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

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-764/S011

20-604/S012

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Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-764/S011

20-604/S012

APPROVAL LETTER

JUL 19 2000

[redacted]
NDA 20-604/S-012

Serono Laboratories, Inc.
Attention: Pamela Williamson Joyce
Executive Director, Regulatory Operations
100 Longwater Circle
Norwell, MA 02061

Dear Ms. Williamson Joyce:

Please refer to your supplemental new drug applications dated April 4, 2000, received April 5, 2000, for Saizen (somatropin [rDNA origin] for injection) and dated April 3, 2000, received April 4, 2000, for Serostim (somatropin [rDNA origin] for injection) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act.

We acknowledge receipt of your submissions (2) dated June 26, 2000.

These supplemental new drug applications provide for: (1) [redacted] (2) [redacted] and (3) the addition of [redacted]

We have completed the review of these supplemental applications and they are 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, call Crystal King, P.D., M.G.A., Regulatory Project Manager, at (301) 827-6423.

Sincerely,

Stephen K. Moore 7/18/2000
Stephen K. Moore, Ph.D.
Chemistry Team Leader I for
Division of Metabolic and
Endocrine Drug Products (HFD-510)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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) [redacted] (2) the addition of [redacted] and (3) the addition of [redacted]

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-764/S011

20-604 /S012

CHEMISTRY REVIEW(S)

JUL 11 2000

CHEMISTS REVIEW	1. ORGANIZATION	2. NDA NUMBER
	DMEDP II, HFD-510	see below
3. NAME AND ADDRESS OF APPLICANT		4. SUPPLEMENT NUMBER, DATE
Serono Laboratories 100 Longwater Circle Norwell MA 02061		20-604, SCS-012, 03-Apr-00 [redacted]04-Apr-00
5. PROPRIETARY NAME	6. NAME OF THE DRUG	7. AMENDMENTS, REPORT, DATE
Serostim® and Saizen®	Somatropin (rDNA origin) for injection	26-June-00 (20-604) 26-June-00 (19-764)
8. SUPPLEMENT PROVIDES FOR		
a. [redacted] b. [redacted] c. the addition of [redacted]		
9. PHARMACOLOGICAL CATEGORY	10. HOW DISPENSED	11. RELATED IND, NDA, DMF
Growth hormone	RX	
12. DOSAGE FORM	13. POTENCY	
Lyophilized powder for injection	5 and 10 mg/vial	
14. CHEMICAL NAME AND STRUCTURE		
See Chemistry Review #1		
15. COMMENTS		
[redacted] Included in the tables below is a comparison of their current process to the [redacted]-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	18. REVIEWERS SIGNATURE	19. DATE COMPLETED
Janice T. Brown	Janice T. Brown	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

Withheld Track Number: Chemistry- 20-60+/
5012

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-764/S011

20-604/S012

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-764/S-011

APR 10 2000

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

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 [redacted] chromatogram [redacted] Ms. Mills replied that during [redacted] of [redacted] lot, [redacted] chromatogram. [redacted] 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 [redacted] 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 [redacted] 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

Serono
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

SCS-011
BC

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
CSO ACTION:
☒ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS 7/18/00 DATE

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NDA NO. 19.764 REF. NO. C11

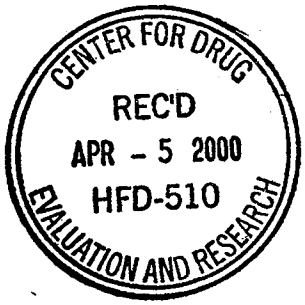
NDA SUPPL FOR SC3

Serono
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

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. [redacted]
2. [redacted] and
3. the addition of [redacted]

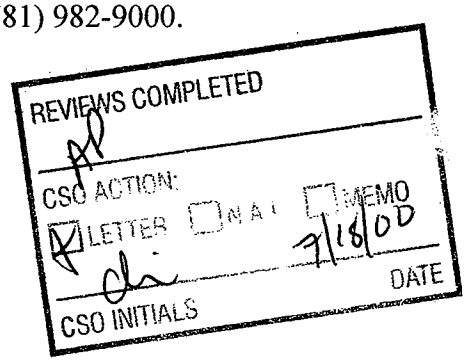
Please note that Serono Laboratories, Inc. considers this application and all correspondence related thereto as confidential proprietary information and hereby claims protection from disclosure under the applicable sections of Title 18 of the United States Code and Title 21 of the Code of Federal Regulations.

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

Sincerely,

Lisa Mills for

Pamela Williamson Joyce
Executive Director, Regulatory Operations



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

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

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
Saizen

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:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

2. TELEPHONE NUMBER *(Include Area Code)*
(781) 982-9000

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.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ 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 *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ 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

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

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
for Pamela Williamson Joyce	Executive Director, Regulatory Operations	4 April 2000

FORM FDA 3397 (5/98)