

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER

21-379

CORRESPONDENCE

2579 MIDPOINT DRIVE  
PORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: [atrixlab@frii.com](mailto:atrixlab@frii.com)  
<http://www.atrixlabs.com>

**TELECOPIER INFORMATION**

This transmission is from an NEC/NEFAX 430. If you do not receive all the pages being transmitted or if you have any questions regarding the material you receive, please call Laura Eder at 970/482-5868, Ext.328.

To transmit to us, please use FAX number 970/482-9735.

  15   Page(s) being transmitted including cover.

**DATE:** July 18, 2002  
**TO:** Ms. Archana Reddy, MPH  
FDA Project Manager  
**FAX:** (301) 827-4267  
**PHONE:** (301) 827-4260  
**FROM:** Johanna Matz  
**SUBJECT:** ELIGARD™ 22.5mg NDA 21-379, Amendment #014

---

Dear Archana:

A desk copy of ELIGARD™ 22.5 mg NDA 21-379, Amendment #014 is attached to this fax. This amendment contains the mockups of the carton, pouch labels, and syringe labels that we promised in yesterday in Amendment #013.

The official archive and review copies are being sent today via FedEx. Thanks for your prompt assistance in this matter. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail ([JMatz@atrixlabs.com](mailto:JMatz@atrixlabs.com)).

Sincerely

A handwritten signature in black ink, appearing to read "Johanna J. Matz".

Johanna J. Matz  
Regulatory Affairs Project Leader

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



ORIGINAL

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

July 18, 2002

RECEIVED

JUL 19 2002

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

HFD-580/CDER

CONFIDENTIAL

ORIG AMENDMENT

BL

**Subject: NDA 21-379, Amendment #014  
Labeling Amendment – Mockups of Syringe Labels, Pouch Labels,  
and Carton**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is Amendment #014 to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. We accepted all of the Agency's labeling changes sent to Atrix via facsimile on July 15, 2002 and submitted clean copies of the proposed text of the ELIGARD™ 22.5 mg package insert and the carton, pouch and syringe labels in NDA 21-379 Amendment #013 on July 17, 2002. This submission contains the mockups of the carton, pouch and syringe labels. We appreciate your prompt responses during the review of our labeling.

This amendment consists of one volume and we have included one archive copy and two review copies. An additional copy of this amendment was forwarded to the Denver District Office and a copy of the Field Copy Certification Letter is included. A desk copy was also sent via facsimile to the project manager for this product, Ms. Archana Reddy, MPH. Finally, we sent another copy to CDER's Central Document room, which contained a CD-R disk with electronic copies of the mockups (PDF format). Atrix certifies that the CD-R disk has been scanned for viruses using Norton AntiVirus Corporate Edition version 7.60.0.926 with virus definition and is virus free.

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

Thank you for your assistance. If you have any questions or require further information, please contact Johanna Matz by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,



Larry Tamura  
Director, Regulatory Affairs

**CONFIDENTIAL**

LT/jm

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: [atrilab@friu.com](mailto:atrilab@friu.com)  
<http://www.atrilabs.com>

#### TELECOPIER INFORMATION

This transmission is from an NEC/NEFAX 430. If you do not receive all the pages being transmitted or if you have any questions regarding the material you receive, please call Laura Eder at 970/482-5868, Ext.328.

To transmit to us, please use FAX number 970/482-9735.

30 29 Page(s) being transmitted including cover.

**DATE:** July 17, 2002  
**TO:** Ms. Archana Reddy, MPH  
FDA Project Manager  
**FAX:** (301) 827-4267  
**PHONE:** (301) 827-4260  
**FROM:** Johanna Matz  
**SUBJECT:** ELIGARD™ 22.5mg NDA 21-379, Amendment #013

Dear Archana:

A desk copy of ELIGARD™ 22.5 mg NDA 21-379, Amendment #013 is attached to this fax. This amendment contains clean copies of the proposed text of the package insert, carton, pouch labels, and syringe labels. We will submit mockups as soon as they are available.

The official archive and review copies will follow. Thanks for your assistance in this matter. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail ([JMatz@atrilabs.com](mailto:JMatz@atrilabs.com)).

Sincerely

A handwritten signature in black ink, appearing to read "Johanna J. Matz". The signature is fluid and cursive, with the first name being the most prominent.

Johanna J. Matz  
Regulatory Affairs Project Leader

ORIG AMENDMENT



ORIGINAL

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

July 17, 2002

N-156

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

RECEIVED

JUL 19 2002

HFD-580/CDER

**Subject: NDA 21-379, Amendment #013  
Labeling Amendment**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is Amendment #013 to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. We have accepted all of the Agency's changes sent to Atrix via facsimile on July 15, 2002. This amendment contains a clean copy of the proposed text of the ELIGARD™ 22.5 mg package insert and the carton, pouch and syringe labels. As we discussed in our July 16, 2002 teleconference, two minor changes were made to Table 1 of the package insert to correct typographical errors: 1) the "U" in "Genitourinary" was changed to lower case, and 2) a percent sign was added after "6.0." Mock-ups of the carton, pouch and syringe labels will be submitted as soon as they are available. We appreciate your prompt responses during the review of our labeling.

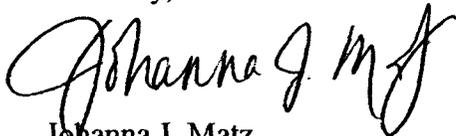
This amendment consists of one volume and we have included one archive copy and two review copies. An additional copy of this amendment was forwarded to the Denver District Office and a copy of the Field Copy Certification Letter is included. A desk copy was sent via facsimile to the project manager for this product, Ms. Archana Reddy, MPH. Finally, we sent another copy to CDER's Central Document room, which contained a CD-R disk with electronic copies of the proposed labels (Microsoft WORD and PDF formats). Atrix certifies that the CD-R disk has been scanned for viruses using Norton AntiVirus Corporate Edition version 7.60.0.926 with virus definition and is virus free.

REVIEWS COMPLETED
CSO ACTION:
<input type="checkbox"/> LETTER <input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO

CONFIDENTIAL

Thank you for your assistance. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,

A handwritten signature in black ink, appearing to read "Johanna J. Matz". The signature is fluid and cursive, with the first name being the most prominent.

Johanna J. Matz  
Regulatory Affairs Project Leader

**CONFIDENTIAL**

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



DUPLICATE

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

July 17, 2002

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

RECEIVED  
JUL 18 2002  
HFD-580/CDER

*BC*  
ORIG AMENDMENT

**Subject: NDA 21-379, Amendment #012  
LA-2550 22.5 mg (ELIGARD™ 22.5 mg)  
CMC Amendment**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is a Chemistry, Manufacturing, and Controls Amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. This amendment contains additional photostability information, residual solvent information and updated specifications.

This amendment consists of one volume and we have included one archive copy and one review copy. A desk copy was also sent to Ms. Archana Reddy, MPH, the project manager for this product, and a Field Copy was sent to the Denver District Office. All copies contain a copy of the Field Copy Certification Letter.

Thank you for your assistance. If you have any questions or require further information, please contact Johanna Matz by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,

A handwritten signature in cursive script that reads "Larry Tamura".

Larry Tamura  
Director, Regulatory Affairs

LT/jm

CONFIDENTIAL

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



DUPLICATE

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

RECEIVED

July 12, 2002

ORIG AMENDMENT

JUL 15 2002

HFD-580/CDER CONFIDENTIAL

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

N-13C

**Subject: NDA 21-379, Amendment #011  
LA-2550 22.5 mg (ELIGARD™ 22.5 mg)  
CMC Amendment**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is a Chemistry, Manufacturing, and Controls Amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. This amendment is a response to a teleconference with the Agency held on July 11, 2002.

