CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-653/S-021 & 19-697/S-016

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: 11/02/1999

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-021 & 19-697/S-016

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Approvable Letter	X
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Summary Review	
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Medical Review(s)	
Chemistry Review(s)	X
Environmental Assessment	
Pharmacology Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Clinical Pharmacology/Biopharmaceutics Review(s)	
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-021 & 19-697/S-016

APPROVAL LETTER

NDA 19-653/S-021
NDA 19-697/S-016

OCT - 2

The R.W. Johnson Pharamceutical Research Institute
Attention: Donna Panasewicz
Director, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869

NOV - 2 1999

Dear Ms. Panasewicz:

Please refer to your supplemental new drug applications dated November 10, 1998, received November 12, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ortho-Cyclen Tablets and Ortho Tri-Cyclen Tablets.

We acknowledge receipt of your submission dated July 1, 1999. Your submission of July 1, 1999 constituted a complete response to our May 12, 1999 action letter.

We note that these supplements were submitted as 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

These supplemental new drug applications provide for changes in the packaging equipment in which the current equipment is replaced with a newer version of the same basic operating design and principle.

We have completed the review of these supplemental applications and they are 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, contact Jennifer Mercier, B.S., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

10/29/99

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

cc:
Archival NDAs 19-653, 19-697
HFD-580/Div. Files
HFD-580/J.Mercier
HFD-580/Rhee/Lin
HFD-095/DDMS-IMT
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: JM/October 25, 1999
Initialed by: Rumble10.27.99/Lin10.28.99/Rhee10.28.99/Lin10.29.99
final: October 29, 1999
filename: 19653S21.WPD

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-020 & 19-697/S-015

APPROVABLE LETTER

NDA 19-697/S-016
NDA 19-653/S-021

R.W. Johnson
Attention: Donna M. Panasewicz
Manager, Regulatory Affairs
920 Route 202 South
P.O. Box 300
Rariton, NJ 08869-0602

MAY 12 1999

Dear Ms. Panasewicz:

Please refer to your supplemental new drug applications dated November 10, 1998, received November 12, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ORTHO-TRI-CYCLEN (norgestimate/ethinyl estradiol) Tablets and ORTHO-CYCLEN (norgestimate/ethinyl estradiol) Tablets, NDA 19-697 and NDA 19-653, respectively.

We acknowledge receipt of your submission dated December 2, 1998.

We note that these supplements were submitted as 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

These supplements propose the following change: a change in packaging equipment in which the current equipment is replaced with a newer version of the same basic operating design and principle. Your submission stated December 12, 1998 as the implementation date for the changes.

We have completed the review of these applications, as amended, and they are approvable. Before these applications may be approved, however, it will be necessary for you to address the following:

1. Provide the following long-term stability data of the drug product which has been packaged in the new blister pack:

   a) 18-months on one batch at 25^0 C/60% RH, and
   b) 12-months on two batches at 25^0 C/60% RH.

2. Provide the results of the leak testing on the new empty blister packs.

3. Commit to provide the following additional stability data:

   a) 24-months on one batch at 25^0 C/60% RH, and
   b) 18-months on two batches at 25^0 C/60% RH.

Within 10 days after the date of this letter, you are required to amend the supplemental applications, notify us of your intent to file amendments, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the applications. Any amendment should respond to all the deficiencies listed. We will not process a

partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, contact Jennifer Mercier, Regulatory Health Project Manager, at (301) 827-4260.

