CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-701/S-009

Trade Name: Crinone

Generic Name: Progesterone gel

Sponsor: Columbia Laboratories

Approval Date: 04/20/2001

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APPLICATION NUMBER:

NDA 20-701/S-009

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APPLICATION NUMBER:

NDA 20-701/S-009

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-701/S-009

Columbia Research Laboratories, Inc.
Attention: Howard Levine, Pharm.D.
Vice President
100 No. Village Avenue/Suite 32
Rockville Centre, NY 11570

Dear Dr. Levine:

Please refer to your supplemental new drug application dated December 20, 2000, received December 22, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Crinone® (progesterone gel), 4% and 8%.

We acknowledge receipt of your submissions dated January 22, February 9, and April 18, 2001.

This supplemental new drug application provides for a new applicator design for the delivery of Crinone® progesterone gel.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted on April 18, 2001, and immediate container and carton labels submitted February 9, 2001).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-701/S-009." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Reproductive and Urologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

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 Diane Moore, BS, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, 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

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/s/

Amit K. Mitra
4/20/01 04:41:54 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-701/S-009

CHEMISTRY REVIEW(S)

CHEMIST REVIEW OF **SUPPLEMENT**

1. ORGANIZATION	Columbia Research Laboratories, Inc.
2. NDA NUMBER:	20-701
3. SUPPLEMENT NUMBERS/DATES: **Letterdate:** **Stampdate:**	S-009 December 20, 2000 December 22, 2000
4. AMENDMENTS/REPORTS/DATES:	2/9/01
5. RECEIVED BY CHEMIST:	January 10, 2001
6. APPLICANT NAME AND ADDRESS:	Columbia Research Laboratories, Inc. 100 No. Village Avenue/Suite 32 Rockville Center, NY 11570
7. NAME OF DRUG:	CRINONE®
8. NONPROPRIETARY NAME:	Progesterone gel
9. CHEMICAL NAME/STRUCTURE:	Pregn-4ene-3,20-dione
10. DOSAGE FORM(S):	Gel
11. POTENCY:	4% and 8%
12. PHARMACOLOGICAL CATEGORY:	Treatment of secondary amenorrhea
13. HOW DISPENSED:	Rx
14. RECORDS & REPORTS CURRENT:	Yes
15. RELATED IND/NDA/DMF:	20-756 (8%)
16. SUPPLEMENT PROVIDES FOR:	Improved applicator design

17. SPECIAL PRODUCTS: YES _ NO _x__.

(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

18. COMMENTS:

This supplement is provided for the use of an **improved applicator design** for delivery of Progesterone gel (CRINONE®). The data confirm that the change of applicator has no effect on the overall quality of the fished product and the changes made in applicator will only result in slight change in the appearance (narrower) of the applicator and fill weight of the gel (1.45g).

19. CONCLUSIONS AND RECOMMENDATIONS:

The supplement may be approved from the chemistry point of view.

20. REVIEWER NAME: **Rajiv Agarwal**

SIGNATURE
DATE COMPLETED: **2-20-01**

cc: Original:
HFD-580/NDA 20-701
HFD-580/Ragarwal/MRhee/DMoore

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of trade secret and/or

confidential commercial

information from

Chemistry Review #1

/s/

Rajiv Agarwal
2/23/01 08:54:12 AM
CHEMIST

Team laeder [MJ] has sign off the paper copy on 2-20-01

Moo-Jhong Rhee
2/27/01 11:16:46 AM
CHEMIST
I concur

CHEMIST REVIEW OF **SUPPLEMENT**

1. ORGANIZATION	Columbia Research Laboratories, Inc.
2. NDA NUMBER:	20-701
3. SUPPLEMENT NUMBERS/DATES: **Letterdate:** **Stampdate:**	S-009 December 20, 2000 December 22, 2000
4. AMENDMENTS/REPORTS/DATES:	**4/18/01**
5. RECEIVED BY CHEMIST:	**April 20, 2001**
6. APPLICANT NAME AND ADDRESS:	Columbia Research Laboratories, Inc. 100 No. Village Avenue/Suite 32 Rockville Center, NY 11570
7. NAME OF DRUG:	Crinone®
8. NONPROPRIETARY NAME:	Progesterone gel
9. CHEMICAL NAME/STRUCTURE:	Pregn-4ene-3,20-dione
10. DOSAGE FORM(S):	Gel
11. POTENCY:	4% and 8%
12. PHARMACOLOGICAL CATEGORY:	Treatment of secondary amenorrhea
13. HOW DISPENSED:	Rx
14. RECORDS & REPORTS CURRENT:	Yes
15. RELATED IND/NDA/DMF:	20-756 (8%)
16. SUPPLEMENT PROVIDES FOR:	Improved applicator design