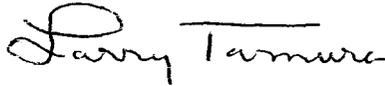
The first issue discussed during the teleconference was the acceptance criteria for the PLG polymer molecular weight. Atrix agrees to use the PLG polymer molecular weight acceptance criteria (  ) recommended by the Agency in their June 26, 2002 Information Request Letter. If we wish to widen these specifications in the future, we will consult with the Agency and submit a postapproval supplement.

Also in the June 26, 2002 Information Request Letter, the Agency asked Atrix to narrow the acceptance criteria for the extended release 18-hour sampling timepoint from  to %. Atrix now agrees to change the limits to the Agency's suggested criteria. Also, Atrix will revise the instructions to clarify that Tier 2 testing will be performed if any of the three conditions (mean, 5 of 6 units, individual units) fail to meet the acceptance criteria. Finally, Atrix will define extended release acceptance criteria and report individual and mean extended release assay results as integers rather than to one decimal place.

This amendment consists of one volume and we have included one archive copy and one review copy. A desk copy was sent via facsimile to Ms. Archana Reddy, MPH, the project manager for this product, and a Field Copy was sent to the Denver District Office. All copies contain a copy of the Field Copy Certification Letter.

Thank you for your assistance. If you have any questions or require further information, please contact Johanna Matz by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,

A handwritten signature in cursive script that reads "Larry Tamura". The signature is written in black ink and is positioned below the word "Sincerely,".

Larry Tamura  
Director, Regulatory Affairs

CONFIDENTIAL

LT/jm

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



RECEIVED N-000 BL

JUL 11 2002

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

11 cc  
July 10, 2002

ORIGINAL

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

CONFIDENTIAL

BL  
ORIG AMENDMENT

**Subject: NDA 21-379, Amendment #010**  
**Response to June 21, 2002 Labeling Comments**  
**ELIGARD™ 22.5 mg**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is a Labeling Amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. Atrix has previously submitted labeling amendments (#003 dated March 19, 2002 and #005 dated May 13, 2002) to NDA 21-379. On June 21, 2002, the Agency sent comments via facsimile to Atrix on the proposed ELIGARD™ 22.5 mg labeling (package insert and the carton, pouch, and syringe labels). In response to the Agency's June 21, 2002 comments regarding the Syringe B label, Atrix submitted Amendment #008 on June 27, 2002. In that amendment, Atrix proposed deleting the text, "For Subcutaneous Use", from the Syringe B label due to space limitations and for consistency with the approved labeling for the related monthly formulation, ELIGARD™ 7.5 mg. On July 1, 2002, the project manager, Ms. Archana Reddy, MPH, called to inform Atrix that Amendment #008 had been reviewed and the Agency agreed to the deletion of the "For Subcutaneous Use" text from the Syringe B label.

In Amendment #008, Atrix also committed to forwarding a complete response to the remaining June 21, 2002 labeling comments as soon as possible. Atrix's response is the subject of this amendment. The following information is provided under Tabs A, B and C.

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
DATE	

Tab A: This tab contains the package insert with Atrix's proposed changes to the Agency's June 21, 2002 version of the package insert indicated via the track changes feature of Microsoft WORD (redline/strike-out). Justifications for the proposed changes are included in the text.

Tab B: This tab contains the syringe, pouch, and carton (product) labeling with Atrix's proposed changes to the Agency's June 21, 2002 version of the labeling indicated via the track changes feature of Microsoft WORD. Atrix's proposed changes will make the labeling consistent with the labeling approved by the Agency for the related monthly product, ELIGARD™ 7.5 mg. Regarding the Syringe A label, the additional text suggested by the Agency cannot be added due to space limitations and is not required under the labeling regulation 21 CFR §201.10(h)(2)(i), which describes what text must appear on a label if there are space limitations. Also, the deletion of the product name and additional text on the Syringe A label and Syringe A pouch implies that the ATRIGEL® Delivery System may be injected without first mixing with the leuprolide acetate in Syringe B. Please note that the needle cannot be attached to Syringe A and that ELIGARD™ 22.5 mg will be administered by health care professionals in a physician-based practice, rather than by patients, so the chance for confusion is minimal.

**The Syringe A label and Syringe A pouch label contained in this submission are urgently needed by our manufacturing group to meet printing deadlines. Atrix would greatly appreciate the Agency's immediate review and feedback on at least the proposed changes to the Syringe A label and Syringe A pouch label.**

Tab C: This tab contains mock-ups of the currently-approved ELIGARD™ 7.5 mg product labeling (NDA 21-343) for comparison to facilitate review of Atrix's proposed changes to the ELIGARD™ 22.5 mg labeling.

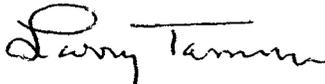
Once Atrix and the Agency agree on the proposed labeling, Atrix will provide the mock-ups of the ELIGARD™ 22.5 mg carton, pouch and syringe labeling.

CONFIDENTIAL

This amendment consists of one volume and we have included one archive copy and two review copies. Three additional copy of this amendment were also sent – one to the Denver District Office, one via facsimile to Ms. Reddy, and a third to CDER's Central Document Room. All copies contain a copy of the Field Copy Certification Letter. The copy sent to the Central Document Room contains a CD-R disk with electronic copies of the package insert, syringe labels, pouch labels, and carton. Atrix certifies that the CD-R disk has been scanned for viruses using Norton AntiVirus Corporate Edition version 7.60.0.926 with virus definition and is virus free.

Thank you for your assistance. Please contact Johanna Matz at 970-482-5868 if there are any questions regarding this submission.

Sincerely,



Larry Tamura  
Director, Regulatory Affairs

CONFIDENTIAL

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: [atrixlab@frii.com](mailto:atrixlab@frii.com)  
<http://www.atrixlabs.com>

July 10, 2002

Denver District Director  
U.S. Food and Drug Administration  
Denver District  
Federal Center/Building 20  
Denver, CO 80225-0087

CONFIDENTIAL

Subject: Submission of a Field Copy of Response to June 21, 2002  
Labeling Comments  
NDA 21-379, Amendment #010  
LA-2550 22.5 mg (ELIGARD™ 22.5 mg)

Pursuant to 21 CFR §314.50(k)(3), enclosed is a field copy of NDA 21-379, Amendment #010 for ELIGARD™ 22.5 mg, an extended-release formulation of leuprolide acetate designed for the palliative treatment of advanced prostate cancer. This field copy is one volume containing Atrix's response to the Agency's June 21, 2002 labeling comments. This letter certifies that the enclosed volume is a true copy of the information that was submitted in the archival and review copies of this amendment.

Thank you for your assistance. If you have any questions or require further information, please contact Johanna Matz by phone (970-482-5868), fax (970-482-9735), or e-mail ([JMatz@atrixlabs.com](mailto:JMatz@atrixlabs.com)).

Sincerely,

A handwritten signature in cursive script that reads "Larry Tamura".

Larry Tamura  
Director, Regulatory Affairs

LT/le

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



DUPLICATE

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

July 3, 2002

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

RECEIVED

JUL 05 2002

HFD-580/CDER

BC  
ORIG AMENDMENT

**Subject: NDA 21-379, Amendment #009  
LA-2550 22.5 mg (ELIGARD™ 22.5 mg)  
Response to Request for Information  
Chemistry Amendment**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is a Chemistry amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. This amendment is a response to a series of questions/requests from the Agency.

