CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202107Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 202107 SUPPL # N/A HFD # 510

Trade Name Korlym

Generic Name mifepristone 300 mg Tablets

Applicant Name CORCEPT

Approval Date, If Known February 16, 2012

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)(2)

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

YES ☒ NO ☐

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

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

d) Did the applicant request exclusivity?

YES ☒ NO ☐

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

7

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?

N/A

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# 020687 Mifeprex (mifepristone) Tablets

NDA#

NDA#

2. Combination product.

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

N/A 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:
C1073-400 (efficacy)
C1073-415 (safety), long-term extension study

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"):

C1073-400 (efficacy)
C1073-415 (safety), long-term extension study

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 # 076480	YES ☒	! NO ☐
		! Explain:

Investigation #2		!
		!
IND # 076480	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?

N/A

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:

N/A

==========

Name of person completing form: Jena M. Weber
Title: Project Manager
Date: February 9, 2012

Name of Office/Division Director signing form: Mary Parks, M.D.
Title: Division Director, DMEP

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

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

/s/

JENA M WEBER
02/18/2012

MARY H PARKS
02/19/2012

Corcept
THERAPEUTICS

February 17, 2012

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets
Amendment to a Pending Application: Final Labeling

Dear Ms. Weber:

Attached please find the final Package Insert for Korlym 300 mg Tablets. We consider this, together with the final Medication Guide that was submitted via e-mail to you today, as the Final Printed Labeling for Korlym. This label is being sent to you via e-mail, and also will be submitted officially to the NDA.

Please let me know if you have any questions regarding this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

505(b)(2) ASSESSMENT

Application Information		
NDA # 202107	NDA Supplement: N/A	Efficacy Supplement Type : N/A
Proprietary Name: Korlym Established/Proper Name: mifepristone Dosage Form: Tablets Strengths: 300 mg		
Applicant: Corcept Therapeutics		
Date of Receipt: April 18, 2011		
PDUFA Goal Date: February 18, 2012	Action Goal Date: **February 17, 2012**	
Proposed Indication: This new drug application provides for the use of Korlym (mifepristone) for the control of hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have diabetes mellitus type 2 or glucose intolerance and have failed surgery or are not candidates for surgery.		

GENERAL INFORMATION

1) Is this application for a recombinant or biologically-derived product and/or protein or peptide product *OR* is the applicant relying on a recombinant or biologically-derived product and/or protein or peptide product to support approval of the proposed product?

YES ☐ NO ☒

*If "**YES** "contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

INFORMATION PROVIDED VIA RELIANCE (LISTED DRUG OR LITERATURE)

2) List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug or by reliance on published literature. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

Source of information* (e.g., published literature, name of referenced product)	Information provided (e.g., pharmacokinetic data, or specific sections of labeling)
NDA 20687 Mifeprex (mifepristone) Tablets	Nonclinical data

*each source of information should be listed on separate rows

3) Reliance on information regarding another product (whether a previously approved product or from published literature) must be scientifically appropriate. An applicant needs to provide a scientific "bridge" to demonstrate the relationship of the referenced and proposed products. Describe how the applicant bridged the proposed product to the referenced product(s). (Example: BA/BE studies).

This 505(b)(2) application for (b) (4) (mifepristone) relies in part on the nonclinical fertility and teratogenicity data in the Mifeprex® label (NDA 2068, mifepristone, Population Council). The nonclinical toxicology studies conducted under IND 76480 are considered sufficient to bridge the nonclinical findings in the Mifeprex® label to (b) (4).

RELIANCE ON PUBLISHED LITERATURE

4) (a) Regardless of whether the applicant has explicitly stated a reliance on published literature to support their application, is reliance on published literature necessary to support the approval of the proposed drug product (i.e., the application *cannot* be approved without the published literature)?

YES ☐ NO ☒
*If "**NO**," proceed to question #5.*

(b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

YES ☐ NO ☐
*If "**NO**", proceed to question #5.*
*If "**YES**", list the listed drug(s) identified by name and answer question #4(c).*

(c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?

YES ☐ NO ☐

RELIANCE ON LISTED DRUG(S)

Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #5-9 accordingly.

5) Regardless of whether the applicant has explicitly referenced the listed drug(s), does the application **rely** on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?

