

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-764/S011

20-604/S012

Trade Name: Saizen Injection

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

Sponsor: Serono Laboratories Inc.

Approval Date: July 18, 2000

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APPLICATION NUMBER:

19-764/S011

20-604/S012

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APPLICATION NUMBER:

19-764/S011

20-604/S012

APPROVAL LETTER

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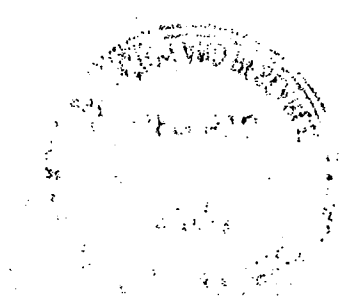
cc:

Archival NDAs 19-764, 20-604
HFD-510/Div. Files
HFD-510/C.King
HFD-510/Reviewers and Team Leaders
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: C.King 07.12.00
Initialed by: S.Moore 07.12.00
final: C.King 07.19.00
filename: mydoc/NDA/19764/s-011ap

APPROVAL (AP)

FOI: Please redact, "(1) /
(2) the addition of
and (3) the addition of /



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APPLICATION NUMBER:

19-764/S011

20-604 /S012

CHEMISTRY REVIEW(S)

JUL 11 2000

CHEMISTS REVIEW		1. ORGANIZATION DMEDP II, HFD-510	2. NDA NUMBER see below
3. NAME AND ADDRESS OF APPLICANT Serono Laboratories 100 Longwater Circle Norwell MA 02061		4. SUPPLEMENT NUMBER, DATE 20-604, SCS-012, 03-Apr-00 20-604, SCS-012, 04-Apr-00	
5. PROPRIETARY NAME Serostim® and Saizen®	6. NAME OF THE DRUG Somatotropin (rDNA origin) for injection	7. AMENDMENTS, REPORT, DATE 26-June-00 (20-604) 26-June-00 (19-764)	
8. SUPPLEMENT PROVIDES FOR a. _____ b. _____ c. the addition of _____			
9. PHARMACOLOGICAL CATEGORY Growth hormone	10. HOW DISPENSED RX	11. RELATED IND, NDA, DMF	
12. DOSAGE FORM Lyophilized powder for injection	13. POTENCY 5 and 10 mg/vial		
14. CHEMICAL NAME AND STRUCTURE See Chemistry Review #1			
15. COMMENTS _____ _____ Included in the tables below is a comparison of their current process to the _____ -scale increase. Continued on the next page			
16. CONCLUSION AND RECOMMENDATION The application has satisfactorily addressed issues related to this supplement. The sponsor has also commitment to submitting the results of the their stability testing for batches PGRA9906, PGRA9909, and PGRA9911 in their next annual report. Issue a Approval letter.			
17. NAME Janice T. Brown	18. REVIEWERS SIGNATURE <i>Janice T. Brown</i>	19. DATE COMPLETED 22-Jun-00	
DISTRIBUTION: ORIGINAL JACKET CSO REVIEWER DIVISION FILE			

AP

Stephen Moore
7/11/2000



5 Page(s) Withheld

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

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

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APPLICATION NUMBER:

19-764/S011

20-604/S012

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**



NDA 19-764/S-011

APR 10 2000

Food and Drug Administration
Rockville MD 20857

Serono Laboratories, Inc.
100 Longwater Circle
Norwell, MA 02061

Attention: Pamela Williamson Joyce
Exec. Director, Regulatory Operations

Dear Ms. Joyce:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Saizen® [somatropin (rDNA origin) for injection]
NDA Number: 19-764
Supplement Number: S-011
Date of Supplement: April 4, 2000
Date of Receipt: April 5, 2000

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on June 4, 2000, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Metabolic and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Attention: Document Control Room 14B-19
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Enid Galliers
Chief, Project Management Staff
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

NDA 19764/S-011
Page 2

cc:

Original NDA 19764/S-011
HFD-510/Div. Files
HFD-510/CSO/King

filename:

SUPPLEMENT ACKNOWLEDGEMENT

Serono Laboratories, Inc. 100 Longwater Circle Norwell, MA 02061

FAX

Date: 23 June 2000

Number of pages including cover sheet: 1

CONFIDENTIAL

To: Dr. Janice Brown
 Microbiologist, DNDCII
 CDER, FDA

re: Serostim NDA 20-604 / S-012
Saizen NDA 19-764 / S-011

Phone: (301) 827 5579

Fax phone: (301) 827 5586

From: Lisa S. Mills
 Regulatory Affairs

Phone: (781) 681-2273

Fax phone: (781) 878-5001

REMARKS: Urgent For your review Reply ASAP Please comment


Dear Dr. Brown,

In response to your request regarding **Serostim NDA 20-604 / S-012** and **Saizen NDA 19-764 / S-011**:

- The stability profile for the scaled-up process batches and the stability profile for the current process batches are comparable.
- The company commits to include the ongoing stability results in the Annual Report.

I hope this meets your needs.

Sincerely,



Lisa S. Mills
 Manager, Regulatory Affairs

RECORD OF TELEPHONE CONVERSATION/MEETING**Date:** 22 and 23-Jun-00

On June 22, 00, I called Ms. Lisa Mills requesting some additional information regarding these supplements. On June 23, 00, she returned my call with Serono's response. A summary of our conversation is provided below.

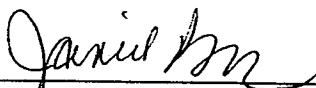
1. I asked for an explanation of the ~~chromatogram~~ of ~~lot~~, ~~chromatogram~~. Ms. Mills replied that during ~~of~~ of

2. I requested a written commitment that the results following their approved protocol (page 48) be submitted in the next annual report for lots PGRA9906, PGRA9909, and PGRA9911. She replied that a written commitment would be submitted to the file.

3. The current submission included ~~manufactured~~ manufactured before the change and no comparison was provided for the scaled-up lots on stability. I explained that when demonstrating product comparability, our current guidance recommends three lots manufactured before the change and three lots after the change. I emphasized that future submissions should include the recommended comparisons. Ms. Mills agreed that future submissions would include this data.

I explained that the stability results did not include a comparison or trend to determine whether the ~~month~~ month data using the scaled-up process is consistent with their current process. I asked whether the stability profile is consistent with batches manufactured using their current process. She replied that the results were compared with previous batches and the same trend was observed.

Name:


Janice T. Brown

NDA#:
20-604, SCS-012, 03-Apr-00
19-764, SCS-011, 04-Apr-00**Telecon/Meeting
initiated by:** Janice Brown Applicant/Sponsor
 FDA**By:** Telephone**Product Name:**
Serostim® and Saizen®**Firm Name:**
Serono Laboratories, Inc.**Name and Title of Person
with whom conversation was
held:**
Lisa Mills, Manager,
Regulatory Affairs**Phone:** (781) 982-9000



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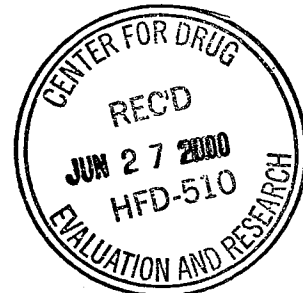
NDA SUPP AMEND

SLS-011
 BC



PART OF THE ARES-SERONO GROUP

SERONO LABORATORIES, INC.
 100 LONGWATER CIRCLE
 NORWELL, MA 02061 / USA
 (800) 283-8088
 TEL (781) 982-9000
 FAX (781) 871-6754



June 26, 2000

John Jenkins, M.D.
 Acting Director, Division of Metabolism and Endocrine
 Drug Products, HFD-510
 Center for Drug Evaluation and Research
 Attn: Document Control Room, 14B-04
 Food and Drug Administration
 5600 Fishers Lane
 Rockville, MD 20857

NDA 19-764
 Saizen® [somatropin (rDNA origin) for injection]
 Response to FDA Request for Information (S-011)

Dear Dr. Jenkins:

Reference is made to NDA 19-764 for Saizen® [somatropin (rDNA origin) for injection] approved on October 8, 1996. Further reference is made to Supplemental New Drug Application (SNDA) S-011 submitted on April 4, 2000, to a telephone conversation with the Agency on June 23, 2000 during which additional information was requested, and to a FAX sent on June 23, 2000 containing the requested information.