Sincerely,

5/12/99

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

cc:
Archival NDAs 19-697, 19-653
HFD-580/Div. Files
HFD-580/T.Rumble/Mercier
HFD-580/Rarick/Mann/Rhee/Lin
HFD-95/DDMS
DISTRICT OFFICE

Drafted by: tfr/May 11, 1999
Initialed by: Rarick,5.12.99/Mann,5.11.99/Rhee,5.11.99/Lin,5.11.99
Final: Rumble.5.12.99
Filename: 19653.WPF

APPROVABLE (AE)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-021 & 19-697/S-016

CHEMISTRY REVIEW(S)

MAY 10 1999

CHEMIST REVIEW
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 19-697/SCM-016
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 10-NOV-1998
   Stampdate: 12-NOV-1998
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate: 02-DEC-1998
   Stampdate: 03-DEC-1998
5. **RECEIVED BY CHEMIST:** 20-NOV-1998

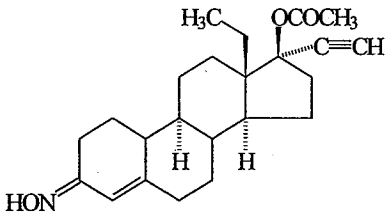
6. **APPLICANT NAME AND ADDRESS:**
   R.W. Johnson Pharmaceutical Research Institute
   920 Route 202 South
   P.O. Box 300
   Raritan, NJ 08869-0602

7. **NAME OF DRUG:**
   Ortho Tri-Cyclen Tablets

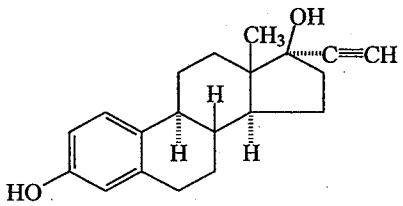
8. **NONPROPRIETARY NAME:**
   Norgestimate/ethinyl estradiol (NGM/EE)

9. **CHEMICAL NAME/STRUCTURE:**

a. Norgestimate: a) (+)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one oxime acetate
b) 18,19-Dinor-17-pregn-4-en-20-yn-3-one,17-(acetyloxy)-13-ethyl-, oxime, (17α)-(+)



b. Ethinyl estradiol: a) 19-Nor-17α-pregn-1,3,5(10)-trien-20-yne-3,17-diol
b) 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17α)



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

11. **POTENCY:**
    180 μg /35 μg, 215 μg /35 μg, and 250 μg /35 μg Norgestimate/ethinyl estradiol

12. **PHARMACOLOGICAL CATEGORY:**
    Progestin, estrogen/Contraception

13. HOW DISPENSED:
RX

14. RECORDS & REPORTS CURRENT:
Yes

15. RELATED IND/NDA/DMF:
NDA 19-653/SCM-021

16. SUPPLEMENT PROVIDES FOR:
Change in packaging equipment in which the current equipment is replaced with a newer version of the same basic operating design and principle.

17. COMMENTS
The company will be replacing the current Dialpak Tablet Dispenser with Dialpak III Tablet Dispenser. This involves the replacement of the current packaging equipment with new equipment. The new equipment are newer versions of the currently used equipment and the packaging operation will remain the same. In addition the same [ ] and aluminum foil will be used for the blister package. The blister packages from the two dialpaks are similar, but not the same.

The equipment change does not involve a change in operating principle or design, and therefore would be considered a level 1 SUPAC IR manufacturing change. However, there is a difference in the blister packages. The sponsor will need to demonstrate both the equivalency between the two blister packages and equal stability between the drug product in the two blister packages. Thus the sponsor's commitment to placing the first production batch of the product on long term stability testing and reporting the results in the annual report is not considered to be adequate.

18. CONCLUSIONS AND RECOMMENDATIONS:
This CBE Supplement is approvable pending satisfactory resolution of the issues delineated in the draft letter.

19. REVIEWER NAME	**SIGNATURE**	**DATE COMPLETED**
David T. Lin, Ph.D. Review Chemist	5/10/99	10-MAY-1999

cc: Original: NDA 19-697/SCM-016
HFD-580/Division File
HFD-580/JMercier
HFD-580/MRhee/DLin

INIT by MJ Rhee 5/10/99

Filename: S19697.016 (doc)

Draft Letter

The review of the CMC information submitted for NDA 19-653/S-021 has been completed and the following comments and requests should be submitted to the sponsor:

1. Provide the following long term stability data on the drug product which has been packaged in the new blister pack: 1) 18 months on one batch at 25°C/60% RH and 2) 12 months on two batches at 25°C/60% RH.

