# CENTER FOR DRUG EVALUATION AND RESEARCH

**Approval Package for:**

***APPLICATION NUMBER:***

# 19-653/S-033 & 19-697/S-030

***Trade Name:*** Ortho-Cyclen 0.25mg/0.035mg

Ortho Tri-Cyclen 0.18mg/0.035mg, 0.215mg/0.035mg, 0.25mg/0.035mg

***Generic Name:*** norgestimate/ethinyl estradiol tablets

***Sponsor:*** Johnson RW

***Approval Date:*** 09/06/2002

***Indications:*** Ortho-Cyclen & Ortho Tri-Cyclen: For the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception.

Ortho Tri-Cyclen: For the treatment of moderate acne vulgaris in females, greater than or equal to 15 years of age, who have no known contradictions to oral contraceptive therapy, desire contraception, have achieved menarche and are unresponsive to topical anti-acne medications.

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

# 19-653/S-033 & 19-697/S-030

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## Reviews / Information Included in this NDA Review.

| | |
|---|---|
| Approval Letter | X |
| Approvable Letter | |
| Labeling | |
| Summary Review | |
| Officer/Employee List | |
| Office Director Memo | |
| Cross Discipline Team Leader Review | |
| Medical Review(s) | |
| Chemistry Review(s) | X |
| Environmental Assessment | |
| Pharmacology Review(s) | |
| Statistical Review(s) | |
| Microbiology Review(s) | |
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| Risk Assessment and Risk Mitigation Review(s) | |
| Proprietary Name Review(s) | |
| Administrative/Correspondence Document(s) | X |

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**19-653/S-033 & 19-697/S-030**

# APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-653/S-033
NDA 19-697/S-030

Johnson & Johnson Pharmaceutical Research & Development
Attention: Sandy Rathborne
Manager, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Rathborne:

Please refer to your supplemental new drug application dated March 6, 2002, received March 7, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ortho Cyclen® (norgestimate/ethinyl estradiol) Tablets and Ortho Tri-Cyclen® (norgestimate/ethinyl estradiol) Tablets.

This "Changes Being Effected in 30 days" supplemental new drug application provides for two additional analytical testing laboratory sites.

We have completed the review of this supplemental application, and it is approved.

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 Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

*{See appended electronic signature page}*

David Lin, 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/

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David T. Lin
9/6/02 02:31:40 PM
I concur.

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**19-653/S-033 & 19-697/S-030**

## CHEMISTRY REVIEW(S)

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER: NDA 19-653/SCM-033**
3. **SUPPLEMENT NUMBERS/DATES:**
   **Letterdate:** 06-Mar-2002
   **Stampdate:** 07-Mar-2002
4. **AMENDMENTS/REPORTS/DATES:**
   **Letterdate:**
   **Stampdate:**
5. **RECEIVED BY CHEMIST:** 08-Mar-2002

6. **APPLICANT NAME AND ADDRESS:**
   R.W. Johnson Pharmaceutical Research Institute
   920 Route 202 South
   P.O. Box 300
   Raritan, NJ 08869-0602

7. **NAME OF DRUG:**
   ORTHO-CYCLEN® Tablets

8. **NONPROPRIETARY NAME:**
   Norgestimate / Ethinyl Estradiol

9. **CHEMICAL NAME/STRUCTURE:**
   Please refer to the USP Dictionary of USAN and International Drug Names.

10. **DOSAGE FORM(S):**
    Tablet

11. **POTENCY:**
    Norgestimate 250µg/ Ethinyl Estradiol 35µg

12. **PHARMACOLOGICAL CATEGORY:**
    Progestin/Estrogen; Oral Contraception

13. **HOW DISPENSED:**
    RX

14. **RECORDS & REPORTS CURRENT:**
    Yes

**15. RELATED IND/NDA/DMF:**
NDA 19-697/SCM-030.

**16. SUPPLEMENT-CHANGES BEING EFFECTED PROVIDES FOR:**
This CBE 30 Supplement provides for two additional analytical testing laboratory sites.

**17. COMMENTS**
This is a bundled supplement with NDA 19-697 SCM-030. The two additional analytical laboratories are, [redacted] and Janssen Pharmaceutica (for the addresses of these facilities please refer to the attached EER). The two laboratories will perform [redacted] of ORTHO-CYCLEN and ORTHO TRI-CYCLEN tablets.

The sponsor has met the following criteria:
1) The approved methods described in NDA 19-653 and NDA 19-697 will be used.
2) All post-approval commitments related to these test methods have been fulfilled (Method Validation is complete).
3) The new testing facilities have the capability to perform the intended testing (see EER report).
4) An EER was submitted on 26-MAR-2002 and returned as acceptable based on profile on 27-MAR -2002 (see attached EER).

