

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**204412Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

## EXCLUSIVITY SUMMARY

NDA # 204412

SUPPL # N/A

HFD #

Trade Name: Delzicol

Generic Name: **mesalamine**

Applicant Name: Warner Chilcott Company (US Agent: Warner Chilcott (US), LLC)

Approval Date, If Known: February 1, 2013

### **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.

*The study submitted by the sponsor is a BA/BE study entitled "A Study to Assess the Relative Bioavailability of Two WC3045 Formulations in Healthy Subjects, Study PR-08210."*

*The approved Asacol 400 mg tablet and the proposed new WC3045 capsule (NDA 204412) are both delayed-release products, differing only with respect to a plasticizer excipient, and the final presentation (capsules instead of tablets). The dose, dosing regimen, and indication remain unchanged. Thus it was agreed upon that NDA approval can be based upon demonstration of comparable*

*systemic mesalamine exposures (bioequivalence) between the approved (reference) and new (test) formulations via the conduct of a relative bioavailability/bioequivalence 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:

N/A

d) Did the applicant request exclusivity?

YES  NO

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

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?

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#	21830	Asacol HD (mesalamine) Delayed-Release Tablet
NDA#	19651	Asacol (mesalamine) Delayed-Release Tablet
NDA#	22000	Lialda (mesalamine) Delayed-Release Tablet
NDA#	20049	Pentasa (mesalamine) Extended Release Capsule
NDA#	22301	Apriso (mesalamine) Extended Release Capsule
NDA#	19618	Rowasa (mesalamine) enema, rectal
ANDA#	76751	(mesalamine) enema, rectal
ANDA#	76841	(mesalamine) enema, rectal

## 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#

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:

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"):

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 # 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: Anissa Davis  
Title: Senior Regulatory Project Manager

Date: January 25, 2013

Name of Office/Division Director signing form: Joyce Korvick

Title: Deputy Director of Safety

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ANISSA A DAVIS  
01/25/2013

BRIAN K STRONGIN  
01/25/2013

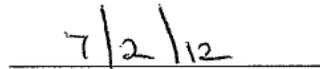
JOYCE A KORVICK  
01/25/2013

**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

CONFIDENTIAL

# ACTION PACKAGE CHECKLIST

<b>APPLICATION INFORMATION<sup>1</sup></b>		
NDA # 204412 BLA # N/A	NDA Supplement # N/A BLA Supplement # N/A	If NDA, Efficacy Supplement Type: N/A
Proprietary Name: Delzicol Established/Proper Name: mesalamine Dosage Form: Delayed-Release Capsule		Applicant: Warner Chilcott Company, LLC Agent for Applicant (if applicable): Warner Chilcott (US), LLC
RPM: CDR Anissa Davis & CDR Stacy Barley		Division: Division of Gastroenterology and Inborn Errors Products ( DGIEP)
<p><b><u>NDA and NDA Efficacy Supplements:</u></b></p> <p>NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)   <input type="checkbox"/> 505(b)(2)            Efficacy Supplement:   <input type="checkbox"/> 505(b)(1)   <input type="checkbox"/> 505(b)(2)</p> <p>(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.)</p>		<p><b><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></b></p> <p>Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> This application does not rely upon a listed drug.  <input type="checkbox"/> This application relies on literature.  <input type="checkbox"/> This application relies on a final OTC monograph.  <input type="checkbox"/> This application relies on (explain)</p> <p><b><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b></p> <p><b><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></b></p> <p><input type="checkbox"/> No changes   <input type="checkbox"/> Updated   Date of check:</p> <p><b>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.</b></p>
<p>❖ <b>Actions</b></p> <ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is <u>02/01/13</u></li> <li>• Previous actions (<i>specify type and date for each action taken</i>)</li> </ul>		<p><input checked="" type="checkbox"/> AP   <input type="checkbox"/> TA   <input type="checkbox"/> CR</p> <p><input checked="" type="checkbox"/> None</p>

<sup>1</sup> 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.

<sup>2</sup> For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

<p>❖ 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 <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a>). If not submitted, explain</p>	<p><input type="checkbox"/> Received</p>
<p>❖ Application Characteristics<sup>3</sup></p> <p>Review priority: <input type="checkbox"/> Standard <input checked="" type="checkbox"/> Priority                  Chemical classification (new NDAs only): Type 3</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch  <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch  <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDA: Subpart H <span style="margin-left: 200px;">BLAs: Subpart E</span>  <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <span style="margin-left: 100px;"><input type="checkbox"/> Accelerated approval (21 CFR 601.41)</span>  <input type="checkbox"/> Restricted distribution (21 CFR 314.520) <span style="margin-left: 100px;"><input type="checkbox"/> Restricted distribution (21 CFR 601.42)</span></p> <p>Subpart I <span style="margin-left: 200px;">Subpart H</span>  <input type="checkbox"/> Approval based on animal studies <span style="margin-left: 100px;"><input type="checkbox"/> Approval based on animal studies</span></p> <p><input type="checkbox"/> Submitted in response to a PMR <span style="margin-left: 200px;">REMS: <input type="checkbox"/> MedGuide</span>  <input type="checkbox"/> Submitted in response to a PMC <span style="margin-left: 100px;"><input type="checkbox"/> Communication Plan</span>  <input type="checkbox"/> Submitted in response to a Pediatric Written Request <span style="margin-left: 100px;"><input type="checkbox"/> ETASU</span>  <span style="margin-left: 400px;"><input type="checkbox"/> MedGuide w/o REMS</span>  <span style="margin-left: 400px;"><input type="checkbox"/> REMS not required</span></p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<p><input type="checkbox"/> Yes, dates</p>
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> <li>• Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
<ul style="list-style-type: none"> <li>• Press Office notified of action (by OEP)</li> </ul>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p>
<ul style="list-style-type: none"> <li>• Indicate what types (if any) of information dissemination are anticipated</li> </ul>	<p><input checked="" type="checkbox"/> None  <input type="checkbox"/> HHS Press Release  <input type="checkbox"/> FDA Talk Paper  <input type="checkbox"/> CDER Q&amp;As  <input type="checkbox"/> Other</p>

<sup>3</sup> 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	
<ul style="list-style-type: none"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> <li>NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>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.</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA #                      and date exclusivity expires:
<ul style="list-style-type: none"> <li>NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(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.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA #                      and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> <li>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.</li> </ul>	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> <li>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.</li> </ul>	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified  21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> <li>[505(b)(2) applications] If the application includes a <b>paragraph III</b> 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).</li> </ul>	<input type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> <li>[505(b)(2) applications] For <b>each paragraph IV</b> 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). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i></li> </ul>	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> 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).*

<p>(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?</p> <p>(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).</p> <p><i>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).</i></p> <p><i>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.</i></p>	<p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p>
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**CONTENTS OF ACTION PACKAGE**

❖ Copy of this Action Package Checklist <sup>4</sup>	2/1/13
<b>Officer/Employee List</b>	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list ( <i>approvals only</i> )	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) Approval 2/1/2013
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	1/30/13
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	8/1/12
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	Asacol (mesalamine) Delayed-Release Tablets- May 2010

<sup>4</sup> Fill in blanks with dates of reviews, letters, etc.

❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling ( <i>write submission/communication date at upper right of first page of each piece</i> )	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	N/A
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	N/A
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	N/A
❖ Labels ( <b>full color</b> carton and immediate-container labels) ( <i>write submission/communication date on upper right of first page of each submission</i> )	
<ul style="list-style-type: none"> <li>• Most-recent draft labeling</li> </ul>	1/16/13
❖ Proprietary Name <ul style="list-style-type: none"> <li>• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>• Review(s) (<i>indicate date(s)</i>)</li> <li>• Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name.</li> </ul>	DMEPA Communication: 1/25/13 1/17/13, 1/11/13, 12/5/12, 10/10/12 Review 1/25/13
❖ Labeling reviews ( <i>indicate dates of reviews and meetings</i> )	<input checked="" type="checkbox"/> RPM 9/28/12 <input checked="" type="checkbox"/> DMEPA 1/9/13 <input type="checkbox"/> DMPP/PLT (DRISK) N/A <input checked="" type="checkbox"/> ODPD (DDMAC) 1/16/2013 <input checked="" type="checkbox"/> SEALD 1/24/13 <input type="checkbox"/> CSS N/A <input type="checkbox"/> Other reviews
<b>Administrative / Regulatory Documents</b>	
❖ Administrative Reviews ( <i>e.g., RPM Filing Review<sup>5</sup>/Memo of Filing Meeting</i> ) ( <i>indicate date of each review</i> )	9/28/12
❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment ( <i>indicate date</i> )	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs only: Exclusivity Summary ( <i>signed by Division Director</i> )	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a>	
<ul style="list-style-type: none"> <li>• Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>• This application is on the AIP               <ul style="list-style-type: none"> <li>○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input type="checkbox"/> Not an AP action
❖ Pediatrics ( <i>approvals only</i> ) <ul style="list-style-type: none"> <li>• Date reviewed by PeRC <u>1/9/13</u> If PeRC review not necessary, explain: _____</li> <li>• Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul>	<input checked="" type="checkbox"/> 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 ( <i>include certification</i> )	<input checked="" type="checkbox"/> Verified, statement is acceptable

<sup>5</sup> Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Outgoing communications ( <i>letters, including response to FD RR (do not include previous action letters in this tab), emails, faxes, telecons</i> )	1/31/13, 1/30/13, 1/25/13, 1/16/13, 1/14/13, 1/8/13, 1/7/13, 1/4/13, 12/14/12, 12/12/12, 12/7/12, 12/5/12, 11/20/12, 11/16/12, 10/25/12, 10/10/12, 9/28/12, 9/19/12, 9/13/12, 9/12/12, 8/13/12
❖ Internal memoranda, telecons, etc.	9/25/12, 9/17/12
❖ Minutes of Meetings	
• Regulatory Briefing ( <i>indicate date of mtg</i> )	<input type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting ( <i>indicate date of mtg</i> )	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting ( <i>indicate date of mtg</i> )	<input type="checkbox"/> No mtg 7/10/12
• EOP2 meeting ( <i>indicate date of mtg</i> )	<input type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) ( <i>indicate dates of mtgs</i> )	Type C Meetings- 11/5/10, 5/20/10
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available ( <i>do not include transcript</i> )	
<b>Decisional and Summary Memos</b>	
❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Division Director Summary Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 2/1/13
Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 2/1/13
PMR/PMC Development Templates ( <i>indicate total number</i> )	<input type="checkbox"/> None Total= 3; 1/31/13
<b>Clinical Information<sup>6</sup></b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) ( <i>indicate date for each review</i> )	(concur with clinical review) 1/24/13, 1/22/13, 12/26/12, 9/10/12
• Clinical review(s) ( <i>indicate date for each review</i> )	1/24/13, 1/22/13, 12/26/12, 9/10/12
• Social scientist review(s) (if OTC drug) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not ( <i>indicate date of review/memo</i> )	See clinical review addendum dated 1/24/13
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers ( <i>indicate date of each review</i> )	<input type="checkbox"/> None 1/11/13 Maternal Health review; 1/30/13 Pediatric review
❖ Controlled Substance Staff review(s) and Scheduling Recommendation ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> Not applicable

<sup>6</sup> Filing reviews should be filed with the discipline reviews.

❖ Risk Management <ul style="list-style-type: none"> <li>REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)</li> <li>REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)</li> <li>Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
❖ DSI Clinical Inspection Review Summary(ies) ( <i>include copies of DSI letters to investigators</i> )	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None
Clinical Microbiology Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None
<b>Biostatistics</b> <input checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None
Statistical Team Leader Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None
Statistical Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None (concur with clinpharm review) 1/11/13, 12/20/12, 9/12/12
Clinical Pharmacology review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 1/11/13, 12/20/12, 9/12/12
❖ DSI Clinical Pharmacology Inspection Review Summary ( <i>include copies of DSI letters</i> )	<input type="checkbox"/> None 1/8/13, 10/3/12
<b>Nonclinical</b> <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
• Supervisory Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None (concur with nonclinical review) 12/20/12, 9/12/12
• Pharm/tox review(s), including referenced IND reviews ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 12/20/12, 9/12/12
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary ( <i>include copies of DSI letters</i> )	<input checked="" type="checkbox"/> None requested

<b>Product Quality</b> <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
<ul style="list-style-type: none"> <li>• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i></li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i></li> </ul>	<input type="checkbox"/> None (concur with CMC reviewer) 2/1/13, 12/12/12 CMC filing review 9/28/12 (concur with Biopharm review) 1/12/13, 12/28/12, 9/10/12
<ul style="list-style-type: none"> <li>• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i></li> </ul>	<input type="checkbox"/> None 2/1/13, 1/12/13, 12/28/12, 12/12/12, 9/10/12
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	claim for categorical exclusion granted on 11/1/12, see page 5 of CMC review dated 12/12/12
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>	
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(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<sup>7</sup>)</i>	Date completed: 2/1/13 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER <i>(date of most recent TB-EER must be within 30 days of action date) (original and supplemental BLAs)</i>	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation <i>(check box only, do not include documents)</i>	<input checked="" type="checkbox"/> Completed (see page 69 of CMC review dated 12/12/12) <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

<sup>7</sup> 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.