On June 26, 2002, Atrix submitted NDA 21-379, Amendment #007, in response to an Information Request Letter from the Agency that contained 19 issues. Item #10 in this letter required Atrix to provide information on the residual solvent in the PLG polymer and include residual solvent content as part of the polymer specification. Atrix committed to providing a test method, test method validation report and data from three lots of polymer to the Agency, but did not give a specific date. That information will be submitted to the Agency on or before July 19, 2002.

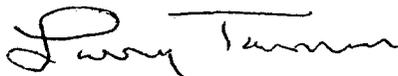
Item #12 of the Agency's letter asked Atrix to narrow the acceptance criteria range for the PLG molecular weight from \_\_\_\_\_ to \_\_\_\_\_. Atrix provided a justification as to why the criteria should remain unchanged in the June 26 response. The Agency requested further clarification from Atrix during a teleconference on July 1, 2002. This submission contains that clarification.

Also, during the July 1, 2002 teleconference, the Agency asked Atrix to change the acceptance criteria for the 18-hour sampling time in the extended release test method for ELIGARD™ 22.5 mg, T549. The Agency recommended narrowing the criteria from \_\_\_\_\_ % to \_\_\_\_\_ %. Atrix's response is also included in this submission.

This amendment consists of one archive and one Chemistry review copy. We also sent a desk copy of this amendment to our project manager, Ms. Archana Reddy, MPH, and a Field copy to the Denver District Office. A copy of the Field Copy Certification Letter is included in this submission.

If you have any questions or require further information, please contact Johanna Matz, Atrix Regulatory Group Leader, by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,

A handwritten signature in cursive script, appearing to read "Larry Tamura".

Larry Tamura  
Director, Regulatory Affairs

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: [atrixlab@frii.com](mailto:atrixlab@frii.com)  
<http://www.atrixlabs.com>

July 3, 2002

Denver District Director  
U.S. Food and Drug Administration  
Denver District  
Federal Center/Building 20  
Denver, CO 80225-0087

Subject: Submission of a Field Copy of Response to Request for Information  
Chemistry Amendment  
NDA 21-379, Amendment #009  
LA-2550 22.5 mg (ELIGARD™ 22.5 mg)

Pursuant to 21 CFR §314.50(k)(3), enclosed is a field copy of NDA 21-379, Amendment #009 for ELIGARD™ 22.5 mg, an extended-release formulation of leuprolide acetate designed for the palliative treatment of advanced prostate cancer. This field copy is one volume containing a response to a request for additional Chemistry, Manufacturing, and Controls Information for ELIGARD™ 22.5 mg. This letter certifies that the enclosed volume is a true copy of the information that was submitted in the archival and review copies of this amendment.

Thank you for your assistance. If you have any questions or require further information, please Johanna Matz by phone (970-482-5868), fax (970-482-9735), or e-mail ([JMatz@atrixlabs.com](mailto:JMatz@atrixlabs.com)).

Sincerely,

A handwritten signature in cursive script that reads "Larry Tamura".

Larry Tamura  
Director, Regulatory Affairs

LT/jm

**ORIGINAL**



2579 MIDPOINT, DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.

**RECEIVED**  
JUL 01 2002  
HFD-580/CDER  
PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrilabs.com

**TELECOPIER INFORMATION**

This transmission is from an NEC/NEFAX 430. If you do not receive all the pages being transmitted or if you have any questions regarding the material you receive, please call Laura Eder at 970/482-3868, Ext.328.

To transmit to us, please use FAX number 970/482-9735.

9 Page(s) being transmitted including cover.

**NEW CORRESP**

**DATE:** June 27, 2002  
**TO:** Ms. Archana Reddy, MPH  
Project Manager  
FDA, DRUDP  
**FAX:** 301-827-4267  
**PHONE:** 301-827-4260  
**FROM:** Johanna Matz  
Regulatory Affairs Project Leader  
**SUBJECT:** NDA 21-379, Amendment #008 - Response to FDA Labeling Comments for  
ELIGARD™ 22.5 mg Syringe B Label

Dear Archana,

Attached please find NDA 21-379, Amendment #008. This is a partial response to the Agency's comments on the ELIGARD™ 22.5 mg labeling that we received on June 21, 2002. This submission addresses the Syringe B label only. We are currently composing a complete response to the Agency's fax and will submit it as soon as possible, but we urgently need the Agency's response to the issue described in the attached amendment.

The hard copy of this amendment will follow. Thanks for all your help. I will contact you on Friday morning to ensure that you receive this fax.

Sincerely,

*Johanna J. Matz*  
Johanna J. Matz

<b>REVIEWS COMPLETED</b>	
GSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
GSO INITIALS	DATE

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
<http://www.atrixlabs.com>

RECEIVED

JUL 01 2002

HFD-580/CDER

June 27, 2002

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

**Subject: NDA 21-379, Amendment #008  
Response to FDA Labeling Comments for ELIGARD™ 22.5 mg  
Syringe B Label**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is a Labeling Amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. On June 21, 2002, the Agency faxed a copy of its comments on labeling for ELIGARD™ 22.5 mg (leuprolide acetate for injectable suspension) that we submitted to NDA 21-379 in Amendments #003 (March 19, 2002) and #005 (May 13, 2002). Atrix is currently working on a complete reply to the Agency's fax, but we urgently request your response to the following.

The Agency is proposing adding "For Subcutaneous Use" to the Syringe B label, but Atrix contends that this statement should not be added to this label. A side-by-side comparison of the two proposed labels and Atrix's justification for not including the "For Subcutaneous Use" statement follow.

NDA 21-379  
 Amendment #008  
 26 June 2002  
 Page 2 of 2

### FDA Proposed Syringe B Label

<p><b>Syringe B</b>      <b>E-922</b>          Eligard™ 22.5 mg          leuprolide acetate for          injectable suspension  <b>Delivers 22.5 mg</b>  <b>leuprolide acetate</b>          Actual content 28.2 mg          lyophilized leuprolide acetate  <del>For Subcutaneous Use</del>          Mfd. For Sanofi-Synthelabo Inc.          New York, NY 10016  <b>sanofi-synthelabo</b>          Lot&lt;XXXX&gt;      04107 Rev. 0 5/02          Exp. &lt;xx-xxxx&gt;</p>
--

### Atrix Proposed Syringe B Label

<p><b>Syringe B</b>      <b>E-922</b>          Eligard™ 22.5 mg          leuprolide acetate for          injectable suspension  <b>Delivers 22.5 mg</b>  <b>leuprolide acetate</b>          Actual content 28.2 mg          lyophilized leuprolide acetate          Mfd. For Sanofi-Synthelabo Inc.          New York, NY 10016  <b>sanofi-synthelabo</b>          Lot&lt;XXXX&gt;      04107 Rev. 0 5/02          Exp. &lt;xx-xxxx&gt;</p>
---

#### Justification for Omitting "For Subcutaneous Use" Statement:

The size of the Syringe B label makes it impossible to add any statements to the labeling, without reducing the font to an unreadable size. Increasing the size of the label is also impossible due to the size of the syringe – a larger label would wrap around the barrel and overlap onto itself making it impossible to read. Also, a nearly identical statement ("For subcutaneous injection" versus "For Subcutaneous Use") already exists on the Syringe A pouch label, the Syringe B pouch label, the large outer pouch label, the carton label, and in the package insert. The statement is not included on the Syringe A label. Therefore, the user is fully informed prior to opening the Syringe B pouch that the contents of Syringe B is for subcutaneous use.