2. Provide the results of the leak testing on the new empty blister packs.

3. Commit to provide the following additional stability data: 1) 24 months on one batch at 25°C/60% RH and 2) 18 months on two batches at 25°C/60% RH.

18.1

OCT 22 1999

CHEMIST REVIEW #2
OF **SUPPLEMENT**

1. **ORGANIZATION:** DRUDP HFD-580
2. **NDA NUMBER:** 19-697/SCM-016
3. **SUPPLEMENT NUMBERS/DATES:**
   Letterdate: 10-NOV-1998
   Stampdate: 12-NOV-1998
4. **AMENDMENTS/REPORTS/DATES:**
   Letterdate: 01-JUL-1999
   Stampdate: 02-JUL-1999
5. **RECEIVED BY CHEMIST:** 12-JUL-1999

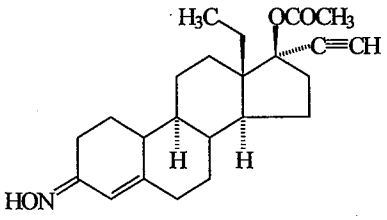
6. **APPLICANT NAME AND ADDRESS:**
R.W. Johnson Pharmaceutical Research Institute
920 Route 202 South
P.O. Box 300
Raritan, NJ 08869-0602

1. **NAME OF DRUG:**
Ortho Tri-Cyclen Tablets

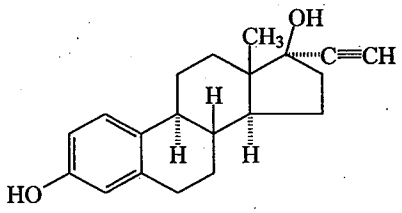
2. **NONPROPRIETARY NAME:**
Norgestimate/ethinyl estradiol (NGM/EE)

3. **CHEMICAL NAME/STRUCTURE:**

a. Norgestimate: a) (+)-13-Ethyl-17-hydroxy-18,19-dinor-17α-pregn-4-en-20-yn-3-one oxime acetate
b) 18,19-Dinor-17-pregn-4-en-20-yn-3-one,17-(acetyloxy)-13-ethyl-, oxime, (17α)-(+)



b. Ethinyl estradiol: a) 19-Nor-17α-pregn-1,3,5(10)-trien-20-yne-3,17-diol
b) 19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17α)



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

5. **POTENCY:**
180 µg /35 µg, 215 µg /35 µg, and 250 µg /35 µg Norgestimate/ethinyl estradiol

6. **PHARMACOLOGICAL CATEGORY:**
Progestin, estrogen/Contraception

7. HOW DISPENSED:
RX

8. RECORDS & REPORTS CURRENT:
Yes

9. RELATED IND/NDA/DMF:
NDA 19-653/SCM-02[illegible]

10. SUPPLEMENT PROVIDES FOR:
Change in packaging equipment in which the current equipment is replaced with a newer version of the same basic operating design and principle.

11. COMMENTS
The company will be replacing the current Dialpak Tablet Dispenser with Dialpak III Tablet Dispenser. This involves the replacement of the current packaging equipment with new equipment. The new equipment is a newer version of the currently used equipment and the packaging operation will remain the same. In addition the same [ ] and aluminum foil will be used for the blister package. The blister packages from the two dialpaks are similar, but not the same.

The equipment change does not involve a change in operating principle or design, and therefore would be considered a level 1 SUPAC IR manufacturing change. However, there is a difference in the blister packages. The sponsor will need to demonstrate both the equivalency between the two blister packages and equal stability between the drug product in the two blister packages. Thus the sponsor's commitment to placing the first production batch of the product on long term stability testing and reporting the results in the annual report is not considered to be adequate.

In the July 1, 1999 amendment the sponsor has responded to the May 12, 1999 FDA approvable letter. See the review notes section for more detailed comments.