Therefore sponsor has met and fulfilled all the criteria for this supplement to qualify and be approved as a CBE supplement under the PAC-ALTS Guidance (Postapproval Changes-Analytical Testing Laboratory Sites).

**18. CONCLUSIONS AND RECOMMENDATIONS:**
This CBE-30 Supplement may be approved. **Issue an approval letter.**

| **19. REVIEWER NAME** | **SIGNATURE** | **DATE COMPLETED** |
|---|---|---|
| Jila H. Boal, Ph.D.<br>Review Chemist | | 30-AUG-2002 |

**cc: Original: NDA 19-653/SCM-033**
**HFD-580/Division File**
**HFD-580/JMercier**
**HFD-580/DTLin/JBoal**

**INIT by DTLin, Ph.D.**

Filename: NDA 19-653/SCM-033

14-AUG-2002 FDA CDER EES Page 1 of 1
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 19653/033
Stamp: 07-MAR-2002
Regulatory Due: 07-SEP-2002
Applicant: ORTHO MCNEIL PHARM
1000 ROUTE 202 SOUTH
RARITAN, NJ 088690602
Priority: 14S
Org Code: 580

Action Goal:
District Goal: 02-JUN-2002
Brand Name: ORTHO CYCLEN-28
Estab. Name:
Generic Name: ETHINYL ESTRADIOL/NORGESTIMATE

Dosage Form: (TABLET)
Strength: 235 UG/35 UG NMG/EE

Application Comment: THE [ ] FACILITY IS FOR [ ] OF THE TABLETS ACCORDING TO THE APPROVED METHODS IN THE NDA. (on 26-MAR-2002 by J. BOAL (HFD-580) 301-827-4259)

FDA Contacts: J. MERCIER (HFD-580) 301-827-4260 , Project Manager
J. BOAL (HFD-580) 301-827-4259 , Review Chemist
D. LIN (HFD-580) 301-827-4230 , Team Leader

Overall Recommendation: ACCEPTABLE on 27-MAR-2002 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: 2242843
JANSSEN PHARMACEUTICA INC
1125 TRENTON HARBOURTON RD
TITUSVILLE, NJ 08560

DMF No: AADA:
Responsibilities: FINISHED DOSAGE STABILITY TESTER
Profile: CTL OAI Status: NONE
Estab. Comment:

| Milestone Name | Date | Req. Type | Insp. Date | Decision & Reason | Creator |
|---|---|---|---|---|---|
| SUBMITTED TO OC | 26-MAR-2002 | | | | BOALJ |
| OC RECOMMENDATION | 27-MAR-2002 | | | ACCEPTABLE BASED ON PROFILE | DAMBROGIOJ |

Establishment: [ ]

DMF No: AADA:
Responsibilities: [ ]
Profile: CTL OAI Status: NONE
Estab. Comment: THE JANSSEN PHARMACEUTICA IS FOR STABILITY TESTING OF THE TABLETS ACCORDING TO THE APPROVED METHODS IN THE NDA. (on 26-MAR-2002 by J. BOAL (HFD-580) 301-827-4259)

| Milestone Name | Date | Req. Type | Insp. Date | Decision & Reason | Creator |
|---|---|---|---|---|---|
| SUBMITTED TO OC | 26-MAR-2002 | | | | BOALJ |
| OC RECOMMENDATION | 27-MAR-2002 | | | ACCEPTABLE BASED ON PROFILE | DAMBROGIOJ |

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/s/

Jila Boal
9/5/02 05:44:19 PM
CHEMIST

David T. Lin
9/5/02 06:12:59 PM
CHEMIST
I concur.

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER: NDA 19-697/SCM-030**
3. **SUPPLEMENT NUMBERS/DATES:**
   **Letterdate:** 06-Mar-2002
   **Stampdate:** 07-Mar-2002
4. **AMENDMENTS/REPORTS/DATES:**
   **Letterdate:**
   **Stampdate:**
5. **RECEIVED BY CHEMIST:** 08-Mar-2002

6. **APPLICANT NAME AND ADDRESS:**
   R.W. Johnson Pharmaceutical Research Institute
   920 Route 202 South
   P.O. Box 300
   Raritan, NJ 08869-0602

7. **NAME OF DRUG:**
   ORTHO-TRI-CYCLEN® Tablets

8. **NONPROPRIETARY NAME:**
   Norgestimate / Ethinyl Estradiol

9. **CHEMICAL NAME/STRUCTURE:**
   Please refer to the USP Dictionary of USAN and International Drug Names.