YES ☒ NO ☐
*If "**NO**," proceed to question #10.*

6) Name of listed drug(s) relied upon, and the NDA/ANDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

Name of Drug	NDA/ANDA #	Did applicant specify reliance on the product? (Y/N)
Mifeprex (mifepristone) Tablets	NDA 20687	Y

Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

7) If this is a (b)(2) supplement to an original (b)(2) application, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?

N/A ☒ YES ☐ NO ☐

*If this application is a (b)(2) supplement to an original (b)(1) application or not a supplemental application, answer **"N/A"**.*
*If "**NO**", please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

8) Were any of the listed drug(s) relied upon for this application:
   a) Approved in a 505(b)(2) application?

YES ☐ NO ☒
*If "**YES**", please list which drug(s).*

Name of drug(s) approved in a 505(b)(2) application:

   b) Approved by the DESI process?

YES ☐ NO ☒
*If "**YES**", please list which drug(s).*

Name of drug(s) approved via the DESI process:

   c) Described in a monograph?

YES ☐ NO ☒
*If "**YES**", please list which drug(s).*

Name of drug(s) described in a monograph:

   d) Discontinued from marketing?

YES ☐ NO ☒
*If "**YES**", please list which drug(s) and answer question d) i. below.*
*If "**NO**", proceed to question #9.*

Name of drug(s) discontinued from marketing:

   i) Were the products discontinued for reasons related to safety or effectiveness?

YES ☐ NO ☐

(Information regarding whether a drug has been discontinued from marketing for reasons of safety or effectiveness may be available in the Orange Book. Refer to

section 1.11 for an explanation, and section 6.1 for the list of discontinued drugs. If a determination of the reason for discontinuation has not been published in the Federal Register (and noted in the Orange Book), you will need to research the archive file and/or consult with the review team. Do not rely solely on any statements made by the sponsor.)

9) Describe the change from the listed drug(s) relied upon to support this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsule to solution").

This application provides for a new indication, to reduce the effects of hypercorisolism in patients with endogenous Cushing's syndrome, and a new dosage strength.

The purpose of the following two questions is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval that should be referenced as a listed drug in the pending application.

*The assessment of pharmaceutical equivalence for a recombinant or biologically-derived product and/or protein or peptide product is complex. If you answered **YES to question #1**, proceed to question #12; if you answered **NO to question #1**, proceed to question #10 below.*

10) (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved (via an NDA or ANDA)?

*(**Pharmaceutical equivalents** are drug products in identical dosage forms that: **(1)** contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; **(2)** do not necessarily contain the same inactive ingredients; **and** **(3)** meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c)).*

***Note** that for proposed combinations of one or more previously approved drugs, a pharmaceutical equivalent must also be a combination of the same drugs.*

YES ☐ NO ☒

*If "**NO**" to (a) proceed to question #11.*
*If "**YES**" to (a), answer (b) and (c) then proceed to question #12.*

(b) Is the pharmaceutical equivalent approved for the same indication for which the 505(b)(2) application is seeking approval?

YES ☐ NO ☐

(c) Is the listed drug(s) referenced by the application a pharmaceutical equivalent?

YES ☐ NO ☐

*If "**YES**" to (c) and there are no additional pharmaceutical equivalents listed, proceed to question #12.*
*If "**NO**" or if there are additional pharmaceutical equivalents that are not referenced by the application, list the NDA pharmaceutical equivalent(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

Pharmaceutical equivalent(s):

11) (a) Is there a pharmaceutical alternative(s) already approved (via an NDA or ANDA)?

*(**Pharmaceutical alternatives** are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)*

***Note** that for proposed combinations of one or more previously approved drugs, a pharmaceutical alternative must also be a combination of the same drugs.*

YES ☒ NO ☐
*If "**NO**", proceed to question #12.*

(b) Is the pharmaceutical alternative approved for the same indication for which the 505(b)(2) application is seeking approval?

YES ☐ NO ☒

(c) Is the approved pharmaceutical alternative(s) referenced as the listed drug(s)?

YES ☒ NO ☐

*If "**YES**" and there are no additional pharmaceutical alternatives listed, proceed to question #12.*

*If "**NO**" or if there are additional pharmaceutical alternatives that are not referenced by the application, list the NDA pharmaceutical alternative(s); you do not have to individually list all of the products approved as ANDAs, but please note below if approved generics are listed in the Orange Book. Please also contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

Pharmaceutical alternative(s): Mifeprex (mifepristone) Tablets

PATENT CERTIFICATION/STATEMENTS

12) List the patent numbers of all unexpired patents listed in the Orange Book for the listed drug(s) for which our finding of safety and effectiveness is relied upon to support approval of the (b)(2) product.

