

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

***APPLICATION NUMBER:***

**50-767**

**CHEMISTRY REVIEW(S)**

AUG 18 1999

**DIVISION OF SPECIAL PATHOGENS AND IMMUNOLOGIC DRUG  
PRODUCTS**

**Review of Chemistry, Manufacturing, and Controls**

**NDA #:** 50-767

**CHEM.REVIEW #:** 1

**REVIEW DATE:** 8/13/99

<b><u>SUBMISSION/TYPE</u></b>	<b><u>DOCUMENT DATE</u></b>	<b><u>CDER DATE</u></b>
ORIGINAL	10/13/98	10/14/98
Amendment (BC)	3/22/99	3/25/99
Amendment (BC)	7/8/99	7/8/99
Amendment (BC)	7/13/99	7/14/99
Amendment (NC)	7/20/99	8/2/99
Amendment (NC)	7/21/99	7/22/99
Amendment (BL)	7/27/99	7/27/99
Amendment (BL)	8/5/99	8/6/99
Amendment (BC)	8/6/99	8/9/99
Amendment (NC)	8/10/99	8/11/99
Amendment (BL)	8/12/99	8/13/99

**NAME & ADDRESS OF APPLICANT:**

Pharmacia & Upjohn  
7000 Portage Road  
Kalamazoo, MI 49001  
Ph# (616) 833-9164

**CONTACT:**

Carl DeJuliis, Regulatory Affairs

**DRUG PRODUCT NAME:**

**Proprietary:** CLEOCIN Vaginal Ovules  
**Established:** clindamycin phosphate vaginal suppositories  
**Code #:** -

**PHARMACOLOGICAL CATEGORY/INDICATION:**

Treatment of bacterial vaginosis.

**DOSAGE FORM:** Vaginal Suppositories

**STRENGTHS:** 100 mg

**ROUTE OF ADMINISTRATION:** Intravaginal

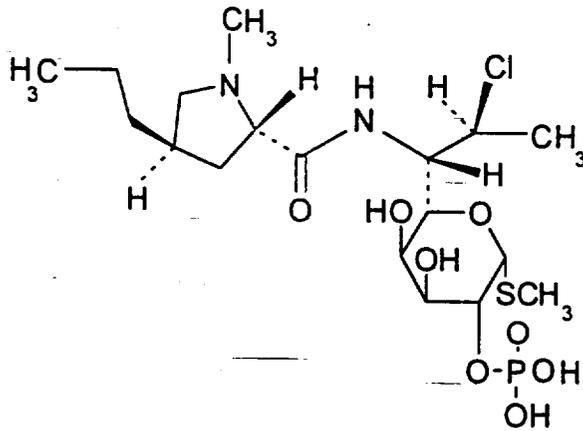
**Rx/OTC:** Rx

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,  
MOLECULAR WEIGHT:**

Clindamycin phosphate,  $C_{18}H_{34}ClN_2O_8PS$ , MW=504.97

- (1) *threo*- $\alpha$ -D-galacto-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[[(1-methyl-4-propyl-2-pyrrolidiny)carbonyl]amino]-1-thio-, 2-(dihydrogen phosphate), (2S-trans)-
- (2) Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*- $\alpha$ -D-galacto-octopyranoside 2-(dihydrogen phosphate)

CAS 024729-96-2



**SUPPORTING DOCUMENTS:**

\_\_\_\_\_

**RELATED DOCUMENTS:**

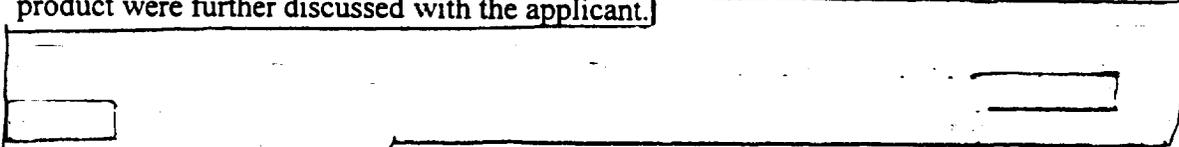
NDA 50-680;

