

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-701

CHEMISTRY REVIEW(S)

JUL 21 1997

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

NDA # 20-701 **Chemistry Review # 2** **Review Date: 6-30-97**
AMENDMENT: BL

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	2-28-97	3-4-97	3-12-97
Amendment	6-30-97	6-30-97	6-30-97

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 (45 and 90 mg b.i.d).

STRENGTHS: Progesterone 4 and 8% gel. Each applicator contains 2.6 g 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
C₂₁H₃₀O₂, Molecular Weight: 314.47

SUPPORTING DOCUMENTS: DMF
IND

RELATED DOCUMENTS
None

CONSULTS
None

REMARKS/COMMENTS
These amendments were submitted in response to the deficiencies recorded in chemistry review #1.

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

A commitment by the sponsor is made to add the storage condition on carton, overwrap and packaging insert as follows. "Store at controlled room temperature below 25° C".

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

cc: NDA original
HFD-580/A. K. Mitra/6-30-97
HFD-580/M. J. Rhee
HFD-580/D. Moore
R/D. Init. By-

M. Mitra 7/21/97

Amit K. Mitra 7-21-97

Amit K. Mitra, Ph.D

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

NDA # 20-701 Chemistry Review # 1 Review Date: 6-30-97
AMENDMENT:

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Original	8-23-97	8-23-96	8-23-96

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

DRUG PRODUCT NAME

Proprietary: Crinone^a
 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. 4,615,697- Composition and Method of Use
2. US Patent Application Serial No. 081122,371- Method of Use

PHARMACOL. CATEGORY/INDICATION: Crinone^a is indicated for the treatment of secondary amenorrhea and abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as fibroids or uterine cancer.

DOSAGE FORM: 1) Progesterone 4% gel (45 mg), each applicator contains 2.6 g of gel and delivers 1.125 g of gel; Progesterone 8% gel (90 mg), each applicator contains 2.6 g of gel and delivers 1.125 g of gel.

STRENGTHS: Progesterone 8% and 4% gels

ROUTE OF ADMINISTRATION: Vaginal

DISPENSED: By prescription

CHEMICAL NAME. STRUCTURAL FORMULA. MOLECULAR FORMULA. MOL.WT.:

Pregn-4-ene-3,20-dione

C₂₁H₃₀O₂, Molecular Weight: 314.47**SUPPORTING DOCUMENTS:** DMF

IND (COL-1620 progesterone gel), NDA 20-701 (Crinone 4 and 8% gel)

RELATED DOCUMENTS

None

CONSULTS

1. Proposed Trademark, "Crinone", was sent to the Labeling Committee on 8-18-96. The Trademark is acceptable.
2. EER was sent on 9-16-96. The response is back from compliance with satisfactory results of the inspections on 1-14-97
3. The firm's Environmental Assessment and FONSI were prepared, reviewed and signed by Ms. N. Sager on 5-13-97.

REMARKS/COMMENTS

The application was declared fileable on 7-1-97

As shown in the Deficiency 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.

CONCLUSION AND RECOMMENDATIONS

The Chemistry Manufacturing and Control information in NDA 20-701 was reviewed earlier with NDA 20-756 and the reviewed deficiencies are the same. The NDA is approvable pending satisfactory resolution of those deficiencies.

cc: NDA original
HFD-580/A. K. Mitra/6-30-97
HFD-580/M. J. Rhee
HFD-580/D. Moore
R/D. Init. By-

Amit K. Mitra, Ph.D