

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203667Orig1s000

CHEMISTRY REVIEW(S)

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: May 8, 2013
FROM: Raymond P. Frankewich, Ph.D., Review Chemist, Branch IV, DNDQA II/ONDQA
THROUGH: Moo-Jhong Rhee, Ph.D., Branch Chief, Branch IV, DNDQA II/ONDQA
TO: NDA 203-667
SUBJECT: Final Recommendation

The previous CMC Review #1, dated 3-28-2013, made a recommendation of not approval of this NDA because of the following unresolved issues:

1. Final recommendation from the Office of Compliance has not been received.
2. Label/labeling issues were not satisfactorily resolved from the CMC perspective.

The Office of compliance has issued an overall “Acceptable” recommendation on **May 8, 2013 (Attachment 1)**.

Labels/labeling were revised according to our recommendations in CMC Review #1 (**Attachment 2**). Updated container labels were submitted on April 30, 2013. Updated package insert was submitted on May 3, 2013.

Shelf life for this drug product is 24 months (see CMC Review #1, sections P.8.1 (Stability Summary and Conclusions) and P.8.3 (Stability Data)).

Recommendation:

Therefore, from the ONDQA’s perspective, this NDA is now recommended for **APPROVAL**.

Attachments

Attachment 1 EES Report

FDA CDER EES ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application:	NDA 203667/000	Sponsor:	WARNER CHILCOTT LLC
Org. Code:	580		UNION ST RD 195 KM 1 1
Priority:	5		FAJARDO, PR 00738
Stamp Date:	09-JUL-2012	Brand Name:	WC3040 (norethindrone acetate and ethiny
PDUFA Date:	09-MAY-2013	Estab. Name:	
Action Goal:		Generic Name:	
District Goal:	10-MAR-2013	Product Number; Dosage Form; Ingredient; Strengths	001; TABLET (IMMED./COMP. RELEASE), UNCOATED, CHEWABLE NORETHINDRONE ACETATE; 1MG 001; TABLET (IMMED./COMP. RELEASE), UNCOATED, CHEWABLE ETHINYL ESTRADIOL; .2MG

FDA Contacts:	R. FRANKEWICH	Prod Qual Reviewer		3017961354
	K. JENNINGS	Product Quality PM		3017962919
	P. LUCARELLI	Regulatory Project Mgr	(HFD-580)	3017963961
	D. CHRISTNER	Team Leader		3017961341

Overall Recommendation:	ACCEPTABLE	(b) (4)	(HFD-320)	3017964753
	PENDING	on 03-MAY-2013	by EES_PROD	
	ACCEPTABLE	(b) (4)	()	3017964463
	PENDING	on 02-NOV-2012	by EES_PROD	

Establishment:	CFN: (b) (4)	FEI: (b) (4)	(b) (4)
DMF No:	(b) (4)		
Responsibilities:	DRUG SUBSTANCE OTHER TESTER	AADA:	
Profile:	CONTROL TESTING LABORATORY	OAI Status:	NONE
Last Milestone:	OC RECOMMENDATION		
Milestone Date:	06-AUG-2012		
Decision:	ACCEPTABLE		
Reason:	BASED ON PROFILE		

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Establishment: CFN: (b) (4) FEI: (b) (4)
(b) (4)
DMF No: (b) (4) AADA:
Responsibilities: DRUG SUBSTANCE (b) (4)
Profile: NON-STERILE API BY CHEMICAL SYNTHESIS OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 06-AUG-2012
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Establishment: CFN: (b) (4) FEI: (b) (4)
(b) (4)
DMF No: (b) (4) AADA:
Responsibilities: DRUG SUBSTANCE MANUFACTURER
Profile: NON-STERILE API BY CHEMICAL SYNTHESIS OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 08-MAY-2013
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Establishment: CFN: FEI: (b) (4)
(b) (4)
DMF No: (b) (4) AADA:
Responsibilities: DRUG SUBSTANCE OTHER TESTER
FINISHED DOSAGE OTHER TESTER
Profile: CONTROL TESTING LABORATORY OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 06-AUG-2012
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Attachment 2

Labeling – Package Insert – selected sections

Highlights section

NORETHINDRONE ACETATE AND ETHINYL ESTRADIOL CHEWABLE TABLETS AND FERROUS FUMARATE TABLETS, for oral use **Initial U.S. Approval: 1968**

“Full Prescribing Information” section

3: Dosage Forms and Strengths

Norethindrone acetate and ethinyl estradiol chewable tablets and ferrous fumarate tablets is available in blister packs.