Listed drug/Patent number(s):

No patents listed ☒ *proceed to question #14*

13) Did the applicant address (with an appropriate certification or statement) all of the unexpired patents listed in the Orange Book for the listed drug(s) relied upon to support approval of the (b)(2) product?

YES ☐ NO ☐

*If "**NO**", list which patents (and which listed drugs) were not addressed by the applicant.*

Listed drug/Patent number(s):

14) Which of the following patent certifications does the application contain? *(Check all that apply and identify the patents to which each type of certification was made, as appropriate.)*

☐ No patent certifications are required (e.g., because application is based solely on published literature that does not cite a specific innovator product)

☐ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)

☒ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)

Patent number(s): **4626531, 4447424, 4386085**

☐ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)

Patent number(s): Expiry date(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification). *If Paragraph IV certification was submitted, proceed to question #15.*

☐ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the NDA holder/patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above). *If the applicant has a licensing agreement with the NDA holder/patent owner, proceed to question #15.*

☐ 21 CFR 314.50(i)(1)(ii): No relevant patents.

☐ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a

statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)

Patent number(s):
Method(s) of Use/Code(s):

15) Complete the following checklist ***ONLY*** for applications containing Paragraph IV certification and/or applications in which the applicant and patent holder have a licensing agreement:

(a) Patent number(s):
(b) Did the applicant submit a signed certification stating that the NDA holder and patent owner(s) were notified that this b(2) application was filed [21 CFR 314.52(b)]?

YES ☐ NO ☐

*If "**NO**", please contact the applicant and request the signed certification.*

(c) Did the applicant submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)]? This is generally provided in the form of a registered mail receipt.

YES ☐ NO ☐

*If "**NO**", please contact the applicant and request the documentation.*

(d) What is/are the date(s) on the registered mail receipt(s) (i.e., the date(s) the NDA holder and patent owner(s) received notification):

Date(s):

(e) Has the applicant been sued for patent infringement within 45-days of receipt of the notification listed above?

***Note** that you may need to call the applicant (after 45 days of receipt of the notification) to verify this information **UNLESS** the applicant provided a written statement from the notified patent owner(s) that it consents to an immediate effective date of approval.*

YES ☐ NO ☐ Patent owner(s) consent(s) to an immediate effective date of approval ☐

JMarchick AC 2/14/TBourcier 2/15/12

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

/s/

JENA M WEBER
02/15/2012

February 12, 2012

Dr. Mary Parks
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets
Proposed Labeling

Dear Dr. Parks:

Thank you very much for your division's careful attention to our NDA and for your personal involvement. We feel like a great deal of progress was made last week in our mutual goal of creating the most useful label possible for Korlym. As you will see, we have incorporated almost of the changes contained in your latest version verbatim and have added the drug interaction table that you requested.

Our shared goal is that we bring a potentially valuable treatment to the relatively small number of patients who have refractory Cushing's syndrome. We want our indication statement to be clear to physicians and, frankly, to insurers who are likely to pay for this treatment. We want to leave both groups certain that Korlym is intended to be used in patients with endogenous Cushing's syndrome for whom surgery has been ineffective or impossible and who are diabetic or glucose intolerant. We want both groups to understand that this is NOT a medication for the infinitely larger group of patients who have diabetes and who do not have Cushing's syndrome. While the group of patients with refractory Cushing's syndrome and manifestions of hyperglycemia is small, we want their physicians to consider each one of them for treatment with Korlym.

As such, we propose rewording the indication statement for Korlym as follows:

INDICATIONS AND USAGE

(b) (4)

149 Commonwealth Drive • Menlo Park, CA 94025 • Tel 650.327.3270 • Fax 650.327.3218

[redacted] (b) (4)

This wording emphasizes the use of the drug only in patients with Cushing's syndrome and disturbed glucose metabolism. This wording provides clearer instruction to physicians regarding the diagnostic criteria that should be considered in the decision to prescribe Korlym and outlines the hierarchical list of diagnostic criteria that should be applied:

1. The patient must have endogenous Cushing's syndrome
2. The patient must also have failed surgery or not be a candidate for surgery
3. The patient must have diabetes mellitus type 2 or glucose intolerance

[redacted] (b) (4)

[redacted] (b) (4) reinforces that the major evidence by which Korlym will be approved is its effect on glycemic control in patients with Cushing's syndrome.