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/s/  
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ANISSA A DAVIS  
02/01/2013

STACY R BARLEY  
02/01/2013

## Davis, Anissa

---

**From:** Davis, Anissa  
**Sent:** Thursday, January 31, 2013 4:33 PM  
**To:** 'Wei Zhuang'  
**Subject:** NDA 204412 Delzicol (mesalamine)

**Importance:** High

Hi Wei:

We wish to determine if the following testing site is redundant.

Regarding the specific manufacturing responsibilities concerning the Warner Chilcott UK testing laboratory in Larne, UK, please provide the following:

- The specific tests performed at the site for drug product release and stability testing

Please provide a statement to indicate if these tests are/are not performed at other sites listed in your application in support of commercial operations.

**Please provide your response by 10:00am tomorrow, February 1, 2013.**

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

*(301) 796-9904 (fax)*

***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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/s/  
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ANISSA A DAVIS  
02/01/2013

**Davis, Anissa**

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**From:** Davis, Anissa  
**Sent:** Wednesday, January 30, 2013 8:35 AM  
**To:** 'Wei Zhuang'  
**Cc:** Barley, Stacy  
**Subject:** NDA 204412 Delzicol (mesalamine) Delayed- Release Capsules  
**Attachments:** annotlabel-1.30.13 Sponsor's copy.rtf; annotlabel-1.30.13 Sponsor's copy.pdf

Hello Wei:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Delzicol (mesalamine) Delayed-Release Capsules 400mg.

Please review and make the minor edits noted in the attached PI and forward a courtesy track change word version to me by noon today. The Carton/Container labels has been reviewed and accepted. There are no other comments at this time.

Thank you.

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

*(301) 796-9904 (fax)*

**[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)**

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ANISSA A DAVIS  
01/30/2013

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Cc:** [Barley, Stacy](#)  
**Subject:** NDA 204412 Delzicol (mesalamine) Delayed-Release Capsule  
**Date:** Friday, January 25, 2013 5:46:40 PM  
**Attachments:** [annotlabel 1.25.13-Sponsor"s copy.doc](#)  
[annotlabel 1.25.13-Sponsor"s copy.pdf](#)

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Good Afternoon Wei,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Delzicol (mesalamine) Delayed-Release Capsules 400mg.

We are continuing the process of reviewing your label for NDA 204412. Please see the attached revisions. Ensure all edits made by you are in track change format. If you are in agreement with the FDA revisions, accept the track changes (additions and/or deletions). Do not accept track changes to your own revisions. Additionally, if you are in agreement with the FDA track changes, please update the highlight section to reflect those changes as well. **Again, please do not accept your own track changes.**

Referring to the July 31, 2012 submission of your Labeling Carton and Container information, the team has the following comments:

- You removed the statement [REDACTED] <sup>(b) (4)</sup> from the principal display panels of the container and carton labeling. This statement should be returned to the label since this is a safety issue.
- Please insert your approved proprietary name in the Carton and Container.

**Please submit the revised Carton and Container label and Package Insert by noon on Tuesday, January 29, 2013.**

Thank you.

**Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.**  
CDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration/Center for Drug Evaluation and Research  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
(301) 796-5016 (office)  
(301) 796-9904 (fax)  
[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)

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*have received this document in error, please notify us immediately by telephone at (301) 796-0069. Thank you.*

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ANISSA A DAVIS  
01/25/2013



NDA 204412

**PROPRIETARY NAME REQUEST  
CONDITIONALLY ACCEPTABLE**

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

ATTENTION: Wei Zhuang  
Senior Manager, Regulatory Affairs

Dear Ms. Zhuang:

Please refer to your New Drug Application (NDA) dated July 31, 2012, received August 1, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Mesalamine Delayed-release Capsules, 400 mg.

We also refer to your January 18, 2013, correspondence, received January 18, 2013, requesting review of your proposed proprietary name, Delzicol. We have completed our review of the proposed proprietary name, Delzicol, and have concluded that it is acceptable.

The proposed proprietary name, Delzicol, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you. Additionally, if **any** of the proposed product characteristics as stated in your January 18, 2013 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Phong Do, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4795. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Anissa Davis, at (301) 796-5016.

Sincerely,

*{See appended electronic signature page}*

Carol Holquist, RPh

Director

Division of Medication Error Prevention and Analysis

Office of Medication Error Prevention and Risk Management

Office of Surveillance and Epidemiology

Center for Drug Evaluation and Research

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CAROL A HOLQUIST  
01/25/2013

MEMORANDUM

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

**MEETING DATE:** January 17, 2013  
**TIME:** 1:30 PM  
**LOCATION:** WO 22 Room 4440  
**APPLICATION:** NDA 204412  
**DRUG NAME:** (b) (4) (mesalamine) delayed-release capsules, 400 mg  
**TYPE OF MEETING:** Proposed Proprietary Name

**MEETING CHAIR:** Lubna Merchant

**MEETING RECORDER:** Phong Do

**FDA ATTENDEES:**

Lubna Merchant, Pharm.D., M.S., Team Leader, DMEPA  
Phong Do, Pharm.D., SRPM

**EXTERNAL CONSTITUENT ATTENDEES:**

Wei Zhuang, Sr. Manager, Regulatory Affairs  
Alvin Howard, Sr. Vice President, Regulatory Affairs  
Matthew Lamb

**Background**

Warner Chilcott Co, LLC submitted the proposed primary proprietary name, (b) (4) for NDA 202241, mesalamine delayed-release capsules, 400 mg on December 14, 2012.

DMEPA requested this teleconference to inform Warner Chilcott Pharmaceuticals of preliminary concerns identified during the review of the proposed proprietary name, (b) (4)

**Product Information**

- Active Ingredient: Mesalamine
- Indication of Use: Treatment of mildly to moderately active ulcerative colitis and maintenance of remission of ulcerative colitis
- Route of Administration: Oral
- Dosage Form: Delayed-release Capsules
- Strength: 400 mg

- Dose and Frequency: 800 mg by mouth three times daily or 1600 mg by mouth daily in divided doses
- How Supplied: Bottles of 180 capsules
- Storage: Room temperature
- Container and Closure System: Child-resistant cap

### **Meeting Objectives**

This is a courtesy call to notify Warner Chilcott, Inc. of DMEPA's preliminary findings and safety concerns with regards to the proposed proprietary name, (b) (4) submitted December 14, 2012.

### **Discussion**

DMEPA's preliminary review has identified that the proposed proprietary name, (b) (4) is unacceptable from a promotional perspective for the following reasons:

“(b) (4) can be broken up into “(b) (4) The term (b) (4) evokes the phrase (b) (4) (http://unabridged.merriam-webster.com/cgi-bin/unabridged; accessed 1/3/13). Therefore, the proposed proprietary name implies a unique representation over other drugs with the same active ingredient, suggesting that the drug is a new form of mesalamine associated with a better efficacy profile. Given that the active ingredient is a common substance, this suggestion is misleading.

As a result of OPDP's decision for this name, and to try to meet the PDUFA deadline, DMEPA proceeded to evaluate your alternate proprietary name, Delzicol, which has been found to be acceptable preliminarily.

### **Regulatory Options**

1. Wait for DMEPA to complete the review of (b) (4) by the OSE PDUFA goal date of March 14, 2013 and issue a formal decision (most likely a denial of the name).
2. Withdraw the proposed name, (b) (4) and formally submit alternate name, Delzicol, for review.

The sponsor agreed to withdrawal the proposed name, (b) (4) and will formally submit Delzicol for proprietary name review.

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PHONG DO  
01/17/2013

From: [Barley, Stacy](#)  
To: ["Wei Zhuang"](#)  
Cc: [Davis, Anissa](#)  
Subject: NDA 204412 (mesalamine) Delayed-Release Capsules: PMR discussion  
Date: Wednesday, January 16, 2013 4:40:40 PM

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Hello Wei,

We are in the process of reviewing your application: NDA 204412 mesalamine Delayed-Release Capsules. Please review the two post-marketing requirements below and provide feedback by COB 1/18/13. Contact me if you have any questions.

**Study 1: A randomized, double-blind study in pediatric patients ages 5 to 17 years with active mild to moderate ulcerative colitis (UC) using an age-appropriate formulation to evaluate the pharmacokinetics, safety, and clinical response of pediatric patients undergoing six weeks of oral mesalamine therapy. The study should compare at least two different dose levels of mesalamine and enroll at least 40 pediatric patients in each dosing arm.**

**Protocol Submission Date: 8/31/2013  
Study Completion Date: 5/31/2015  
Final Report Submission: 9/30/2015**

**Study 2: A randomized, double-blind study in pediatric patients ages 5 to 17 years using an age-appropriate formulation for the maintenance of remission of UC.**

**Protocol Submission Date: 8/31/2013  
Study Completion Date: 5/31/2016  
Final Report Submission: 9/30/2016**

*Stacy Barley, RN, M.S.N., M.H.A.  
CDR, USPHS Commissioned Corps  
Senior Regulatory Project Manager  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
CDER/FDA  
(301) 796-2137 (office)  
(301) 796-9905 (fax)  
stacy.barley@fda.hhs.gov*

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/s/  
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STACY R BARLEY  
01/16/2013

**From:** [Davis, Anissa](#)  
**To:** ["Wei Zhuang"](#)  
**Cc:** [Barley, Stacy](#)  
**Subject:** NDA 204412 (mesalamine) Delayed- Release Capsules: Labeling, Carton & Container Information  
**Date:** Monday, January 14, 2013 5:19:54 PM  
**Attachments:** [annotlabel- Sponsor"s copy.docx](#)  
[annotlabel- Sponsor"s copy.pdf](#)

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Good Afternoon Wei,

We are continuing the process of reviewing your label for NDA 204412. Please see the attached revisions. Ensure all edits made by you are in track change format. If you are in agreement with the FDA revisions, accept the track changes (additions and/or deletions). Do not accept track changes to your own revisions. Additionally, if you are in agreement with the FDA track changes, please update the highlight section to reflect those changes as well. **Again, please do not accept your own track changes.**

**Please submit the revisions to your Package Insert to the Agency by close of business Tuesday, January 15, 2013.**

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. Referring to the July 31, 2012 submission of your Labeling Carton and Container information, the team has the following comments:

1. **All Label and Labeling (container label [180 count] sample container label [12 count], and sample carton labeling [12 count])**
  - a. Update all labels and labeling to remove reference to the proprietary name, (b) (4) as this name has been denied.
  - b. Although it appears the established name is printed in letters that are at least half as large as the letters comprising the proprietary name, the prominence of the established name is lessened due to the small font thickness in relation to the proprietary name. Revise the presentation of the established name taking into account all pertinent factors, including font thickness, typography, layout, contrast and other printing features in accordance with 21 CFR 201.10(g)(2).
  - c. Remove the statement "per capsule" as the dosage form ('capsule') is already stated and therefore this statement is redundant.
  - d. Locate the strength statement ('400 mg') to appear just below the dosage form ('delayed-release capsules').
  - e. The lines incorporated into the graphic are too prominent and interfere with the readability of other information such as the net quantity statement. Please revise or delete the lines.
  - f. Revise the presentation of the "Rx Only" statement, the net quantity

statement (“12 capsules”) and the statement “Sample-Not for Sale” appearing at the lower part of the principal display panel to improve its readability. The use of overly fanciful font makes such statements difficult to read.

g. Add this important dosing message on to the label: “Take each dose at least one hour before or 2 hours after a meal”.

h. Incorporate space between all statements on the principal display panel to assist with readability.

## **2. Sample Tray**

See Recommendations A(1)(a) and A(1)(b).

## **3. Container Label (180 count) and Sample Carton Labeling (12 count)**

Ensure that the “New formulation” alert is implemented only for the first six months of new product marketing.

## **4. Sample Carton Labeling**

Revise the presentation of the “Rx Only” statement, the net quantity statement (“12 capsules”) and the statement “Sample-Not for Sale” appearing at the lower part of the principal display panel to improve its readability. The use of the yellow outline with white lettering makes these statements difficult to read on the images provided to the Agency.

## **5. Sample Container Label**

Consider moving the lot and expiration date to the side panel for the sample container label to accommodate the above recommendations

**Please submit your revisions to the Labeling Carton and Container to the Agency by Thursday, January 17, 2013 or sooner, if possible.**

**Also, please copy Stacy Barley on all email correspondence related to this application.**

**Thank you**

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

*(301) 796-9904 (fax)*

***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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/s/  
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ANISSA A DAVIS  
01/14/2013



NDA 204412

**PROPRIETARY NAME REQUEST  
WITHDRAWN**

Warner Chilcott Company, LLC  
100 Enterprise Drive  
Rockaway, NJ 07866

ATTENTION: Wei Zhuang  
Senior Manager, Regulatory Affairs

Dear Ms. Zhuang:

Please refer to your New Drug Application (NDA) dated July 31, 2012, received August 1, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Mesalamine Delayed-release Capsules, 400 mg.