Each blister pack contains 28 tablets in the following order:

- 24 white, round, (active) chewable tablets imprinted with “WC” on one side and “535” on the other side, and each containing 1 mg norethindrone acetate and 20 mcg ethinyl estradiol.
- 4 brown, round (non-hormonal placebo) tablets imprinted with “WC” on one side and “624” on the other side, and each containing 75 mg ferrous fumarate. The ferrous fumarate tablets do not serve any therapeutic purpose.

#11: Description

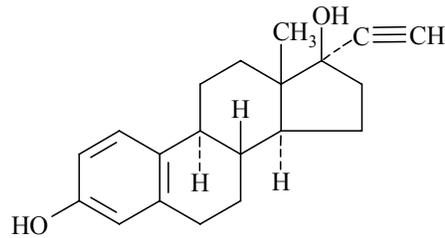
Norethindrone acetate and ethinyl estradiol chewable tablets and ferrous fumarate tablets provides an oral contraceptive regimen consisting of 24 white active chewable tablets that contain the active ingredients, followed by 4 brown non-hormonal placebo tablets as specified below:

- 24 white, round tablets each containing 1 mg norethindrone acetate and 20 mcg ethinyl estradiol.
- 4 brown, round tablets each containing 75 mg ferrous fumarate

Each white active chewable tablet also contains the following inactive ingredients: acacia, lactose monohydrate, magnesium stearate, modified starch, confectioner’s sugar and talc.

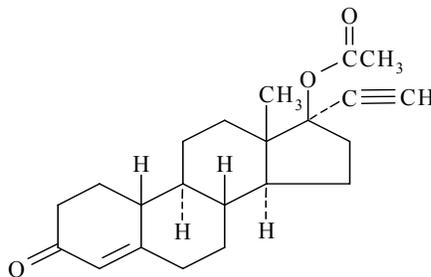
Each brown placebo tablet contains ferrous fumarate, mannitol, povidone, microcrystalline cellulose, sodium starch glycolate, magnesium stearate, sucralose and spearmint flavor. The ferrous fumarate tablets do not serve any therapeutic purpose.

The empirical formula of ethinyl estradiol is $C_{20}H_{24}O_2$ and the structural formula is:



The chemical name of ethinyl estradiol is [19-Norpregna-1,3,5(10)-trien-20-yne-3,17-diol, (17 α)-]. The molecular weight of ethinyl estradiol is 296.40.

The empirical formula of norethindrone acetate is C₂₂H₂₈O₃ and the structural formula is:



The chemical name of norethindrone acetate is [19-Norpregn-4-en-20-yn-3-one, 17-(acetyloxy)-, (17 α)-]. The molecular weight of norethindrone acetate is 340.46.

#16: How Supplied/Storage and Handling

16.1 How Supplied

Norethindrone acetate and ethinyl estradiol chewable tablets and ferrous fumarate tablets is available in blister cards (dispensers) containing 28 tablets:

NDC 0430-0535-50 Cartons of 5 blister cards (dispensers)

Each blister card contains 28 tablets in the following order:

- 24 white, round (active) tablets imprinted with “WC” on one side and “535” on the other side, and each containing 1 mg norethindrone acetate and 20 mcg ethinyl estradiol.
- 4 brown, round (non-hormonal placebo) tablets imprinted with “WC” on one side and “624” on the other side, and each containing 75 mg ferrous fumarate. The ferrous fumarate tablets do not serve any therapeutic purpose.

16.2 Storage Conditions

Store at 20 - 25° C (68 - 77° F); excursions permitted to 15 - 30° C (59 - 86° F) [see USP Controlled Room Temperature].

Keep this drug and all drugs out of the reach of children.

Labeling – selected container and carton labels

Trade pouch label



(b) (4)

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

RAYMOND P FRANKEWICH
05/08/2013

MOO JHONG RHEE
05/08/2013
Chief, Branch IV

NDA 203667

**Norethindrone acetate and ethinyl estradiol chewable tablets
and ferrous fumarate tablets**

Warner Chilcott Company, LLC

Raymond P. Frankewich, Ph.D.

