CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022573Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 022573 SUPPL # HFD #

Trade Name

Generic Name norethindrone and ethinyl estradiol chewable tablets and ferrous fumarate chewable tablets

Applicant Name Warner Chilcott

Approval Date, If Known December 22, 2010

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☒ NO ☐

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES ☒ NO ☐

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES ☒ NO ☐

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

No

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☒

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES ☐ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☒ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# See Attached Sheet

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered “NO” for original approvals of new molecular entities.)
IF “YES,” GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES ☒ NO ☐

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☒ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☒

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☒

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☒

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Study PR-00207

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES ☐ NO ☒

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☒

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a

similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

PR-00207

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 ! !
IND # 076629 YES ☒ ! NO ☐
! Explain:

Investigation #2 ! !
IND # YES ☐ ! NO ☐
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 ! !
YES ☐ ! NO ☐

Explain:	! Explain:
Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐ NO ☒

If yes, explain:

==========

Name of person completing form: Pam Lucarelli
Title: Regulatory Health Project Manager
Date: December 7, 2010

Name of Office/Division Director signing form: Scott Monroe
Title: Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

List of approved drug products containing the active moiety:

N016659 NORINYL 1+50 28-DAY
N016954 MICRONOR
N017060 NOR-QD
N017354 LOESTRIN FE 1/20
N017355 LOESTRIN FE 1.5/30
N017565 NORINYL 1+35 21-DAY
N017565 NORINYL 1+35 28-DAY
N017576 OVCON-50
N017716 OVCON-35
N017735 MODICON 28
N017743 BREVICON 28-DAY
N017875 LOESTRIN 21 1.5/30
N017876 LOESTRIN 21 1/20
N017919 ORTHO-NOVUM 1/35-28
N018405 AYGESTIN
N018977 TRI-NORINYL 28-DAY
N018985 ORTHO-NOVUM 7/7/7-28
N020130 ESTROSTEP FE
N020870 COMBIPATCH
N020870 COMBIPATCH
N020907 ACTIVELLA
N020907 ACTIVELLA
N021065 FEMHRT
N021065 FEMHRT
N021490 FEMCON FE
N021871 LOESTRIN 24 FE
N020071 DESOGEN
N021090 CYCLESSA
N020301 ORTHO-CEPT
N020713 MIRCETTE
N021676 YAZ
N021098 YASMIN
N022532 BEYAZ
N021187 NUVARING
N022262 LOSEASONIQUE
N021840 SEASONIQUE
N021544 SEASONALE
N021864 LYBREL
N018782 NORDETTE-28
N021180 ORTHO EVRA
N021490 FEMCON FE
N017565 NORINYL 1+35 21-DAY
N018985 ORTHO-NOVUM 7/7/7-28
N017735 MODICON 28

N017919 ORTHO-NOVUM 1/35-28
N017716 OVCON-35
N017576 OVCON-50
N018977 TRI-NORINYL 28-DAY
N017743 BREVICON 28-DAY
N017565 NORINYL 1+35 28-DAY
N021065 FEMHRT
N021065 FEMHRT
N021871 LOESTRIN 24 FE
N017876 LOESTRIN 21 1/20
N017875 LOESTRIN 21 1.5/30
N020130 ESTROSTEP FE
N017354 LOESTRIN FE 1/20
N017355 LOESTRIN FE 1.5/30
N021241 ORTHO TRI-CYCLEN LO
N019697 ORTHO TRI-CYCLEN
N019653 ORTHO CYCLEN-28
N017802 LO/OVRAL-28

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

/s/

PAMELA LUCARELLI
12/22/2010

SCOTT E MONROE
12/22/2010

3. DEBARMENT CERTIFICATION

I hereby certify that Warner Chilcott Company, LLC did not and will not use in any capacity the services of any person debarred under section 306(a) and (b) of the Federal Food, Drug and Cosmetic Act in connection with this New Drug Application.

_____ _____

Alvin Howard
Senior Vice President, Regulatory Affairs
Warner Chilcott (US), LLC on behalf of
Warner Chilcott Company, LLC.

Date

Reference ID: 2885900

SIGNATURES

Signed by	Date	Justification
Alvin Howard	Nov-18-2009, 19:54:30 PM, UTC	Regulatory Affairs Approval

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 022573 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: N/A Established/Proper Name: norethindrone and ethinyl estradiol chewable tablets and ferrous fumarate chewable tablets Dosage Form: 0.8 mg norethindrone and 0.025 mg ethinyl estradiol and 75 mg ferrous fumarate tablets		Applicant: Warner Chilcott Agent for Applicant (if applicable):
RPM: Pamela Lucarelli		Division: Division of Reproductive and Urologic Products

NDAs:
NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)

505(b)(2) Original NDAs and 505(b)(2) NDA supplements:
Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):

Provide a brief explanation of how this product is different from the listed drug.

If no listed drug, explain.
- ☐ This application relies on literature.
- ☐ This application relies on a final OTC monograph.
- ☐ Other (explain)

Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.

On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.

☐ No changes ☐ Updated Date of check:

If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.

❖ Actions	
• Proposed action • User Fee Goal Date is December 26, 2010	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ None

[1] The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

Reference ID: 2885900

❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____	☐ Received
❖ Application Characteristics [2]	

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): 5

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation

☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ REMS not required

Comments:

BLAs only: Ensure *RMS-BLA Product Information Sheet for TBP* and *RMS-BLA Facility Information Sheet for TBP* have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	☐ Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Press Office notified of action (by OEP)	☒ Yes ☐ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ HHS Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

[2] Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

Exclusivity	
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application)? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☐ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? *(Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☐ Verified 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ No paragraph III certification Date patent will expire
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☐ N/A (no paragraph IV certification) ☐ Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

  Answer the following questions for **each** paragraph IV certification:

  (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? ☐ Yes ☐ No

  (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))).

  *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).*

  (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.*

  *If "**No**," continue with question (3).*

  (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? ☐ Yes ☐ No

  (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).

  *If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*

  (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? ☐ Yes ☐ No

  *If "**Yes,**" there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).*

  *If "**No**," continue with question (5).*

(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (*Summary Reviews*).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.*	☐ Yes ☐ No

CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist[3]	☒ Included
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included
Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Approved December 22, 2010
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	☒ Included Final PI
• Original applicant-proposed labeling	☒ Included
• Example of class labeling, if applicable	

[3] Fill in blanks with dates of reviews, letters, etc.

Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☐ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☒ None
• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.	
• Original applicant-proposed labeling	
• Example of class labeling, if applicable	
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	☒ Included Original and Final
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s))*	Unacceptable: (b) (4) - April 6, 2010 – July 27, 2010 September 28, 2010 December 1, 2010
❖ Labeling reviews *(indicate dates of reviews and meetings)*	☐ RPM ☒ DMEPA December 17, 2010 ☐ DRISK ☒ DDMAC September 14, 2010 ☐ CSS ☒ Other reviews SEALD September 22, 2010, December 20, 2010 (2)

Administrative / Regulatory Documents

❖ Administrative Reviews *(e.g., RPM Filing Review[4]/Memo of Filing Meeting) (indicate date of each review)*	☒ Included February 2, 2010
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	☒ Not a (b)(2)
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment *(indicate date)*	☒ Not a (b)(2)
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP ○ If yes, Center Director's Exception for Review memo *(indicate date)* ○ If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC August 18, 2010 If PeRC review not necessary, explain: _____ • Pediatric Page/Record *(approvals only, must be reviewed by PERC before finalized)*	☒ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent *(include certification)*	☒ Verified, statement is acceptable

[4] Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Outgoing communications *(letters (except action letters), emails, faxes, telecons)*	☒ Included
❖ Internal memoranda, telecons, etc.	
❖ Minutes of Meetings	
• Regulatory Briefing *(indicate date of mtg)*	☒ No mtg
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	☐ No mtg July 20, 2009
• EOP2 meeting *(indicate date of mtg)*	☒ No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	Pre-IND March 16, 2007
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available *(do not include transcript)*	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	☐ None December 22, 2010
Cross-Discipline Team Leader Review *(indicate date for each review)*	☐ None December 22, 2010
PMR/PMC Development Templates *(indicate total number)*	☒ None
Clinical Information[5]	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	See CDTL Review
• Clinical review(s) *(indicate date for each review)*	October 6, 2010
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not *(indicate date of review/memo)*	☒ Included
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ Not applicable
❖ Risk Management • REMS Documents and Supporting Statement *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	☒ None
❖ DSI Clinical Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☐ None requested 2 sites included

[5] Filing reviews should be filed with the discipline reviews.

Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☐ None
Clinical Microbiology Review(s) *(indicate date for each review)*	☐ None
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☒ None
Statistical Team Leader Review(s) *(indicate date for each review)*	☒ None
Statistical Review(s) *(indicate date for each review)*	☐ None January 8, 2010, September 17, 2010
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ None
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☒ None
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None February 1, 2010, September 1, 2010, December 21, 2010
❖ DSI Clinical Pharmacology Inspection Review Summary *(include copies of DSI letters)*	☒ None
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ None
• Supervisory Review(s) *(indicate date for each review)*	☒ None
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☐ None January 22, 2010
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary *(include copies of DSI letters)*	☒ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ None
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☒ None
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☐ None January 13, 2010 (2), July 29, 2010, August 31, 2010, September 9, 2010, September 20, 2010, December 20, 2010
❖ Microbiology Reviews ☐ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) *(indicate date of each review)*	☒ Not needed
Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None

❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	See Product Quality Review, September 9, 2010 Page 123
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☐ NDAs: Facilities inspections (include EER printout) *(date completed must be within **2 years** of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[6])*	Date completed: April 16, 2010 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER *(date of most recent TB-EER must be within **30 days** of action date) (original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

[6] I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

(1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
(2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
(3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations(see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
(2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
(3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
(2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
(3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

MEMORANDUM

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

DATE: December 15, 2010

TO: Division of Medication Error Prevention and Analysis, Denise Baugh

FROM: Division or Reproductive and Urologic Products, Pamela Lucarelli

SUBJECT: Request for Review of Carton and Container Labels

APPLICATION/DRUG: NDA 022573

The correspondence below is a request to review the carton and container labels for NDA 022573. This product has no approved tradename.

Lucarelli, Pamela K

From: Lucarelli, Pamela K
Sent: Wednesday, December 15, 2010 10:32 AM
To: Baugh, Denise; Wasilik, Maria
Cc: Soule, Lisa; Bridges, Todd
Subject: RE: NDA 022573 - Revised draft container labels to remove name (b) (4)

Hi Denise,

Do you plan to enter a review of the carton and container labels in DARRTS?

Pam

Pamela Lucarelli
Regulatory Health Project Manager
FDA/Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
WO22 - Room 5323
10903 New Hampshire Avenue
Silver Spring, MD 20903

Phone 301.796.3961
Fax 301.796.9897
pamela.lucarelli@fda.hhs.gov

From: Baugh, Denise
Sent: Monday, December 13, 2010 1:59 PM
To: Lucarelli, Pamela K; Wasilik, Maria
Cc: Soule, Lisa; Bridges, Todd
Subject: RE: NDA 022573 - Revised draft container labels to remove name (b) (4)

Hi, Pam,
The labels and labeling submitted are acceptable.

Denise (Baugh)
DMEPA

From: Lucarelli, Pamela K
Sent: Monday, December 13, 2010 9:57 AM
To: Baugh, Denise; Wasilik, Maria
Cc: Soule, Lisa
Subject: RE: NDA 022573 - Revised draft container labels to remove name (b) (4)

Please let me know if you have any comments.

Pam

From: Lucarelli, Pamela K
Sent: Friday, December 10, 2010 6:43 AM
To: Baugh, Denise; Wasilik, Maria; Chang, Jane; Christner, Donna
Cc: Soule, Lisa
Subject: NDA 022573 - Revised draft container labels to remove name (b) (4)

Attached are the carton and container labels with the established name only - no tradename. Please review and let me know if the Applicant needs to make any changes.

Thanks,
Pam

Pamela Lucarelli
Regulatory Health Project Manager
FDA/Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
WO22 - Room 5323
10903 New Hampshire Avenue
Silver Spring, MD 20903

Phone 301.796.3961
Fax 301.796.9897
pamela.lucarelli@fda.hhs.gov

From: Ileana Brown [mailto:IBrown@wcrx.com]
Sent: Thursday, December 09, 2010 3:24 PM
To: Lucarelli, Pamela K
Subject: NDA 022573 - Revised draft container labels to remove name (b) (4)

Hi Pam,

We have revised the container labels to remove (b) (4) and increase the prominence of the established name. I am informally providing the revised container labels at this time for the Division's review and will submit them to the NDA next week along with the updated SPL per our conversation this afternoon. Attached are the:

- trade credit card and carton
- physician's sample credit card, carton and tray
- overwrap

The day label did not change and is therefore not included.

Thanks Pam.

Ileana

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/s/

PAMELA LUCARELLI
12/17/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 022573

PROPRIETARY NAME REQUEST UNACCEPTABLE

Warner Chilcott Company, LLC
c/o Warner Chilcott (US), LLC
100 Enterprise Drive
Rockaway, New Jersey 07866

ATTENTION: Ileana Brown
Director, Regulatory Affairs

Dear Ms. Brown:

Please refer to your New Drug Application (NDA) dated November 26, 2009, received November 26, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norethindrone and Ethinyl Estradiol Tablets, 0.8 mg/0.025 mg.

We also refer to your October 7, 2010, correspondence, received October 8, 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

(b) (4)

(b) (4)

We recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names,* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Maria Wasilik, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Pamela Lucarelli at (301) 796-3961.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
12/06/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 022573

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Warner Chilcott, LLC
c/o Warner Chilcott (US), LLC
100 Enterprise Drive
Rockaway, New Jersey 07866

ATTENTION: Ileana Brown
Director, Regulatory Affairs

Dear Ms. Brown:

Please refer to your New Drug Application (NDA) dated November 26, 2009, received November 26, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norethindrone and Ethinyl Estradiol Tablets, 0.8 mg/0.025 mg.

We also refer to your August 17, 2010, correspondence, received August 19, 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

(b) (4)

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names,* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Maria Wasilik, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Pamela Lucarelli at (301) 796-3961.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
10/01/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022573

REVIEW EXTENSION – MAJOR AMENDMENT

Warner Chilcott
Attention: Alvin Howard
Senior Vice President, Regulatory Affairs
100 Enterprise Drive
Rockaway, NJ 07866

Dear Mr. Howard:

Please refer to your November 26, 2009, New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets.

On September 21, 2010, we received your solicited major amendment to this application. The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is December 26, 2010.

In addition, we are establishing a new timeline for communicating labeling changes and/or postmarketing requirements/commitments in accordance with "PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES – FISCAL YEARS 2008 THROUGH 2012." If major deficiencies are not identified during our review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by November 26, 2010.

If you have any questions, please call Pamela Lucarelli, Regulatory Health Project Manager, at (301) 796-3961.

Sincerely,

{See appended electronic signature page}

Jennifer Mercier
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

JENNIFER L MERCIER
09/24/2010

MEMORANDUM

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

DATE: August 26, 2010

TO: Warner Chilcott, Ileana Brown

FROM: Division or Reproductive and Urologic Products, Pamela Lucarelli

SUBJECT: CMC Information Request

APPLICATION/DRUG: NDA 022573

The correspondence below is a CMC information request.

Lucarelli, Pamela K

From: Ileana Brown [IBrown@wcrx.com]
Sent: Thursday, August 26, 2010 12:21 PM
To: Lucarelli, Pamela K
Cc: 'Geoffrey Millington'
Subject: Re: NDA 022573 Information Request

Hi Pam,

We received your e-mail. I just left you an e-mail message regarding the SPL request.

Ileana
-----"Lucarelli, Pamela K" <Pamela.Lucarelli@fda.hhs.gov> wrote: -----

> To: "'Ileana Brown'" <IBrown@wcrx.com>, "'Geoffrey Millington'" <GMillington@wcrx.com>
> From: "Lucarelli, Pamela K" <Pamela.Lucarelli@fda.hhs.gov>
> Date: 08/26/2010 11:43AM
> Subject: NDA 022573 Information Request
>
> Ileana and Geoffrey,
>
> Please find below and information request from our chemistry reviewer.
>
> 1. The established name for the inactive tablets should be "ferrous fumarate chewable tablets". That is, the established name for the drug product should be "norethindrone and ethinyl estradiol chewable tablets and ferrous fumarate chewable tablets".
> 2. Provide updated mock-up labels with the revised established name.
> 3. Provide an updated Drug Listing Data Elements in the Structured Product Labeling per the FDA 7/16/2010 Information Request Letter.
>
> Confirm receipt of this email. If you have any questions, please let me know.
>
> Pam
>
> Pamela Lucarelli
> Regulatory Health Project Manager
> FDA/Center for Drug Evaluation and Research
> Division of Reproductive and Urologic Products
> WO22 - Room 5323
> 10903 New Hampshire Avenue
> Silver Spring, MD 20903
>
> Phone 301.796.3961
> Fax 301.796.9897
> pamela.lucarelli@fda.hhs.gov

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********** Thank you **********

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

PAMELA LUCARELLI
08/27/2010

MEMORANDUM

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

DATE: August 8, 2010

TO: Warner Chilcott, Ileana Brown

FROM: Division or Reproductive and Urologic Products, Pamela Lucarelli

SUBJECT: Information Request

APPLICATION/DRUG: NDA 022573

The correspondence below is an information request.

Lucarelli, Pamela K

From: Ileana Brown [IBrown@wcrx.com]
Sent: Monday, August 09, 2010 9:27 AM
To: Lucarelli, Pamela K
Subject: Re: NDA 022573 Comments

Hi Pam,

I received this e-mail.

Thanks

Ileana

From: "Lucarelli, Pamela K" <Pamela.Lucarelli@fda.hhs.gov>
To: "'Ileana Brown'" <IBrown@wcrx.com>
Cc: "Tran-Zwanetz, Catherine" <Catherine.TranZwanetz@fda.hhs.gov>, "McKnight, Rebecca" <Rebecca.McKnight@fda.hhs.gov>, "'Geoffrey Millington'" <GMillington@wcrx.com>
Date: 08/06/2010 02:26 PM
Subject: NDA 022573 Comments

Hi Ileana,

Please review the following comments:

1. The proposed dissolution method for the norethindrone (NE)/ethinyl estradiol (EE) tablets (0.025M sodium acetate with 0.15% of sodium dodecyl sulphate buffer, pH 5, (b) (4), 75 rpm) will be acceptable as interim since the data you presented indicate that the method is not discriminating. It appears that considering different method conditions such as lower paddle speed (i.e. 50 rpm), lower concentration of surfactant, and different surfactant will result in a more robust and discriminating method. You will have one year after the expedition of this letter to submit data supporting a more discriminating dissolution method for EE/NE tablets.