This wording will help clinicians understand the relationship between the mode of action of the drug and its effects on glucose metabolism. It will make it clear that it is not a drug for general diabetes use and will ensure that Korlym is not considered simply as a new antidiabetic drug. It could also be useful to clinicians in their interactions with insurance providers in explaining their choice of this approach to glucose control in their patients with Cushing's syndrome.

In addition to the proposed wording for the Indication, we have addressed the following items:

2 Dosage and Administration: Recommended wording for Dose Increases was added at the recommendation of the reviewers. This information is based on how dose escalation was done in the clinical study, and incorporates manifestations of Cushing's syndrome that would give the practitioner guidance on when to increase the dose.

12.3 Pharmacokinetics: Table 2, Summary Table of Korlym Drug-Drug Interaction Effects, was added [redacted] (b) (4)

14.1 Cushing's Syndrome: Clearer wording was added from the clinical study protocol on how the dose was escalated to provide further guidance on increasing the dose of Korlym.

We look forward to your feedback.

Yours sincerely,

Joseph K. Belanoff, MD
Chief Executive Office
Corcept Therapeutics

149 Commonwealth Drive • Menlo Park, CA 94025 • Tel 650.327.3270 • Fax 650.327.3218

February 9, 2012

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets
Amendment to a Pending Application: Revised Container Labels

Dear Ms. Weber:

Attached please find Corcept's response to the questions sent via e-mail on February 8, 2012 on the container labels for Korlym. Each comment is shown in bold followed by the response. The revised labels are attached. Note that no carton labels are planned for Korlym.

Container Labels (28 tablets and 280 tablets)

1. **Delete the proprietary name (b) (4) and use the established name on the container label.**

   Corcept response: The proprietary name (b) (4) has been deleted and replaced with the approved name 'Korlym' that will be used in conjunction with the established name, mifepristone.

2. **Once the proprietary name is identified, ensure the size of the established name is at least ½ size the letters comprising the proprietary name and has prominence consistent with the proprietary name (type, size, color, font) in accordance with 21 CFR 201.10(g)(2).**

   Corcept response: The respective size of the proprietary name, Korlym, and established name, mifepristone, have been modified to be in accordance with 21 CRF 201.10(g)(2).

3. **Delete or reduce size of (b) (4) in accordance with 21 CFR 202.1(a)(1). This (b) (4) is intervening matter that decreases the visibility of the proprietary name. Additionally, this (b) (4) is prominent and distracting. However, the proprietary and established names, dosage form, and strength should be the most prominent items on the principle display panel.**

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Corcept response: The [redacted] (b) (4) has been deleted from the labels.

4. **Add the statement to the principle display panel that reads "Take tablets whole. Do not split, crush, or chew". We request this change because this information is important for the correct administration of the product and thus, should be made more prominent.**

Corcept response: The statement "Take tablets whole. Do not split, crush, or chew has been added to the label.

5. **Increase the prominence of the strength by increasing the font size. As currently presented, the strength and the net quantity (i.e., 28 tablets or 280 tablets) appear in the same prominence. As a result, the net quantity may be misinterpreted as the strength.**

Corcept response: The font size of the strength "300 mg" has been increased to be larger than the font for the net quantity.

6. **Change medication guide statement to be consistent with other medication guide statements for other product. For example, you medication guide statement can read as follows "ATTENTION PHARMACIST: Dispense attached Medication Guide to each patient".**

Corcept response: The statement on providing the Medication Guide has been revised to "ATTENTION PHARMACIST: Dispense attached Medication Guide to each patient"

Please let me know if you have any questions regarding this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

February 8, 2012

Dr. Mary Parks
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets
Amendment to a Pending Application: Response to Questions

Dear Dr. Parks:

We have reviewed the Division's proposed changes to the draft labeling for Korlym, sent to us yesterday by Ms Jena Weber. A new version with some additional changes we are proposing is attached.

While we agree with most of the changes that were made by the Division, we disagree with the proposed wording for the indication for use. The Division suggested the wording "Korlym (mifepristone) is a cortisol receptor blocker indicated to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have diabetes mellitus type 2 or glucose intolerance and have failed surgery or are not candidates for surgery". (b) (4) [redacted].