To paraphrase the labeling regulation in 21 CFR §201.10(h)(2)(i), a drug packaged in a container too small to accommodate a label with sufficient space to bear the information required for compliance with section 502(e)(1)(A)(ii) and (B) of the act shall be exempt from compliance provided that the label:

- Bears the proprietary name of the drug, the established name of the drug, an identifying lot or control number, and the name of the manufacturer, packer, or distributor, and
- All information required to appear on the label by the act and the regulations appears on the carton or other outer container or wrapper.

Atrix's proposed Syringe B label contains the information required by the regulations.

NDA 21-379  
Amendment #008  
26 June 2002  
Page 2 of 2

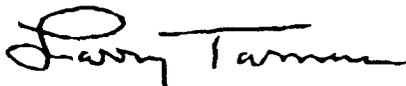
Additionally, this product cannot be injected intramuscularly because the needle included with the package is too short. Also, the lyophilized leuprolide acetate in Syringe B would have to be mixed with the ATRIGEL<sup>®</sup> Delivery System in Syringe A to make it injectable.

Finally, Atrix's proposed label is based upon the approved Syringe B label for ELIGARD<sup>™</sup> 7.5 mg, so adding the statement "For Subcutaneous Use" is inconsistent with the Agency's previous actions. Atrix has already manufactured a commercial scale lot of the leuprolide acetate filled syringes at considerable expense. If Atrix is required to create and print revised labels, this product may have to be discarded. Therefore, we urgently request your immediate reply to this submission, preferably by initiating a teleconference on Friday, June 28, 2002.

This amendment consists of one volume and we have included one archive copy and two review copies. An additional copy of this amendment was forwarded to the Denver District Office and a copy of the Field Copy Certification Letter is included. We also faxed a desk copy to our project manager, Ms. Archana Reddy, MPH.

Thank you for your assistance. Please contact Johanna Matz at 970-482-5868 to schedule a time for the teleconference.

Sincerely,



Larry Tamura  
Director, Regulatory Affairs

LT/jm

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frij.com  
http://www.atrxdabs.com

June 27, 2002

Denver District Director  
U.S. Food and Drug Administration  
Denver District  
Federal Center/Building 20  
Denver, CO 80225-0087

**Subject: Submission of a Field Copy of Response to FDA Labeling Comments for  
ELIGARD™ 22.5 mg Syringe B Label  
NDA 21-379, Amendment #008  
LA-2550 22.5 mg (ELIGARD™ 22.5 mg)**

Pursuant to 21 CFR §314.50(k)(3), enclosed is a field copy of NDA 21-379, Amendment #008 for ELIGARD™ 22.5 mg, an extended-release formulation of leuprolide acetate designed for the palliative treatment of advanced prostate cancer. This field copy is one volume containing a response to labeling comments from the Agency for the ELIGARD™ 22.5 mg Syringe B label. This letter certifies that the enclosed volume is a true copy of the information that was submitted in the archival and review copies of this amendment.

Thank you for your assistance. If you have any questions or require further information, please Johanna Matz by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,

Larry Tamura  
Director, Regulatory Affairs

LT/jm

DOCUMENT ROOM

ORIGINAL



NEW CORRESP

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrilabs.com

~~REPORT~~

NC

TELECOPIER INFORMATION

This transmission is from an NEC/NEFAX 430. If you do not receive all the pages being transmitted or if you have any questions regarding the material you receive, please call Laura Eder at 970/482-5868, Ext.328.

To transmit to us, please use FAX number 970/482-9735.

3 Page(s) being transmitted including cover.

RECEIVED  
JUL 03 2002  
HFD-580/CDER

**DATE:** June 28, 2002  
**TO:** Ms. Archana Reddy  
FDA Project Manager  
**FAX:** (301) 827-4267  
**PHONE:** (301) 827-4260  
**FROM:** Johanna Matz  
**SUBJECT:** ELIGARD™ 22.5mg NDA 21-379  
Information you requested

Dear Archana:

Per today's conversation, here is the information you requested. If you have any questions, please contact me at (970) 482-5868.

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

Fax  
ELIGARD 22.5 mg  
Atrix Laboratories Inc.

## REQUESTED CLINICAL INFORMATION

On June 17, 2002, a conference call was held with Dr. Ashok Batra, FDA Medical Officer and Ms. Archana Reddy, FDA Project Manager. During this call, the Atrix participants were: Mr. Graham Carron, Biostatistics Supervisor; Dr. Steven Garrett, Clinical Research; Ms. Johanna Matz, Regulatory Group Leader; Ms. Barbara Pons, Database Management Specialist; Dr. Soe Than, V.P. Clinical Research; and Mr. Larry Tamura, Director Regulatory Affairs. The purpose of the call was to discuss clinical questions that Dr. Batra has after reviewing the proposed package insert for ELIGARD 22.5 mg NDA 21-379.

Dr. Batra indicated that they were close to completing the reviews and he had some questions regarding the clinical data. He requested that Atrix submit information to his questions via fax. Atrix agreed to fax the information. We have summarized Dr. Batra's questions and have provided the requested information. They are as follows:

1. *Dr. Batra question: What is the race of the "1 Other" that appears in the Race subsection of the Pharmacokinetics section of the proposed package insert?*

Atrix Information: The Case Report Form describes the race for this patient as Other → Puerto Rican. Atrix contacted the investigator site for this patient in order to gain more information. The coordinator at this site indicated that this patient should be categorized as Hispanic.

2. *Dr. Batra question: During the pivotal trial, Dr. Batra noted that two patients withdrew from the study due to disease progression. Does Atrix have any further follow up information on these two patients beyond what was reported in the NDA application?*

Atrix Information: After reviewing the records, Atrix cannot find any other information on these patients beyond what was reported in the application.

3. *Dr. Batra question: In the Systemic Adverse Events subsection of the proposed package, it is reported that less than 2% of the patients experienced possibly or probably treatment-related sweating and hypotension/hypertension. Are the patients who experienced these events the same and did any patient experience anaphylaxis?*

Contained in the list of possibly or probably related systemic adverse events reported by fewer than 2% of patients (i.e., reported by only one patient), are clamminess, night sweats, sweating increased (all in the Skin Body System), and hypertension and hypotension (both in the Vascular Body System).

Fax  
ELIGARD 22.5 mg  
Atrix Laboratories Inc.

Each of these events was reported by a different patient as follows:

Body System	Adverse Event	Patient #
Skin	Clamminess	2612
	Night Sweats	2610
	Sweating Increased	0401
Vascular	Hypertension	3101
	Hypotension	3103

The adverse event information for these patients can be found in more detail in the NDA submission, Appendix 2.7.1 of the study report. No patient experienced anaphylaxis in this study.

APPEARS THIS WAY  
ON ORIGINAL

APPEARS THIS WAY  
ON ORIGINAL

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



DUPLICATE

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrilabs.com

June 26, 2002

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

RECEIVED  
JUN 27 2002  
HFD-580/CDER

BZ  
ORIG AMENDMENT

**Subject: NDA 21-379, Amendment #007  
LA-2550 22.5 mg (ELIGARD™ 22.5 mg)  
Response to Information Request Letter  
Microbiology Amendment  
Chemistry Amendment**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed is a Chemistry amendment and a Microbiology amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. This amendment is a response to the Agency's Information Request Letter in which the Agency made a series of 19 comments and information requests related to the chemistry and microbiology sections of NDA 21-379. Atrix has addressed these issues in this amendment.