2. In addition, the proposed dissolution specifications for both EE/NE tablets and Ferrous Fumarate tablets are too permissive. The following dissolution specification is recommended for EE/NE tablets as interim until you submit a more discriminating dissolution method:

(b) (4)

This recommendation is based on mean dissolution values from clinical drug product release and drug

product stability testing. Please revise the specifications accordingly.

3. The following dissolution specification is recommended for the Ferrous Fumarate Tablets based on mean dissolution values from clinical drug product release and drug product stability testing:

Specification	
	(Q)
(b) (4)	(Q) of ferrous fumarate is dissolved in 30 min.

Please revise the specifications accordingly.

Confirm receipt of this email. If you have any questions, please let me know.

Thanks,
Pam

Pamela Lucarelli
Regulatory Health Project Manager
FDA/Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
WO22 - Room 5323
10903 New Hampshire Avenue
Silver Spring, MD 20903

Phone 301.796.3961
Fax 301.796.9897
pamela.lucarelli@fda.hhs.gov

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********** Thank you **********

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

PAMELA LUCARELLI
08/19/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 022573 **INFORMATION REQUEST**

Warner Chilcott Company, LLC
Attention: Geoffrey Millington
Director, Regulatory Affairs
100 Enterprise Drive
Rockaway, New Jersey 07866

Dear Mr. Millington:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for norethindrone and ethinyl estradiol Tablets, 0.8 mg/0.025 mg.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a response by August 23, 2010 in order to continue our evaluation of your supplemental application.

1. Either you conform to a (b) (4) expiration dating period or provide the 30 months long-term stability data for Lot 80537F. Even though you stated in the cover letter of the 8/11/2010 amendment that 30 months long term stability data for Lot 80537F were provided, the data were missing in the amendment. Therefore, the stability data provided to date could only support an expiration dating period of (b) (4) as stated in the FDA Information Request Letter dated July 16, 2010 (Item 2).

2. Please clarify whether lot (b) (4) (Section 3.2.P.8.3) provided in the 8/11/2010 amendment is a typographical error for lot 80547F.

3. Please clarify whether Lot (b) (4) mentioned in the 8/11/2010 amendment is a typographical error for Lot 80157F. Lot (b) (4) had never been mentioned in any of the submissions prior to the 8/11/2010 amendment. The stability data of Lot (b) (4) were provided in the 8/11/2010 amendment, but not Lot 80157F.

If you have questions, call Rebecca McKnight, Regulatory Project Manager, at (301) 796-1765.

Sincerely,

{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
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

MOO JHONG RHEE
08/18/2010
Chief, Branch IV

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADM NISTRATION

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

Please send immediately following the Filing/Planning meeting

TO:	FROM: (Name/Title, Office/Division/Phone number of requestor)
Division of Drug Marketing, Advertising and Communications (DDMAC) Attention: Janice Maniwang 301-796-3821	Division of Reproductive and Urologic Drug Products (HFD-580) Pamela Lucarelli 301-796-3961

REQUEST DATE	IND NO.	NDA/BLA NO.	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)
August 12, 2010		NDA 022573	See Below

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting)
norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets	Standard		September 20, 2010

NAME OF FIRM:	
Warner Chilcott	PDUFA Date: September 24, 2010

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:
(Check all that apply)
- ☑ PACKAGE INSERT (PI)
- ☑ PATIENT PACKAGE INSERT (PPI)
- ☑ CARTON/CONTAINER LABELING
- ☐ MEDICATION GUIDE
- ☐ INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION
- ☑ ORIGINAL NDA/BLA
- ☐ IND
- ☐ EFFICACY SUPPLEMENT
- ☐ SAFETY SUPPLEMENT
- ☐ LABELING SUPPLEMENT
- ☐ PLR CONVERSION

REASON FOR LABELING CONSULT
- ☑ INITIAL PROPOSED LABELING
- ☐ LABELING REVISION

EDR link to submission:
\\CDSESUB1\EVSPROD\NDA022573\022573.ENX

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: April 21, 2010

Labeling Meetings: July 12, 2010 and July 29, 2010

Wrap-Up Meeting: July 29, 2010

SIGNATURE OF REQUESTER
Pamela Lucarelli (delivered through DARRTS)

SIGNATURE OF RECEIVER	METHOD OF DELIVERY (Check one) ☑ eMAIL ☐ HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

PAMELA LUCARELLI
08/12/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 022573

PROPRIETARY NAME REQUEST UNACCEPTABLE

Warner Chilcott Company, LLC
100 Enterprise Drive
Rockaway, New Jersey 07866

ATTENTION: Ileana Brown
Director, Regulatory Affairs

Dear Ms. Brown:

Please refer to your New Drug Application (NDA) dated November 26, 2009, received November 26, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norethindrone and Ethinyl Estradiol Tablets, 0.8 mg/0.025 mg.

We also refer to your April 28 2010, correspondence, received April 28 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

(b) (4)

We recognize this conclusion differs from that of the external study you submitted in support of your proposed proprietary name. However, the external study did not evaluate the name Mircette for potential similarity to (b) (4), nor could it evaluate the name not yet marketed, which accounts for our different conclusions.

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Complete Submission for the Evaluation of Proprietary Names,* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm121568.htm and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Maria Wasilik, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Pamela Lucarelli at (301) 796-3961.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

LAURIE A KELLEY
07/27/2010

CAROL A HOLQUIST
07/27/2010

MEMORANDUM

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

DATE: July 15, 2010

TO: Warner Chilcott, Ileana Brown

FROM: Division or Reproductive and Urologic Products, Pamela Lucarelli

SUBJECT: Clinical Information Request

APPLICATION/DRUG: NDA 022573

The correspondence below is a clinical information request.

Lucarelli, Pamela K

From: Ileana Brown [IBrown@wcrx.com]
Sent: Thursday, July 15, 2010 6:31 PM
To: Lucarelli, Pamela K
Subject: Re: NDA 022573 Information Request

Received.

Ileana

From: "Lucarelli, Pamela K" <Pamela.Lucarelli@fda.hhs.gov>
To: "Ileana Brown" <IBrown@wcrx.com>
Date: 07/15/2010 01:39 PM
Subject: NDA 022573 Information Request

Hi Ileana,

Provide follow up information for the following subjects with significant laboratory abnormalities at the final visit in Study PR-00207.

Subject 208/037 - markedly elevated liver enzymes and bilirubin
Subject 209/005 - triglycerides > 500 mg/dL
Subject 255/015 - markedly elevated liver enzymes and bilirubin

Additionally, provide full narratives.

Confirm receipt of this email. If you have any questions, please let me know.

Pam

Pamela Lucarelli
Regulatory Health Project Manager
FDA/Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
WO22 - Room 5323
10903 New Hampshire Avenue
Silver Spring, MD 20903

Phone 301.796.3961
Fax 301.796.9897
pamela.lucarelli@fda.hhs.gov

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********** Thank you **********

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

PAMELA LUCARELLI
07/20/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 022573 **INFORMATION REQUEST**

Warner Chilcott Company, LLC
Attention: Ileana Brown
Director, Regulatory Affairs
100 Enterprise Drive
Rockaway, New Jersey 07866

Dear Ms. Brown:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for norethindrone and ethinyl estradiol Tablets, 0.8 mg/0.025 mg.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a response by July 21, 2010 in order to continue our evaluation of your supplemental application.

1. (b) (4)

2. Please revise the proposed expiration dating period to (b) (4). Your proposed expiration dating period of 36 months is not acceptable unless acceptable long-term stability data at 30-months for Lots 80537F and 80547F are provided. Per ICH Q1E, when significant change at accelerated condition is observed and no significant change is observed at intermediate condition, the proposed expiration dating period can be up to one-and-half times as long as,

but should not be more than 6 months beyond the period covered by long-term data. To date, long-term data for Lots 80537F and 80547F were provided only up to 24 months.

3. Limit the hold time of bulk tablets to (b) (4) under 25°C/60% RH unless acceptable stability data are provided for both the bulk tablets and the drug product packaged from bulk tablets held after the proposed hold time.

4. Please provide the revised specifications for three colorant excipients per the 5/5/2010 Information Request Letter (Item 13). The revised specifications were not submitted in the 6/29/2010 amendment.

5. Regarding labeling:
   a. For the blister card and carton labels, the font size of the established name should be at least half as large as that of the proprietary name per 21 CFR 201.10(g)(2). The size of letter (b) (4) should be used as basis of measurement. Please provide the revised mock-up labels.
   b. Drug Listing Data Elements in the Structured Product Labeling:
      1. Replace (b) (4) as the established name to "norethindrone and ethinyl estradiol kit". Only the active ingredients are included in the established name.
      2. Revise the established name listed in Part 1 of 2 from (b) (4) to "norethindrone and ethinyl estradiol tablet, chewable".