We acknowledge receipt of your December 14, 2012, correspondence, on December 14, 2012, notifying us that you are withdrawing your request for a review of the proposed proprietary name (b) (4). This proposed proprietary name request is considered withdrawn as of December 14, 2012.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Phong Do, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4795. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager.

Sincerely,

*{See appended electronic signature page}*

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

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CAROL A HOLQUIST  
01/11/2013

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Subject:** RE: NDA 204412 (mesalamine) Delayed-Release Capsules: Information Request  
**Date:** Tuesday, January 08, 2013 10:59:56 AM

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Hello Wei:

Below is the language you can utilize to submit your response to bullet one in the Information Request forwarded to you yesterday, January 7, 2013-see email below:

**(Name of Sponsor) certifies that the clinical study of (name of drug) in pediatric patients will be conducted with due diligence at the earliest possible time. (Name of Sponsor) also certifies that all statements made in the request for partial waiver and deferral of pediatric studies are true and correct, and that the information included is believed to adequately support the Request for a Partial Waiver and Deferral of Pediatric Studies.**

Please type it, sign/date, and submit to the application today. Also, please provide me with a courtesy copy via email.

Additionally, thank you for providing the location of your responses to bullet two in your January 4, 2013 submission to the application.

Thanks

**Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.**  
CDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration/Center for Drug Evaluation and Research  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
(301) 796-5016 (office)  
(301) 796-9904 (fax)  
[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)

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**From:** Davis, Anissa  
**Sent:** Monday, January 07, 2013 4:34 PM  
**To:** 'Wei Zhuang'  
**Subject:** NDA 204412 (mesalamine) Delayed-Release Capsules: Information Request

Good Afternoon Wei,

Please refer to your New Drug Application (NDA) 204412 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

- Provide the certification(s) required by FDCA Section 505B(a)(3) and (4) for the request for partial waiver and deferral of pediatric studies submitted with this application.
- Provide a response ( official withdrawal letter) to the following request that Catherine Tran-Zwanetz forwarded to you on December 7, 2012:
  - You are proposing to use two drug substance suppliers, (b) (4). However, all the data that you have submitted is for drug product batches manufactured with drug substance from (b) (4). Therefore, please withdraw the (b) (4) as a drug substance supplier.

**Please provide a response by January 8, 2013. If responses are not received, this will impact the review of this application.**

Thank you.

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

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***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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/s/  
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ANISSA A DAVIS  
01/08/2013

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Subject:** NDA 204412 (mesalamine) Delayed-Release Capsules: Information Request  
**Date:** Monday, January 07, 2013 4:33:37 PM

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Good Afternoon Wei,

Please refer to your New Drug Application (NDA) 204412 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

- Provide the certification(s) required by FDCA Section 505B(a)(3) and (4) for the request for partial waiver and deferral of pediatric studies submitted with this application.
- Provide a response ( official withdrawal letter) to the following request that Catherine Tran-Zwanetz forwarded to you on December 7, 2012:
  - You are proposing to use two drug substance suppliers, (b) (4) (b) (4). However, all the data that you have submitted is for drug product batches manufactured with drug substance from (b) (4). Therefore, please withdraw the (b) (4) as a drug substance supplier.

**Please provide a response by January 8, 2013. If responses are not received, this will impact the review of this application.**

Thank you.

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

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***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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ANISSA A DAVIS  
01/07/2013

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Subject:** NDA 204412 (mesalamine) Delayed-Release Capsule- Label Revision  
**Date:** Friday, January 04, 2013 3:25:38 PM  
**Attachments:** [annotlabel2-Sponsor"s copy.doc](#)  
[annotlabel2-Sponsor"s copy.pdf](#)

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Hello Wei:

We are in the process of reviewing your label for NDA 204412. Please see the attached revisions. Ensure **all edits made by you are in track change format** . If you are in agreement with the FDA revisions, accept the track changes (additions and/or deletions). **Do not accept track changes to your own revisions.**

Additionally, if you are in agreement with the FDA track changes, please update the highlight section to reflect those changes as well. Again, please do not accept your own track changes.

**Please submit your revisions to the Agency by close of business Tuesday, January 8, 2013.**

Thank you

**Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.**  
*CDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration/Center for Drug Evaluation and Research  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
(301) 796-5016 (office)  
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[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)*

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ANISSA A DAVIS  
01/04/2013

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Subject:** RE: NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request  
**Date:** Thursday, December 13, 2012 3:21:20 PM

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Hello Wei:

Thanks for the information. I have forwarded this email to the CMC review team's RPM, Catherine Tran-Zwanetz to review and respond accordingly. If needed, you can contact her via email at [Catherine.TranZwanetz@fda.hhs.gov](mailto:Catherine.TranZwanetz@fda.hhs.gov)

As it relates to the pediatric study information, thank you and I look forward to your response on 12/19/12.

Thanks

**Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.**  
CDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration/Center for Drug Evaluation and Research  
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**From:** Wei Zhuang [mailto:wei.zhuang@wcrx.com]  
**Sent:** Thursday, December 13, 2012 1:02 PM  
**To:** Davis, Anissa  
**Cc:** 'Wei Zhuang'  
**Subject:** Re: NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request

Hi Anissa,

Thanks for reaching out to me for the Agency's information request!

Our team discussed the Agency's request to revise the specification for dissolution testing at pH7.2 from 90 minutes to 75 minutes. The proposed dissolution specification (90 minutes) in NDA 204412 is based on USP <711> mesalamine delayed-release tablets and the specifications of the current approved Asacol and Asacol HD tablets. The dissolution testing is also a part of the stability testing, and 90 minute time point is reported in the stability study based on the proposed specification. There are no stability dissolution testing data at 75 minutes to support changing dissolution testing at pH7.2 from 90 minutes to 75 minutes.

Warner Chilcott acknowledges the Agency's suggestion to change dissolution testing at pH7.2 from 90

minutes to 75 minutes. We propose to collect stability dissolution data at the 75 minute time point at pH7.2, make an evaluation and report these data to the Agency (b) (4). If the stability data supports changing the dissolution testing at pH7.2 from 90 minutes to 75 minutes, the specification of the dissolution will be revised accordingly.

Could you please discuss this proposal with the Chemistry reviewer and see if it is acceptable? If the proposal is not acceptable, might it be possible to have a teleconference with Chemistry reviewer to discuss it?

If acceptable, the formal response for this CMC request outlining our proposal will be submitted to the Agency on Wednesday (12/19).

Lastly, we are working on the pediatric study request and will submit that to the Agency on Wednesday (12/19) as well.

Thanks again for your help!

Wei

---

*Wei Zhuang*  
*Senior Manager, Regulatory Affairs*  
*Wamer Chilcott (US), LLC*  
*100 Enterprise Drive*  
*Rockaway, NJ 07866*  
*973.907.7063 (office)*  
*973.647.8139 (BB)*  
*973.442.3280 (fax)*  
[wei.zhuang@wcrx.com](mailto:wei.zhuang@wcrx.com)

From: "Davis, Anissa" <[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)>  
To: ""Wei Zhuang"" <[wei.zhuang@wcrx.com](mailto:wei.zhuang@wcrx.com)>  
Date: 12/12/2012 01:18 PM  
Subject: NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request

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Good Afternoon Wei,

Please refer to your New Drug Application (NDA) 204412 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

- **We have reviewed your Pediatric Plan and note that it does not contain your plan to fully address** (b) (4)

- **Submit a timeline for the completion of your studies (must include at least dates for protocol submission, study completion, and studies submission). Provide the dates in a month/day/year format.**
- **The dissolution data provided in your NDA appear to support the acceptance criterion of Q=80% at 75 minutes in the medium of pH 7.2 using the proposed dissolution conditions (USP II, 50 rpm). We recommend that you implement this criterion and provide the revised specification table for your drug product**

**Provide your responses before or by 12/19/2012.**

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***  
*CDR, USPHS Commissioned Corps*  
*Regulatory Project Manager*  
*Food and Drug Administration/Center for Drug Evaluation and Research*  
*Division of Gastroenterology/Inborn Errors Products*  
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***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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ANISSA A DAVIS  
12/14/2012

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Subject:** NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request  
**Date:** Wednesday, December 12, 2012 1:18:22 PM

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Good Afternoon Wei,

Please refer to your New Drug Application (NDA) 204412 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

- We have reviewed your Pediatric Plan and note that it does not contain your plan to fully address  (b) (4)  
  

- Submit a timeline for the completion of your studies (must include at least dates for protocol submission, study completion, and studies submission). Provide the dates in a month/day/year format.
- The dissolution data provided in your NDA appear to support the acceptance criterion of Q=80% at 75 minutes in the medium of pH 7.2 using the proposed dissolution conditions (USP II, 50 rpm). We recommend that you implement this criterion and provide the revised specification table for your drug product

Provide your responses before or by 12/19/2012.

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

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***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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/s/  
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ANISSA A DAVIS  
12/12/2012



NDA 204412

**INFORMATION REQUEST**

Warner Chilcott Company, LLC.  
US Agent: Warner Chilcott (US) LLC.  
Attention: Wei Zhuang, Senior Manager  
100 Enterprise Drive  
Rockaway, NJ 07866

Dear Ms. Zhuang:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mesalamine Delayed-Release Capsules, 400 mg.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- Since all core tablets for the drug product registration batches were manufactured by the “alternative process” described in Sec. 2.3.P.3.3.2.2. Please amend your application to indicate that only the “alternative process” will be used in manufacturing the commercial product, and withdraw the “original process” from the application.
- Please provide information regarding the composition of the white ink solution used to imprint the capsules. If this information can be found in a DMF, provide the DMF number, page number, and a letter of authorization from the DMF holder for FDA to review that DMF.
- Please add testing for (b) (4) to your drug product specification (release and stability).
- You have committed to alternate stability testing of the 180-count and 12-count bottles on an annual basis. Please revise that commitment to test the 180-count bottle annually (testing of the 12-count bottle is optional) and report stability failures to FDA per 21 CFR 314.81(b)(1)(ii).
- You are proposing to use two drug substance suppliers, (b) (4). However, all the data that you have submitted is for drug product batches manufactured with drug substance from (b) (4). Therefore, please withdraw the (b) (4) as a drug substance supplier.

- Please provide specification for the drug substance, mesalamine.

If you have any questions, call Cathy Tran-Zwanetz, Regulatory Project Manager, at (301) 796-3877.

Sincerely,

*{See appended electronic signature page}*

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

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MOO JHONG RHEE  
12/07/2012  
Chief, Branch IV

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Subject:** NDA 204412 (mesalamine) Delayed-Release Capsules  
**Date:** Friday, December 07, 2012 2:20:56 PM  
**Attachments:** [annotlabel-comments for the Sponsor 12.7.12.pdf](#)  
[annotlabel-comments for the Sponsor 12.7.12.doc](#)  
[annotlabel-Sponsor clean version. 12.7.12.doc](#)

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Hello Wei:

Please refer to your New Drug Application (NDA) 204412 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. Please review our labeling comments and provide revisions by COB December 13, 2012 at 3:00 p.m. (EST).

Accept track changes for all comments that you are in agreement with.

Please contact me if you have any questions or concerns.

Thank you.

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

*(301) 796-9904 (fax)*

**[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)**

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

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ANISSA A DAVIS  
12/07/2012

## Davis, Anissa

---

**From:** Davis, Anissa  
**Sent:** Thursday, December 06, 2012 10:25 AM  
**To:** 'Wei Zhuang'  
**Cc:** Barley, Stacy  
**Subject:** RE: NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request

Thank you very much for the information, Wei.

Have a nice day!

**Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.**

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

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[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)

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**From:** Wei Zhuang [<mailto:wei.zhuang@wcrx.com>]  
**Sent:** Wednesday, December 05, 2012 3:34 PM  
**To:** Davis, Anissa  
**Subject:** Re: NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request

Dear Anissa,

The requested information is presented in the original NDA section 2.7.1, Table 12 (page 21) and the individual data is also presented in CTD section 2.7.1, Table 21 (page 31).

If you have further question, please don't hesitate to contact me.

Thanks,

Wei

---

*Wei Zhuang*  
*Senior Manager, Regulatory Affairs*  
*Warner Chilcott (US), LLC*  
*100 Enterprise Drive*  
*Rockaway, NJ 07866*  
*973.907.7063 (office)*  
*973.647.8139 (BB)*  
*973.442.3280 (fax)*  
[wei.zhuang@wcrx.com](mailto:wei.zhuang@wcrx.com)

From: "Davis, Anissa" <[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)>  
To: "Wei Zhuang" <[wei.zhuang@wcrx.com](mailto:wei.zhuang@wcrx.com)>  
Date: 12/05/2012 01:57 PM  
Subject: NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request

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Good Afternoon Wei,

Please refer to your New Drug Application (NDA) 204412 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

**Provide dissolution data for your product collected at 75 minutes during the stage of pH 7.2 (Type II Paddle 50 RPM).**

**Provide a response before or by 12/28/2012.**

Contact me if you have any questions.