The Division's proposed indication would limit the use of Korlym to the treatment of Cushing's patients who are diabetic or glucose intolerant. (b) (4) [redacted].

(b) (4) [redacted]

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This indication is consistent with the data, is meaningful to clinicians, and prevents the disenfranchisement of a substantial subset of patients with this rare disease.

Attached is Corcept's proposed label with specific changes shown using track changes. A clean version with changes accepted is also provided. We look forward to your feedback.

Yours sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Attachment: Photographs from NDA submission of April 15, 2011 (provided on CD); Patients 11-004 and 22-001, Baseline vs Visit 12/Wk 24, Frontal

January 23, 2012

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets
Amendment to a Pending Application: Clinical

Dear Ms. Weber:

Submitted in this amendment is the response to the request sent via e-mail on January 18, 2012. Attached are the cited literature references.

FDA request: Provide the background rate for the following adverse events among subjects with endogenous Cushing's syndrome:

- **Major adverse cardiovascular events (MI, stroke, cardiovascular death)**

Corcept response: Estimation of the background rate of major adverse cardiovascular events in subjects with endogenous Cushing's syndrome is difficult due to very limited published data. Whereas there are studies that give estimates for mortality due to serious events in this population, Corcept has not been able to find much data to support morbidity numbers. Below is a summary of literature that was reviewed to ascertain an estimate of the background rate. Based on this review, we estimate the background rate of a major adverse cardiovascular event, such as MI, stroke, or cardiovascular death, to be >20% in subjects with endogenous Cushing's syndrome.

The hypercortisolemia of Cushing's syndrome leads to a multisystem disorder that can affect many tissues and organs in the body and is associated with an increased mortality rate. Untreated Cushing's syndrome has a 50% five year mortality[1]. Even when treated, the mortality rate in Cushing's syndrome is increased. The standardized mortality ratio (SMR) in patients with Cushing's syndrome who remain hypercortisolemic after surgery is approximately 4 to 5[2,3,4]. The causes of death in Cushing's syndrome are mainly due to cardiovascular complications although patients with underlying malignant tumors as the cause of Cushing's syndrome generally die of their malignancy (i.e. adrenal cancer, neuroendocrine cancer). Importantly, the risk of death is independently increased with co-existing diabetes mellitus and/or hypertension.[5] Other vascular complications (i.e. stroke and pulmonary embolism) are important causes of Cushing's associated morbidity and mortality[4,5,6].

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The literature regarding cardiovascular events focuses on mortality related to these factors. In the Stoke-on-Trent UK cohort of 60 patients with Cushing's disease who were followed for a median of 15 years, there were 13 deaths including seven due to ischemic heart disease or congestive heart failure, and four due to cerebrovascular events[5] (see supplementary table 1). Lindholm, et al.[4] described a similar pattern of deaths in patients with Cushing's syndrome; in a subset of 90 patients with at least five years of follow up (median 8.3 – 10.0 years) there were 10 deaths including one ruptured aortic aneurysm, one myocardial infarction and two strokes. Dekkers, et al.[7] reported four cardiovascular and one cerebrovascular deaths among 74 patients with Cushing's syndrome who were followed for a mean of 10 years; there were 12 total deaths in this group. Because Cushing's is a rare disorder, the true rates of these major cardiovascular events (myocardial infarction, stroke, cardiovascular death) are not well understood. Mancini, et al.[8] evaluated the cardiovascular risk in 49 Cushing's syndrome patients according to World Health Organization/International Society of Hypertension guidelines. Eighty percent of the study population was found to have a 20% 10-year risk of a major cardiovascular event. Based on these data, we estimate the 10-year risk of major cardiovascular event to be 15% in Cushing's syndrome overall. Given the long delay in the diagnosis of Cushing's syndrome and the high rate of persistent hypercortisolemia after initial surgical treatment, the background rate is likely to be 20% or greater.

Please let me know if you have any questions regarding this submission.

Sincerely,

Tania Bellerman

for

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Corcept
THERAPEUTICS

January 19, 2012

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets
Amendment to a Pending Application: Clinical

Dear Ms. Weber:

Submitted in this amendment are responses to the request sent via e-mail today, January 19, 2012. Provided below is each request noted in bold followed by Corcept's response. Supplemental data are provided as attachments as noted below.

1) Were HbA1c measurements in Study 400 done in a central laboratory for the patients in the glucose intolerance/diabetes group?