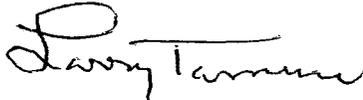
Atrix would also like to make two minor changes to the \_\_\_\_\_ procedure for the bulk polymer as it was described in the original NDA 21-379, Volume 1.3, Section 4.9.3.1, Page 90. The first part of the section entitled *Preparation of ATRIGEL® Delivery System, Syringe A* describes the *Delivery System Formulation*. During scale up operations, Atrix manufacturing discovered that, to ensure adequate \_\_\_\_\_ volume of delivery system components, PLG and NMP, we needed to 1) \_\_\_\_\_

\_\_\_\_\_ 2) \_\_\_\_\_  
A redline strike out version of this section is included in Tab H of this submission.

This amendment consists of one archive, one Chemistry review copy, and one Microbiology review copy. We also sent a desk copy of this amendment to our project manager, Ms. Archana Reddy, MPH, and a Field copy to the Denver District Office. A copy of the Field Copy Certification Letter is included in this submission.

If you have any questions or require further information, please contact Johanna Matz, Atrix Regulatory Group Leader, by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,

A handwritten signature in black ink, appearing to read "Larry Tamura". The signature is written in a cursive style with a large initial "L" and a long horizontal stroke extending to the right.

Larry Tamura  
Director, Regulatory Affairs

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



DUPLICATE

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

May 30, 2002

RECEIVED

MAY 31 2002

HFD-580/CDER

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

SU  
NDA ORIG AMENDMENT

**Subject: NDA 21-379, Amendment #006**  
**LA-2550 22.5 mg (ELIGARD™ 22.5 mg)**  
**Safety Update Report**

Dear Dr. Shames,

Pursuant to Section 21 CFR §314.50(d)(5)(vi)(b), enclosed is the safety report for NDA 21-379 for LA-2550 22.5 mg (ELIGARD™ 22.5 mg), a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer.

We are providing an archival and clinical copy of this submission. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Best regards,

A handwritten signature in black ink that reads "Johanna J. Matz".

Johanna J. Matz  
Regulatory Affairs Project Leader

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



DUPLICATE

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

May 13, 2002

RECEIVED  
MAY 14 2002  
HFD-580/CDER

CONFIDENTIAL

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

BL  
NDA ORIG AMENDMENT

**Subject: NDA 21-379, Amendment #005  
Labeling Amendment**

Dear Dr. Shames,

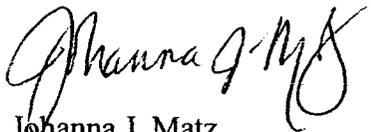
Pursuant to 21 CFR §314.60, enclosed is a Labeling Amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. The labeling consists of the syringe, pouch, and carton labels for the ELIGARD™ 22.5 mg drug product. This material was originally submitted as part of NDA 21-379, Amendment #004. At the request of Ms. Archana Reddy, the project manager for NDA 21-379, we are resubmitting this material as a separate amendment. Ms. Reddy called on May 6, 2002 to ask that we submit the labeling separately to avoid confusion during review. She also asked that we submit electronic copies of the labels in Microsoft WORD format for the reviewers' convenience. Therefore, this submission contains:

- Original syringe and pouch labels submitted in NDA 21-379 with changes indicated via the redline strikeout feature of Microsoft WORD
- Clean copies of the new syringe and pouch labels with the changes accepted
- Carton label in Microsoft WORD format
- Mockups of the new syringe, pouch, and carton label

This amendment consists of one volume and we have included one archive copy and two review copies. An additional copy of this amendment was forwarded to the Denver District Office and a copy of the Field Copy Certification Letter is included. Two desk copies were also sent to Ms. Reddy. Electronic copies of the proposed labels (Microsoft WORD and PDF formats) are provided on the CD-R disk included with the archive and field copies. Atrix certifies that the CD-R disks have been scanned for viruses using Norton AntiVirus Corporate Edition version 7.60.0.926 with virus definition and are virus free.

Thank you for your assistance. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,



Johanna J. Matz  
Regulatory Affairs Project Leader

CONFIDENTIAL

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: [atrixlab@frii.com](mailto:atrixlab@frii.com)  
<http://www.atrixlabs.com>

April 25, 2002

RECEIVED

CONFIDENTIAL

APR 26 2002

HFD-580/CDER

Denver District Director  
U.S. Food and Drug Administration  
Denver District  
Federal Center/Building 20  
Denver, CO 80225-0087

**Subject: Field Copy Submission NDA 21-379, Amendment #004  
ELIGARD™ 22.5 mg  
Chemistry, Manufacturing, and Controls Amendment  
Pharmacology/Toxicology Amendment  
Microbiology Amendment  
Labeling Amendment**

Pursuant to 21 CFR §314.50(k)(3), enclosed is a field copy of NDA 21-379, Amendment #004 for ELIGARD™ 22.5 mg, an extended-release formulation of leuprolide acetate designed for the palliative treatment of advanced prostate cancer. This field copy is two volumes containing additional Chemistry, Manufacturing and Controls, Microbiology, Pharmacology/Toxicology, and Labeling information. This letter certifies that the enclosed volume is a true copy of the information that was submitted in the archival and review copies of this amendment.

Thank you for your assistance. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail ([JMatz@atrixlabs.com](mailto:JMatz@atrixlabs.com)).

Best regards,

A handwritten signature in cursive script that reads "Johanna J. Matz".

Johanna J. Matz  
Regulatory Affairs Project Leader

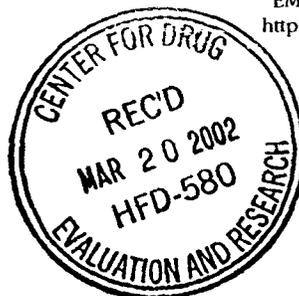
2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



ORIGINAL

PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrilabs.com

PACKAGE INSERT



CONFIDENTIAL

March 19, 2002

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

BZ

NDA ORIG AMENDMENT

**Subject: NDA 21-379, Amendment #003  
Chemistry, Manufacturing, and Controls Amendment  
Microbiology Amendment  
Labeling Amendment**

Dear Dr. Shames,

Pursuant to 21 CFR §314.60, enclosed are a Chemistry, Manufacturing, and Controls amendment and a Microbiology amendment to NDA 21-379 for ELIGARD™ 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. This submission contains amended CMC information and labeling as requested by Jeanine Best, the project manager, during a telephone conversation on February 12, 2002. Ms. Best asked us to amend the ELIGARD™ 22.5 mg CMC information to reflect the changes we made to the ELIGARD™ 7.5 mg CMC information (NDA 21-343, Approved January 23, 2002). Atrix has reviewed the NDA 21-343 CMC amendments and applied the Agency's comments to the NDA 21-379 CMC section. We also revised the package insert to reflect the changes we made to the ELIGARD™ 7.5 mg package insert. Additionally, we reviewed the NDA 21-343 November 19, 2001 Microbiology Discipline Review Letter and answered the questions that were relevant for the Microbiology section of NDA 21-379.

This amendment consists of one archive copy, one chemistry review copy, and one microbiology review copy, each consisting of one volume. An additional copy of this amendment was forwarded to the Denver District Office and a copy of the Field Copy Certification Letter is included. A desk copy was also sent to Ms. Best. Electronic

REVIEWS COMPLETED	
CSO ACTION:	
<input type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

LAB A  
Package Insert

is of the package insert text (redline strikeout and clean) are provided on the CD-R included with each copy. Atrix certifies that the CD-R discs have been scanned for us using Norton AntiVirus 5.02.00 with virus definition and are virus free.

Thank you for your assistance. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail (matz@atrixlabs.com).