If you have questions, call Rebecca McKnight, Regulatory Project Manager, at (301) 796-1765.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

MOO JHONG RHEE
07/16/2010
Chief, Branch IV

MEMORANDUM

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

DATE: June 30, 2010

TO: Warner Chilcott, Ileana Brown

FROM: Division or Reproductive and Urologic Products, Pamela Lucarelli

SUBJECT: Clinical Information Request

APPLICATION/DRUG: NDA 022573

The correspondence below is a clinical information request.

Lucarelli, Pamela K

From: Ileana Brown [IBrown@wcrx.com]
Sent: Wednesday, June 30, 2010 4:37 PM
To: Lucarelli, Pamela K
Subject: Re: NDA 022573 Information Request

Hi Pam,

I received the e-mail.

Regards,

Ileana

From: "Lucarelli, Pamela K" <Pamela.Lucarelli@fda.hhs.gov>
To: "Ileana Brown" <IBrown@wcrx.com>
Date: 06/30/2010 04:32 PM
Subject: NDA 022573 Information Request

Ileana,

Below is a clinical information request:

1. It appears possible that Subject 261/009 was a “during treatment” pregnancy. Provide a Pearl Index and life table analysis based on 19 “during treatment” pregnancies in women 35 years and younger in PR-00207.

2. On page 13 of 297 (Report RR-03009) you indicated that there were 70 investigational sites for Protocol PR-00207. On page 58 of 297 you stated that this multicenter study was performed at 68 investigational sites. Please clarify.

3. In study report RR-03009 you provide information on protocol deviations leading to subject withdrawal. Provide summary information for the protocol deviations for the subjects who remained in the study and whether any of these deviations would have affected evaluation of product efficacy.

4. Clarify the term “new user” in report RR-03009. How many subjects were first time users of a combination oral contraceptive?

5. For the treated population in PR-00207 provide the number of completed 28 day cycles, number of partially completed 28 day cycles and total women-years of exposure.

6. Some of the follow-up and hospital information on Subject 238/031 (22 year old with diagnosis of angina pectoris) was not very legible. Provide a full summary for this subject with any additional follow-up that is available and assess the etiology for the angina.

7. Do the mean median duration of intracyclic bleeding and spotting in Table 12 and the mean median

duration of withdrawal bleeding in Table 15 of RR-03009 apply only to the “Cycle 2 through Cycle 13” row in the table? Please clarify exactly how you calculate “mean median duration.”

8. Provide the mean number of days of withdrawal bleeding for the MITT population per cycle in PR-00207.

9. Provide ranges and quartiles for the following by cycle in PR-00207:

- Days of intracyclic bleeding/spotting
- Days of intracyclic bleeding only
- Days of intracyclic spotting only
- Days of withdrawal bleeding

10. We were unable to verify that Subject 209042 had a cycle excluded for efficacy analysis while she was taking Plan B. Please clarify. Provide a table that includes all subjects who used other hormonal products “during treatment with study drug” in PR-00207. Include subjects who used other combination oral contraceptives, progestins, emergency contraception, etc. Provide subject number, name of hormone, cycle of use and duration of use (days). Also specify how many cycles were excluded from the Pearl Index calculation based on use of other hormonal products.

Provide responses as soon as possible. If you have any questions, please let me know.

Confirm receipt of this email.

Thanks,
Pam

Pamela Lucarelli
Regulatory Health Project Manager
FDA/Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
WO22 - Room 5323
10903 New Hampshire Avenue
Silver Spring, MD 20903

Phone 301.796.3961
Fax 301.796.9897
pamela.lucarelli@fda.hhs.gov

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********** Thank you **********

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

PAMELA LUCARELLI
07/02/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022573 **INFORMATION REQUEST**

Warner Chilcott Company, LLC
Ileana Brown
Director, Regulatory Affairs
100 Enterprise Drive
Rockaway, New Jersey 07866

Dear Ms. Brown:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for norethindrone and ethinyl estradiol Tablets, 0.8 mg/0.025 mg.

We are reviewing the Quality section of your submission and have the following comments and information requests. We request a written response by 30 June 2010 in order to continue our evaluation of your NDA:

Regarding the drug substance:

1. Revise the norethindrone drug substance specification (b) (4) .
2. Revise the ethinyl estradiol drug substance specification (b) (4) .
3. Provide information on analytical method and method validation data (b) (4) .

Regarding the drug product:

4. Address the following items regarding the drug product specification:
   a. Adopt two-tier assay acceptance criteria for ethinyl estradiol: (b) (4) . The lower limit of the release specification should be further (b) (4) to ensure that your product will meet the stability specification at the end of the expiration dating period. (b) (4)

b. Tighten the limits for ethinyl estradiol related substances, including specified impurities and total impurities. Revise the limit for each specified impurity to (b) (4) to comply with the ICH Q3B qualification threshold. (b) (4) the limit for the sum of (b) (4) to (b) (4) Alternatively, data (e.g. toxicology or stability) could be provided to justify the proposed limits.

c. Include microbial limits test per USP <1111>. Certificates of analysis for norethindrone and mannitol (b) (4) do not include testing for microbial limits. Therefore, testing should be performed to ensure absence of pathogens in the drug product.

d. Tightened the acceptance criteria for hardness and (b) (4) to (b) (4) and NMT (b) (4), respectively. Your proposed acceptance criteria are much wider than the release and stability data.

5. Regarding HPLC method DP-56 (PD.PAP.089-1):

a. Please address the concern of inadequate method specificity for assay of ethinyl estradiol. (b) (4) .

You may address this issue by determining assay of ethinyl estradiol for an aged drug product, e.g. Lot 80537F, (b) (4) .

b. Revise the method for calculation of assay for norethindrone and ethinyl estradiol so as not to correct for actual weight of tablets. The calculations should be revised as following:

(b) (4)

6. Please perform statistical analysis on the stability data of WC3026-5C tablets. Your proposed expiration dating period of (b) (4) for the drug product is not acceptable. Stability data for Lots 80537F and 80547F showed a decreasing trend for EE assay. The statistical analysis should consider the lower limit of EE assay at release and use a 95% lower confidence interval (LCL) of EE assay to project the time point where a maximum reduction of EE assay is allowed. For example, if the lower limit of EE assay is proposed to be 95.0%, the time point when a decrease of 5.0% (95.0% - 90.0% = 5.0%) in EE assay based on the 95% LCL should be determined.

7. Please revise your manufacturing process (b) (4) .

8. Regarding HPLC method (b) (4) (PD.PAP.093) method validation:

   a. Provide HPLC method (b) (4) validation data for linearity, accuracy, and detection and quantitation limits for norethindrone and ethinyl estradiol. The data are required as norethindrone and ethinyl estradiol are used for determination of unspecified impurities.

   b. Provide information as to how the HPLC relative response factors were determined for the specified impurities.

   c. Provide information on total impurities for NE and EE for the drug product, Lot 80157T, under the forced degradation study.

9. Please provide the hold time for ethinyl estradiol (b) (4). Stability data should be provided if prolonged hold time is proposed. The data should include stability data of ethinyl estradiol (b) (4) and stability data of three batches of finished product manufactured from three batches of ethinyl estradiol (b) (4) after the proposed hold time.

10. Testing for content uniformity of finished product (Section 3.2.P.5.1) should be performed for routine batch manufacture. Testing for content uniformity of in-process dosage unit (Table 5 in Section 3.2.P.3.4) should be performed minimally through validation batches. The proposed omission of testing is unacceptable. The following statement was provided in Section 4.2 of 3.2.P.3.4.

    "In-process content uniformity testing will be performed in lieu of unit dose testing for routine batch manufacture."

    Please clarify the frequency of sampling for content uniformity of in-process dosage unit during compression.

11. Please revise the acceptance criteria for assay of final (b) (4) of WC3026-5C from "RSD ≤ 6.0% and all individual within 85.0% - 115.0% of label claim" to "RSD ≤ 5.0% and all individual within ± 10% of the mean".

12. Address the concern as to whether the ICH Class 1 or 2 solvents are present in mannitol [redacted] (b) (4) spearmint flavor, and povidone. Either include a test for residual solvents in the specifications for these excipients or provide a statement to certify that no ICH Class 1 or 2 solvents are used in the manufacture of these excipients. Alternatively, the testing can be performed on the finished product.

13. Revise the specifications for [redacted] (b) (4) excipients for the acceptance criteria of identification and color tests. The acceptance criteria for identification test for FD&C Yellow #6 Aluminum Lake and FD&C Blue #1 Aluminum Lake, [redacted] (b) (4) should be revised so that the results of sample correspond to, not "compare to", that of the reference standard.

14. Please clarify whether analytical testing was performed on both the bulk tablets and finished product. Release testing should be performed on the finished product. The batch analysis data of the drug product provided in Section 3.2.P.5.4 appear to be data of bulk tablets. The analytical data for Lots 80547T, 80278T, and 80019T are identical to those of the initial time point of Lot 80547F, 80278F, and 80019F, respectively.

15. Provide information on the supplier, batch number, and purity for the reference standards of the specified impurities, including the reference standards for [redacted] (b) (4).