Thank you.

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***  
*CDR, USPHS Commissioned Corps*  
*Regulatory Project Manager*  
*Food and Drug Administration/Center for Drug Evaluation and Research*  
*Division of Gastroenterology/Inborn Errors Products*  
*Office of Drug Evaluation III*  
*(301) 796-5016 (office)*  
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**[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)**

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\*\*\*\*\* WC Confidentiality Note: \*\*\*\*\*

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\*\*\*\*\* Thank you \*\*\*\*\*

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ANISSA A DAVIS  
12/07/2012

**From:** [Davis, Anissa](#)  
**To:** ["Wei Zhuang"](#)  
**Subject:** NDA 204412 (mesalamine) Delayed-Release Capsule: Information Request  
**Date:** Wednesday, December 05, 2012 1:56:47 PM

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Good Afternoon Wei,

Please refer to your New Drug Application (NDA) 204412 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

**Provide dissolution data for your product collected at 75 minutes during the stage of pH 7.2 (Type II Paddle 50 RPM).**

**Provide a response before or by 12/28/2012.**

Contact me if you have any questions.

Thank you.

***Anissa Davis, RN, B.S.N., M.P.H., C.P.H.M.***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

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***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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ANISSA A DAVIS  
12/05/2012

MEMORANDUM

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

**MEETING DATE:** December 4, 2012  
**TIME:** 3:30 PM  
**LOCATION:** WO 22 Room 4311  
**APPLICATION:** NDA 204412  
**DRUG NAME:** (b) (4) (mesalamine) delayed-release capsules, 400 mg  
**TYPE OF MEETING:** Proposed Proprietary Name

**MEETING CHAIR:** Denise Baugh

**MEETING RECORDER:** Phong Do

**FDA ATTENDEES:**

Lubna Merchant, Pharm.D., M.S., Team Leader, DMEPA  
Denise Baugh, Pharm.D., Safety Evaluator, DMEPA  
Franklin Stephenson, M.S., SRPM Team Leader  
Phong Do, Pharm.D., SRPM

**EXTERNAL CONSTITUENT ATTENDEES:**

Wei Zhuang, Sr. Manager, Regulatory Affairs  
Alvin Howard, Sr. Vice President, Regulatory Affairs

**Background**

Warner Chilcott Co, LLC submitted the proposed primary proprietary name, (b) (4) for NDA 202241, (b) (4) (mesalamine) delayed-release capsules, 400 mg on October 2, 2012.

DEMPEA requested this teleconference to inform Warner Chilcott Pharmaceuticals of preliminary concerns identified during the review of the proposed proprietary name, (b) (4)

**Product Information**

- Active Ingredient: Mesalamine
- Indication of Use: Treatment of mildly to moderately active ulcerative colitis and maintenance of remission of ulcerative colitis
- Route of Administration: Oral
- Dosage Form: Delayed-release Capsules

- Strength: 400 mg
- Dose and Frequency: 800 mg by mouth three times daily or 1600 mg by mouth daily in divided doses
- How Supplied: Bottles of 180 capsules
- Storage: Room temperature
- Container and Closure System: Child-resistant cap

## **Meeting Objectives**

This is a courtesy call to notify Warner Chilcott, Inc. of DMEPA's preliminary findings and safety concerns with regards to the proposed proprietary name, (b) (4) submitted August 7, 2012.

## **Discussion**

DMEPA's preliminary review has identified that the proposed proprietary name, (b) (4) is unacceptable from a look-alike and sound-alike perspective for the following reasons;

1. The name is similar in spelling and phonetically similar to the marketed product, (b) (4) Tablet. The name pair shares four of the 6 letters in identical positions (b) (4) differing only by two letters (b) (4). In addition, the name pair has (b) (4) syllables with similar stresses in each syllable. The (b) (4) syllables (b) (4) are identical in sound and (b) (4) syllables (b) (4) sound similar. The similar spelling and pronunciation makes the names indistinguishable in speech and gives the name a similar appearance when scripted as well. The similar sound was confirmed in our simulated voice prescription study where a participant stated (b) (4) sounded like (b) (4). Therefore, DMEPA objects to the proposed name based on 21 CFR 201.10(c)(5), which states "The labeling of a drug may be misleading by reason of designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."
2. During our review of the proposed name, (b) (4) we identified an identical foreign name which is the active ingredient for (b) (4) and is marketed in Mexico. U.S. proprietary names that are identical to or almost identical in spelling or pronunciation to foreign names can cause confusion that can lead to medication errors such as wrong drug errors and the retrieval of wrong drug information. We can provide real world examples of how these errors have happened in the past so that you are aware of how they can occur (*details are provided below should the Applicant request them*). Additionally, using a proprietary name in the U.S. that is identical to or almost identical in spelling or pronunciation to a foreign name may inhibit your ability to obtain a global proprietary name if that is your goal. Please take this advice into consideration when submitting future proprietary names for this product.

### **Regulatory Options**

1. Wait for DMEPA to complete the review of (b) (4) by the OSE PDUFA goal date of January 1, 2013 and issue a formal decision (most likely a denial of the name).
2. Withdraw the proposed name, (b) (4) and submit another name for review.

The sponsor agreed to withdrawal the proposed name, (b) (4) and will submit a new name and additional alternates as soon as possible.

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PHONG DO  
12/05/2012

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Subject:** NDA 204412 WC3045 (mesalamine) Delayed-Release Capsules- Information Request  
**Date:** Tuesday, November 20, 2012 8:58:45 AM

---

Hello Wei,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NDA 204412, WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

- **For the NDA study PR08210, please submit descriptive stats and bioequivalence (BE) analyses (using the reference-scaled BE approach) for the following partial area under the curve (AUC) parameters: AUC0-12 and AUC12-48.**

**We request response by November 27, 2012.**

Please let me know if you have any questions or concerns.

Thank you.

**Anissa Davis, RN, BSN, CPHM**  
CDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration/Center for Drug Evaluation and Research  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
(301) 796-5016 (office)  
(301) 796-9904 (fax)  
[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)

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ANISSA A DAVIS  
11/20/2012

**From:** [Davis, Anissa](#)  
**To:** ["Wei Zhuang"](#)  
**Subject:** NDA 204412: WC3045 (mesalamine) Delayed-Release Capsule-Information Request  
**Date:** Friday, November 16, 2012 10:39:35 AM

---

Hello Wei,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NDA 204412, WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

**Please provide the Agency a copy of the pediatric plan for this application. If you have already submitted a pediatric plan, please provide the location.**

**The Agency request a response to this Information Request (IR) by November 26, 2012.**

Thank you and contact me if you have any questions.

***Anissa Davis, RN, BSN, CPHM***

*CDR, USPHS Commissioned Corps*

*Regulatory Project Manager*

*Food and Drug Administration/Center for Drug Evaluation and Research*

*Division of Gastroenterology/Inborn Errors Products*

*Office of Drug Evaluation III*

*(301) 796-5016 (office)*

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***[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)***

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ANISSA A DAVIS  
11/16/2012

**From:** [Davis, Anissa](#)  
**To:** ["Wei Zhuang"](#)  
**Subject:** NDA 204412 WC3045 (mesalamine) Delayed-Release Capsule- Information Request  
**Date:** Wednesday, October 24, 2012 3:58:06 PM

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Good Afternoon Wei,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for WC3045 (mesalamine) Delayed-Release Capsules 400mg. In reviewing your submission, the team has the following request for information:

**Please send the SAS codes used in the bioequivalence analysis of the PK data.**

**We request a response by October 31, 2012.**

Please let me know if you have any questions.

Thank you.

**Anissa Davis, RN, BSN, CPHM**  
CDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration/Center for Drug Evaluation and Research  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
(301) 796-5016 (office)  
(301) 796-9904 (fax)  
[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)

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ANISSA A DAVIS  
10/24/2012

STACY R BARLEY  
10/25/2012



NDA 204412

**PROPRIETARY NAME  
REQUEST WITHDRAWN**

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

Attention: Wei Zhuang  
Senior Manager, Regulatory Affairs

Dear Ms. Zhuang:

Please refer to your New Drug Application (NDA) dated July 31, 2012, received August 1, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Mesalamine Delayed-release Capsules, 400 mg.

We acknowledge receipt of your September 26, 2012, correspondence, on September 26, 2012, notifying us that you are withdrawing your request for a review of the proposed proprietary name (b) (4). This proposed proprietary name request is considered withdrawn as of September 26, 2012.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Franklin Stephenson, Team Leader, Project Management Staff in the Office of Surveillance and Epidemiology, at (301) 796-3872. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Anissa Davis, at (301) 796-5016.

Sincerely,

*{See appended electronic signature page}*

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

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FRANKLIN T STEPHENSON  
10/10/2012

CAROL A HOLQUIST  
10/10/2012



NDA 204412

**FILING COMMUNICATION**

Warner Chilcott Company, LLC  
c/o Warner Chilcott (US), LLC  
Attention: Wei Zhuang  
Senior Manager, Regulatory Affairs  
100 Enterprise Drive  
Rockaway, NJ 07866

Dear Ms. Zhuang:

Please refer to your New Drug Application (NDA) dated July 31, 2012, received August 1, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for WC3045 (mesalamine) Delayed-Release Capsules 400mg.

We also refer to your amendments dated August 7, 2012, September 6, 2012, September 14, 2012, September 18, 2012, September 25, 2012, and September 26, 2012.

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 **Priority**. Therefore, the user fee goal date is February 1, 2013.

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 requirement/commitment requests by January 11, 2013.

During our filing review of your application, we identified the following potential review issues and request you submit the following information, if applicable:

1. The scientific rationale and data to support partial waiver (e.g. epidemiologic information

and use data for Asacol and other mesalamine products in pediatric patients) was not included.

2. Due to the lack of a food effect study, there will be restrictive language in regard to dosing if the NDA is approved.
3. We recommend that you evaluate if alcohol induces dose dumping for your product. First, you should conduct the *in vitro* alcohol induced dose dumping testing. Depending on the result of this testing, you may have to follow-up with an *in vivo* alcohol-dose dumping study.

The following points should be considered during the evaluation of the *in vitro* alcohol induced dose dumping of your MR product:

- i. Dissolution testing should be conducted using the optimal dissolution apparatus and agitation speed. Dissolution data should be generated from 12 dosage units (n=12) at multiple time points to obtain a complete dissolution profile.
- ii. The following alcohol concentrations for the *in vitro* dissolution studies are recommended in the currently proposed media: 0%, 5%, 10%, 20%, and 40%.
- iii. The shape of the dissolution profiles should be compared to determine if the modified release characteristics are maintained, especially in the first 2 hours.
- iv. The  $f_2$  values assessing the similarity (or lack thereof) between the dissolution profiles should be estimated (using 0% alcohol as the reference).
- v. The report with the complete data (i.e., individual, mean, SD, comparison plots,  $f_2$  values, etc.) collected during the evaluation of the *in vitro* alcohol induced dose dumping study should be provided for review.

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. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues:

4. Highlights Limitation (HL) Statement: The bolded HL Limitation Statement must be on the line immediately beneath the HL heading and must state: “These highlights do not include all the information needed to use (insert name of drug product in UPPER CASE) safely and effectively. See full prescribing information for (insert name of drug product in UPPER CASE).” Please note that you did not capitalize drug name in the last sentence.

5. Revision Date: Bolded revision date (i.e., “Revised: MM/YYYY or Month Year”) must be at the end of HL. Do not include numbers at this time.
6. Cross-references: Submit references in title case rather than in all capital letters. For example, [*see Warnings and Precautions (5.2)*].

We request that you resubmit labeling that addresses these issues by October 15, 2012. The resubmitted labeling will be used for further labeling discussions.

Please respond only to the above requests for 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.

### **PROMOTIONAL MATERIAL**

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

### **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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a partial waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial waiver request is denied.

We acknowledge receipt of your request for a partial deferral of pediatric studies for this application. Once we have reviewed your request, we will notify you if the partial deferral request is denied.

If you have any questions, call Anissa Davis, Regulatory Project Manager, at (301) 796-5016.

Sincerely,

*{See appended electronic signature page}*

Andrew Mulberg, M.D., F.A.A.P., C.P.I.  
Deputy Director  
Division of Gastroenterology and Inborn Errors  
Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/  
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ANDREW E MULBERG

09/28/2012

signing on behalf of Donna Griebelm, MD

## MEMORANDUM OF TELECON

DATE: September 24, 2012

APPLICATION NUMBER: NDA 204412 (mesalamine)

BETWEEN:

Name: Wei Zhuang  
Phone: 973-907-7063  
Representing: Warner Chilcott Company, LLC (US Agent: Warner Chilcott (US), LLC)

AND

Name: Anissa Davis, RN, CPHM, Regulatory Project Manager, Division of Gastroenterology and Inborn Errors Products (DGIEP)

Stacy Barley, RN, MSN, MHA, Senior Regulatory Project Manager, DGIEP

SUBJECT: To Verify and Confirm Information Pertaining to the Application.

