

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-640/S020

Trade Name: Humatrope 5/mg/vial

Generic Name: [somatropin (rDNA origin) for injection]

Sponsor: Eli Lilly and Company

Approval Date: June 13, 1997

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APPLICATION NUMBER:

19-640/S020

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**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

19-640/S020

APPROVAL LETTER



NDA 19-640/S-020

Eli Lilly and Company
Attention: Jennifer Stotka, M.D.
Director, U.S., Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

JUN 13 1997

Dear Dr. Stotka:

Please refer to your supplemental new drug application dated January 13, 1997, received January 15, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Humatrope [somatotropin (rDNA origin) for injection], 5 mg/vial.

We acknowledge receipt of your submission dated May 19, 1997. The User Fee goal date for this application is July 15, 1997.

The supplemental application provides for a change in the bulk drug substance ~~anhydrous~~ potency specification limits from "NLT ~~—~~ $\mu\text{g}/\text{mg}$ and NMT ~~—~~ $\mu\text{g}/\text{mg}$ " to "NLT ~~×~~ $\mu\text{g}/\text{mg}$ and NMT ~~—~~ $\mu\text{g}/\text{mg}$ " based upon the new WHO reference standard [88/624] for growth hormone.

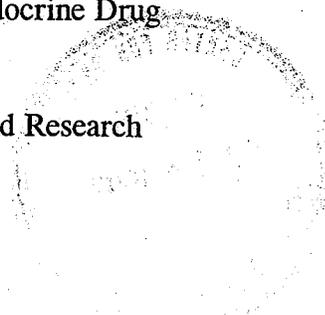
We have completed the review of this supplemental application and it is approved.

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

If you have any questions, please contact Michael F. Johnston, R.Ph., Consumer Safety Officer, at (301) 443-3490.

Sincerely yours,

Stephen K. Moore, Ph.D.
Chemistry Team Leader I, DNDC II
Division of Metabolic and Endocrine Drug
Products (HFD-510)
Office of Drug Evaluation II
Center for Drug Evaluation and Research



NDA 19-640/S-020

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cc:

Original NDA 19-640
HFD-510/Div. Files
HFD-510/CSO/M.F.Johnston
HFD-510/WBerlin/SMoore/EGalliers
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

NOTE TO FOI: Please redact the phrase: "NLT ~~—~~ $\mu\text{g}/\text{mg}$ and NMT ~~—~~ $\mu\text{g}/\text{mg}$ " to "NLT ~~—~~ vg/mg and NMT ~~—~~ $\mu\text{g}/\text{mg}$," from the above.

Drafted by: Mjohnston6.13.97

Initialed by: SMoore6.13.97/EGalliers6.13.97

final:

APPROVAL (AP)

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

19-640 /S020

CHEMISTRY REVIEW(S)

(Comments continued)

The Agency agreed with the Sponsor's request to change, however it seemed appropriate

Therefore, the reviewer requested that the Sponsor amend the application to include specification limits for the bulk potency of NLT ~~1020~~ $\mu\text{g}/\text{mg}$ and NMT 1020 $\mu\text{g}/\text{mg}$. The amendment of 5-19-97 contained revised specifications which are consistent with the Agency's request (see attached copy of the proposed specifications for the bulk drug substance).

/ Page(s) Withheld

 ✓ § 552(b)(4) Trade Secret /
Confidential

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry- 19-640
5020

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APPLICATION NUMBER:

19-640/S020

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

Lilly

Lilly Research Laboratories
A Division of Eli Lilly and Company

Lilly Corporate Center
Indianapolis, Indiana 46285
(317) 276-2000

May 19, 1997

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrine
Drug Products, HFD-510
Attn: Document Control Room 14B-03
5600 Fishers Lane
Rockville, MD 20875-1706

SCS-020 ORIGINAL
NDA SUPPL AMENDMENT



SUPPLEMENT AMENDMENT

Re: NDA 19-640, Supplement Amendment, Humatrope® Bulk Drug Substance

Reference is made to the supplemental application (January 13, 1997, S-020) submitted to the referenced NDA. This amendment provides for requested additional information to supplement S-020.

This amendment to supplement number S-020 is provided in response to a request from Dr. William Berlin during telephone conversations with Lilly personnel on February 5, 1997 and April 28, 1997. The following information was requested:

- data comparison of the Lilly vs. the WHO standard
- clarification/definition of the Dr. Riggins letter that was included in the supplement to identify ~~the~~ that is being discussed
- supplement potency range be amended to "Not less than ~~1~~ g/mg and not more than ~~1~~ µg/mg"

Please call Mr. Steve C. Thomas at (317) 276-9436 or me at (317) 276-7055 if you require any additional information or if there are any questions. Thank you for your continued cooperation and assistance.

