CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-756

CHEMISTRY REVIEW(S)

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS (HFD-580)
REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS

NDA # 20-756 **Chemistry Review # 2** **Review Date**: 5-8-97
AMENDMENT: BL

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	2-28-97	3-4-97	3-12-97
Amendment	4-14-97	4-16-97	4-16-97

NAME AND ADDRESS OF APPLICANT
COLUMBIA RESEARCH LABORATORIES
100 NORTH VILLAGE AVENUE
ROCKVILLE CENTRE, NY 11570

DRUG PRODUCT NAME
Proprietary: Crinone®
Non-proprietary/USAN: Progesterone gel
Compendium: does not apply
Code name/number: None
Chem. Type/Ther. Class: 3 S

ANDA SUITABILITY PETITION/DESI/PATENT STATUS:
1. US Patent No. 4,615697- Composition and Method of Use
2. US Patent Application Serial No. 081122,371- Method of Use

PHARMACOL. CATEGORY/INDICATION: Crinone® is indicated Artificial Reproductive Technology (Artificial fertilization).

DOSAGE FORM: Topical (vaginal) dosage form (90 mg b.i.d).

STRENGTHS: Progesterone 8% gel (90 mg), each applicator contains 2.6 g of gel and delivers 1.125 g of gel.

ROUTE OF ADMINISTRATION: Vaginal

DISPENSED: By prescription

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT.:
Pregn-4-ene-3,20-dione
$C_{21}H_{30}O_2$, Molecular Weight: 314.47

SUPPORTING DOCUMENTS: DMF
IND NDA 20-701 (Crinone 4 and 8% gel)

RELATED DOCUMENTS
None

CONSULTS
1. Proposed Trademark was sent to the Labeling Committee on 8-18-96. The Trademark is acceptable.

2. EER was sent on 2-07-97. A response from compliance with satisfactory results of the inspections was received.

3. A FONSI was prepared on 4-25-97. The FONSI is acceptable.

REMARKS/COMMENTS
The application was declared fileable on 1-12-1997.

A deficiency letter was sent to the sponsor of this NDA on 3-25-97

A response to the above deficiencies was received on 4-16-97.

A deficiency letter was sent to the DMF holder of the Drug substance on 5-5-97. The DMF responses are satisfactory.

A commitment by the sponsor is made to add the storage condition on carton, overwrap and packaging insert as follows.

CONCLUSION AND RECOMMENDATIONS
The application can be approved with respect to Chemistry, Manufacturing and Controls.

Amit K. Mitra, Ph.D

cc: NDA original
HFD-580/A. K. Mitra/5-08-97
HFD-580/M. J. Rhee
HFD-580/D. Moore
R/D. Init. By 5/8/97

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS (HFD-580)
REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS

NDA # 20-756 **Chemistry Review # 1** **Review Date**: 3-4-97 **AMENDMENT:**

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original	11-13-96	11-13-96	11-20-96

NAME AND ADDRESS OF APPLICANT
COLUMBIA RESEARCH LABORATORIES
100 NORTH VILLAGE AVENUE
ROCKVILLE CENTRE, NY 11570

DRUG PRODUCT NAME
Proprietary: Crinone®
Non-proprietary/USAN: Progesterone gel
Compendium: does not apply
Code name/number:None
Chem. Type/Ther. Class: 3 S

ANDA SUITABILITY PETITION/DESI/PATENT STATUS:
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$C_{21}H_{30}O_2$, Molecular Weight: 314.47

SUPPORTING DOCUMENTS: DMF
IND NDA 20-701 (Crinone 4 and 8% gel)

RELATED DOCUMENTS
None

CONSULTS
1. Proposed Trademark was sent to the Labeling Committee on 8-18-96. The Trademark is acceptable.

2. EER was sent on 2-07-97. The response is not back from compliance with results of the inspections.

REMARKS/COMMENTS
The application was declared fileable on 1-12-1997.

As shown in the attached Review Notes and Draft Letter, the firm must provide additional information before the application can be approved.

The labeling states that the product is manufactured by The product will be marketed in the US by Columbia Laboratories, Rockville Center, NY.

The firm's Environmental Assessment is reviewed separately.

CONCLUSION AND RECOMMENDATIONS
The application cannot be approved until the firm has responded to the questions in the Draft Deficiency Letter in the NDA review and all responses have been reviewed and found satisfactory.

The Tradename Crinone^{R} is acceptable.

Establishments evaluations for IND and NDA 20-701 are complete with satisfactory results. However, the sites need to be approved for NDA 20-756. The sites for all three applications are same.

A FONSI is being initiated

Amit K. Mitra, Ph.D

cc: NDA original
HFD-580/A. K. Mitra/3-4-97
HFD-580/M. J. Rhee
HFD-580/D. Moore
R/D. Init. By- 3/5/97