Sincerely,



Hanna J. Matz  
Regulatory Affairs Project Leader

CONFIDENTIAL

Redline Strikeout

Clean

Doc. No. S0271-C

1392.004

ORIGINAL

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@frii.com  
http://www.atrixlabs.com

NDA ORIG AMENDMENT

March 8, 2002

CONFIDENTIAL

Daniel Shames, MD, Acting Director  
Division of Reproductive and Urologic Drugs, HFD-580  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Attn: Document Control, 17-B-20  
5600 Fishers Lane  
Rockville, MD 20857

N-000-1313

Subject: NDA 21-379, Amendment #002  
Human Pharmacokinetics and Bioavailability Information

Pursuant to 21 CFR §314.60, enclosed is a Human Pharmacokinetics and Bioavailability amendment to NDA 21-379 for LA-2550 22.5 mg, a leuprolide acetate extended-release formulation for the palliative treatment of advanced prostate cancer. As requested by the Biopharmaceutics Reviewer through Jeanine Best on February 13, 2002, this submission contains a table with the following data for the 22 evaluable patients in the pharmacokinetics subset of the AGL9909 clinical study:

- subject number
- body weight
- full profile for all time points for leutenizing hormone, leuprolide acetate, and testosterone

This submission consists of one archive and one review copy, each consisting of one volume. A desk copy was also sent to the project manager, Jeanine Best. If you have any questions or require further information, please contact me by phone (970-482-5868), fax (970-482-9735), or e-mail (JMatz@atrixlabs.com).

Sincerely,

Johanna J. Matz  
Regulatory Affairs Project Leader

REVIEWS COMPLETED
CSD ACTION:
<input type="checkbox"/> LETTER <input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSD INITIALS
DATE



<b>Dosage Form, Route of Administration, and Dosing Regime</b>	LA-2550 22.5 mg is designed as a parenteral drug product that consists of a sterile syringe containing the lyophilized active drug substance, leuprolide acetate, a sterile syringe containing the polymeric ATRIGEL® Delivery System, and a sterile needle for injection. The ATRIGEL® Delivery System is composed of poly (DL-lactide-co-glycolide) (PLG) dissolved in <i>N</i> -methyl-2-pyrrolidone (NMP). The drug product is mixed immediately before patient administration and injected subcutaneously. The drug product is designed to deliver a nominal 22.5 mg of leuprolide acetate over a three-month period. The injection mass is approximately _____ mL
--	---

Atrix also manufactures ELIGARD™ 7.5 mg, a similar product designed to deliver 7.5 mg of leuprolide acetate over a one-month period. Atrix submitted NDA 21-343 for ELIGARD™ 7.5 mg on March 23, 2001 and requested comment from OPDRA on the ELIGARD™ 7.5 mg name in an NDA amendment (NDA 21-343, Amendment #007, October 12, 2001). The Agency approved NDA 21-343 on January 23, 2002, thereby accepting the name.

This submission consists of one archive and two review copies. I have also sent a desk copy to our project manager, Jeanine Best. You may contact me by phone (970-482-5868), fax (970-482-9735), or e-mail ([Jmatz@atrixlabs.com](mailto:Jmatz@atrixlabs.com)) if I can provide additional information or if you have any questions regarding the enclosed material.

Please inform me of OPDRA's decision us as soon as possible. Thank you very much for your assistance.

Best regards,



Johanna J. Matz  
Regulatory Affairs Project Leader

CONFIDENTIAL

2579 MIDPOINT DRIVE  
FORT COLLINS, CO 80525-4417  
U.S.A.



PHONE: (970) 482-5868  
FAX: (970) 482-9735  
EMAIL: atrixlab@ftri.com  
http://www.atrilabs.com

September 25, 2001



**CONFIDENTIAL**

Food and Drug Administration  
Center for Drug Evaluation and Research  
Central Document Room  
12229 Wilkins Avenue  
Rockville, MD 20852

**RECEIVED**  
**SEP 26 2001**  
**CDR/CDER**

**Subject:** Submission of an original New Drug Application  
(NDA) 21-379 for LA-2550 22.5 mg

Pursuant to Section 505(b) of the Federal Food, Drug and Cosmetic Act and 21 CFR §314, enclosed are an archival copy (92 Volumes) and review sections of an original NDA for LA-2550 22.5 mg, a sustained-release formulation of leuprolide acetate designed for the palliative treatment of advanced prostate cancer. In accordance with 21 CFR §314.50, the NDA contains the following information:

<b>Volume</b>	<b>Description</b>
1.1	Form, Statements, Certifications, Letters of Authorization, NDA Summary, Electronic Copy of Selected Data
1.2 - 1.15	Chemistry, Manufacturing and Controls Technical Section
1.16 - 1.24	Nonclinical Pharmacology and Toxicology Technical Section
1.25 - 1.58	Human Pharmacokinetics and Bioavailability Technical Section
1.59 - 1.60	Microbiology Information (Sterility and Endotoxin Testing)
1.61 - 1.92	Clinical/Statistical Technical Section including Case Report Forms and Tabulations

As required by 21 CFR 314.50(e)(2)(i), three additional copies of Volume 1.1 and Volumes 1.2 through 1.15 (Chemistry, Manufacturing and Controls technical section) containing the analytical methods and related descriptive information (methods validation package), have been included with the archival copy. An additional copy of Volumes 1.1 through 1.15 was forwarded to the Denver District office. A copy of the Field Copy Certification Letter is provided in Volume 1.1 of this submission. Six additional desk copies of Volume 1.1 have also been sent to our project manager.

Electronic copies of the proposed labeling, text of the Human Pharmacokinetics and Bioavailability Technical Section, text of the Clinical Technical Section (including the integrated summaries of safety and efficacy and risk/benefit summary), text of clinical studies AGL9909, AGL9802 and AGL9904, line listings of the AGL9909 data and AGL9909 SAS transport files are provided on the CD-R disks included with each copy of Volume 1.1. Atrix certifies that the CD-R discs have been scanned for viruses using Norton AntiVirus 7.51.CE with virus definition are virus free.

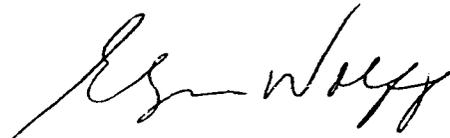
The user fee of \$309,647.00 (user fee I.D. number 4147) was sent by courier on September 25, 2001 to:

Food and Drug Administration (360909)  
Mellon Client Service Center RM 670  
500 Ross Street  
Pittsburgh, PA 15262-0001

We are providing two samples of LA-2550 22.5 mg. A material safety data sheet is included with the samples.

We look forward to your review of our application. Please contact me if I can provide additional information or if you have any questions regarding the enclosed material.

Best regards,

A handwritten signature in black ink, appearing to read 'Elyse Wolff', written in a cursive style.

Elyse Wolff, MT (ASCP)  
Regulatory Project Leader II

CONFIDENTIAL



Food and Drug Administration  
 Center for Drug Evaluation and Research  
 Office of Drug Evaluation III

**FACSIMILE TRANSMITTAL SHEET**

**DATE:** July 24, 2002

<b>To:</b> Johanna Matz Cc: Larry Tamura	<b>From:</b> Archana Reddy, M.P.H. Regulatory Project Manager
<b>Company:</b> Atrix Laboratories, Inc.	Division of Division of Reproductive and Urologic Drug Products
<b>Fax number:</b> 970-482-9735	<b>Fax number:</b> 301-827-4267
<b>Phone number:</b> 970-482-5868	<b>Phone number:</b> 301-827-4260
<b>Subject:</b> Fax of July 11 <sup>th</sup> CMC teleconference for Eligard <sup>™</sup> 22.5 mg	

**Total no. of pages including cover:** 4

**Comments:**

Johanna,

Attached are the minutes from the July 11<sup>th</sup> CMC tcon for Eligard<sup>™</sup> 22.5 mg (leuprolide acetate for injectable suspension).