**CONSULTS:**

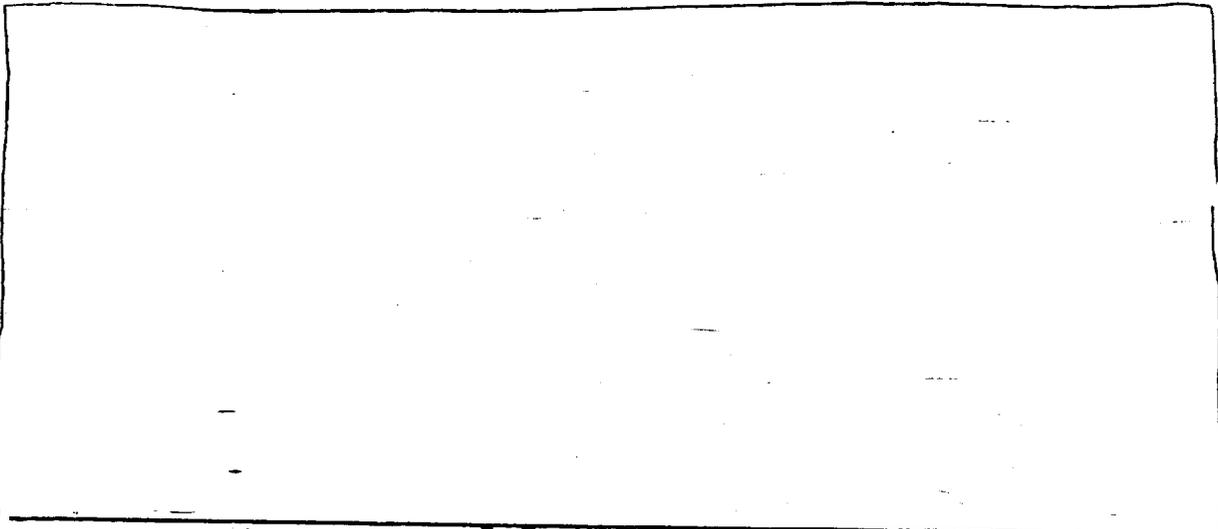
Trademark review (acceptable on March 11, 1999).  
Site inspection (acceptable on March 16, 1999).  
Microbiology consult (completed on May 9, 1999).  
Environmental Assessment (categorical exclusion request acceptable).

**REMARKS/COMMENTS:**

This NDA submitted by Pharmacia & Upjohn provides for clindamycin phosphate vaginal suppositories, 100 mg, as a three days treatment for bacterial vaginosis. The NDA submission and amendments provide acceptable information on the chemistry, manufacturing and controls for the production of clindamycin phosphate vaginal suppositories. Several issues in the manufacturing of both drug substance and drug product were further discussed with the applicant.



In addition, two following Phase IV CMC commitments are included in the action letter for this NDA:



The applicant agreed to that in the 8/10/99 amendment. The faxes containing the comments and questions on these issues that were communicated to the applicant are attached in the end of this review.

**CONCLUSIONS & RECOMMENDATIONS:**

The NDA submission and amendments provide acceptable information on the chemistry, manufacturing and controls for the production of Cleocin Vaginal Ovules (clindamycin phosphate vaginal suppositories). The related GMP and product specific inspections of the manufacturing facilities have been completed and found satisfactory. From the chemistry, manufacturing and controls viewpoint, the NDA is recommended for approval.

/S/

Dorota Matecka, Ph.D.  
Review Chemist, HFD-590

/S/

Norman R. Schmuff, Ph.D.  
Team Leader, HFD-590

8/18/99

cc: Org. NDA 50-767  
HFD-590/Division File  
HFD-590/Team Leader/NSchmuff  
HFD-830/DivDir/CChen  
HFD-590/Chem/DMatecka  
HFD-590/MO/JWinfield  
HFD-590/Pharm/OMcMaster  
HFD-590/CSO/CChi  
District Office