16. Provide samples of the drug product, including both the active and inactive tablets, in the to-be-marketed container closure system.

17. Please correct the typographical errors for norethindrone, which was abbreviated as "NA" and "AA" in Table 1: Stability Commitment: Test Schedule for WC3026-5C tablets in Section 3.2.P.8.2. Norethindrone has been abbreviated as NE throughout the application.

18. [redacted] (b) (4)

19. Establish acceptance criteria for hardness and [redacted] (b) (4) for ferrous fumarate tablets specification. The proposed acceptance criterion of [redacted] (b) (4) for each test is unacceptable.

20. Regarding labeling:

    a. Revise the established name to "norethindrone and ethinyl estradiol chewable tablets and ferrous fumarate tablets" on all labeling. That is, "chewable" should be in front of "tablets" for the active tablets.

    b. Add the following statement to Section 11 DESCRIPTION:

       The molecular formula of norethindrone is $C_{20}H_{26}O_2$. The molecular formula of ethinyl estradiol is $C_{20}H_{24}O_2$.

c. For the blister card and carton labels, the font size of the established name should be at least half as large as that of the proprietary name per 21 CFR 201.10(g)(2). Provide the revised mock-up labels.

d. Provide structured product labeling.

If you have any questions, call Jeannie David, Regulatory Project Manager for Quality, at (301) 796-4247.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Chief, Branch III
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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MOO JHONG RHEE
05/05/2010
Chief, Branch III

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 022573

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Warner Chilcott Company, LLC
100 Enterprise Drive
Rockaway, New Jersey 07866

ATTENTION: Ileana Brown
Director, Regulatory Affairs

Dear Ms. Brown:

Please refer to your New Drug Application (NDA) dated November 26, 2009, received November 26, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Norethindrone and Ethinyl Estradiol Tablets, 0.8 mg/0.025 mg.

We also refer to your January 12, 2010, correspondence, received January 13, 2010, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

(b) (4)

(b) (4)

We recognize this conclusion differs from that of the external study you submitted in support of your proposed proprietary name. However, the external study did not evaluate the names Alinia, Aclaro, or Oralone for potential similarity to (b) (4), which accounts for our different conclusion.

We note that you have proposed an alternate proprietary name in your submission dated January 12, 2010. In order to initiate the review of the alternate proprietary name, (b) (4), submit a new complete request for proprietary name review. The review of this alternate name will not be initiated until the new submission is received.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Maria Wasilik, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0567. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Pamela Lucarelli, at 301-796-3961.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

DENISE P TOYER on behalf of CAROL A HOLQUIST
04/06/2010

DSI CONSULT: Request for Clinical Inspections

Date: March 15, 2010

To: Tejashri Purohit-Sheth, M.D., Branch Chief, GCP2
Roy Blay, Ph.D., Reviewer
Division of Scientific Investigations, HFD-45
Office of Compliance/CDER

Through: Gerald Willett, M.D., Clinical Reviewer
Lisa Soule, M.D., Clinical Team Leader
Division of Reproductive and Urologic Products

From: Pam Lucarelli, Regulatory Health Project Manager
Division of Reproductive and Urologic Products

Subject: **Request for Clinical Site Inspections**
NDA 022573 (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

I. General Information

Application#:	NDA 022573
Applicant:	Warner Chilcott
Authorized U.S. Agent:	N/A 100 Enterprise Drive Rockaway, NJ 07866
Contact:	Ileana Brown – Director, Regulatory Affairs
Phone:	973-442-3229
E-mail:	IBrown@wcrx.com
Proposed Proprietary Name:	(b) (4)
NME:	No
Review Priority:	Standard
Study Population includes < 17 years of age:	No
Is this for Pediatric Exclusivity:	No
Proposed New Indication(s):	Prevention of pregnancy
PDUFA:	September 26, 2010
Action Goal Date:	September 24, 2010
Inspection Summary Goal Date:	July 24, 2010

II. Protocol/Site Identification

Site # (Name,Address, Phone number, email, fax#)	Protocol ID	Number of Subjects	Indication
Site # 205 Dr. Joe Blumenau Research Across America RHD Professional Plaza 4 9 Medical Parkway, Suite 202 Dallas, TX 75234 972-241-1222	PR-00207	43 Subjects Enrolled	Prevention of pregnancy
Site # 246 Dr. Robert Lamar Parker 2927 Lyndhurst Avenue Winston Salem, NC 27103 336-765-9350	PR-00207	51 Subjects Enrolled	Prevention of pregnancy

III. Site Selection/Rationale

Sites 205 and 246 are the two of the top accruing sites for Protocol PR-00207 and have not been inspected recently.

Domestic Inspections:

Reasons for inspections (please check all that apply):

- _X_ Enrollment of large numbers of study subjects
- ____ High treatment responders (specify):
- _X_ Significant primary efficacy results pertinent to decision-making
- ____ There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
- ____ Other (specify):

Should you require any additional information, please contact Pam Lucarelli, Regulatory Health Project Manager at 301-796-3961 or Dr. Gerald Willett, Medical Officer at 301-796-1024.

Concurrence:
Gerald Willett M.D.
Medical Reviewer

Lisa Soule M.D.
Medical Team Leader

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

PAMELA LUCARELLI
03/15/2010

LISA M SOULE
03/15/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022573 **FILING COMMUNICATION**

Warner Chilcott
Attention: Alvin Howard
Senior Vice President, Regulatory Affairs
100 Enterprise Drive
Rockaway, NJ 07866

Dear Mr. Howard:

Please refer to your new drug application (NDA) dated November 25, 2009, received November 26, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets.

We also refer to your submission dated January 12, 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is September 26, 2010.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team, and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by August 17, 2010.

During our filing review of your application, we identified the following potential review issues:

1. The proposed dissolution method for the norethindrone/ethinyl estradiol tablets (0.025 M sodium acetate with 0.15% of sodium dodecyl sulphate buffer, pH 5, (b) (4), and 75 rpm) is different from that established in the USP monograph for this product. Submit a report of your dissolution method development and validation for norethindrone/ethinyl estradiol tablets, chewable. These data should also include tabulated values of individual and mean % dissolved under the conditions tested.

2. Please provide information, (e.g., the formulation) for the spearmint flavor. Alternatively, a reference to the DMF, with an authorization letter from the holder, will suffice.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Pamela Lucarelli, Regulatory Health Project Manager, at (301) 796-3961.

Sincerely,

{See appended electronic signature page}

Scott Monroe, M.D.
Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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

/s/

SCOTT E MONROE
02/04/2010

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements (except SE8 and SE9)

Application Information		
NDA # 022573 BLA#	NDA Supplement #:S- BLA STN #	Efficacy Supplement Type SE-
Proprietary Name: Established/Proper Name: norethindrone/ethinyl estradiol chewable and ferrous fumarate Dosage Form: tablets Strengths: norethindrone 0.8 mg/ethinyl estradiol 0.025 mg and ferrous fumarate		
Applicant: Warner Chilcott Agent for Applicant (if applicable):		
Date of Application: November 25, 2009 Date of Receipt: November 26, 2009 Date clock started after UN:		
PDUFA Goal Date: September 26, 2010	Action Goal Date (if different):	
Filing Date: January 10, 2010	Date of Filing Meeting: January 7, 2010	
Chemical Classification: (1,2,3 etc.) (original NDAs only) 5		
Proposed indication(s)/Proposed change(s): prevention of pregnancy		
Type of Original NDA: AND (if applicable)	☒ 505(b)(1) ☐ 505(b)(2)	
Type of NDA Supplement: ***If 505(b)(2): Draft the "505(b)(2) Assessment" form found at:*** ***http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/ucm027499.html*** ***and refer to Appendix A for further information.***	☐ 505(b)(1) ☐ 505(b)(2)	
Review Classification: ***If the application includes a complete response to pediatric WR, review classification is Priority.*** ***If a tropical disease priority review voucher was submitted, review classification is Priority.***	☒ Standard ☐ Priority ☐ Tropical Disease Priority Review Voucher submitted	
Resubmission after withdrawal? ☐	Resubmission after refuse to file? ☐	
Part 3 Combination Product? ☐ ***If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults***	☐ Drug/Biologic ☐ Drug/Device ☐ Biologic/Device	
☐ Fast Track ☐ Rolling Review ☐ Orphan Designation ☐ Rx-to-OTC switch, Full ☐ Rx-to-OTC switch, Partial ☐ Direct-to-OTC Other:	☐ PMC response ☐ PMR response: ☐ FDAAA [505(o)] ☐ PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] ☐ Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) ☐ Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)	

Collaborative Review Division (*if OTC product*):				
List referenced IND Number(s): IND 076629				
Goal Dates/Names/Classification Properties	**YES**	**NO**	**NA**	**Comment**
PDUFA and Action Goal dates correct in tracking system? ***If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.***	X			
Are the proprietary, established/proper, and applicant names correct in tracking system? ***If not, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking system.***	X			
Are all classification properties [e.g., orphan drug, 505(b)(2)] entered into tracking system? ***If not, ask the document room staff to make the appropriate entries.***	X			
Application Integrity Policy	**YES**	**NO**	**NA**	**Comment**
Is the application affected by the Application Integrity Policy (AIP)? ***Check the AIP list at: http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm***		X		
If yes, explain in comment column.				
If affected by AIP, has OC/DMPQ been notified of the submission? **If yes,** date notified:				
User Fees	**YES**	**NO**	**NA**	**Comment**
Is Form 3397 (User Fee Cover Sheet) included with authorized signature?	X			

User Fee Status	Payment for this application:
If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send UN letter and contact user fee staff.	☒ Paid ☐ Exempt (orphan, government) ☐ Waived (e.g., small business, public health) ☐ Not required
If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.	Payment of other user fees: ☒ Not in arrears ☐ In arrears

Note: *505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. All 505(b) applications, whether 505(b)(1) or 505(b)(2), require user fees unless otherwise waived or exempted (e.g., small business waiver, orphan exemption).*

505(b)(2) **(NDAs/NDA Efficacy Supplements only)**	**YES**	**NO**	**NA**	**Comment**
Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?				
Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (see 21 CFR 314.54(b)(1)).				
Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug (see 21 CFR 314.54(b)(2))? ***Note:*** *If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).*				
Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? ***Check the Electronic Orange Book at:*** ***http://www.fda.gov/cder/ob/default.htm*** **If yes**, please list below:				

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 108(b)(2).Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.