Archana Reddy

PM

DRUDP

**Document to be mailed:**                      X YES                      NO

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.**

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.

-----  
**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
-----

/s/

-----  
Archana Reddy  
7/24/02 10:24:43 AM  
CSO

Confirmation Report - Memory Send

Page : 001  
Date & Time: Jul-10-02 12:15pm  
Line 1 : 301-827-4267  
Line 2 :  
Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number : 369  
Date : Jul-10 12:14pm  
To : 919704829735  
Number of pages : 004  
Start time : Jul-10 12:14pm  
End time : Jul-10 12:15pm  
Pages sent : 004  
Status : OK

Job number : 369

\*\*\* SEND SUCCESSFUL \*\*\*



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: July 10, 2002

To: Johanna Matz Cc: Larry Tamura	From: Archana Reddy, M.P.H. Regulatory Project Manager
Company: Atrix Laboratories, Inc.	Division of Division of Reproductive and Urologic Drug Products
Fax number: 970-482-9735	Fax number: 301-827-4267
Phone number: 970-482-5868	Phone number: 301-827-4260

Subject: Fax of clinical teen minutes for Eligard held on June 17, 2002

Total no. of pages including cover: 4

Comments:

Johanna,  
Attached are the minutes from the June 17th teleconference held for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).  
Archana Reddy  
PM  
DRUDP

Document to be mailed:  YES  NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

---

---

**FACSIMILE TRANSMITTAL SHEET**

---

---

**DATE: July 10, 2002**

<b>To:</b> Johanna Matz Cc: Larry Tamura	<b>From:</b> Archana Reddy, M.P.H. Regulatory Project Manager
<b>Company:</b> Atrix Laboratories, Inc.	Division of Division of Reproductive and Urologic Drug Products
<b>Fax number:</b> 970-482-9735	<b>Fax number:</b> 301-827-4267
<b>Phone number:</b> 970-482-5868	<b>Phone number:</b> 301-827-4260

**Subject:** Fax of clinical tcon minutes for Eligard held on June 17, 2002

---

**Total no. of pages including cover: 4**

---

**Comments:**

Johanna,

Attached are the minutes from the June 17th teleconference held for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).

Archana Reddy

PM

DRUDP

---

**Document to be mailed:**             YES             NO

---

---

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.**

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.

Confirmation Report - Memory Send

Page : 001  
 Date & Time: Jul-10-02 02:20pm  
 Line 1 : 301-827-4267  
 Line 2 :  
 Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number : 372  
 Date : Jul-10 02:19pm  
 To : 919704829735  
 Number of pages : 004  
 Start time : Jul-10 02:19pm  
 End time : Jul-10 02:20pm  
 Pages sent : 004  
 Status : OK

Job number : 372 \*\*\* SEND SUCCESSFUL \*\*\*



Food and Drug Administration  
 Center for Drug Evaluation and Research  
 Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: July 10, 2002

To: Johanna Metz Cc: Larry Tamura Company: Atrix Laboratories, Inc.	From: Archana Reddy, M.P.H. Regulatory Project Manager Division of Division of Reproductive and Urologic Drug Products
Fax number: 970-482-9735	Fax number: 301-827-4267
Phone number: 970-482-5868	Phone number: 301-827-4260

Subject: Fax of CMC tcon minutes for Ellgard held on July 1, 2002

Total no. of pages including cover: 4

Comments:

Johanna,  
 Attached are the minutes from the July 1<sup>st</sup> teleconference held for Ellgard™ 22.5 mg (icuprolide acetate for injectable suspension).  
 Archana Reddy  
 PM  
 DRUDP

Document to be mailed:  YES  NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

---

---

**FACSIMILE TRANSMITTAL SHEET**

---

---

**DATE: July 10, 2002**

<b>To:</b> Johanna Matz Cc: Larry Tamura	<b>From:</b> Archana Reddy, M.P.H. Regulatory Project Manager
<b>Company:</b> Atrix Laboratories, Inc.	Division of Division of Reproductive and Urologic Drug Products
<b>Fax number:</b> 970-482-9735	<b>Fax number:</b> 301-827-4267
<b>Phone number:</b> 970-482-5868	<b>Phone number:</b> 301-827-4260

**Subject:** Fax of CMC tcon minutes for Eligard held on July 1, 2002

---

**Total no. of pages including cover: 4**

---

**Comments:**

Johanna,

Attached are the minutes from the July 1<sup>st</sup> teleconference held for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).

Archana Reddy

PM

DRUDP

---

**Document to be mailed:**             YES             NO

---

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.**

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

---

---

**FACSIMILE TRANSMITTAL SHEET**

---

---

**DATE: June 21, 2002**

<b>To:</b> Johanna Matz Cc: Larry Tamura	<b>From:</b> Archana Reddy, M.P.H. Regulatory Project Manager
<b>Company:</b> Atrix Laboratories, Inc.	Division of Division of Reproductive and Urologic Drug Products
<b>Fax number:</b> 970-482-9735	<b>Fax number:</b> 301-827-4267
<b>Phone number:</b> 970-482-5868	<b>Phone number:</b> 301-827-4260
<b>Subject:</b> Fax of revised label for Eligard	

---

**Total no. of pages including cover: 22**

---

**Comments:**

Johanna,

Attached is the revised labeling for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension) for your agreement.

Thanks,

Archana Reddy

PM

DRUDP

---

**Document to be mailed:**             YES             NO

---

---

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.**

**If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.**

22 pages redacted from this section of  
the approval package consisted of draft labeling

Confirmation Report - Memory Send

Page : 001
Date & Time: Jun-21-02 11:25am
Line 1 : 301-827-4267
Line 2 :
Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number : 263
Date : Jun-21 11:22am
To : 919704829735
Number of pages : 022
Start time : Jun-21 11:22am
End time : Jun-21 11:25am
Pages sent : 022
Status : OK

Job number : 263 \*\*\* SEND SUCCESSFUL \*\*\*



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: June 21, 2002

Table with 2 columns: To/From, Company, Fax number, Phone number, Subject. To: Johanna Matz, Cc: Larry Tamura, Company: Aurix Laboratories, Inc. From: Archana Reddy, M.P.H., Regulatory Project Manager, Division of Division of Reproductive and Urologic Drug Products.

Total no. of pages including cover: 22

Comments:

Johanna,
Attached is the revised labeling for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension) for your agreement.
Thanks,
Archana Reddy
PM
DRUDP

Document to be mailed: [ ] YES [X] NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.



NDA 21-379

## INFORMATION REQUEST LETTER

Atrix Laboratories, Inc.  
Attention: Johanna Matz  
Regulatory Affairs Project Leader  
2579 Midpoint Drive  
Fort Collins, CO 80525-4417

Dear Ms. Matz:

Please refer to your September 25, 2001, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).