Wei Zhuang, representative for Warner Chilcott Company was notified via telephone at 2:25pm to discuss the pending application NDA# 204412. Discussion points were as follows:

- 1) Sponsor verified that they will submit the English translation of the Batch records today.
- 2) Sponsor will submit a revised FDA Form 356h to reflect the dosage form as "Delayed-Release Capsule".
- 3) Sponsor will submit a revised FDA Form 3674 with corrected date under item #2 of the form (changing 7/30/2010 to 7/30/2012).
- 4) Sponsor verified that name and signature on FDA Form 3454 represents the and not the US Agent.
- 5) Sponsor will confirm with her labeling team regarding the status of the Patient Information Labeling.
- 6) The Pediatric Drug Development plan was not submitted with the application. Sponsor was notified and was notified that a formal request will be issued in an official correspondence.

The Sponsor verbalized understanding. The call ended at 2:31pm.

Anissa Davis, RN, CPHM  
Regulatory Project Manager  
Division of Gastroenterology and Inborn Errors  
Product

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/s/  
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ANISSA A DAVIS  
09/24/2012

STACY R BARLEY  
09/25/2012

**From:** [Davis, Anissa](#)  
**To:** "Wei Zhuang"  
**Cc:** [Barley, Stacy](#)  
**Subject:** RE: NDA 204412 mesalamine: Information request update  
**Date:** Wednesday, September 19, 2012 1:41:08 PM

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Our review team has ongoing discussion regarding your approach as mentioned in the email below.

The regulations require the batch records; therefore, it appears that your description does not provide enough information. A translated English version of both the Master and executed Batch records is needed. Please amend your NDA with a commitment statement that you will provide the documents in English translation no later than October 15, 2012.

We will contact you with any additional comments in the near future.

**Anissa Davis, RN, BSN, CPHM**  
CDR, USPHS Commissioned Corps  
Regulatory Project Manager  
Food and Drug Administration/Center for Drug Evaluation and Research  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
(301) 796-5016 (office)  
(301) 796-9904 (fax)  
[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)

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**From:** Wei Zhuang [mailto:wei.zhuang@wcrx.com]  
**Sent:** Thursday, September 13, 2012 6:20 PM  
**To:** Barley, Stacy  
**Cc:** Davis, Anissa  
**Subject:** Re: NDA 204412 mesalamine: Information request 9/13/12

Hi Stacy,

I left a voice mail message for you and would like to get clarity on the below Agency request.

In the FDA guidance for drug product, the Agency recommends to provide master batch record or a comparable detailed description of product process. We provided the detailed description of manufacturing process for WC3045 capsules in section 3.2.P.3.3, since the manufacturing site is in (b) (4) and the batch records are in (b) (4). Could you please let me know if this approach is acceptable? If not, could you please let me know if we need to provide both the Executed Batch Record and the Master Batch Record in English? Lastly, if the batch records need to be translated, would it be helpful if we provide the (b) (4) batch records immediately and follow-up as quickly as

possible with the translated version of the batch records.

If you would like to discuss, please call me on 973-647-8139.

Thanks & Kind Regards,

Wei

---

*Wei Zhuang*  
*Senior Manager, Regulatory Affairs*  
*Warner Chilcott (US), LLC*  
*100 Enterprise Drive*  
*Rockaway, NJ 07866*  
*973.907.7063 (office)*  
*973.647.8139 (BB)*  
*973.442.3280 (fax)*  
[wei.zhuang@wcrx.com](mailto:wei.zhuang@wcrx.com)

From: "Barley, Stacy" <[Stacy.Barley@fda.hhs.gov](mailto:Stacy.Barley@fda.hhs.gov)>  
To: ""Wei Zhuang" <[wei.zhuang@wcrx.com](mailto:wei.zhuang@wcrx.com)>  
Cc: "Davis, Anissa" <[Anissa.Davis@fda.hhs.gov](mailto:Anissa.Davis@fda.hhs.gov)>  
Date: 09/13/2012 02:51 PM  
Subject: NDA 204412 mesalamine: Information request 9/13/12

---

Hello Wei,

I am covering for Anissa Davis and have the following information request regarding NDA 204412:

We are unable to locate the Regional Information section of your submission. In particular, we are unable to find the Executed Batch Record nor the Master Batch Record. If you have submitted these documents, please specify the location in which we would be able to retrieve them. If the documents have not been submitted, please formally submit them immediately to help facilitate the continuation of our review. Thank you!

***Stacy Barley, RN, M.S.N., M.H.A.***  
***CDR, USPHS Commissioned Corps***  
***Senior Regulatory Project Manager***  
***Division of Gastroenterology/Inborn Errors Products***  
***Office of Drug Evaluation III***  
***CDER/FDA***  
***(301) 796-2137 (office)***  
***(301) 796-9905 (fax)***  
***[stacy.barley@fda.hhs.gov](mailto:stacy.barley@fda.hhs.gov)***

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\*\*\*\*\* WC Confidentiality Note: \*\*\*\*\*

This email transmission and any documents accompanying this email transmission contain information from Warner Chilcott, PLC, which is confidential.  
The information is intended only for the use of the intended recipient. If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution or the taking of any action in reliance on the contents of this email information is strictly prohibited, and that the documents should be returned to Warner Chilcott immediately. If you have received this email in error please notify us immediately by replying to the email address set forth above.

\*\*\*\*\* Thank you \*\*\*\*\*

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/s/  
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ANISSA A DAVIS  
09/19/2012

## MEMORANDUM OF TELECON

DATE: September 17, 2012

APPLICATION NUMBER: NDA 204412 (mesalamine)

BETWEEN:

Name: Wei Zhuang  
Phone: 973-907-7063  
Representing: Warner Chilcott Company, LLC (US Agent: Warner Chilcott (US), LLC)

AND

Name: Anissa Davis, RN, CPHM, Regulatory Project Manager, Division of Gastroenterology and Inborn Errors Products (DGIEP)  
  
Stacy Barley, RN, MSN, MHA, Senior Regulatory Project Manager, DGIEP

SUBJECT: To Clarify Questions and Responses related to the Information Requests Submitted by the FDA on September 12 and 13, 2012.

Wei Zhuang, representative for Warner Chilcott Company was notified via telephone at 12:04pm to discuss the pending application NDA# 204412. Three topics of discussion were as follows:

- 1) Status of their response and question to the FDA information request dated 9/13/12 for additional chemistry information
- 2) A response to their question regarding notification of review classification (Priority vs Standard)
- 3) Their response to the FDA information request dated 9/12/12 regarding an annotated label

The Sponsor was notified that their clarification question regarding the FDA's information request for the chemistry batch record is currently being reviewed by the team. The FDA will provide a response as soon as possible, at which time the Sponsor can submit all supporting documents to the application.

The Sponsor was informed that the notification regarding the review classification will be issued by day 60 in an official letter.

The sponsor was notified to edit their label using "track changes" format and submit a courtesy copy via email. If the format is acceptable, they will be notified to submit the annotated label to the application.

The sponsor verbalized understanding. The call ended at 12:12pm.

Anissa Davis, RN, CPHM  
Regulatory Project Manager  
Division of Gastroenterology and Inborn Errors Product

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ANISSA A DAVIS  
09/17/2012

STACY R BARLEY  
09/17/2012

**From:** Barley, Stacy  
**Sent:** Thursday, September 13, 2012 3:56 PM  
**To:** 'Wei Zhuang'  
**Cc:** Davis, Anissa  
**Subject:** NDA 204412 mesalamine: Information request 9.13.12 (contact information)  
 Hello Wei,

Please provide me with the following missing information **highlighted in red** font by close of business 9/18/12 (formally to the application as well as a courtesy copy via email):

<b>Facility #1 (Clinical Sites)</b> Name: Worldwide Clinical Trials Drug Development Solutions Address: 2455 N.E. Loop 410, Suite 150 San Antonio, TX 78217 (Tel) 210 635-1500 (Fax)	 (b) (4) (Tel) (Fax)
Clinical Investigator: Dr. Cynthia Zamora (email)	<b>Principal Analytical Investigator:</b> (email)
<b>Facility #2</b> Comprehensive Clinical Development Address: 3400 Enterprise Way Miramar, FL 33025 (Tel) (Fax)	
Clinical Investigator: Dr. Maria J. Gutierrez (email)	
<b>Facility #3</b> Comprehensive Clinical Development Address: 3745 Broadway Ave, Suite 100 Fort Myers, FL 33901 (Tel) 239-461-8600 (Fax)  Clinical Investigator: Dr. Pedro Ylisastigui (email)	

Thank you!

**Stacy Barley, RN, M.S.N., M.H.A.**  
**CDR, USPHS Commissioned Corps**  
**Senior Regulatory Project Manager**  
**Division of Gastroenterology/Inborn Errors Products**  
**Office of Drug Evaluation III**  
**CDER/FDA**  
**(301) 796-2137 (office)**  
**(301) 796-9905 (fax)**  
**stacy.barley@fda.hhs.gov**

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STACY R BARLEY  
09/13/2012

**From:** [Barley, Stacy](#)  
**To:** ["Wei Zhuang"](#)  
**Cc:** [Davis, Anissa](#)  
**Subject:** NDA 204412 mesalamine: Information request 9/13/12  
**Date:** Thursday, September 13, 2012 2:51:00 PM

Hello Wei,

I am covering for Anissa Davis and have the following information request regarding NDA 204412:

We are unable to locate the Regional Information section of your submission. In particular, we are unable to find the Executed Batch Record nor the Master Batch Record. If you have submitted these documents, please specify the location in which we would be able to retrieve them. If the documents have not been submitted, please formally submit them immediately to help facilitate the continuation of our review. Thank you!

*Stacy Barley, RN, M.S.N., M.H.A.  
CDR, USPHS Commissioned Corps  
Senior Regulatory Project Manager  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
CDER/FDA  
(301) 796-2137 (office)  
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stacy.barley@fda.hhs.gov*

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STACY R BARLEY  
09/13/2012

**From:** [Barley, Stacy](#)  
**To:** ["Wei Zhuang"](#)  
**Cc:** [Davis, Anissa](#)  
**Subject:** NDA 204412 mesalamine: Information request 9/13/12  
**Date:** Thursday, September 13, 2012 2:51:00 PM

---

Hello Wei,

I am covering for Anissa Davis and have the following information request regarding NDA 204412:

We are unable to locate the Regional Information section of your submission. In particular, we are unable to find the Executed Batch Record nor the Master Batch Record. If you have submitted these documents, please specify the location in which we would be able to retrieve them. If the documents have not been submitted, please formally submit them immediately to help facilitate the continuation of our review. Thank you!

*Stacy Barley, RN, M.S.N., M.H.A.  
CDR, USPHS Commissioned Corps  
Senior Regulatory Project Manager  
Division of Gastroenterology/Inborn Errors Products  
Office of Drug Evaluation III  
CDER/FDA  
(301) 796-2137 (office)  
(301) 796-9905 (fax)  
stacy.barley@fda.hhs.gov*

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/s/  
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STACY R BARLEY  
09/13/2012

**From:** [Davis, Anissa](#)  
**To:** ["Wei Zhuang"](#)  
**Cc:** [Barley, Stacy](#)  
**Subject:** Request for Information (NDA# 204412)  
**Date:** Wednesday, September 12, 2012 3:27:52 PM

---

Good Afternoon Wei,

We are in the process of reviewing your application, NDA 204412, and request the following information:

- Please provide an annotated word copy of your label as a formal submission to your application as well as a courtesy copy via email
- Provide a projected plan regarding removal of your previously approved product (application NDA 019651) from the market. Include the date in which manufacturing will cease. This information is necessary for us to determine if the application (NDA 204412) will be a priority or standard review if filed.

If you have any questions, please contact me and copy Stacy Barley at [stacy.barley@fda.hhs.gov](mailto:stacy.barley@fda.hhs.gov)

Thank you,

Anissa

***Anissa Davis, RN, BSN, CPHM***  
*CDR, USPHS Commissioned Corps*  
*Regulatory Project Manager*  
*Division of Gastroenterology/Inborn Errors Products*  
*Office of Drug Evaluation III*  
*CDER/FDA*  
*(301) 796-5016 (office)*  
*(301) 796-9905 (fax)*  
[\*\*\*Anissa.Davis@fda.hhs.gov\*\*\*](mailto:Anissa.Davis@fda.hhs.gov)

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ANISSA A DAVIS  
09/12/2012

**From:** [Davis, Anissa](#)  
**To:** "[ahoward@wcrx.com](mailto:ahoward@wcrx.com)"  
**Subject:** Request for Information (NDA# 204412)  
**Date:** Tuesday, September 04, 2012 11:46:48 AM

---

Dear Mr. Howard,

As mentioned earlier this morning, I will be the new RPM managing NDA 204412/mesalamine delayed-release capsules. The team is preparing for a meeting related to this application and has the following request for information. We request a response by September 7, 2012. You may provide your initial response by email, however, please also send this information to your NDA for the administrative record.