Exclusivity	**YES**	**NO**	**NA**	**Comment**
Does another product have orphan exclusivity for the same indication? ***Check the Electronic Orange Book at:*** ***http://www.fda.gov/cder/ob/default.htm***		X		
If another product has orphan exclusivity, is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? ***If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)***				
Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? ***(NDAs/NDA efficacy supplements only)*** **If yes**, # years requested: 3 ***Note:*** *An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	X			

Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use (***NDAs only***)?		X		
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? ***If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.***				

Format and Content				
Do not check mixed submission if the only electronic component is the content of labeling (COL).	☐ All paper (except for COL) ☒ All electronic ☐ Mixed (paper/electronic) ☐ CTD ☐ Non-CTD ☐ Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?				
Overall Format/Content	**YES**	**NO**	**NA**	**Comment**
If electronic submission, does it follow the eCTD guidance[1]? **If not,** explain (e.g., waiver granted).	X			
Index: Does the submission contain an accurate comprehensive index?	X			
Is the submission complete as required under 21 CFR 314.50 (*NDAs/NDA efficacy supplements*) or under 21 CFR 601.2 (*BLAs/BLA efficacy supplements*) including: ☒ legible ☒ English (or translated into English) ☒ pagination ☒ navigable hyperlinks (electronic submissions only) **If no**, explain.	X			
Controlled substance/Product with abuse potential: Is an Abuse Liability Assessment, including a proposal for scheduling, submitted? ***If yes,*** *date consult sent to the Controlled Substance Staff:*			X	
BLAs only: Companion application received if a shared or divided manufacturing arrangement? **If yes**, BLA #				

Forms and Certifications				
Electronic *forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise,* ***paper*** *forms and certifications with hand-written signatures must be included.* ***Forms*** *include: user fee cover sheet (3397), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674);* ***Certifications*** *include: debarment certification, patent certification(s), field copy certification, and pediatric certification.*				
Application Form	**YES**	**NO**	**NA**	**Comment**
Is form FDA 356h included with authorized signature? ***If foreign applicant, both the applicant and the U.S. agent must sign the form.***	X			
Are all establishments and their registration numbers listed on the form/attached to the form?	X			
Patent Information **(NDAs/NDA efficacy supplements only)**	**YES**	**NO**	**NA**	**Comment**
Is patent information submitted on form FDA 3542a?	X			
Financial Disclosure	**YES**	**NO**	**NA**	**Comment**
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature? ***Forms must be signed by the APPLICANT, not an Agent.*** ***Note:*** *Financial disclosure is required for bioequivalence studies that are the basis for approval.*	X			
Clinical Trials Database	**YES**	**NO**	**NA**	**Comment**
Is form FDA 3674 included with authorized signature?	X			
Debarment Certification	**YES**	**NO**	**NA**	**Comment**
Is a correctly worded Debarment Certification included with authorized signature? ***(Certification is not required for supplements if submitted in the original application)*** ***If foreign applicant, both the applicant and the U.S. Agent must sign the certification.*** ***Note:*** *Debarment Certification should use wording in FD&C Act section 306(k)(l) i.e.,"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge…"*	X			

Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? ***Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)*** ***If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.***				

Pediatrics	YES	NO	NA	Comment
PREA Does the application trigger PREA? ***If yes, notify PeRC RPM (PeRC meeting is required)*** ***Note****: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.*	X			
If the application triggers PREA, are the required pediatric assessment studies or a full waiver of pediatric studies included?	X			
If studies or full waiver not included, is a request for full waiver of pediatric studies OR a request for partial waiver and/or deferral with a pediatric plan included? ***If no, request in 74-day letter***				
If a request for full waiver/partial waiver/deferral is included, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3) ***If no, request in 74-day letter***	X			
BPCA (NDAs/NDA efficacy supplements only): Is this submission a complete response to a pediatric Written Request? ***If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)***		X		

Proprietary Name	**YES**	**NO**	**NA**	**Comment**
Is a proposed proprietary name submitted? ***If yes, ensure that it is submitted as a separate document and routed directly to OSE/DMEPA for review.***	X			
Prescription Labeling	☐ **Not applicable**			
Check all types of labeling submitted.	☒ Package Insert (PI) ☒ Patient Package Insert (PPI) ☐ Instructions for Use (IFU) ☐ Medication Guide (MedGuide) ☒ Carton labels ☒ Immediate container labels ☐ Diluent ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is Electronic Content of Labeling (COL) submitted in SPL format? ***If no, request in 74-day letter.***	X			
Is the PI submitted in PLR format?	X			
If PI not submitted in PLR format, was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted**, what is the status of the request? ***If no waiver or deferral, request PLR format in 74-day letter.***				
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to DDMAC?		X		
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (*send WORD version if available*)		X		
REMS consulted to OSE/DRISK?		X		
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA?	X			
OTC Labeling	☐ **Not Applicable**			
Check all types of labeling submitted.	☐ Outer carton label ☐ Immediate container label ☐ Blister card ☐ Blister backing label ☐ Consumer Information Leaflet (CIL) ☐ Physician sample ☐ Consumer sample ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is electronic content of labeling (COL) submitted? ***If no, request in 74-day letter.***				

Are annotated specifications submitted for all stock keeping units (SKUs)? ***If no, request in 74-day letter.***				
If representative labeling is submitted, are all represented SKUs defined? ***If no, request in 74-day letter.***				
All labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEPA?				
Consults	**YES**	**NO**	**NA**	**Comment**
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) ***If yes, specify consult(s) and date(s) sent:***		X		

Meeting Minutes/SPAs	**YES**	**NO**	**NA**	**Comment**
End-of Phase 2 meeting(s)? **Date(s):** ***If yes, distribute minutes before filing meeting***		X		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? **Date(s):** June 23, 2009 Pre-IND Meeting on February 15, 2007 ***If yes, distribute minutes before filing meeting***	X			
Any Special Protocol Assessments (SPAs)? **Date(s):** ***If yes, distribute letter and/or relevant minutes before filing meeting***		X		

[1] http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf

ATTACHMENT

MEMO OF FILING MEETING

DATE: January 7, 2010

BLA/NDA/Supp #: NDA 022573

PROPRIETARY NAME:

ESTABLISHED/PROPER NAME: norethindrone/ethinyl estradiol chewable and ferrous fumarate

DOSAGE FORM/STRENGTH: norethindrone 0.8 mg/ethinyl estradiol 0.025 mg chewable and ferrous fumarate

APPLICANT: Warner Chilcott

PROPOSED INDICATION(S)/PROPOSED CHANGE(S): Prevention of pregnancy

BACKGROUND: Norethindrone (NE)/ethinyl estradiol (EE) and ferrous fumarate is developed for the primary indication of prevention of pregnancy. NE/EE and ferrous fumarate contains 24 tablets of NE 0.8 mg /EE 0.025 mg and four tablets of ferrous fumarate to complete a 28-day regimen.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Pam Lucarelli	Y
	CPMS/TL:	Jennifer Mercier	Y
Cross-Discipline Team Leader (CDTL)	Lisa Soule		Y
Clinical	Reviewer:	Gerald Willett	Y
	TL:	Lisa Soule	Y
Social Scientist Review (*for OTC products*)	Reviewer:		
	TL:		
OTC Labeling Review (*for OTC products*)	Reviewer:		
	TL:		
Clinical Microbiology (*for antimicrobial*	Reviewer:		

products)			
	TL:		

Clinical Pharmacology	Reviewer:	Christian Grimstein	Y
	TL:	Myong-Jin Kim	Y
Biostatistics	Reviewer:	Sonia Castillo	Y
	TL:	Mahboob Sobhan	N
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Krishan Raheja	N
	TL:	Alex Jordan	N
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Immunogenicity (assay/assay validation) *(for BLAs/BLA efficacy supplements)*	Reviewer:		
	TL:		
Product Quality (CMC)	Reviewer:	Jane Chang	Y
	TL:	Moo-Jhong Rhee Donna Christner - PAL	N Y
Quality Microbiology *(for sterile products)*	Reviewer:		
	TL:		
CMC Labeling Review *(for BLAs/BLA supplements)*	Reviewer:		
	TL:		
Facility Review/Inspection	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name)	Project Manager:	Maria Wasilik	N
	TL:		
OSE/DRISK (REMS)	Reviewer:		
	TL:		
Bioresearch Monitoring (DSI)	Reviewer:	Roy Blay	N