We are reviewing the Microbiology and Chemistry section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Provide the results of dose mapping studies conducted on loads of Syringe A sterilized at the \_\_\_\_\_ facility. A diagram of dosimeter placement in the loads should be provided along with high and low dose sites, a dose map, certificates of exposure, and proof of the uniformity and reproducibility of the \_\_\_\_\_ process. The validation data provided in Tab A is sufficient for establishing the \_\_\_\_\_ but insufficient for validating the \_\_\_\_\_ sterilization process at \_\_\_\_\_.
2. Provide an adequate description of the WFI system or the frequency and procedures for microbial and endotoxin testing of the system.
3. Provide a description of how the drug product is transferred from the clean room to the lyophilizer. Provide the duration of the maximum hold time between filling and lyophilization.
4. Provide maps and descriptions of air pressure differentials and material/product/personnel flow throughout the facility.
5. Describe how the lyophilization equipment is sterilized.
6. Address the following issues with regard to media fills conducted on syringe B:
  - a. According to the tables on pp. 196 and 197 of volume 1.59, a portion of the filled

- syringes were not \_\_\_\_\_ Explain what happened to the vials that were not \_\_\_\_\_
- b. Media fills should be conducted more frequently than once per year (p. 194, vol. 1.59).
7. Provide a detailed description of personnel monitoring. Include the frequency and location of monitoring on personnel (e.g. hands, arms, chest).
  8. The container closure integrity test should evaluate the ability of the package to serve as a barrier against microbial ingress. Describe in detail how the integrity tests conducted on the syringe A package accomplish this.
  9. Conduct sterility testing on syringe A prior to product release. We will not consider parametric release for a drug product (as proposed on p. 5 of Amendment 3) until a significant amount of experience has been obtained with the \_\_\_\_\_ sterilization procedure.
  10. Please provide information on the residual solvent in Poly (d,l-lactide-co-glycolide), 75:25 PLG. We recommend including a residual solvent content should be a part of specifications for 75:25 PLG.
  11. Based on the data provided, please adjust the acceptance criterion for the total impurities of the drug product to \_\_\_\_\_%.
  12. The acceptance criterion of PLG molecular weight should be adjusted to \_\_\_\_\_ based on the COA and stability data of the different lots.
  13. The upper range acceptance criterion of NMP should be changed to \_\_\_\_\_% from the present level of \_\_\_\_\_%.
  14. We recommend that a polydispersity specification be added to the drug product.
  15. Provide information on the use of \_\_\_\_\_ (DMF \_\_\_\_\_) and add the information in the container closure section of the NDA.
  16. We recommend that the following additional photostability studies be performed:
    - Two additional batches from \_\_\_\_\_ should be tested to assure the photostability of the drug substance.
    - Photostability study of the syringe A containing the Atrigel Delivery System is not included. A photostability study should be performed on the Syringe A as recommended by ICHQ1B guidance.
  17. The stability commitment should be revised to indicate that expiration dating period for the drug product may be extended in an annual report based on real time data from the first three production lots.

18. Based on the stability data provided, we recommend an 18-month expiration date for the drug product.
19. Please submit three copies of the method validation package including a list of samples and equipment, which will be provided for the analysis of the methods.

If you have any questions, call Archana Reddy, M.P.H., Regulatory Project Manager, at 301-827-4260.

Sincerely,

*{See appendix electronic signature page}*

David Lin, 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

-----  
**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
-----

/s/

-----  
David T. Lin  
6/7/02 05:23:40 PM  
I concur.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

NDA 21-379

Atrix Laboratories, Inc.  
Attention: Richard Jackson, Ph.D.  
Senior Vice President, Research and Development  
2579 Midpoint Drive  
Fort Collins, CO 80525-4417

Dear Dr. Jackson:

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: LA-2550 22.5 mg (leuprolide acetate for injectable suspension)  
Review Priority Classification: Standard (S)  
Date of Application: September 25, 2001  
Date of Receipt: September 26, 2001  
Our Reference Number: NDA 21-379

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 November 25, 2001 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be July 26, 2002 and the secondary user fee goal date will be September 26, 2002.

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](http://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., Senior Regulatory Associate, at (301) 827-4260.

Sincerely,

*{See appended electronic signature page}*

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

-----  
**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
-----

/s/

-----  
Jeanine Best  
9/27/01 02:43:44 PM  
Signing for Terri Rumble

Confirmation Report - Memory Send

Page : 001  
Date & Time: Jul-24-02 11:03am  
Line 1 : 301-827-4267  
Line 2 :  
Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number : 466  
Date : Jul-24 11:00am  
To : 919704829735  
Number of pages : 018  
Start time : Jul-24 11:00am  
End time : Jul-24 11:03am  
Pages sent : 018  
Status : OK

Job number : 466 \*\*\* SEND SUCCESSFUL \*\*\*



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: July 24, 2002

To: Johanna Matz Cc: Larry Tamura; Elyse Wolf Company: Arix Laboratories, Inc.	From: Archana Reddy, M.P.H. Regulatory Project Manager Division of Division of Reproductive and Urologic Drug Products
Fax number: 970-482-9735	Fax number: 301-827-4267
Phone number: 970-482-5868	Phone number: 301-827-4260
Subject: Fax of approval letter for Eligard™ 22.5 mg	

Total no. of pages including cover: 18

Comments:  
Johanna,  
Attached is the approval letter for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).  
Archana Reddy  
PM  
DRUDP

Document to be mailed: X YES NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.



**Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III**

**FACSIMILE TRANSMITTAL SHEET**

**DATE: July 24, 2002**

<b>To:</b> Johanna Matz Cc: Larry Tamura; Elyse Wolf	<b>From:</b> Archana Reddy, M.P.H. Regulatory Project Manager
<b>Company:</b> Atrix Laboratories, Inc.	Division of Division of Reproductive and Urologic Drug Products
<b>Fax number:</b> 970-482-9735	<b>Fax number:</b> 301-827-4267
<b>Phone number:</b> 970-482-5868	<b>Phone number:</b> 301-827-4260
<b>Subject:</b> Fax of approval letter for Eligard™ 22.5 mg	

**Total no. of pages including cover: 18**

**Comments:**

Johanna,  
Attached is the approval letter for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).  
Archana Reddy  
PM  
DRUDP

**Document to be mailed:                      X YES                      NO**

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.**

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.

Confirmation Report - Memory Send

Page : 001  
Date & Time: Jul-15-02 04:52pm  
Line 1 : 301-827-4267  
Line 2 :  
Machine ID : FDA/CDER/OND/ODE3/DRUDP

Job number : 404  
Date : Jul-15 04:49pm  
To : 919704829735  
Number of pages : 022  
Start time : Jul-15 04:49pm  
End time : Jul-15 04:52pm  
Pages sent : 022  
Status : OK

Job number : 404 \*\*\* SEND SUCCESSFUL \*\*\*



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: July 15, 2002

To: Johanna Metz Cc: Larry Tamura Company: Arix Laboratories, Inc.	From: Archana Reddy, M.P.H. Regulatory Project Manager Division of Division of Reproductive and Urologic Drug Products
Fax number: 970-482-9735	Fax number: 301-827-4267
Phone number: 970-482-5868	Phone number: 301-827-4260

Subject: Fax of revised label for Eligard

Total no. of pages including cover: 22

Comments:

Johanna,  
Attached is the final DRUDP labeling for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).  
Thanks,  
Archana Reddy  
PM  
DRUDP

Document to be mailed:  YES  NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

---

---

**FACSIMILE TRANSMITTAL SHEET**

---

---

**DATE:** July 15, 2002

<b>To:</b> Johanna Matz Cc: Larry Tamura	<b>From:</b> Archana Reddy, M.P.H. Regulatory Project Manager
<b>Company:</b> Atrix Laboratories, Inc.	Division of Division of Reproductive and Urologic Drug Products
<b>Fax number:</b> 970-482-9735	<b>Fax number:</b> 301-827-4267
<b>Phone number:</b> 970-482-5868	<b>Phone number:</b> 301-827-4260
<b>Subject:</b> Fax of revised label for Eligard	

---

**Total no. of pages including cover:** 22

---

**Comments:**

Johanna,

Attached is the final DRUDP labeling for Eligard™ 22.5 mg (leuprolide acetate for injectable suspension).

Thanks,

Archana Reddy

PM

DRUDP

---

**Document to be mailed:**             YES             NO

---

---

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.**

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-4260. Thank you.