Review Chemist

**Office of New Drug Quality Assessment
Division of New Drug Quality Assessment II
Branch IV**

**CMC REVIEW
For the Division of Reproductive and Urologic Products
(CDER/ODEIII/DRUP, HFD-580)**

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CMC Review Data Sheet

CMC Review Data Sheet

1. NDA 203667
2. REVIEW #: 1
3. REVIEW DATE: 28-March-2013
4. REVIEWER: Raymond P. Frankewich, Ph.D.
5. PREVIOUS DOCUMENTS: NDA 21-871 (Loestrin 24 Fe)
6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original Submission	July 9, 2012
Correspondence (C)	
Amendment (BC)	October 1, 2012 (Package Insert)
Amendment (BC)	November 26, 2012
Amendment	January 22, 2013
Amendment	February 27, 2013

7. NAME & ADDRESS OF APPLICANT:

Name: Warner Chilcott Company, LLC
Address: Union Street, Road 195 Km 1.1
Fajardo, PR 00738-1005
Representative: Warner Chilcott (US), LLC
100 Enterprise Drive
Rockaway, New Jersey 07866
Telephone: 973 – 442 – 3280

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: None
- b) Non-Proprietary Name: Norethindrone acetate and ethinyl estradiol chewable tablets and ferrous fumarate
- c) Code Name/# (ONDQA only): WC3040

CMC Review Data Sheet

d) Chem. Type/Submission Priority (ONDQA only):

- Chem. Type: 6
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

10. PHARMACOL. CATEGORY: Contraceptives/Oral (3010600)

11. DOSAGE FORM: Chewable tablet

12. STRENGTH/POTENCY: 1 mg NA / 0.020 mg EE

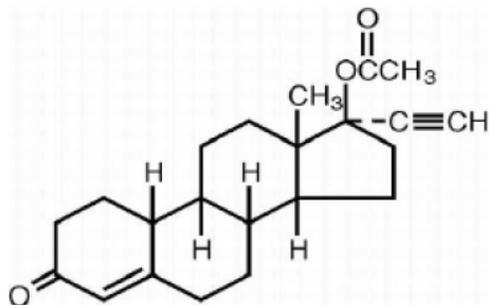
13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: Rx OTC15. [SPOTS \(SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM\):](#) SPOTS product – Form Completed Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Norethindrone acetateChemical name: 3-oxo-19-nor-17 α -pregn-4-en-20-yn-17 β -yl acetate

Structural formula:

Molecular Formula: C₂₂H₂₈O₃

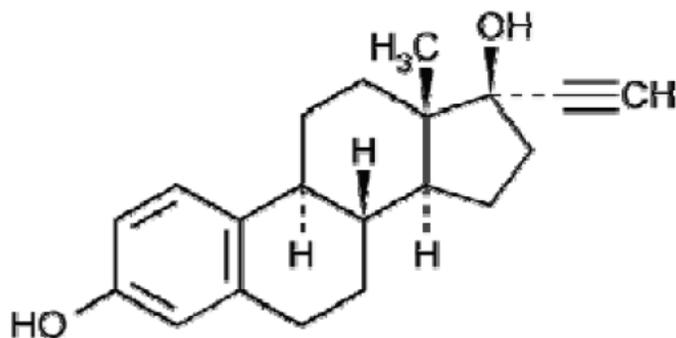
Relative Mass: 340.46

CMC Review Data Sheet

Ethinyl estradiol

Chemical name:

Structural formula:



Molecular Formula: C₂₀H₂₄O₂

Molecular Mass: 296.40

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Norethindrone acetate	1	Adequate	April 28, 2011	
	II		Ethinyl estradiol (b) (4)	1	Adequate	August 27, 2012	
	IV			1	Adequate	November 6, 2012	
	III			1	Adequate	October 25, 2012	
	III			1	Adequate	March 18, 2009	
	III			1	Adequate	March 10, 2010	

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 –Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

CMC Review Data Sheet

- 5 – Authority to reference not granted
- 6 – DMF not available
- 7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND		
NDA		

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NA		
EES	Pending		
Pharm/Tox	NA		
Biopharm	NA*		
LNC	NA		
Methods Validation	NA, according to the current ONDQA policy		
DMEPA	NA		
EA	Categorical exclusion (see review)		
Microbiology	NA		

*No Biopharm review was requested because the drug product is currently approved, and the proposed dissolution test and acceptance criteria are the same as the approved product.