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

13. REVIEWER NAME	**SIGNATURE**	**DATE COMPLETED**
David T. Lin, Ph.D. Review Chemist	10/25/99	21-OCT-1999

cc: Original: NDA 19-697/SCM-016
HFD-580/Division File
HFD-580/JMercier
HFD-580/MRhee/DLin

INIT by MJ Rhee 10/26/99

Filename: S19697BC.016 (doc)

1 Page(s) Withheld

Chemistry Review #2 (19-697/S-016)

X § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-653/S-021 & 19-697/S-016

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ORIGINAL

NDA SUPP AMEND

S-016-BL

THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

JUL - 1 1999

Dr. Lisa Rarick
U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and
Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attn: Document Control Room 14B-03
5600 Fishers Lane
Rockville, MD 20857

~~NDA 19-653~~ (S-021)
ORTHO-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

Please cross-refer to:

NDA 19-697 (S-016)
ORTHO TRI-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

Amendment to Special Supplements – Changes Being Effected

Dear Dr. Rarick:

Reference is made to our approved New Drug Application for ORTHO-CYCLEN Tablets NDA 19-653, and ORTHO TRI-CYCLEN Tablets NDA 19-697, our norgestimate/ethinyl estradiol containing oral contraceptive products. Further reference is made to the above referenced Special Supplements – Changes Being Effected dated 10 November 1998 (copy attached) which provided for a change in packaging equipment in which the current equipment is replaced with a newer version of the same basic operating design and principle.

We further refer to your letter dated 12 May 1999 (copy attached)in which you advise that these applications are approvable with the provision that we:

1. Provide the following long-term stability data of the drug product which has been packaged in the new blister pack:
   a) 18-months on one batch at 25 °C/60% RH, and
   b) 12-months on two batches at 25 °C/60% RH.

2. Provide the results of the leak testing on the new empty blister packs.

3. Commit to provide the following additional stability data:
   c) 24-months on one batch at 25 °C/60% RH, and
   d) 18-months on two batches at 25 °C/60% RH.

As outlined in our letter of 21 May 1999 (copy attached), we are hereby submitting the following information which we committed to supply for each of the referenced supplemental NDAs to support approval of these applications:

1. Stability Data:
   a) 12-months on one batch of ORTHO-CYCLEN at[ ]°C/[ ]% RH (Batch 18H100)
   b) 12-months on one batch of ORTHO TRI-CYCLEN at [ ] °C/[ ]% RH (Batch 18D594)
   c) 18-months on one batch of ORTHO -CYCLEN at[ ]°C/[ ]% RH (Batch 18G596)
   d) 18-months on one batch of ORTHO TRI-CYCLEN at[ ]°C/[ ]% RH (Batch 27M058B)
2. Leak testing results on the new empty blister packs.

Please be advised that stability testing was carried out at[ ]°C/[ ]% RH as specified in our NDA. The additional requested stability results will be provided on or before 1 January 2000.

We trust that this amendment will fulfill the requirements set forth in your letter of 12 May 1999.

In accordance with 21 CFR Part 314.70 (a), identical field copies of this correspondence have been filed with our local FDA District Offices.

Should you have any questions or comments concerning this submission, please contact me directly at (908) 218-6140 or call our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

The R.W. Johnson
Pharmaceutical Research Institute

Donna Panasewicz
Director
Regulatory Affairs

REVIEWS COMPLETED
CSO ACTION:
☒ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE

Field Copy: Newark District Office, North Brunswick
San Juan District Office, San Juan, Puerto Rico

NDA SUPP AMEND

SUPPL-016 BL

DEC -3 1998
HFD-580
EVALUATION AND RESEARCH

THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

Received
See Chem. Rev.
And ltr 5/26/99
DJC
5/24/99

DEC 02 1998

Lisa Rarick, M.D., Director
Division of Reproductive and Urologic
Drug Products
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II, HFD-580
Attn.: Document Control Room 14B-03
5600 Fishers Lane
Rockville, Maryland 20857-1706

SUPAC IR Guidance
Section VI.A. Level 1

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

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

Response to Agency Request

Dear Dr. Rarick:

Reference is made to our approved NDA's, 19-653 (ORTHO-CYCLEN Tablets) and 19-697 (ORTHO TRI-CYCLEN Tablets) and our SUPAC IR submission dated November 10, 1998 (S-021 ORTHO-CYCLEN Tablets, S-016 ORTHO TRI-CYCLEN Tablets).