**Please clarify whether a food-effect PK study was conducted with the new mesalamine formulation. If yes, provide the location of the study report and datasets in the NDA. If no, provide the rationale in this regard.**

If you have any questions, please contact me.

***Anissa Davis, RN, BSN, CPHM***  
*CDR, USPHS Commissioned Corps*  
*Regulatory Project Manager*  
*Division of Gastroenterology/Inborn Errors Products*  
*Office of Drug Evaluation III*  
*CDER/FDA*  
*(301) 796-5016 (office)*  
*(301) 796-9905 (fax)*  
[\*\*\*Anissa.Davis@fda.hhs.gov\*\*\*](mailto:Anissa.Davis@fda.hhs.gov)

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ANISSA A DAVIS  
09/12/2012



NDA 204412

**NDA ACKNOWLEDGMENT**

Warner Chilcott Company, LLC  
c/o Warner Chilcott (US), LLC  
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: WC3045 (mesalamine) Delayed-Release Capsules

Date of Application: July 31, 2012

Date of Receipt: August 1, 2012

Our Reference Number: NDA 204412

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 September 30, 2012, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

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 Gastroenterology and Inborn Errors Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to [SecureEmail@fda.hhs.gov](mailto:SecureEmail@fda.hhs.gov). Please note that secure email may not be used for formal regulatory submissions to applications. If you have any questions, call CDR Stacy Barley, Senior Regulatory Project Manager, at (301) 796-2137.

Sincerely,

*{See appended electronic signature page}*

Stacy Barley, R.N., M.S.N., M.H.A.  
CDR/USPHS  
Senior Regulatory Project Manager  
Division of Gastroenterology and Inborn Errors  
Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/  
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STACY R BARLEY  
08/13/2012



IND 026093

**MEETING MINUTES**

Warner Chilcott  
Attention: Wei Zhuang  
Senior Manager, Regulatory Affairs  
100 Enterprise Drive  
Rockaway, NJ 07866

Dear Ms. Zhuang:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Asacol (mesalamine).

We also refer to the meeting between representatives of your firm and the FDA on June 13, 2012. The purpose of the meeting was to discuss plans for submitting a new formulation of the Asacol product in which the dibutyl phthalate is replaced with the alternate plasticizer, dibutyl sebacate.

A copy of the official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-2302.

Sincerely,

*{See appended electronic signature page}*

Kevin Bugin, MS, RAC  
Regulatory Health Project Manager  
Division of Gastroenterology and Inborn Errors Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure:  
Meeting Minutes



**FOOD AND DRUG ADMINISTRATION**  
CENTER FOR DRUG EVALUATION AND RESEARCH

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** Type B  
**Meeting Category:** Pre-Submission

**Meeting Date and Time:** June 13, 2012, from 1:00 to 2:00 PM, EST  
**Meeting Location:** 10903 New Hampshire Avenue  
White Oak Building 22, Conference Room: 1313  
Silver Spring, Maryland 20903

**Application Number:** IND 026093  
**Product Name:** Asacol (mesalamine) Capsules  
**Indication:** ulcerative colitis  
**Sponsor/Applicant Name:** Warner Chilcott

**Meeting Recorder:** Kevin Bugin  
**Meeting Chair:** Anil Rajpal

**FDA ATTENDEES**

Donna Griebel, M.D., Director,  
Division of Gastroenterology and Inborn Errors Products (DGIEP)  
Andrew Mulberg, M.D., F.A.A.P., C.P.I., Deputy, DGIEP  
Joyce Korvick, MD, MPH, Deputy Director of Safety, DGIEP  
Anil Rajpal, M.D., M.P.H., Clinical Team Leader, DGIEP  
Laurie Muldowney, M.D., Clinical Reviewer, DGIEP  
Sushanta Chakder, Ph.D., Nonclinical Reviewer, DGIEP  
Sue Chih Lee, Ph.D., Clinical Pharmacology Team Leader,  
Office of Clinical Pharmacology (OCP)  
Kristina Estes, Ph.D., Clinical Pharmacology Reviewer, OCP  
Mike Welch, Ph.D., Biometrics Team Leader, Office of Biometrics  
Marie Kowblansky, Ph.D., Quality Assessment Team Leader, Office of New Drug  
Quality Assessment (ONDQA)  
Angelica Dorantes, Ph.D., Biopharmaceutics Team Leader, ONDQA  
John Duan, Ph.D., Biopharmaceutics Reviewer, ONDQA  
Kevin Bugin, M.S., R.A.C., Regulatory Project Manager, DGIEP  
Mildred Wright, Project Manager, Pediatric and Maternal Health Staff (PMHS)  
Hari Sachs, M.D., Clinical Team Leader, PMHS  
Erica Radden, M.D., Clinical Reviewer, PMHS  
Chantal Phillips, R.N., Safety Regulatory Project Manager, DGIEP

Chitra Mahadevan, Project Manager, Office of Generic Drugs  
Valerie Gooding, electronic Submission Support Team, Office of Business Informatics

**SPONSOR ATTENDEES**

Tina deVries, PhD	Vice President, Clinical Pharmacology
Philip Krieter, PhD	Director, Clinical Pharmacology
Herman Ellman, MD	Senior Vice President, Clinical Development
Hans Griek, MD	Vice President, Medical Affairs
Cathy Coulter, PhD	Vice President, Pharmaceutical Development
Alvin Howard	Senior Vice President, Regulatory Affairs
Matthew Lamb, PharmD	Senior Director, Regulatory Affairs
Wei Zhuang	Senior Manager, Regulatory Affairs

## 1.0 BACKGROUND

Per FDA recommendations Warner Chilcott has developed a new formulation of Asacol (WC3045) in which dibutyl phthalate is replaced with the alternate plasticizer, dibutyl sebacate. In preparation for filing a new NDA to support marketing the new formulation, Warner Chilcott submitted a pre-submission, Type B, meeting request to the Division of Gastroenterology and Inborn Errors Products on April 24, 2012. The Division granted the meeting and scheduled it for June 13, 2012, at 1:00 PM, EST.

## 2. DISCUSSION

[Sponsor's questions are in plain font. Agency preliminary responses are in **bold** and discussion at the meeting is captured in *bold italics*.]

### CMC

1. Warner Chilcott has conducted the special dissolution study based on the Agency's advice received during the teleconference between the Agency and Warner Chilcott on November, 2, 2010 and detailed in the meeting minutes. The study demonstrated the similarity of dissolution profiles for the approved Asacol tablets, 400 mg and WC3045 capsules, 400 mg in multi-pH media. Does the Agency concur with the conclusion drawn from the special dissolution study?

#### **FDA Response:**

**Yes, we agree with your conclusion.**

2. Warner Chilcott proposes to submit 6 months stability data on 3 batches of WC3045 capsules at the time of submission and provide an additional 3 months stability data (9 months total) during the NDA review.

a. Does the Agency agree with this proposal in support of filing and review of the WC3045 NDA and agree that provision of the additional 3 months stability data during the review will not be classified as a major amendment and extend the PDUFA action date by 3 months?

#### **FDA Response:**

**It will be acceptable for you to submit six months of stability data (long term and accelerated) and to submit an additional 3 months of data while the NDA is under review, provided the supplementary data are received no later than at the midpoint of the review clock.**

b. The current shelf-life for approved Asacol (mesalamine) delayed-release tablets, 400 mg is 36 months. Does the Agency agree an 18 month shelf life at time of approval is appropriate given the available stability data and supporting information?

#### **FDA Response:**

**Expiration dating for your product will be based on the stability data that you submit for your newly formulated product.**

### **Clinical**

3. Warner Chilcott has conducted a PK study (Study PR-08210) of WC3045 capsules compared to Asacol (mesalamine) delayed-release tablets using a methodology suitable for highly variable drugs. Warner Chilcott recognizes that the results of this study need to be considered in light of the fact that within-subject standard deviation for the reference product exceeds 0.83 (CV>100 %) (see Question 4), and this may raise questions about the suitability of the methodology used in this study.

- a. Does the Agency conclude that WC3045 capsules have comparable PK profiles and are bioequivalent to Asacol (mesalamine) delayed-release tablets?

#### **FDA Response:**

**You need to submit the final study report with raw data for the Agency to make conclusions. Although we note that the study appears to have met the criteria for the reference scaled average bioequivalence method, we have the following two concerns:**

- **the mean profiles had appreciable differences between the new product and the approved product;**
- **samples were not collected beyond 48 hours.**

#### **Discussion:**

*The Sponsor agrees to provide the final study report with raw data as part of the NDA submission. The Agency emphasized that profile of the test drug should be similar to the reference, which is the major concern. However, the outliers will be taken into consideration for the difference between the reference and the test. The individual profiles will be reviewed in totality to determine if the difference in mean profile has implications in bioequivalence.*

*The Sponsor noted that in the current study (PR-08210) only 17% of subjects had measurable concentrations at 48 hours and any additional data from sampling beyond 48 hours would not have an impact on the study conclusion. The Agency will review the data and evaluate the impact in the overall establishment of bioequivalence.*

- b. Does the Agency agree with the evaluation of the pharmacokinetic parameter (b) (4)

#### **FDA Response:**

**We cannot agree at this time. We note that you did not perform sampling beyond 48 hours. Please submit your justification.**

#### **Discussion:**

*The Sponsor will provide the justification in the NDA.*

4. Does the Agency believe it is necessary to generate clinical efficacy and safety data to confirm the results of the special dissolution study and PK study given the within-subject variability for Cmax of the reference product in Study PR-08210 was approximately 200%, well exceeding the 100 percent threshold?

- a. If yes, can these clinical data be generated as part of a post-marketing requirement not to delay introduction of Asacol 400 mg dibutyl phthalate free capsules or will these data be required for the initial approval and have to be submitted as part of the original NDA submission?

**FDA Response:**

**No. Bioequivalence should be shown through a combination of PK studies and in vitro dissolution testing. We do not recommend comparative clinical endpoint studies to show bioequivalence for this product.**

5. If a clinical study is required, does the Agency agree that we can schedule a subsequent meeting to discuss the general design of the clinical study?

**FDA Response:**

**See the Response to Question 4.**

**NDA Review Process**

6. Does the FDA concur that a Priority Review designation with a 6-month review cycle may be appropriate for the WC3045 NDA, given the Agency's concern with the potential safety issue for the dibutyl phthalate excipient?

**FDA Response:**

**Although there is alternative available therapy, there is a safety advantage for your product relative to your currently marketed product and we will be committed to complete the review in a timely manner. The final decision on review priority will be made at the time of filing of the application.**

**Labeling Approach**

7. If an additional clinical study is not required, does the demonstration of bioequivalence using data from the PK study and the special dissolution study allow for the prescribing information in the labeling for Asacol, (mesalamine) delayed-release tablets, to be copied to the WC3045 capsule labeling? Warner Chilcott also recognizes that the labeling for WC3045 capsules would need to comply with the content and format labeling requirement of 21CFR201.56 (d) and 21CFR201.57 (PLR format). Does the Agency concur with this labeling approach?

**FDA Response:**

**The proposed labeling approach appears to be reasonable. We note that the change in dosage form and the formulation differences would need to be accounted for in the labeling. The final decision on labeling wording will be made during the course of the review of the NDA, and will likely include the recommendations of the Agency's Study Endpoints and Labeling Development team, Office of Prescription Drug Promotion, and Division of Medication Error Prevention and Analysis.**

**Cross-reference**

8. If a NDA submission based on currently available information including special dissolution and PK data is acceptable, Warner Chilcott plans to cross reference NDA 19-651 (Asacol 400-mg tablets) and intends on providing the following CTD sections in the WC3045 NDA:

- o Module 2
  - a. Section 2.3 – Quality Overall Summary
  - b. Section 2.5 – Clinical Overview
  - c. Section 2.7.1 – Summary of Biopharmaceutic studies
  - d. Section 2.7.4 – Summary of Clinical Safety (WC plans to provide the summary of safety information in this BE study only)
  - e. Section 2.7.5 - Reference
  - f. Section 2.7.6 – Synopses of Individual Studies
- o Module 3
  - a. Section 3.2.D – Drug Product
- o Module 5
  - a. Section 5.2 Tabular Listing of Studies
  - b. Section 5.3.1.2 (Comparative BA and BE study reports and related information).

The cross referenced information will be provided in CTD section 1.4.4 (Cross Reference to Other Applications) of WC3045 NDA and the information of those related cross reference sections will not be provided in the WC3045 NDA submission.

Does the Agency concur with this submission approach?

**FDA Response:**

**Yes. A PDF table should be placed in m1.4.4 (cross reference to other applications) with a description of what is being cross referenced, and where the original document resides. Hyperlinks to those documents are optional, but could be of help to reviewers, if provided. The table should include the following information, but not limited to, (1) the application number, (2) the date of submission (e.g., letter date), (3) the document name, (4) the submission identification (e.g., submission serial/sequence number, Module, eCTD Section etc.).**

9. NDA 19-651 for Asacol tablets, 400 mg was approved prior to the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c). (b) (4)

[REDACTED]

(b) (4) The pediatric study requirement for ages 0 to 4 years was waived because studies are impossible or highly impractical due to the small number of pediatric ulcerative colitis patients less than 5 years of age. Does the Agency concur that (b) (4)

**FDA Response:**

pediatric assessment must also be reviewed by the Pediatric Review Committee (PeRC).