Corcept response: Yes, the HbA1c measurements were performed in the central laboratory for all Study 400 participants.

2) Were glucose measurements for calculation of AUCglucose in the oral glucose tolerance test done at a central laboratory; if not were they done at each site?

Corcept response: Yes, the glucose measurements used for the calculation of AUCglucose for all Study 400 participants were performed in the central laboratory.

3) Do you have access to any HbA1c data in the extension study 415 for the patients who were part of the glucose intolerance/diabetes group in Study 400? If so, can you submit such data by individual patient?

Corcept response: No data are available because HbA1c measurements were not performed as part of Study 415.

4) Do you have anywhere in the package the individual HOMA-IR and insulin data by patient ID (baseline, end of trial and intermediary time points)? Same for weight? If not please submit such a table.

Corcept response: Provided in Attachment 1 are the individual HOMA-IR data for patients with diabetes/impaired glucose tolerance (C-DM) and hypertension (C-HT). These data

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were calculated using fasting glucose and insulin levels (0 minute time point on the oral glucose tolerance test). Figures 14.2.6.1 through 14.2.6.4 of the original NDA showed plots of the HOMA data for the C-DM patients not taking insulin and for the C-HT patients.

The individual insulin data by patient were included in Listing 16.2.6.1.6 (Listing of Insulin Concentration Data) submitted with the original NDA. A copy of the listing is provided here in Attachment 2 for convenience.

The individual weight data by patient were included in Listing 16.2.9.1 (Listing of Vital Sign Data) in the original NDA. A separate listing of only the weight data by patient has been prepared and is submitted here in Attachment 3. Percent change in weight was also presented graphically for the mITT population in Figure 14.2.9.1 (Scatter Plot of Percent Change from Baseline in Weight versus Time: Individual Subject in C-DM and C-HT Cohorts) that was submitted in the original NDA.

Please let me know if you have any questions regarding this submission.

Sincerely,

Tania Bikerman
for L. Staiger

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Attachments

1 HOMA-IR data for patients in Study 400 with diabetes/impaired glucose tolerance (C-DM) and hypertension (C-HT)

2 Listing 16.2.6.1.6 (Listing of Insulin Concentration Data) from Study 400 Clinical Study Report

3 Individual weight data from Listing 16.2.9.1 (Listing of Vital Sign Data) of Study 400 Clinical Study Report

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202107

GENERAL ADVICE

Corcept Therapeutics
Attention: Launa Staiger
Regulatory Affairs
149 Commonwealth Drive
Menlo Park, CA 94025

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) submitted April 15, 2011, received April 18, 2011, under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Korlym (mifepristone) Tablets.

We also refer to your July 20, October 19, November 21, and December 14 2011, submissions, containing Biopharmaceutics information.

We have reviewed the referenced material and have the following comments/recommendations:

- Your proposed dissolution method (b) (4) SMA.COR.007 and acceptance criterion of Q= (b) (4) at 30 minutes is acceptable. We encourage you to update the analysis method from direct UV to HPLC post approval. (b) (4)

If you have any questions, call Swati Patwardhan, Regulatory Project Manager, at (301) 796-4085.

Sincerely,

{See appended electronic signature page}

Ali Al-Hakim, Ph.D.
Branch Chief, Branch VII
Division of New Drug Quality Assessment III
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

ALI H AL HAKIM
01/06/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202107

MEETING MINUTES

CORCEPT Therapeutics
Attention: Luana Staiger
Regulatory Affairs
149 Commonwealth Drive
Menlo Park, CA 94025

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Korlym (mifepristone) 300 mg Tablets.

We also refer to the telecon between representatives of your firm and the FDA on December 13, 2011. The purpose of the meeting was to discuss your proposed REMS (including Medication Guide, Communication Plan, ETASU, Implementation System, and Timetable for Submission of Assessments).

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

If you have any questions, please call me at 301-796-1306.

