CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20582/S001

CORRESPONDENCE

SEP 10 1998

NDA 20-582/S-001

Organon, Inc.
Attention: Mr. Albert P. Mayo
Director, Regulatory Affairs
375 Mt. Pleasant Avenue
West Orange, NJ 07052

Dear Mr. Mayo:

Please refer to your pending May 18, 1998, supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Follistim™ (follitropin beta for injection), USP.

We have completed our review of the Clinical Pharmacology and Biopharmaceutics section of your submission and have the following comment and information request:

> Because the effect of the proposed change in the drug product on its bioavailability is unknown, an *in vivo* bioavailability study should be conducted, or a biowaiver should be requested by providing scientific rationale for not conducting such a study.

We would appreciate your prompt written response so we can continue our evaluation of your supplemental application.

This comment is being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If you choose to respond to the issues raised in this letter during this review cycle, depending on the timing of your response, as per the user fee reauthorization agreements, we may or may not be able to consider your response prior to taking an action on your application during this review cycle.

If you have any questions, contact Ms. Diane Moore, Project Manager at (301) 827-4260.

Sincerely,

/S/ 9/8/98

Lana L. Pauls, M.P.H.
Chief, Project Management Staff
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Archival NDA 20-582
HFD-580/Div. Files
HFD-580/D.Moore
HFD-580/LRarick/MMann/MRhee/RBennett/KRaheja
HFD-580/AParekh/VJarugula
HFD-510/DWu
HFD-820/DNDC Division Director (only for CMC related issues)
DISTRICT OFFICE

Drafted by: dm/August 21, 1998

filename: N20582IRS001.DOC

Concurrence:
TRumble 09.03.98/VJarugula, AParekh 09.04.98/MMann, LRarick 09.04.98

INFORMATION REQUEST (IR)

/S/ 9/4/98

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-582/S-001

MAY 27 1998

Organon Inc.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

Attention: Albert P. Mayo
Director, Regulatory Affairs

Dear Mr. Mayo:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Follistim (follitropin beta for injection)
NDA Number:	20-582
Supplement Number:	S-001
Date of Supplement:	May 18, 1998
Date of Receipt:	May 19, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on July 18, 1998 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 Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely, /S/

Lana L. Pauls, M.P.H.
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-582/S-001
HFD-580/Div. Files
HFD-580/CSO/A. Dunson

SUPPLEMENT ACKNOWLEDGEMENT

AKZO NOBEL

ORIGINAL

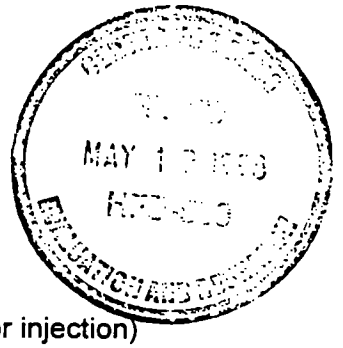
Organon Inc.

CONFIDENTIAL

May 18, 1998

Lisa Rarick, M.D., Director
Division of Reproductive and Urologic Drug Products
Center for Drug Evaluation and Research (HFD-580)
Office of Drug Evaluation II
Document Control Room 17B20
5600 Fishers Lane
Rockville, MD 20857

NDA NO. 20-582 REF. NO. 001
NDA SUPPL FOR SCE



NDA 20-582
Follistim™ (follitropin beta for injection)
Supplement - Sterile Water for Injection, USP
Expedited Review Requested

Dear Dr. Rarick:

Reference is made to our approved New Drug Application, NDA No. 20-582, for Follistim™ (follitropin beta for injection). Reference is also made to our telephone conversation with Alvis Dunson of your Division on February 25, 1998. In accordance with 314.70(b)(2)(i), we are herewith submitting a Supplement for changing diluent from 0.45% NaCl to Sterile Water for Injection, USP. We are doing this to enhance patient comfort during dose administration. Included in this submission are the following attachments:

Attachment 1: Drug Master File No. authorization letter on behalf of a wholly owned subsidiary.

Attachment 2: July 11, 1996 Pharmaceutical Development Report PDR-572 "Compatibility Study Report for Org 32489 Injection with Stoppers Using Water for Injection as a Diluent".

Attachment 3: Six copies of each printed material revised to reflect the change in diluent from 0.45% NaCl to Sterile Water for Injection, USP. (single vial carton for 75 IU product vial and 5 ML diluent vial ; vial boot for 75 IU product vial and 5 mL diluent vial; and five vial carton for 75 IU product vials and 5 mL diluent vials; Sterile Water for Injection, USP vial labels). The vial boot for 75 IU was modified to accommodate the 5 mL diluent vial.

Attachment 4: Clean and Red Line versions of the revised package insert on diskette in Word format. Hard copies of both clean and redline versions are also included in this submission.

Organon

Organon Inc.
375 Mt. Pleasant Avenue
West Orange
New Jersey 07052
USA
Tel.: (973) 325-4500
Fax: (973) 325-4589

Should you have any questions related to this supplement, please contact the undersigned at (973) 325-4855.

Sincerely,

Carole Ann Cartier

Carole Ann Cartier
Senior Regulatory Associate
Regulatory Affairs

CAC:cjw

Attachments
FDA form 356H

Submitted in Duplicate
via Federal Express Airbill No. 805407589383

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

Copy to:

FDA North Brunswick Residence
120 North Center Drive, Building C
New Brunswick, NJ 08902
ATTN: Preapproval Monitor

Submitted via Federal Express Airbill No. 80540789410