	TL:		

Other reviewers	Sandra Suarez (DCPII)	Y
Other attendees	Scott Monroe (DRUP)	Y

FILING MEETING DISCUSSION:

GENERAL • 505(b)(2) filing issues? **If yes,** list issues:	☒ Not Applicable ☐ YES ☐ NO
• Per reviewers, are all parts in English or English translation? **If no**, explain:	☒ YES ☐ NO
• Electronic Submission comments **List comments**: None	☐ Not Applicable
CLINICAL **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical study site(s) inspections(s) needed? **If no,** explain:	☒ YES ☐ NO
• Advisory Committee Meeting needed? **Comments**: ***If no, for an original NME or BLA application, include the reason. For example:*** o ***this drug/biologic is not the first in its class*** o ***the clinical study design was acceptable*** o ***the application did not raise significant safety or efficacy issues*** o ***the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a***	☐ YES Date if known: ☒ NO ☐ To be determined Reason:

disease	

• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? **Comments**:	☒ Not Applicable ☐ YES ☐ NO
CLINICAL MICROBIOLOGY **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL PHARMACOLOGY **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical pharmacology study site(s) inspections(s) needed?	☐ YES ☒ NO
BIOSTATISTICS **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY) **Comments**:	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
IMMUNOGENICITY (BLAs/BLA efficacy supplements only) **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC)	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE

Comments:	☐ Review issues for 74-day letter

Environmental Assessment • Categorical exclusion for environmental assessment (EA) requested? **If no**, was a complete EA submitted? **If EA submitted**, consulted to EA officer (OPS)? **Comments**:	☐ Not Applicable ☒ YES ☐ NO ☐ YES ☐ NO ☐ YES ☐ NO
Quality Microbiology (for sterile products) • Was the Microbiology Team consulted for validation of sterilization? (**NDAs/NDA supplements only**) **Comments**:	☒ Not Applicable ☐ YES ☐ NO
Facility Inspection • Establishment(s) ready for inspection? ▪ Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ? **Comments**:	☐ Not Applicable ☒ YES ☐ NO ☒ YES ☐ NO
Facility/Microbiology Review (BLAs only) **Comments**:	☐ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CMC Labeling Review (BLAs/BLA supplements only) **Comments**:	☐ Review issues for 74-day letter

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: Scott Monroe, Division Director **21st Century Review Milestones (see attached)** (optional): **Comments**:	
REGULATORY CONCLUSIONS/DEFICIENCIES	
☐	The application is unsuitable for filing. Explain why:
☒	The application, on its face, appears to be suitable for filing. Review Issues: ☐ No review issues have been identified for the 74-day letter. ☒ Review issues have been identified for the 74-day letter. List (optional): Review Classification: ☒ Standard Review ☐ Priority Review
ACTIONS ITEMS	
☒	Ensure that the review and chemical classification properties, as well as any other pertinent properties (e.g., orphan, OTC) are correctly entered into tracking system.
☐	If RTF, notify everybody who already received a consult request, OSE PM, and Product Quality PM (to cancel EER/TBP-EER).
☐	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
☐	BLA/BLA supplements: If filed, send 60-day filing letter
☐	If priority review: • notify sponsor in writing by day 60 (For BLAs/BLA supplements: include in 60-day filing letter; For NDAs/NDA supplements: see CST for choices) • notify DMPQ (so facility inspections can be scheduled earlier)
☐	Send review issues/no review issues by day 74
☐	Other

Appendix A (NDA and NDA Supplements only)

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

An original application is likely to be a 505(b)(2) application if:

(1) it relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application,
(2) it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval, or
(3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies),

(2) No additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application, and.

(3) All other “criteria” are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely

for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2),

(2) The applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement, or

(3) The applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your OND ADRA or OND IO.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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

/s/

PAMELA LUCARELLI
02/01/2010

JENNIFER L MERCIER
02/02/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022573

NDA ACKNOWLEDGMENT

Warner Chilcott
Attention: Alvin Howard
Senior Vice President, Regulatory Affairs
100 Enterprise Drive
Rockaway, NJ 07866

Dear Mr. Howard:

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

Name of Drug Product: norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets

Date of Application: November 26, 2009

Date of Receipt: November 26, 2009

Our Reference Number: NDA 022573

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on January 25, 2010, in accordance with 21 CFR 314.101(a).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Reproductive and Urologic Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, please call Pamela Lucarelli, Regulatory Health Project Manager at (301) 796-3961.

Sincerely,

{See appended electronic signature page}

Jennifer Mercier
Chief, Project Management Staff
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22573	ORIG-1	WARNER CHILCOTT INC	(b) (4) (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets)

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/s/

JENNIFER L MERCIER
12/10/2009

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

IND 76,629

Warner Chilcott
Attention: Ileana Brown
Director, Regulatory Affairs
100 Enterprise Drive
Rockaway, New Jersey 07866

Dear Ms. Brown:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for WC3026 (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets) 0.8 mg/25 mcg.

We also refer to your April 14, 2009, correspondence, requesting a teleconference to seek concurrence from the Division regarding suitability and sufficiency of the clinical program and nonclinical pharmacology and toxicology information conducted in support of your upcoming NDA submission.

On June 19, 2009, we provided our draft preliminary responses to the questions presented in your May 21, 2009, meeting package. After receipt and review of these draft responses, you informed the Division via telephone communication on June 22, 2009, that a meeting was not necessary at this time and you requested to cancel the meeting.

A copy of the preliminary responses is attached for your information.

If you have any questions, please call Pamela Lucarelli, Regulatory Health Project Manager at (301) 796-3961.

Sincerely,

Lisa Soule, M.D.
Medical Team Leader
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

MEMORANDUM OF MEETING COMMUNICATION

SCHEDULED MEETING DATE: June 23, 2009

DATE CANCELLED: June 22, 2009

APPLICATION: IND 76,629

DRUG NAME: WC3026 (norethindrone and ethinyl estradiol tablets, chewable and ferrous fumarate tablets) 0.8 mg/25 mcg

SPONSOR'S QUESTIONS AND DIVISION'S RESPONSES:

1. *Does the Division concur that the nonclinical pharmacology and toxicity of norethindrone and ethinyl estradiol is well documented and that reference to Warner Chilcott's approved NDA 17-576 for Ovcon 50 (norethindrone and ethinyl estradiol tablets, USP) and current review of the literature will be sufficient for the nonclinical pharmacology and toxicology evaluation of NE and EE in support of the NDA to be submitted under Section 505(b)(1)?*

   DIVISION RESPONSE: Yes.

2. *Does the Division concur that in support of the NDA to be submitted under Section 505(b)(1) the nonclinical pharmacology and toxicology of the inactive ingredients in WC3026 is well established (i.e., per the Inactive Ingredient Database or GRAS regulations) and that no additional nonclinical studies are needed?*

   DIVISION RESPONSE: Yes.

3. *Does the Division concur that it is appropriate and sufficient to address the nonclinical pharmacology and toxicology summaries of the active and inactive ingredients in WC3026 as written summaries within section 2.6.6 Toxicology Written Summary and indicate that Module 4 is not applicable unless there are nonclinical literature references in which case they will be located in section 4.3 Literature References?*

   DIVISION RESPONSE: Yes.

4. *Does the Division concur that the clinical pharmacology program is sufficient and adequate in support of the filing of the NDA?*

   DIVISION RESPONSE: The clinical pharmacology program appears to be adequate. However, it is premature to address the filability of the NDA at this time.

5. *Does the Division concur that the clinical program is sufficient and adequate in support of the filing of the NDA under Section 505(b)(1) for this new chewable oral contraceptive tablet?*

   DIVISION RESPONSE: The clinical program appears to be adequate; however, it is premature to address the filability of the NDA at this time. There appear to be the requested number of treatment cycles. It is unclear whether the (b) (4) evaluable cycles include all women or just the cohort aged 18-35 using no other method of contraception.

   The Division has the following comments about the Synopsis of PR-00207:

   - The description of pregnancies used in the calculation of the Pearl Index is not in accord with the Division's definition of "on drug" pregnancies: all conceptions that occur from Day 1 (the initiation of study drug) to seven days after the final tablet (i.e., the last Fe tablet) in the pill pack is taken. If the pills are stopped prior to completing a 28-day pill pack, "on drug" pregnancies are defined as conceptions from Day 1 to seven days after the final tablet is taken.
   - The synopsis does not state how data for bleeding and cycle control will be handled. For the parameters concerning bleeding/spotting, provide, at a minimum, the mean, median and range for the number of observed days of bleeding and/or spotting within each reference period. In addition, stratify the most important analyses for days of bleeding and/or spotting by: BMI, weight, age, parity, smoking (yes/no), history of prior hormonal contraceptive use, and untreated chlamydia infection.