A partial waiver for the 0 to 4 year age group appears appropriate. However, you must submit the scientific rationale and data to support your partial waiver request. Consider submitting data such as epidemiologic information and use data for Asacol and other mesalamine products in pediatric patients to support your request.

**Additional FDA comment:**

We remind you that you will need to adequately justify the safety of dibutyl sebacate as an excipient in the new formulation.

**Additional Discussion:**

*The Sponsor requested additional clarity regarding the limit of 100% intra-subject variability as noted in the August 2010 response to the Citizen's Petition, considering the Asacol product has been shown to have a variability (b) (4)%. Furthermore, the Sponsor requested clarity regarding sample size and the adequacy of 80% powering for future studies.*

*The Agency will follow-up and provide clarification as a post-meeting comment or as Advice at a later date.*

**Additional FDA Post-Meeting Comments:**

- 1. The intra-subject variability of (b) (4) will be acceptable so long as the study was properly conducted.*
- 2. We note that the new WC3045 capsule is size (b) (4) which is larger than the prior Asacol 400 mg tablets, and may be difficult for pediatric patients to swallow. PREA requires you to make reasonable attempts to produce an age appropriate pediatric formulation. If you are unable to develop an age-appropriate formulation, you must provide data to support this claim for review by the Division, and the submitted report will be publicly posted. Also, you may need to conduct a palatability/ability to swallow study to determine pediatric patient's ability to ingest the formulation.*

### 3.0 PRESCRIBING INFORMATION

Proposed prescribing information (PI) submitted with your application must conform to the content and format regulations found at 21 CFR 201.56 and 201.57.

Summary of the Final Rule on the Requirements for Prescribing Information for Drug and Biological Products, labeling guidances, sample tool illustrating Highlights and Table of Contents, an educational module concerning prescription drug labeling, and fictitious prototypes of prescribing information are available at:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm>. We encourage you to review the information at this website and use it as you draft prescribing information for your application.

### 4.0 MANUFACTURING FACILITIES

To facilitate our inspectional process, the Office of Manufacturing and Product Quality in CDER's Office of Compliance requests that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

**5.0 ATTACHMENTS AND HANDOUTS**

Warner Chillcott Slides

**WC3045**  
**Pre-NDA Meeting**

Warner Chilcott  
June 13, 2012



(b) (4)





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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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KEVIN B BUGIN  
07/10/2012



IND 026093

**MEETING MINUTES**

Warner Chilcott  
Attention: Matthew Lamb, Pharm.D.  
Senior Director, Regulatory Affairs  
100 Enterprise Drive  
Rockaway, NJ 07866

Dear Dr. Lamb:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Asacol (mesalamine) Delayed Release Tablets, 400 mg and Asacol HD (mesalamine) Delayed Release Tablets, 800 mg.

We also refer to the teleconference between representatives of your firm and the FDA on November 2, 2010. The purpose of the meeting was to discuss the requirements of special dissolution and pharmacokinetic testing necessary to establish bioequivalence between the currently marketed Asacol and Asacol HD tablets and those undergoing reformulation with the alternate plasticizer, dibutyl sebacate.

A copy of the official minutes of the teleconference is attached for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-3827.

Sincerely,

*{See appended electronic signature page}*

Roland Girardet, M.H.S., M.S., M.B.A.  
Regulatory Health Project Manager  
Division of Gastroenterology Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure



FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** C  
**Meeting Category:** Other

**Meeting Date and Time:** November 2, 2010, 9:00 a.m. – 10:00 a.m. EDT  
**Meeting Location:** Teleconference

**Application Number:** IND 026093  
**Product Name:** Asacol (mesalamine) Delayed Release Tablets, 400 mg and Asacol HD (meslamine) Delayed Release Tablets, 800 mg  
**Indication:** Mild to moderately active ulcerative colitis  
**Sponsor/Applicant Name:** Warner Chilcott

**Meeting Chair:** Robert Fiorentino, M.D., M.P.H., Acting Clinical Team Leader  
**Meeting Recorder:** Roland Girardet, M.H.S., M.S., M.B.A., Regulatory Health Project Manager

**FDA ATTENDEES**

**Division of Gastroenterology Products**

Donna Griebel, M.D., Director  
Robert Fiorentino, M.D., M.P.H., Acting Clinical Team Leader  
Ii-Lun Chen, M.D., Clinical Reviewer  
Kevin Bugin, M.S., R.A.C., Regulatory Health Project Manager  
Roland Girardet, M.H.S., M.S., M.B.A., Regulatory Health Project Manager

**Office of Regulatory Policy**

Patrick Raulerson, J.D., Regulatory Counsel

**Office of New Drug Quality Assessment**

Patrick Marroum, Ph.D., Biopharmaceutics Lead  
John Duan, Ph.D., Biopharmaceutics Reviewer

**Office of Translational Sciences**

Sue Chih Lee, Ph.D., Clinical Pharmacology Team Leader, Division of Clinical Pharmacology III

Meeting Minutes  
[Insert Meeting Type]  
DATE

[Insert Office/Division]

Kristina Estes, Pharm.D., Clinical Pharmacology Reviewer, Division of Clinical  
Pharmacology III  
Milton Fan, Ph.D., Biometrics Reviewer, Division of Biometrics III

**Office of Generic Drugs**

Xinyuan Zhang, Ph.D., Scientific Advisor

**European Medicines Agency**

Michael Berntgen, Ph.D., M.D.R.A., Head of Rheumatology, Respiratory,  
Gastroenterology and Immunology, Safety and Efficacy of Medicines, European  
Medicines Agency.

**SPONSOR ATTENDEES**

**Warner Chilcott**

Alvin Howard, Sr VP, Regulatory Affairs  
Matthew Lamb, PharmD, Sr Director, Regulatory Affairs  
Tina deVries, PhD, VP, Clinical Pharmacology  
Phil Krieter, PhD, Director, Clinical Pharmacology  
Herman Ellman, MD, Sr VP, Clinical Development  
John Caminis, MD, VP, Clinical Development  
Miriam Annette, PhD, Director, Biostatistics

(b) (4)

Cathy Coulter, PhD VP, Pharmaceutical Development

## 1.0 BACKGROUND

Warner Chilcott is in the process of reformulating Asacol and Asacol HD to replace dibutyl phthalate with the alternate plasticizer, dibutyl sebacate. During a Type C teleconference between the FDA's Division of Gastroenterology Products (DGP) and Warner Chilcott which was held on April 22, 2010, the FDA informed Warner Chilcott that as an alternative to conducting trials with clinical endpoints, it would be possible to establish bioequivalence between the two formulations through pharmacokinetic (PK) and special dissolution studies. During this teleconference, the FDA encouraged Warner Chilcott to request a meeting to discuss the details of the PK and special dissolution study requirements.

On August 5, 2010, Warner Chilcott submitted a meeting request to discuss the PK and special dissolution studies. The meeting was granted on August 23, 2010. The briefing package for the meeting was received on October 5, 2010. The FDA's preliminary comments to the questions in the briefing package were communicated to Warner Chilcott on October 29, 2010. The teleconference between Warner Chilcott and the DGP was held as scheduled on November 2, 2010.

## 2.0 DISCUSSION

(Questions in the briefing package are shown in plain font. FDA's preliminary responses are shown in **boldface**. Discussion at the meeting is shown in *bold italics*.)

### Question 1

Warner Chilcott proposes special dissolution testing over a range of pHs reflective of the characteristic release profile of Asacol (400 mg) and Asacol HD (800 mg) in addition to testing according to the drug product release test method (same as USP). Specifically, multipoint dissolution profiles will be obtained using (b) (4)

minutes to characterize the performance of the delayed-release tablets. The reformulated product should meet the USP specification and should have release profile comparable to that of the approved product. Does the Agency agree with this proposal for special dissolution testing?

### **FDA Response:**

**No. We recommend the following:**

**Apparatus: USP Apparatus 2 (paddle)**

**Pretreatment Stage: 2 hours in 0.1 N HCl at 100 rpm**

**Evaluation Stage: Each of**

- (1) pH 4.5 Acetate buffer at 50 rpm**
- (2) pH 6.0 Phosphate buffer at 50 rpm**
- (3) pH 6.5 Phosphate buffer at 50 rpm**

- (4) pH 6.8 Phosphate buffer at 50 rpm
- (5) pH 7.2 Phosphate buffer at 50 rpm
- (6) pH 7.5 Phosphate buffer at 50 rpm

**Volume: 900 mL**

**Temperature: 37°C**

**Sample times: 0, 10, 20, 30, 45, 60, 75, 90, 120, 150 minutes or as needed for profile comparison**

**At least 12 tablets from each lot (test and reference) should be used per test. The f2 metric should be used to compare dissolution profiles.**

**Discussion:**

*Warner Chilcott stated that an f2 metric value greater than 50 may not be achieved for all of the conditions. For this reason, Warner Chilcott proposed using alternative testing methods. The FDA stated that Warner Chilcott's proposal seemed appropriate as long as the Guidance for Industry: Dissolution Testing of Immediate Release Solid Oral Dosage Forms (FDA, 1997) was followed and that final agreement would ultimately be a review issue.*

**Question 2**

Asacol and Asacol HD formulations were designed to target drug release to the colon. The conventional pharmacokinetic parameters Cmax, AUC(0-tldc) where tldc is time of last determinable concentration, and AUC(0-infinity) may not meaningfully distinguish between products with materially different mesalamine release profiles at the sites of drug action.

The pharmacokinetic profiles of Asacol and Asacol HD tablets are characterized by a substantial lag-time, relatively long tmax values and the lack of log-linear terminal phase.

The important lag-time characteristic of the pharmacokinetic profile may be captured in an appropriate partial area parameter. AUC(0-t), where t corresponds to the median tmax for each formulation, may characterize and distinguish between products with materially different mesalamine release profiles, e.g. AUC(0-12h) for Asacol and AUC(0-16h) for Asacol HD. The sponsor is evaluating available study data to confirm that these partial areas would enable the unique mesalamine pharmacokinetic profiles for Asacol 400-mg or Asacol HD (800 mg) tablets to be distinguished.

The terminal phase most likely represents a combination of mesalamine absorption and elimination rather than only mesalamine elimination. Because the terminal phase is not loglinear, parameters such as AUC(0-infinity) and mean residence time (MRT) may not be determinable. The sponsor proposes that (b) (4) The sponsor considered whether (b) (4)

[REDACTED] (b) (4)  
[REDACTED]  
[REDACTED]  
[REDACTED]

The sponsor is proposing that the pharmacokinetic parameters [REDACTED] (b) (4) [REDACTED] are useful for determining whether mesalamine from test and reference products is absorbed at the same rate and to the same extent at the colon and rectum.

Does the Agency agree with this approach?

**FDA Response:**

**We agree with the use of partial AUC in addition to the traditional PK parameters (C<sub>max</sub> and AUC) to ensure profile similarity as part of a bioequivalence approach that also includes similarity of dissolution profiles.**

**For partial AUC, we recommend characterizing the latter portion of the PK profile which could include AUC<sub>t<sub>max</sub>-20</sub> or a defined range such as AUC<sub>12-24</sub>, for example.**

**Discussion:**

*Warner Chilcott proposed using [REDACTED] (b) (4) The FDA stated that it could not make a commitment on the appropriateness of the pharmacokinetic parameters at this time and that it would like Warner Chilcott to submit a detailed protocol. The FDA would evaluate the proposed study design and data analysis plan in the protocol and provide comments within 30 days of receipt of the protocol.*

Questions 3, 4 & 5

The Agency in their citizen petition response of August 20, 2010 regarding Asacol and Asacol HD and “follow-on” formulations of delayed release orally administered mesalamine drug products stated the following:

‘Since 2007, FDA’s Office of Generic Drugs has recommended methods for demonstrating bioequivalence in highly variable drugs using PK studies for generic drugs. These methods should be sufficient so long as the within-subject variability of the reference product does not exceed 100 percent, and most studies of Asacol and Asacol HD show within-subject variabilities below this upper bound. Accordingly, we conclude that an applicant seeking to show bioequivalence to Asacol or Asacol HD should be able to employ highly variable drug bioequivalence study methods to address and account for the high variability of plasma mesalamine concentrations associated with these products.’

The estimated within-subject variability for Asacol and Asacol HD in studies evaluated

By Warner Chilcott exceeds 100% for Cmax. The sponsor is relying on the data from Study 2006009 (submitted to IND 26,093 on July 27, 2007) as this was the largest study conducted to evaluate the pharmacokinetics of Asacol and Asacol HD. However, the Sponsor believes it may still be possible to utilize a highly variable drug approach including a replicate design and appropriate sample size to assess the change in plasticizer for Asacol and Asacol HD tablets.