Please find below responses to the Agency's request which were also sent by FAX on June 23, 2000:

- The stability profile for the scaled-up process batches and the stability profile for the current process batches are comparable.
- Serono Laboratories, Inc. commits to include the ongoing stability results in the Annual Report.

Please note that Serono Laboratories, Inc. considers this application and all correspondence related thereto as confidential proprietary information and hereby claims protection from disclosure under the applicable sections of Title 18 of the United States Code and Title 21 of the Code of Federal Regulations.

Should you have any questions regarding this submission, please contact Lisa S. Mills, Manager, Regulatory Affairs, or the undersigned at (781) 982-9000.

Sincerely,

Pamela Williamson Joyce
 Vice President, Regulatory Affairs

REVIEWS COMPLETED	
AS	
CSO ACTION:	
<input checked="" type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
sh	7/18/00
CSO INITIALS	DATE



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Serono

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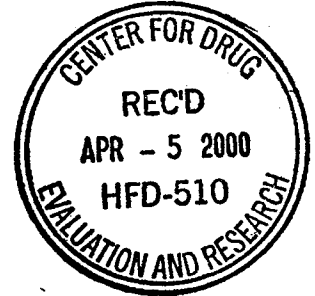
SERONO LABORATORIES, INC.
 100 LONGWATER CIRCLE
 NORWELL, MA 02061 / USA
 (800) 283-8088
 TEL (781) 982-9000
 FAX (781) 871-6754

NDA NO. 19.764 REF. NO. 511
 NDA SUPPL FOR SCS

ORIGINAL

April 4, 2000

John Jenkins, M.D.
 Acting Director, Division of Metabolism and Endocrine
 Drug Products, HFD-510
 Center for Drug Evaluation and Research
 Attn: Document Control Room, 14B-04
 Food and Drug Administration
 5600 Fishers Lane
 Rockville, MD 20857



NDA 19-764
 Saizen® [somatropin (rDNA origin) for injection]
 Supplemental New Drug Application (sNDA) –
 Chemistry, Manufacturing & Controls

Dear Dr. Jenkins:

Reference is made to NDA 19-764 for Saizen® [somatropin (rDNA origin) for injection] approved on October 8, 1996.

Pursuant to 21 CFR 314.70(g)(1), Serono Laboratories, Inc. hereby submits this supplemental New Drug Application (sNDA) to provide for:

1. _____
2. _____ and
3. the addition of _____

Please note that Serono Laboratories, Inc. considers this application and all correspondence related thereto as confidential proprietary information and hereby claims protection from disclosure under the applicable sections of Title 18 of the United States Code and Title 21 of the Code of Federal Regulations.

Should you have any questions regarding this submission, please contact Lisa S. Mills, Manager, Regulatory Affairs, or the undersigned at (781) 982-9000.

Sincerely,

[Handwritten signature]

Pamela Williamson Joyce
 Executive Director, Regulatory Operations

REVIEWS COMPLETED
 CSO ACTION: LETTER MAIL MEMO
 CSO INITIALS *chi* DATE 7/18/00

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

APPLICANT'S NAME AND ADDRESS Serono Laboratories, Inc. 100 Longwater Circle Norwell, MA 02061 USA	3. PRODUCT NAME <p style="text-align: center;">Saizen</p>
2. TELEPHONE NUMBER (Include Area Code) (781) 982-9000	4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW: <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).
5. USER FEE I.D. NUMBER	6. LICENSE NUMBER / NDA NUMBER

7. 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 UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 <i>(Self Explanatory)</i>	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE <i>(See item 7, reverse side before checking box.)</i>
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act <i>(See item 7, reverse side before checking box.)</i>	<input type="checkbox"/> THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act <i>(See item 7, reverse side before checking box.)</i>
<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY <i>(Self Explanatory)</i>	

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"/> AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY	<input type="checkbox"/> AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT
<input type="checkbox"/> BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92	

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


A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

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:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please **DO NOT RETURN** this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 	TITLE Executive Director, Regulatory Operations	DATE 4 April 2000
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