6. *Does the Division concur that it is sufficient for Module 5, section 5.3.1.4 Reports of Bioanalytical and Analytical Methods to provide hypertext links to the respective bioavailability and pharmacokinetic studies which will be submitted as legacy reports each containing a report of the bioanalytical and analytical methods used in the study?*

   DIVISION RESPONSE: Yes.

7. *Does the Division concur with the proposed format of Module 5?*

   DIVISION RESPONSE: Yes.

8. *Does the Division concur with the proposed outline of the NDA as an eCTD?*

   DIVISION RESPONSE: In general, the Division concurs with the proposed outline of the NDA as an eCTD.

   The proposed CMC information appears to be adequate with the following addition:

   In the NDA submission, provide a comprehensive table/list of all facilities involved in production of the drug product with full street address of the actual manufacturing and/or testing site (not the corporate office), **contact information of an individual at the site**, detailed responsibilities of that facility and a date of when the facility was last inspected by the FDA.

This comprehensive table should be attached to the 356h. Full information should still be provided in the appropriate sections of Modules 2 and 3. **Due to a recent software update, inspections cannot be requested unless all the above information is provided. If this information is not provided when the NDA is submitted, it will delay inspection requests and may adversely affect the outcome of a first cycle review decision.**

The proposed Datasets section appears to be adequate with the following addition:

- SAS programs related to efficacy analysis for study PR-00207 should also be included.
- The Division strongly recommends that both SDTM and ADaM datasets be provided. This will facilitate review and likely reduce the queries for customized datasets (see http://www.cdisc.org/standards/index.html for details).

9. *Does the Division concur that at this time a Risk Management Plan for WC3026 is not necessary for inclusion in the NDA?*

   DIVISION RESPONSE: The need for a Risk Management Plan or other postmarketing requirements will be determined during the NDA review.

Linked Applications	Sponsor Name	Drug Name / Subject
IND 76629	WARNER CHILCOTT	WC3026(NORETINDRONE AND ETHINYL ESTRADOL

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/s/

LISA M SOULE
07/20/2009

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

PIND 76,629

Warner Chilcott Co, Inc.
Attention: Ileana Brown
100 Enterprise Drive
Rockaway, NJ 07866

Dear Ms. Brown:

Please refer to your Pre-Investigational New Drug Application (PIND) file for WC3026 (norethindrone and ethinyl estradiol tablets and ferrous fumarate tablets) 0.8 mg/25 μg.

We also refer to the teleconference between representatives of your firm and the FDA on February 15, 2007. The purpose of the teleconference was to discuss the development plan for a new chewable oral contraceptive tablet.

The official minutes of that teleconference are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the teleconference outcomes.

If you have any questions, call Kassandra Sherrod, R.Ph., Regulatory Project Manager, at (301) 796-0997.

Sincerely,

[See appended electronic signature page]

Scott Monroe, M.D.
Acting Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

MEMORANDUM OF TELECONFERENCE MINUTES

MEETING DATE:	February 15, 2007
TIME:	1:00 p.m. to 2:00 p.m.
LOCATION:	Teleconference
APPLICATION:	PIND 76,629
DRUG NAME:	WC3026 (norethindrone and ethinyl estradiol tablets and ferrous fumarate tablets)
TYPE OF MEETING:	Pre-IND
MEETING CHAIR:	Scott Monroe, M.D., Acting Division Director, Division of Reproductive and Urologic Products (DRUP), HFD-580
MEETING RECORDER:	Kassandra Sherrod, R.Ph., Regulatory Project Manager, DRUP, HFD-580

FDA ATTENDEES

Scott Monroe, M.D., Acting Division Director, DRUP, HFD-580
Daniel Davis, M.D., Medical Officer, DRUP, HFD-580
Lynnda Reid, Ph.D., Supervisory Pharmacology Team Leader, DRUP, HFD-580
Kimberly Miller, Ph.D., Pharmacology Reviewer, DRUP, HFD-580
Myong-Jin Kim, Pharm.D, Clinical Pharmacology Acting Team Leader, Office of Clinical Pharmacology, OCP
Kassandra Sherrod, R.Ph., Regulatory Project Manager, DRUP, HFD-580

EXTERNAL CONSTITUENT ATTENDEES

Olu Aloba, Ph.D., Director, Pharmaceutical Development
Ileana Brown, Director, Regulatory Affairs
Tina deVries, Ph.D., Vice President, Clinical Development
Herman Ellman, M.D., Senior Vice President, Clinical Development
Alvin Howard, Senior Vice President, Regulatory Affairs
Brian McNamee, Ph.D., Manager, Clinical Pharmacology
Peter Emodi, Director, Project Management
Jenine Mason, Manager, Project Management

BACKGROUND

Warner Chilcott is developing a new chewable oral contraceptive product consisting of 24 active tablets, each containing 0.8 mg norethindrone and 25 μg ethinyl estradiol, and 4 inactive ferrous fumarate tablets to complete a 28-day dosing regimen.

MEETING OBJECTIVES

To discuss the proposed studies to be conducted in support of the future submission of a new drug application (NDA).

SPONSOR'S QUESTIONS AND THE DIVISION'S RESPONSES

1. *Does the Agency concur that reference to Warner Chilcott's NDA 17,576 for Ovcon 50 is adequate and sufficient for the nonclinical pharmacology and toxicology evaluation of norethindrone and ethinyl estradiol and that no further information on these active ingredients is required in support of the future filing of an NDA under Section 505(b)(1)?*

   Division's Response
   Yes. The daily dose and total monthly dose for both norethindrone (NE) and ethinyl estradiol (EE) are lower than that for the Sponsor's Ovcon 50 product (NDA 17,576). Therefore, no further information is required for the IND submission. At this time, it appears that this data will support filing of an NDA under Section 505(b)(1).

2. *Does the Agency concur that either a demonstration that the quantity of each inactive ingredient found in WC3026 tablets is below the maximum potency provided in FDA's database or the determination that an inactive ingredient is considered GRAS per 21 CFR regulations is adequate and sufficient in support of the future filing of an NDA under Section 505(b)(1)?*

   Division's Response
   Yes. However, a complete listing of the inactive ingredients and their amounts will need to be provided in the IND submission in order to determine safe levels of each excipient.

3. *Does the Agency concur that the proposed Phase 3 study is adequate and sufficient in support of the future filing of an NDA under Section 505(b)(1) and that no additional efficacy and/or safety clinical studies, for example, an oral irritation study, are required?*

   Division's Response
   No. The Division will require the following studies and has the following comments:

   - As the proposed product will provide higher exposure to NE than the Ovcon 35 chewable product, an oral irritation study is requested. [Added post meeting: If the product is to be chewed and not followed by a small quantity of water, it also is likely to remain in contact with the oral mucosa for a longer time than the previously studied product.]
   - The Division requests a total of 10,000 28-day cycles of product exposure in the Phase 3 efficacy and safety trial, including 200 women who complete 13 cycles of use.

(b) (4)

   - The detailed protocol for the proposed Phase 3 trial should be submitted for review by the Division before the trial is initiated.

   Discussion during the Teleconference

(b) (4)

(b) (4)

[redacted]

- The Sponsor stated that they would consider the Division's recommendations regarding the design of the Phase 3 trial and provide a response that would include a revised Phase 3 study design.

4. *Does the Agency concur that the proposed Phase 1 studies will adequately characterize the pharmacokinetics of WC3026?*

Division's Response
Partially. The Sponsor should consider the following:

In Study No. 1,"A single dose, 3-way, 3-period crossover study to characterize the bioavailability of NE and EE …", consider adding an additional fourth arm consisting of WC3026 tablets chewed (with water) to provide bioequivalence data on the chewed tablet taken with and without subsequent water. This will provide data to support labeling regarding the recommended method(s) of administration of the tablet (see Division's response to Question 6).

Discussion during the Teleconference
The Sponsor stated that they would add the requested additional arm: tablets chewed followed by a small amount of water.

5. *Does the Agency concur that the proposed Phase 1 and Phase 3 studies will support labeling that allows WC3026 tablets to be chewed or swallowed?*

Division's Response
Bioequivalence between the two methods of administration (swallowed whole and chewed without water) and demonstrated efficacy and safety of the product regardless of how it is taken would support labeling that allows WC3026 tablets to be taken either by chewing without water or by swallowing whole with water. If the findings from the Phase 3 trial show that the product is efficacious and safe regardless of how the tablets are taken (swallowed or chewed), even if the two administration methods are not bioequivalent, the findings would also support labeling that allows WC3026 tablets to be chewed or swallowed.

Discussion during the Teleconference

(b) (4)

[redacted]

6. (b) (4)

POST MEETING SUBMISSION BY SPONSOR ON FEBRUARY 16, 2007

- The Sponsor confirmed that a third arm, in which the subjects will chew the tablet and then drink a small amount of liquid (approximately 45 ml), will be added to the bioavailability (BA) study.

(b) (4)

Division's Assessment of Sponsor's Proposal

(b) (4)

- The Division cannot comment on the Sponsor's proposed wording for the dosing and administration section of product labeling at this time. The specific wording of this section of labeling will depend upon the findings from the BA study and the design and findings from the Phase 3 study.

ACTION ITEMS

- The Sponsor should submit for Division review and comment the protocols for the BA study and the Phase 3 study prior to initiation of the respective studies.
- Meeting minutes will be provided within 30 days.

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/s/

Scott Monroe
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