10. **DOSAGE FORM(S):**
    Tablet

11. **POTENCY:**
    Norgestimate / Ethinyl Estradiol
    180 µg / 35µg
    215 µg / 35 µg
    250µg / 35µg

12. **PHARMACOLOGICAL CATEGORY:**
    Progestin/Estrogen Oral Contraception

13. **HOW DISPENSED:**
    RX

14. **RECORDS & REPORTS CURRENT:**
    Yes

**15. RELATED IND/NDA/DMF:**
NDA # 19-653/SCM-033.

**16. SUPPLEMENT-CHANGES BEING EFFECTED PROVIDES FOR:**
This CBE 30 Supplement provides for two additional analytical testing laboratory sites.

**17. COMMENTS**
This is a bundled supplement with NDA 19-653 SCM-033. The two additional analytical laboratories are, [ ] and Janssen Pharmaceutica (for the addresses of these facilities please refer to the attached EER). The two laboratories will perform [ ] of ORTHO-CYCLEN and ORTHO TRI-CYCLEN tablets.

The sponsor has met the following criteria:
1) The approved methods described in NDA 19-697 and NDA 19-653 will be used.
2) All post-approval commitments related to these test methods have been fulfilled (Method Validation is complete).
3) The new testing facilities have the capability to perform the intended testing (see EER report).
4) An EER was submitted on 26-MAR-2002 and returned as acceptable based on profile on 27-MAR -2002 (see attached EER).

Therefore sponsor has met and fulfilled all the criteria for this supplement to qualify and be approved as a CBE supplement under the PAC-ALTS Guidance (Postapproval Changes-Analytical Testing Laboratory Sites).

**18. CONCLUSIONS AND RECOMMENDATIONS:**
This CBE-30 Supplement may be approved. **Issue an approval letter.**

| **19. REVIEWER NAME** | **SIGNATURE** | **DATE COMPLETED** |
|---|---|---|
| Jila H. Boal, Ph.D.<br>Review Chemist | | 30-AUG-2002 |

**cc: Original: NDA 19-697/SCM-030**
**HFD-580/Division File**
**HFD-580/JMercier**
**HFD-580/DTLin/JBoal**

**INIT by DTLin, Ph.D.**

Filename: NDA 19-697/SCM-030

14-AUG-2002 FDA CDER EES Page 1 of 1
ESTABLISHMENT EVALUATION REQUEST
DETAIL REPORT

Application: NDA 19697/030
Stamp: 07-MAR-2002
Regulatory Due: 07-SEP-2002
Applicant: ORTHO MCNEIL PHARM
1000 ROUTE 202 SOUTH
RARITAN, NJ 088690602
Priority: 3S
Org Code: 580

Action Goal:
District Goal: 03-AUG-2002
Brand Name: ORTHO TRI-CYCLEN
Estab. Name:
Generic Name: ETHINYL ESTRADIOL/NORGESTIMATE; NORGESTI
Dosage Form: (TABLET)
Strength: SEE COMMENTS

Application Comment: ANALYTICAL TESTING LAB FOR [ ] OF TABLETS BY THE APPROVED METHODS DESCRIBED IN THE NDA. (on 26-MAR-2002 by J. BOAL (HFD-580) 301-827-4259)
THE JANSSEN PHARMACEUTICALS IS THE STABILITY TESTING LAB FOR THE TABLETS ACCORDING TO THE APPROVED METHODS DESCRIBED IN THE NDA. (on 26-MAR-2002 by J. BOAL (HFD-580) 301-827-4259)

FDA Contacts: J. MERCIER (HFD-580) 301-827-4260 , Project Manager
J. BOAL (HFD-580) 301-827-4259 , Review Chemist
D. LIN (HFD-580) 301-827-4230 , Team Leader

Overall Recommendation: ACCEPTABLE on 27-MAR-2002 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: 2242843
JANSSEN PHARMACEUTICA INC
1125 TRENTON HARBOURTON RD
TITUSVILLE, NJ 08560

DMF No: AADA:
Responsibilities: FINISHED DOSAGE STABILITY TESTER
Profile: CTL OAI Status: NONE
Estab. Comment:

| Milestone Name | Date | Req. Type | Insp. Date | Decision & Reason | Creator |
|---|---|---|---|---|---|
| SUBMITTED TO OC | 26-MAR-2002 | | | | BOALJ |
| OC RECOMMENDATION | 27-MAR-2002 | | | ACCEPTABLE BASED ON PROFILE | DAMBROGIOJ |

Establishment: [ ]