3) Can the Agency share the data supporting the statement that within-subject variability for most studies with Asacol and Asacol HD does not exceed 100%?

**FDA Response:**

**Estimates of the within-subject variability can be obtained from replicate design studies (preferred) or from the residual variability in two-way crossover studies. The FDA cannot disclose all specific study numbers that contain this information. Among the data FDA evaluated, the Asacol HD NDA (021830) study 2001095 provided an estimate of residual variability (pooled between fed and fasted state) of less than 100% for AUC.**

**Discussion:**

*There was no discussion of this question during the meeting.*

4) Does the Agency agree that the methods for demonstrating bioequivalence in highly variable drugs using pharmacokinetic studies for generic drugs is suitable for pharmacokinetic characterization of a formulation change such as change in plasticizer for Asacol or Asacol HD?

**FDA Response:**

**Yes, a replicate reference design might be appropriate for this purpose, however, we reserve the right to analyze the data as we deem appropriate.**

**Discussion:**

*There was no discussion of this question during the meeting.*

5) Does the Agency agree that [REDACTED] (b) (4)

[REDACTED]

**FDA Response:**

[REDACTED] (b) (4)

**Discussion:**

*There was no discussion of this question during the meeting.*

Question 6

Warner Chilcott is considering possible reformulation of Asacol 400-mg tablets to an alternate dosage form. One such formulation being considered is a capsule formulation. The sponsor proposes that these special dissolution and pharmacokinetic studies would be adequate to support registration of this reformulation.

Does the Agency agree?

**FDA Response:**

**Yes, we agree that dissolution testing and pharmacokinetic studies would be the necessary studies for a change in dosage form. The adequacy of such data will be a review issue.**

**Discussion:**

*There was no discussion of this question during the meeting.*

**3.0 ISSUES REQUIRING FURTHER DISCUSSION**

There were no issues requiring further discussion.

**4.0 ATTACHMENTS AND HANDOUTS**

There were no attachments or handouts for the meeting minutes.

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ROLAND GIRARDET

11/05/2010



IND 026093

MEETING MINUTES

Warner Chilcott  
Attention: Ann Robbins, Ph.D.  
Regulatory Affairs  
8700 Mason Montgomery Rd.  
Mason, OH 45040

Dear Dr. Robbins:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Asacol (mesalamine) Delayed-Release Tablets, 400 mg and Asacol HD (mesalamine) Delayed-Release Tablets, 800 mg.

We also refer to the teleconference between representatives of your firm and the FDA on April 22, 2010. The purpose of the meeting was to discuss the appropriate non-inferiority margins for study outlines submitted on November 24, 2009.

A copy of the official minutes of the teleconference is attached for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call me at (301) 796-3827.

Sincerely,

*{See appended electronic signature page}*

Roland Girardet, M.H.S., M.S., M.B.A.  
Regulatory Project Manager  
Division of Gastroenterology Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure



**FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH**

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** C  
**Meeting Category:** Other

**Meeting Date and Time:** April 22, 2010, 2:00 to 3:00 p.m. EDT  
**Meeting Location:** Teleconference  
**Application Number:** IND 026093  
**Product Names:** Asacol (mesalamine) Delayed-Release Tablets, 400 mg  
Asacol HD (mesalamine) Delayed-Release Tablets, 800 mg  
**Indications:** Asacol: Treatment of mildly to moderately active  
ulcerative colitis and maintenance of remission  
Asacol HD: Treatment of moderately active ulcerative  
colitis  
**Sponsor/Applicant Name:** Warner Chilcott

**Meeting Chair:** John Hyde, Ph.D., M.D., Medical Team Leader  
**Meeting Recorder:** Roland Girardet, M.H.S., M.S., M.B.A., Regulatory Project  
Manager

**FDA ATTENDEES**

Donna Griebel, M.D., Director, Division of Gastroenterology Products (DGP)  
John Hyde, Ph.D., M.D., Medical Team Leader, DGP  
Ii-Lun Chen, M.D., Medical Reviewer, DGP  
Mike Welch, Ph.D., Deputy Director, Division of Biometrics III  
Milton Fan, Ph.D., Statistical Reviewer, Division of Biometrics III

**SPONSOR ATTENDEES**

Xuelian Chen, Biostatistician  
Tina de Vries, Ph.D., V.P., Clinical Pharmacology  
Preston Dunmon, M.D., F.A.C.P, F.A.C.C., Section head, Global Late Phase Clinical  
Development  
Heman Ellman, M.D., Sr. V.P., Clinical Development  
Alvin Howard, Sr. V.P., Regulatory Affairs

(b) (4)

## 1.0 BACKGROUND

Warner Chilcott is in the process of reformulating Asacol and Asacol HD by replacing the plasticizer, dibutyl phthalate (DBP) with the alternate plasticizer, dibutyl sebacate (DBS). On November 24, 2009, Warner Chilcott submitted (b) (4).

The meeting was granted and scheduled for April 22, 2010. On March 19, 2010, Warner Chilcott submitted a meeting background package. The FDA's preliminary comments to the questions in the background package were communicated to Warner Chilcott on the morning of April 22, 2010. The teleconference took place on April 22, 2010, from 2:00 to 3:00 p.m. EDT.

## 2.0 DISCUSSION

(Questions in the briefing package are shown in plain font. FDA's preliminary responses are shown in **boldface**. Discussion at the meeting is show in *bold italics*.)

### FDA PRELIMINARY COMMENT

**After further consideration and internal discussions with Clinical Pharmacology and Biopharmaceutics regarding the issues associated with conducting a clinical trial to establish bioequivalence based on clinical efficacy, we have determined that it will be acceptable to establish bioequivalence through special dissolution and pharmacokinetic (PK) studies.**

**Clinical studies are still an option for an approval, and may be necessary if bioequivalence cannot be established by those other means.**

**We feel it will be important to have an understanding of how the old and new formulations compare regarding dissolution and PK before we can advise you fully on what, if any, clinical studies you should conduct and what the regulatory considerations would be if clinical studies are necessary. We have provided some responses to your questions below, because they could still be relevant if you conduct a clinical study. However, we defer more complete responses until our discussions with you at the upcoming meeting.**

### Meeting Discussion

*Warner Chilcott requested that the FDA clarify why PK and special dissolution studies would be necessary prior to initiating clinical studies with a locally acting drug.*

*The FDA responded that the FDA's current opinion is that these two testing methods would provide the most sensitive way of comparing test and reference products. Clinical trials are*

*not thought to be sensitive enough to demonstrate bioequivalence of these two formulations. The FDA further stated that PK and dissolution testing was not a requirement prior to initiating clinical trials, but rather that these two testing methodologies could be used instead of a clinical trials.*

*If PK and dissolution testing results are not convincing, then a clinical trial may be necessary to establish equivalence based on clinical endpoints. However, if equivalence of the test and reference drug cannot be established based on the results of the PK and dissolution testing, the need to pursue clinical trials for Asacol and Asacol HD is unclear, because this would bring into question whether or not the new and old formulations are actually equivalent. If the two products are shown to be non-equivalent as a result of the PK and dissolution testing, a clinical trial would need to meet both non-inferiority and non-superiority margins, which may lead to an impractical study design.*

*Warner Chilcott stated that the FDA's comments seem to be dependent on the nature of the products and asked the FDA to elaborate on how the nature of the product may dictate the methods used to establish equivalence. The FDA stated that its comments were specifically for Asacol and Asacol HD, rather than mesalamine products in general.*

*Warner Chilcott stated that, since the PK testing would be done in normal volunteers, it would not be useful in determining efficacy in patients and asked if the PK was intended to serve another purpose. The FDA clarified that the PK testing, which would include evaluating, at a minimum, AUC, C<sub>max</sub>, and T<sub>max</sub>, was not intended to measure efficacy. Instead, the PK testing would be used to create a profile, which, in combination with in vitro dissolution testing at different pH levels, would allow the FDA to compare the reference and test product profiles and determine whether they were equivalent.*

## QUESTIONS AND PRELIMINARY RESPONSES

1. Does the Division agree that our justification for a [REDACTED] (b) (4) [REDACTED] is acceptable?

### FDA Response:

We do not agree. [REDACTED] (b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

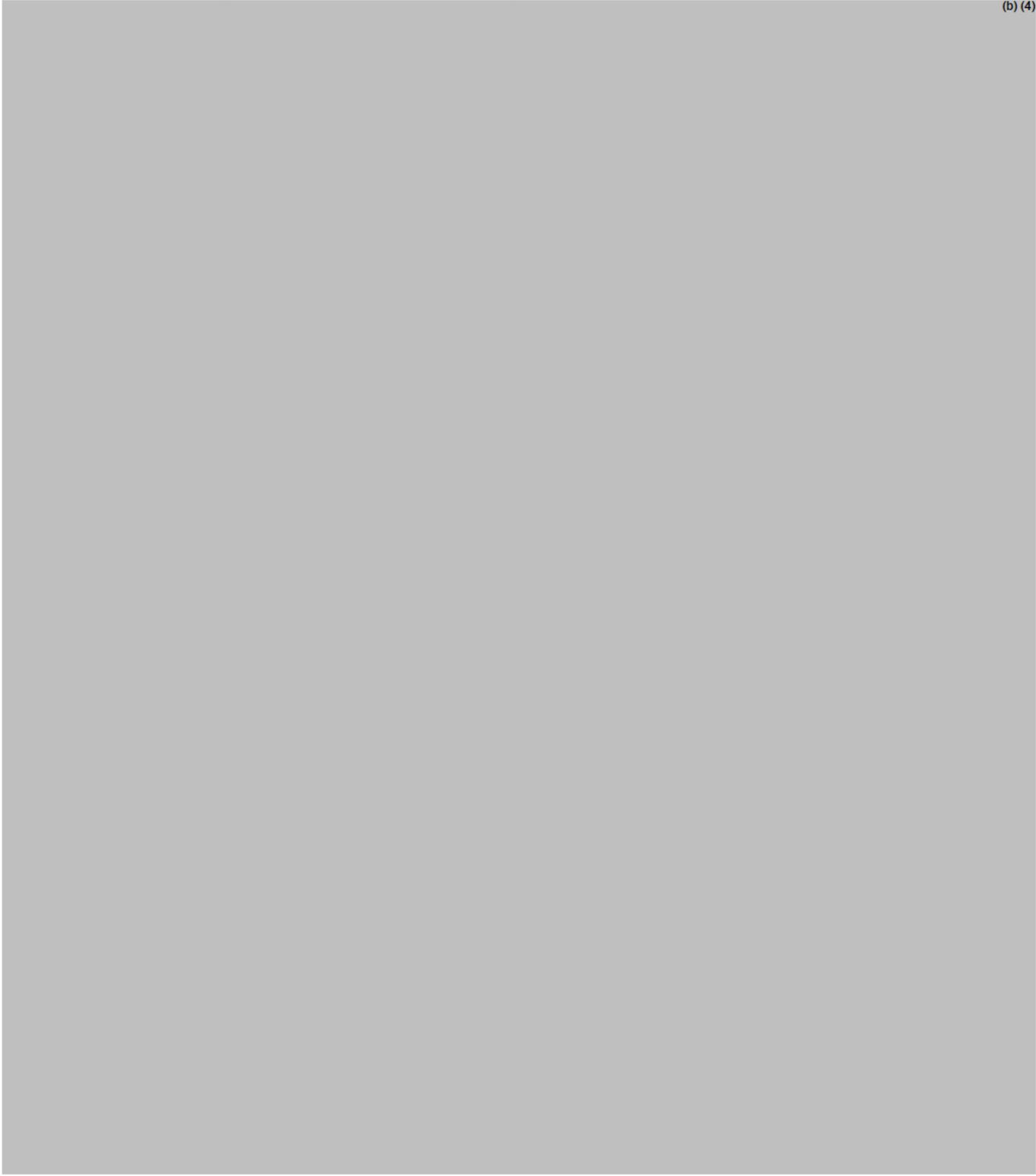
[REDACTED]

[REDACTED]

[REDACTED]

**Meeting Discussion**

(b) (4)



(b) (4)

2. The Division's proposal for a (b) (4)  
(b) (4)  
(b) (4)  
(b) (4)

**FDA Response:**

(b) (4)

**Meeting Discussion**  
*(See discussion under Question 1.)*

**Post-Meeting Comments**

(b) (4)

### 3.0 ISSUES REQUIRING FURTHER DISCUSSION

- **The specific requirements of the special dissolution and PK testing to establish bioequivalence between the old and new Asacol formulations will require further discussion with clinical pharmacology and biopharmaceutics staff. Warner Chilcott committed to requesting an additional meeting with the FDA to discuss these testing methodologies.**

- **Additional discussion will be necessary regarding the** (b) (4)  
[Redacted text block]

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
IND-26093	GI-1	WARNER CHILCOTT PHARMACEUTICA LS INC	5-AMINOSALICYLIC ACID (ASACOL) TABS

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/s/

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ROLAND GIRARDET  
05/20/2010