Executive Summary Section

The CMC Review for NDA 203667

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The Office of Compliance has *not* issued an overall “Acceptable” recommendation for the facilities involved in this application.

Also, issues on labels/labeling are *not* satisfactorily resolved yet.

Therefore, from the ONDQA perspective, this NDA is *not* ready for approval per 21 CFR 314.125(b)(6) and (13) in its present form until the above issues are satisfactorily resolved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

NA

II. Summary of CMC Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

(1) Drug Substance

Two drug substances are Norethindrone Acetate (NA) and Ethinyl Estradiol (EE). NA is a progestin, EE and estrogen. The combination of progestin and estrogen has been shown to be effective in oral contraception. Several currently marketed oral contraceptive products contain the combination of NA and EE as active substances.

(2) Drug Product

The drug product is a tablet that contains 1 mg NA and 0.020 mg (20 µg) EE. It is identified in this NDA as WC3040-1F tablet. It is the same formulation as Loestrin[®] 24 Fe tablets, approved as an oral tablet in NDA 21-871. The only difference in the tablets proposed in this NDA are the markings. The tablet proposed in this NDA is intended to be chewed (followed with liquid) or swallowed. Loestrin[®] 24 Fe tablets were intended to be swallowed (only).

The proposed dosing regimen consists of one WC3040-1F tablet taken daily for 24 days followed by one ferrous fumarate tablet (inactive; identified as placebo) taken daily for 4 days to facilitate ease of drug administration via a 28-day regimen. The

Executive Summary Section

ferrous fumarate (FF) tablets are non-hormonal and do not serve a therapeutic purpose.

The inactive FF tablets contain a sweetener (one separate component) and a flavoring (one separate component) as part of the formulation. The WC3040-1F tablet contains no sweetener or flavoring. (b) (4)

There is a FF tablet used with Loestrin[®] 24 Fe tablets; the FF tablet in this NDA has a different formulation.

B. Description of How the Drug Product is Intended to be Used

Drug product is an oral contraceptive. It is a tablet intended to be chewed (followed by liquid) or swallowed. Dosing is discussed above in II.A(2).

C. Basis for Not-Approval Recommendation

21 CFR 314.125(b)(13)

- Final recommendation from the Office of Compliance has *not* been recommended as of this review (see the **Attachment, p. 89**)

21CFR 314.125(b)(8)

- The label/labeling issues have *not* been resolved as of this review (see the **List of Deficiencies, p. 87**)

III. Administrative**A. Reviewer's Signature:**

(See appended electronic signature page)

Raymond P. Frankewich, Ph.D., Review Chemist, Branch IV, ONDQA

B. Endorsement Block:

(See appended electronic signature page)

Moo Jhong Rhee, Ph.D., Branch Chief, Branch IV, ONDQA

C. CC Block: entered electronically in DFS

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/s/

RAYMOND P FRANKEWICH
04/03/2013

MOO JHONG RHEE
04/03/2013
Chief, Branch IV

Initial Quality Assessment
Branch IV
Division of New Drug Quality Assessment II

OND Division: Division of Reproductive and Urologic Products
NDA: 203667
Applicant: Warner Chilcott
Stamp Date: 09-Jul-2012
PDUFA Date: 09-May-2013
Trademark: TBD
Established Name: Norethindrone acetate/ethinyl estradiol chewable tablets and ferrous fumarate tablets
Dosage Form: Tablet
Route of Administration: Oral
Indication: Prevention of pregnancy

CMC Lead: Donna F. Christner, Ph.D.