DMF No: AADA:
Responsibilities: [ ]
Profile: CTL OAI Status: NONE
Estab. Comment: THE [ ] IS FOR BOTH [ ] OF THE TABLETS ACCORDING TO THE APPROVED METHODS IN THE NDA. (on 26-MAR-2002 by J. BOAL (HFD-580) 301-827-4259)

| Milestone Name | Date | Req. Type | Insp. Date | Decision & Reason | Creator |
|---|---|---|---|---|---|
| SUBMITTED TO OC | 26-MAR-2002 | | | | BOALJ |
| OC RECOMMENDATION | 27-MAR-2002 | | | ACCEPTABLE BASED ON PROFILE | DAMBROGIOJ |

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/s/
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Jila Boal
9/5/02 05:46:42 PM
CHEMIST

David T. Lin
9/5/02 06:15:45 PM
CHEMIST
I concur.

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**19-653/S-033 & 19-697/S-030**

# ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-653/S-033
NDA 19-697/S-030

**CBE-30 SUPPLEMENT**

Johnson & Johnson Pharmaceutical Research & Development
Attention: Sandy Rathborne
Manager, regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Rathborne:

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

| NDA Number | Supplement Number | Drug Name |
|---|---|---|
| 19-653 | 033 | ORTHO-CYCLEN® (norgestimate/ethinyl estradiol) Tablets |
| 19-697 | 030 | ORTHO-TRI-CYCLEN® (norgestimate/ethinyl estradiol) Tablets |

Date of supplement: March 6, 2002

Date of receipt: March 7, 2002

This supplemental application was submitted as a "Supplement - Changes Being Effected in 30 days." The appropriateness of reporting the proposed change(s) as changes being effected in 30 days is under review.

Unless we notify you within 60 days of the 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 May 7, 2002 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Division Document Room, 17B20
5600 Fishers Lane
Rockville, Maryland 20857

If you have any question contact me at (301) 827-4260.

Sincerely,

Jennifer Mercier
Regulatory Project Manager
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

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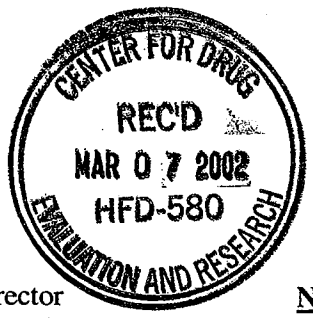
Jennifer L. Mercier
3/12/02 11:00:34 AM

**Johnson & Johnson Pharmaceutical Research & Development, L.L.C.**
920 ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

ORIGINAL




0 6 MAR 2002

NDA NO. 19697 REF. NO. 030
NDA SUPPL FOR Manufacturing

Susan Allen, MD MPH, Director
US Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Attn.: Document Control Room 14B-03
5600 Fishers Lane
Rockville, Maryland 20852-1706

**NDA 19-653**
ORTHO-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

Please cross refer to:

**NDA 19-697**
ORTHO TRI-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

**SUPPLEMENT – CHANGES BEING EFFECTED in 30 DAYS**

Dear Dr. Allen:

Reference is made to the above approved New Drug Applications, NDA 19-697 and NDA 19-653. On behalf of Ortho-McNeil Pharmaceutical, Inc., we are filing a Changes Being Effected in 30 Days Supplement providing for two additional analytical testing laboratory sites.

At this time, we are providing for the following analytical testing site to perform [ ] of ORTHO-CYCLEN and ORTHO TRI-CYCLEN Tablets by the approved methods described in NDA 19-653 and NDA 19-697 respectively:

[ ]

We are also providing for the following analytical testing site to perform routine **stability testing** of ORTHO-CYCLEN and ORTHO TRI-CYCLEN Tablets by the approved methods described in NDA 19-653 and NDA 19-697 respectively:

Janssen Pharmaceutica
1125 Trenton Harbourton Road
Titusville, NJ 08560

The Titusville facility completed a satisfactory general cGMP inspection in July 2001, while [ ] completed their last cGMP inspection in May, 2000. All post-approval

commitments related to these test methods have been fulfilled and the new testing facilities have the capability to perform the intended testing.

A field copy of this submission is being forwarded directly to the FDA district office in North Brunswick and San Juan, Puerto Rico. We certify that the field copies are true copies of the information contained in the archival and review copies of this supplemental application.

Should you have any questions and/or comments, please contact me directly at (908) 704-4687, or our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

Sandy Rathborne

Sandy Rathborne
Manager, Regulatory Affairs
Global CM&C

Enclosure(s)

REVIEWS COMPLETED

CSO ACTION:
[X] LETTER [ ] N.A.I. [ ] MEMO

CSO INITIALS DATE

\\RARUSRARES01\PRIUSREG\ORTHO_CY\LTR\ .DOC\26 February 2002\JU\2