Sincerely,

{See appended electronic signature page}

Jena M. Weber
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE: Meeting Minutes

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Proposed REMS

Meeting Date and Time: Tuesday December 13, 2011
Meeting Location: White Oak Campus (T-con)

Application Number: 202107
Product Name: Korlym (mifepristone) 300 mg Tablets
Indication: Cushing's Syndrome
Applicant Name: CORCEPT

Meeting Chair: Amy Egan, M.D.
Meeting Recorder: Jena Weber, PM

FDA Participants:

Mary Parks, M.D. – Division Director
Amy Egan, M.D. – Deputy Director for Safety
John Bishai, Ph.D. – Project Manager, Safety
Dragos Roman, M.D. – Team Leader, Clinical
Marina Zemskova, M.D. – Clinical Reviewer
Cynthia LaCivita, OSE, DRISK
Claudia Karwoski, OSE, DRISK
Suzanne Berkman Robottom, OSE, DRISK
Jena Weber, BS - Project Manager

CORCEPT Participants:

Tania Bekerman, Manager, Regulatory Affairs
Lorene Campbell, Project Director
Bernadette DeArrmond, M.D., MPH, Post-Marketing & Safety
Coleman Gross, M.D., Medical Director
Johanna Hunt, Program Director
Steven Lo, VP, Commercial Operations
Robert Roe, M.D., President, Corcept
Luana Staiger, Regulatory Affairs
(b) (4)

BACKGROUND

This NDA is under review. Projected action date is February 17, 2012. The purpose of the meeting was to discuss the proposed REMS (including Medication Guide, Communication Plan, ETASU, Implementation System, and Timetable for Submission of Assessments).

QUESTIONS

(b) (4)

FDA Response: We have determined that a REMS is not necessary to ensure that the benefits of Korlym outweigh its risks. Serious risks associated with the use of this product such as adrenal insufficiency, hypokalemia, and drug-drug interactions can be adequately addressed through physician and patient labeling.

2. Is the proposal to provide a Medication Guide with each prescription and not to develop a separate patient package insert acceptable?
FDA Response: While there will be no requirement for a REMS, a Medication Guide will be required as part of labeling.

3. (b) (4) The materials for prescribers will include the Full Prescribing Information, a Prescriber Information and Responsibilities Booklet, and Prescriber Registration and Agreement Form. Prescribers will also be provided with materials to share with patients including the Medication Guide, a Patient Guide, and the Patient Registration and Consent Form. Specialty and Hospital Pharmacies will be provided with the Full Prescribing Information, the Medication Guide and the Pharmacy Registration and Agreement Form. Materials will be available in hard copy and via a website. Does the Agency agree with the nature and scope of the proposed materials to be included in the Communication Plan?
FDA Response: N/A; a REMS is not necessary for the use of Korlym in the Cushing's population. See response to Question 1.

(b) (4)

b. Korlym will be available to outpatients through a limited number of Specialty Pharmacies (b) (4) Hospital Pharmacies that intend to dispense Korlym will be registered (b) (4) (b) (4)

c. All patients must be registered into the program and document that they understand the risks of treatment with Korlym. Female patients of child bearing potential must have a negative pregnancy test prior to receiving Korlym. Does the Agency agree (b) (4)

FDA Response: N/A; a REMS is not necessary for the use of Korlym in the Cushing's population. Reference comments made to Question 1.

We do agree with your proposal to distribute Korlym solely to a "limited number of specialty pharmacies". We anticipate that Korlym would be shipped from these specialty pharmacies directly to patients or hospitals. This should prove more convenient for patients and will facilitate monitoring the use of Korlym to ensure that it is being used in the indicated population.

(b) (4)

FDA Response: N/A; a REMS is not needed for the use of Korlym in the Cushing's population. See reply to Question 1.

(b) (4)

FDA Response: N/A; a REMS is not necessary for the use of Korlym in the Cushing's population. Refer to comments made to Question 1.

(b) (4)

FDA Response: N/A; a REMS is not required for the use of Korlym in the Cushing's population. See comments made in response to Question 1.

(b) (4)

FDA Response: N/A; a REMS is not needed for the use of Korlym in the Cushing's population. See Question 1.

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/s/

JENA M WEBER
01/05/2012
Min from T-con (REMS)

Executive CAC
Date of Meeting: December 13, 2011

Committee: David Jacobson-Kram, Ph.D., OND IO, Chair
Abby Jacobs, Ph.D., OND IO, Member
Paul Brown, Ph.D., OND IO, Member
Todd Bourcier, Ph.D., DMEP, Team Leader
Patricia Brundage, Ph.D., DMEP, Presenting Reviewer

Author of Draft: Patricia Brundage and Todd Bourcier

The following information reflects a brief summary of the Committee discussion and its recommendations.