	YES	NO
ONDQA Fileability:	X	<input type="checkbox"/>
Comments for 74-Day Letter	<input type="checkbox"/>	X

Summary and Critical Issues:

A. Summary

The dosage form is a 28-tablet oral contraceptive regimen consisting of 24 chewable tablets of norethindrone acetate/ethinyl estradiol (1.0 mg/20 mcg) followed by 4 tablets containing 75 mg of ferrous fumarate, which are considered inactive. The active tablets are white, round, flat-faced, beveled edged tablets with “WC” debossed on one side and “535” on the other side. The ferrous fumarate (inert tablets) are round, flat-faced, bevel-edged, brown tablets debossed with “WC” on one side and “624” on the other side. The tablets are packaged in a unit-dose blister card within a foil wrap with desiccant. Secondary (non-functional) packaging will include a rigid (b) (4) card bonded to the unit-dose blister, a (b) (4) pouch, prescriber and patient package inserts and (b) (4) cartons.

B. Critical issues for review

EES was submitted on 06-Aug-2012 by Rebecca McKnight. It should be noted that the Warner Chilcott facility in Fajardo, PR is under an OAI alert and will get an automatic WITHHOLD recommendation if the issue at the facility is not resolved by the PDUFA date.

The specifications are set based on the approved NDA 21-871. Since these are immediate release tablets and the specifications are based on an approved NDA, consultation to ONDQA BioPharm may not be necessary. It is the primary reviewer’s decision on whether a BioPharm review is warranted.

*It should be noted that even though the identical tablets (except for debossing) are used for this drug product, the dosage form will be a **chewable tablet** instead of a tablet. The patient also has the option of swallowing the tablet if she chooses not to chew the tablet. As a new dosage form, a new NDA is warranted.*

(b) (4)

C. Comments for 74-Day Letter

There are no CMC comments to convey at this time.

D. Recommendation:

This NDA is fileable from a CMC perspective. Raymond Frankewich, Ph.D. has been assigned as the primary CMC reviewer.

REGULATORY BRIEFING RECOMMENDATION: Branch level.

Donna F. Christner, Ph.D.

NDA Number: 203667 Type: 5

Established/Proper Name:
Norethindrone acetate/ethinyl
estradiol chewable tablets and
ferrous fumarate tablets

Applicant: Warner
Chilcott

Letter Date: 09-Jul-2012

Stamp Date: 09-Jul-2012

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies. On **initial** overview of the NDA application for filing:

A. GENERAL				
	Parameter	Yes	No	Comment
1.	Is the CMC section organized adequately?	X		
2.	Is the CMC section indexed and paginated (including all PDF files) adequately?	X		
3.	Are all the pages in the CMC section legible?	X		
4.	Has all information requested during the IND phase, and at the pre-NDA meetings been included?	X		

B. FACILITIES*				
	Parameter	Yes	No	Comment
5.	Is a single, comprehensive list of all involved facilities available in one location in the application?	X		
6.	For a naturally-derived API only, are the facilities responsible for critical intermediate or crude API manufacturing, or performing upstream steps, specified in the application? If not, has a justification been provided for this omission? This question is not applicable for synthesized API.		X	N/A

7.	<p>Are drug substance manufacturing sites identified on FDA Form 356h or associated continuation sheet? For each site, does the application list:</p> <ul style="list-style-type: none"> • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable) 	X		
8.	<p>Are drug product manufacturing sites identified on FDA Form 356h or associated continuation sheet. For each site, does the application list:</p> <ul style="list-style-type: none"> • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable) 	X		

9.	<p>Are additional manufacturing, packaging and control/testing laboratory sites are identified on FDA Form 356h or associated continuation sheet. For each site, does the application list:</p> <ul style="list-style-type: none"> • Name of facility, • Full address of facility including street, city, state, country • FEI number for facility (if previously registered with FDA) • Full name and title, telephone, fax number and email for on-site contact person. • Is the manufacturing responsibility and function identified for each facility?, and • DMF number (if applicable) 	X		
10.	Is a statement provided that all facilities are ready for GMP inspection at the time of submission?	X		

* If any information regarding the facilities is omitted, this should be addressed ASAP with the applicant and can be a *potential* filing issue or a *potential* review issue.