Further reference is made to a telephone conversation on November 23, 1998 between Dr. David Lin of your Division and Donna Panasewicz of The R.W. Johnson Pharmaceutical Research Institute in which Dr. Lin requested a sample of both the current DIALPAK blister package and the DIALPAK III blister package.

At this time, we are submitting two each of the above requested samples.

Field copies of this submission are being forwarded directly to the San Juan and Newark District Offices. We certify that the filed copies are true copies of the information contained in the archival and review copies of this supplemental application.

REVIEWS COMPLETED [redacted]
OSO ACTION:
☐ LETTER ☒ N.A.I. ☐ MEMO
OSO INITIALS DATE

N:\NORGESTI\LTR\SUPAC IR GUID 2.DOC/1

Should you have any questions, you may contact me at (908) 704-4600, a number designated for FDA use only, or if you prefer you may contact me directly at (908) 218-6140.

Sincerely yours,

The R.W. Johnson
Pharmaceutical Research Institute

Donna M. Panasewicz
Manager
Regulatory Affairs

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-697/S-016

The R.W. Johnson Pharmaceutical Research Institute
920 Route 202 South
P.O. Box 300
Raritan, New Jersey 08869-0602

NOV 20 1998

Attention Donna Panasewicz,
Manager, Regulatory Affairs

Dear Ms. Panasewicz:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Ortho Tri-Cyclen

NDA Number: 19-697

Supplement Number: S-016

Date of Supplement: November 10,1998

Date of Receipt: November 12,1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on January 11,1999 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

for Lana Pauls
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 19-697/S-016
HFD-580/Div. Files
HFD-580/CSO/Kish,C

SUPPLEMENT ACKNOWLEDGEMENT

SCM-016

ORIGINAL

NDA NO: 19697 REF. NO. SCM-016

NDA SUPPL FOR CMC, (SE)

THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

NOV 10 1998

See Chem. Rev. dated 5/10/99 DTC 5/10/99

Lisa Rarick, M.D., Director
Division of Reproductive and Urologic Drug Products
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II, HFD-580
Attn.: Document Control Room 14B-03
5600 Fishers Lane
Rockville, Maryland 20857-1706

SUPAC IR Guidance
Section VI.A. Level 1

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

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

Dear Dr. Rarick:

Reference is made to our approved NDA's, 19-653 (ORTHO-CYCLEN Tablets) and 19-697 (ORTHO TRI-CYCLEN Tablets).

Reference is also made to our General Correspondence dated 04 October 1995 (Attachment 1), which detailed our plans for a change in packaging equipment, pertinent to the above noted products and to a letter addressed to Dr. Marilyn Apfel dated 28 March 1996 (Attachment 2), requesting guidance and interpretation of the SUPAC guidelines. Specifically, if the SUPAC IR Guidelines apply to a change in packaging equipment in which the current packaging equipment utilized would be replaced with a newer version of the same basic operating design and principle. On 01 May 1996, a response to our request was received from Dr. Apfel (Attachment 3), in which it was confirmed that this type of change would be covered under SUPAC IR.