Sincerely,

ELI LILLY AND COMPANY

Gerald L. Kirschner, Ph.D.
Advisor, Regulatory Affairs (CM&C)

REVIEWS COMPLETED	
<i>Chemistry</i>	
CSO ACTION: AP Ltr	
<input checked="" type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
<i>[Signature]</i>	6/13/97
CSO INITIALS	DATE

enclosure

NDA NO. 19640 REF. NO. 080

NDA SUPPL FOR SCS
Lilly

ORIGINAL
NDA SUPPLEMENT

Lilly Research Laboratories
A Division of Eli Lilly and Company

Lilly Corporate Center
Indianapolis, Indiana 46285
(317) 276-2000

January 13, 1997

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrine
Drug Products, HFD-510
Attn: Document Control Room 14B-03
5600 Fishers Lane
Rockville, MD 20875-1706

SUPPLEMENT



Re: NDA 19-640, Supplement, Humatrope® Bulk Drug Substance

This supplement provides for a change to the anhydrous potency specification for bulk human growth hormone.

Accordingly, this supplement is submitted to the above referenced NDA under the provisions of 21 CFR §314.70(b).

Please call Dr. Gregory Davis at (317) 276-4125 or me at (317) 276-7055 if you require any additional information or if there are any questions. Thank you for your continued cooperation and assistance.

Sincerely,

ELI LILLY AND COMPANY

Gerald L. Kirschner
Gerald L. Kirschner, Ph.D.
Advisor, Regulatory Affairs (CM&C)

REVIEWS COMPLETED	
<i>AP LV - Chomster</i>	
CSO ACTION: <i>AP LV</i>	
<input checked="" type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
<i>my</i>	<i>6/13/97</i>
CSO INITIALS	DATE

enclosure

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION**

Form Approved: OMB No. 0910-0297
Expiration Date: November 30, 1996.

USER FEE COVER SHEET

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Reports Clearance Officer, PHS
Hubert H. Humphrey Building, Room 721-B
200 Independence Avenue, S.W.
Washington, DC 20201
Attn: PRA

and to:

Office of Management and Budget
Paperwork Reduction Project (0910-0297)
Washington, DC 20503

Please DO NOT RETURN this form to either of these addresses.

See Instructions on Reverse Before Completing This Form.

1. APPLICANT'S NAME AND ADDRESS

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

2. USER FEE BILLING NAME, ADDRESS, AND CONTACT

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

C/O Jennifer L. Stotka, M.D.
Director
U.S. Regulatory Affairs

3. TELEPHONE NUMBER (Include Area Code)
(317) 277-1324

4. PRODUCT NAME Humalog

DOES THIS APPLICATION CONTAIN CLINICAL DATA? YES NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

6. USER FEE I.D. NUMBER

7. LICENSE NUMBER/NDA NUMBER

8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

- | | |
|--|--|
| <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED BEFORE 9/1/92 | <input type="checkbox"/> THE APPLICATION IS SUBMITTED UNDER 505(b)(2) (See reverse before checking box.) |
| <input type="checkbox"/> AN INSULIN PRODUCT SUBMITTED UNDER 506 | |
| FOR BIOLOGICAL PRODUCTS ONLY | |
| <input type="checkbox"/> WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION | <input type="checkbox"/> A CRUDE ALLERGENIC EXTRACT PRODUCT |
| <input type="checkbox"/> BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92 | <input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGIC PRODUCT LICENSED UNDER 351 OF THE PHS ACT |

9. a. HAS THIS APPLICATION QUALIFIED FOR A SMALL BUSINESS EXCEPTION? YES NO
(See reverse if answered YES)

b. HAS A WAIVER OF APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO
(See reverse if answered YES)

This completed form must be signed and accompany each new drug or biologic product, original or supplement.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Director	DATE January 13, 1997
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DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: November 30, 1996.

USER FEE COVER SHEET

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Reports Clearance Officer, PHS
Hubert H. Humphrey Building, Room 721-B
200 Independence Avenue, S.W.
Washington, DC 20261
ABB: PRA

and to:

Office of Management and Budget
Paperwork Reduction Project (0910-0297)
Washington, DC 20543

Please DO NOT RETURN this form to either of these addresses.

See Instructions on Reverse Before Completing This Form.

1. APPLICANT'S NAME AND ADDRESS

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

2. USER FEE BILLING NAME, ADDRESS, AND CONTACT

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

C/O Jennifer L. Stotka, M.D.
Director
U.S. Regulatory Affairs

3. TELEPHONE NUMBER (Include Area Code)
(317) 277-1324

4. PRODUCT NAME
Humatrope

DOES THIS APPLICATION CONTAIN CLINICAL DATA? YES NO
IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

6. USER FEE I.D. NUMBER

7. LICENSE NUMBER/NDA NUMBER

8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

- A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED BEFORE 9/1/92
 - AN INSULIN PRODUCT SUBMITTED UNDER 506
 - THE APPLICATION IS SUBMITTED UNDER 505(b)(2) (See reverse before checking box.)
- FOR BIOLOGICAL PRODUCTS ONLY
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 - BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92
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9. a. HAS THIS APPLICATION QUALIFIED FOR A SMALL BUSINESS EXCEPTION? YES (See reverse if answered YES) NO

b. HAS A WAIVER OF APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES (See reverse if answered YES) NO

This completed form must be signed and accompany each new drug or biologic product, original or supplement.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE

TITLE

DATE

Director

May 19, 1997