C. ENVIRONMENTAL ASSESMENT				
	Parameter	Yes	No	Comment
11.	Has an environmental assessment report or categorical exclusion been provided?	X		Categorical exclusion as per 21 CFR 25.31(a)

D. DRUG SUBSTANCE/ACTIVE PHARMACEUTICAL INGREDIENT (DS/API)				
	Parameter	Yes	No	Comment
12.	Does the section contain a description of the DS manufacturing process?	X		DMF (b) (4) for Norethindrone Acetate DMF (b) (4) for Ethinyl Estradiol
13.	Does the section contain identification and controls of critical steps and intermediates of the DS?	X		DMF (b) (4) for Norethindrone Acetate DMF (b) (4) for Ethinyl Estradiol
14.	Does the section contain information regarding the characterization of the DS?	X		DMF (b) (4) for Norethindrone Acetate DMF (b) (4) for Ethinyl Estradiol
15.	Does the section contain controls for the DS?	X		DMF (b) (4) for Norethindrone Acetate DMF (b) (4) for Ethinyl Estradiol
16.	Has stability data and analysis been provided for the drug substance?	X		DMF (b) (4) for Norethindrone Acetate DMF (b) (4) for Ethinyl Estradiol
17.	Does the application contain Quality by Design (QbD) information regarding the DS?		X	Not a filing issue
18.	Does the application contain Process Analytical Technology (PAT) information regarding the DS?		X	Not a filing issue

E. DRUG PRODUCT (DP)				
	Parameter	Yes	No	Comment
19.	Is there a description of manufacturing process and methods for DP production through finishing, including formulation, filling, labeling and packaging?	X		
20.	Does the section contain identification and controls of critical steps and intermediates of the DP, including analytical procedures and method validation reports for assay and related substances if applicable?	X		
21.	Is there a batch production record and a proposed master batch record?	X		
22.	Has an investigational formulations section been provided? Is there adequate linkage between the investigational product and the proposed marketed product?	X		
23.	Have any biowaivers been requested?		X	Not a filing issue
24.	Does the section contain description of to-be-marketed container/closure system and presentations)?	X		
25.	Does the section contain controls of the final drug product?	X		
26.	Has stability data and analysis been provided to support the requested expiration date?	X		24 month expiry requested
27.	Does the application contain Quality by Design (QbD) information regarding the DP?		X	Not a filing issue
28.	Does the application contain Process Analytical Technology (PAT) information regarding the DP?		X	Not a filing issue

F. METHODS VALIDATION (MV)				
	Parameter	Yes	No	Comment
29.	Is there a methods validation package?	X		

G. MICROBIOLOGY				
	Parameter	Yes	No	Comment
30.	If appropriate, is a separate microbiological section included assuring sterility of the drug product?		X	N/A

H. MASTER FILES (DMF/MAF)				
	Parameter	Yes	No	Comment
31.	Is information for critical DMF references (i.e., for drug substance and important packaging components for non-solid-oral drug products) complete?	X		

DMF #	TYPE	HOLDER	ITEM REFERENCED	LOA DATE	COMMENTS
(b) (4)	II	(b) (4)	Norethindrone acetate	(b) (4)	ADEQUATE on 28-Apr-2011. No updates since that time.
	III		(b) (4)		ADEQUATE on 16-Jun-2011. Update submitted on 19-Jul-2012
	III				ADEQUATE on 19-Mar-2009
	III				ADEQUATE on 12-Mar-2010.
	IV				ADEQUATE on 11-Jun-2010. Updates since that time.
	II		Ethinyl estradiol		ADEQUATE on 27-Oct-2011. No updates since that time.

(b) (4)

I. LABELING				
	Parameter	Yes	No	Comment
32.	Has the draft package insert been provided?	X		
33.	Have the immediate container and carton labels been provided?	X		

J. FILING CONCLUSION				
	Parameter	Yes	No	Comment
34.	IS THE PRODUCT QUALITY SECTION OF THE APPLICATION FILEABLE?	X		
35.	If the NDA is not fileable from the product quality perspective, state the reasons and provide filing comments to be sent to the Applicant.		X	N/A
36.	Are there any potential review issues to be forwarded to the Applicant for the 74-day letter?			

{See appended electronic signature page}

Donna F. Christner, Ph.D.
 CMC Lead
 Division of New Drug Quality Assessment II
 Office of New Drug Quality Assessment

Date

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
 Chief, Branch IV
 Division of New Drug Quality Assessment II
 Office of New Drug Quality Assessment

Date

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DONNA F CHRISTNER
09/05/2012

MOO JHONG RHEE
09/06/2012
Chief, Branch IV