17. SPECIAL PRODUCTS: YES _ NO _x__.

18. COMMENTS:

After the review of the supplement (dated 2-20-01), it is noticed that Sponsor has erroneously added [ ] right before the "Description" section in Physician package insert. This concern was communicated to the sponsor via a t-con on 4-18-01. Sponsor has amended the supplement with the corrected version of the physician package insert.

19. CONCLUSIONS AND RECOMMENDATIONS:

The amended supplement may be approved from the chemistry point of view.

20. REVIEWER NAME: **Rajiv Agarwal**

SIGNATURE
DATE COMPLETED: **4-20-01**

cc: Original:
HFD-580/NDA 20-701
HFD-580/Ragarwal/MRhee/DMoore

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/s/

Rajiv Agarwal
4/20/01 03:45:23 PM
CHEMIST

Amit K. Mitra
4/20/01 03:56:47 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-701/S-009

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-701/S-005
NDA 20-701/S-009

Columbia Research Laboratories, Inc.
Attention: Howard Levine, Pharm.D.
Vice President
100 N. Village Ave.
Rockville Centre, NY 11570

Dear Dr. Levine:

We acknowledge receipt of your October 20, 1998 (S-005), and October 15, 2001 (S-009), submissions containing final printed labeling in response to our May 11, 1998 (S-005), and April 20, 2001 (S-009) letters approving your supplemental new drug application for Crinone® (progesterone gel).

We have reviewed the labeling that you submitted in accordance with our May 11, 1998 (S-005), and April 20, 2001 (S-009), letters and we find them acceptable.

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

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Acting Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Daniel A. Shames
12/12/01 11:07:48 AM

Division of Reproductive and Urologic Drug Products

Regulatory Project Manager Review

Application Number: NDA 20-701/S-009

Name of Drug: Crinone® (progesterone gel)

Sponsor: Columbia Research Laboratories, Inc.

Material Reviewed:
FPL for Approved NDA 20-756/S-010

- Package Insert
- Patient Package Insert
- Unit Carton
- Display Carton
- Foil Overwrap

Submission Date: October 15, 2001

Receipt Date: October 17, 2001

Background and Summary Description: Final Printed Labeling (FPL) submitted as FA for approved SNDA 20-701/S-009.

Review:
The FPL is identical to the draft labeling approved on April 20, 2001.

Conclusions:
Issue an Acknowledge and Retain Letter for FPL submitted as FA to SNDA 20-701/S-009.

Jeanine A. Best, M.S.N., R.N.
Senior Regulatory Associate

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/s/

Jeanine Best
12/6/01 09:55:54 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-701/S-009

PRIOR APPROVAL SUPPLEMENT

Columbia Research Laboratories, Inc.
Attention: Howard Levine, Pharm. D.
Vice President
100 North Village Avenue Suite 32
Rockville Center, NY 11570

Dear Dr. Levine:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	CRINONE® (progesterone gel), 4% and 8% Gel
NDA Number:	20-701
Supplement Number:	S-009
Date of Supplement:	December 20, 2000
Date of Receipt:	December 22, 2000

This supplemental application, submitted as a "Changes Being Effected" supplement, proposes the following change: a new applicator design. Changes of this kind cannot be put into effect prior to approval of a supplement. An approved supplement is required for this proposed change prior to distributing drug product made with this change.

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 February 20, 2001, in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be October 22, 2001, and the secondary user fee goal date will be December 22, 2001.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

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 Diane Moore, BS, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

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

/s/

Diane V. Moore
1/2/01 05:23:57 PM