As this time, we wish to inform the Agency that we are instituting the change in packaging equipment for the previously noted products 30 days from your receipt of this letter. We wish to note that initially these products will be utilized for a market test of the DIALPAK III compact, (limited distribution of the product in an isolated area) with an official launch anticipated mid February 1999. In accordance with the SUPAC IR Guidance, we commit to place one batch of each product on long term stability and will report the results in the annual report for each product. In addition, we have also placed one lot of ORTHO-NOVUM® 7/7/7 Tablets on accelerated stability as had been requested by Dr. Rhee of your Division in a previous conversation on this subject. As was agreed with Dr. Rhee, the results of this stability study will be reported in the annual report for this product. It is anticipated that ORTHO-NOVUM® 7/7/7 will be launched in 1999. Prior to its launch, a separate SUPAC supplement will be submitted.

Field copies of this submission are being forwarded directly to the San Juan and Newark District Offices. 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, you may contact me at (908) 704-4600, a number designated for FDA use only, or if you prefer you may contact me directly at (908) 218-6140.

Sincerely yours,

The R.W. Johnson
Pharmaceutical Research Institute

Donna M. Panasewicz
Manager
Regulatory Affairs

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

CSO INITIALS DATE

ORIGINAL

NDA SUPP AMEND
S-016 ~~BE~~ NC

THE R.W. JOHNSON
PHARMACEUTICAL RESEARCH INSTITUTE
ROUTE 202, P.O. BOX 300, RARITAN, NEW JERSEY 08869-0602

MAY 21 1999

Dr. Lisa Rarick
U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and
Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attn: Document Control Room 14B-03
5600 Fishers Lane
Rockville, MD 20857

NDA 19-653 (S-021)
ORTHO-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

Please cross-refer to:

NDA 19-697 (S-016)
ORTHO TRI-CYCLEN® Tablets
(norgestimate/ethinyl estradiol)

Reviewed
The sponsor's commitment is satisfactory.
DTS 5/27/99

Intent to Amend Special Supplements – Changes Being Effected

NDFR 5/27/99

Dear Dr. Rarick:

Reference is made to our approved New Drug Application for ORTHO-CYCLEN Tablets NDA 19-653, and ORTHO TRI-CYCLEN Tablets NDA 19-697, our norgestimate/ethinyl estradiol containing oral contraceptive products. Further reference is made to the above referenced Special Supplements – Changes Being Effected dated 10 November 1998 (copy attached) which provided for a change in packaging equipment in which the current equipment is replaced with a newer version of the same basic operating design and principle.

We further refer to your letter dated 12 May 1999 (copy attached) in which you advise that these applications are approvable with the provision that we:

1. Provide the following long-term stability data of the drug product which has been packaged in the new blister pack:
   a) 18-months on one batch at 25 °C/60% RH, and
   b) 12-months on two batches at 25 °C/60% RH.

2. Provide the results of the leak testing on the new empty blister packs.

3. Commit to provide the following additional stability data:
   c) 24-months on one batch at 25 °C/60% RH, and
   d) 18-months on two batches at 25 °C/60% RH.

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In accordance with 21 CFR 314.120, we wish to notify you of our intent to file an amendment to each of the referenced supplemental NDAs to support approval of these applications. At this time we hereby commit to:

1. Provide the following stability data on or before 1 July 1999:
   a) 12-months on one batch of ORTHO-CYCLEN at[ ] °C/[ ]% RH *
   b) 18-months on two batches of ORTHO TRI-CYCLEN at[ ]°C/[ ]% RH*

2. Provide the leak testing results on or before July 1, 1999

3. Provide the additional stability results on or before 1 January 2000.

*Please be advised that current stability NDA requirements for storage are [ ] °C/[ ]% RH.

We trust that the above will fulfill the requirements set forth in your letter of 12 May 1999.

In accordance with 21 CFR Part 314.70 (a), identical field copies of this correspondence has been filed with our local FDA District Offices.

Should you have any questions or comments concerning this submission, please contact me directly at (908) 218-6140 or call our telephone line dedicated for FDA use at (908) 704-4600.

Sincerely,

The R.W. Johnson
Pharmaceutical Research Institute

Donna Panasewicz
Director
Regulatory Affairs

Field Copy: Newark District Office, North Brunswick
San Juan District Office, San Juan, Puerto Rico

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