NDA #: 202107
Drug Name: Mifepristone
Sponsor: Corcept Therapeutics

Background:
This is a 505(b)(2) application for mifepristone (Korlym®), a glucocorticoid and progesterone receptor antagonist. The proposed indication is for the treatment of the clinical and metabolic effects of hypercortisolism in patients with endogenous Cushing's syndrome. Mifepristone is approved for the acute indication of pregnancy termination (single dose administration) under NDA 20687 (Danco Laboratories/Population Council).

Rat Carcinogenicity Study
Carcinogenic assessment in Sprague Dawley rats was initiated at doses of 0 (vehicle control), 0 (vehicle control), 5, 25, and 125 mg/kg, in accordance with the Committee's dosing recommendations. The vehicle was 0.25% carboxymethylcellulose and 0.2% Tween 80 in sterile water for injection, USP. Drug exposure (mifepristone and its 3 major active metabolites) in the high dose males and females were 0.6X and 1X, respectively, the exposure at the MRHD of 1200 mg/day. Dosing was limited by toxicity. Hepatocellular adenomas, as well as thyroid follicular cell adenomas, carcinomas, and pooled adenomas/carcinomas increased in high dose females. Hyperplasia (thyroid only) and hypertrophy were also noted in the liver and thyroid, mainly in the mid and high dose groups. The sponsor attributes the hepatocellular and follicular cell tumors to a rat-specific chronic induction of enzyme activity in the liver and subsequent increase in thyroid hormone metabolism resulting in thyroid hyperplasia and eventually neoplasia. However, the sponsor did not conduct any mechanistic studies to assess thyroid function or hepatic enzyme activity. Although mifepristone has been shown to cause CYP3A induction, chronic mifepristone treatment has caused elevations in serum TSH and transient decreases in T4 in Cushing's patients as well as in patients with meningioma. The incidence of mammary adenomas/adenocarcinomas was significantly increased in mid dose females by pair-wise comparisons and by trend when the high dose group is left out of the trend analysis.

Mouse Carcinogenicity Study
Carcinogenic assessment in CD-1 mice was initiated at doses of 0 (vehicle control), 12.5, 65, and 125 mg/kg for male mice and 0 (vehicle control), 25, 100, and 300 in female mice. The vehicle was 0.25% carboxymethylcellulose and 0.2% Tween 80 in sterile water for injection, USP. This was in accordance with the Committee's dosing recommendations. Due to the high incidence of mortality in females at 300 mg/kg (main group), the dose level was decreased to 200 mg/kg at Week 36, and subsequently decreased to 125 mg/kg at Week 54. Drug exposure (mifepristone and its 3 major active metabolites) in the high dose males and females was less than clinical exposure at the MRHD of 1200 mg/day. There were no drug-related, statistically significant tumors found in males or females.

Executive CAC Recommendations and Conclusions:

Rat:

- The Committee agreed that the study was adequate, noting prior Exec CAC concurrence with the protocol.

- The Committee concurred that hepatocellular adenomas and thyroid follicular cell adenomas, carcinomas, and combined adenomas/carcinomas in female rats were drug related. It's not clear to what extent these might be related to liver enzyme induction. The relevance to humans cannot be excluded.

- The Committee noted that the absence of an increased incidence of mammary adenomas/ adenocarcinomas in high dose females, despite the statistically significant increase in the mid dose group, might be related to the decreased body weight of the high dose female group.

Mouse:

- The Committee agreed that the study was adequate, although dosing was limited by toxicity, noting prior Exec CAC concurrence with the protocol.

- The Committee concurred that there were no drug-related neoplasms.

David Jacobson-Kram, Ph.D.
Chair, Executive CAC

cc:\
/NDA 202107, DMEP
/Todd Bourcier, DMEP
/Patricia Brundage, DMEP
/Jena Weber, DMEP
/ASeifried, OND IO

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

/s/

ADELE S SEIFRIED
12/19/2011

DAVID JACOBSON KRAM
12/19/2011

Corcept
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INAL

SDN 25

December 14, 2011

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets**
Amendment to a Pending Application: Chemistry, Manufacturing & Controls

Dear Ms. Weber:

Provided in this amendment is Corcept's response to the request sent via e-mail on December 12, 2011 requesting information on the method development for the dissolution method (b)(4) SMA.COR.007. A method development report describing the parameters tested to select the optimal conditions was not prepared; however, details of the testing performed to select the method parameters are discussed in the attached summary.

Please let me know if you have any questions regarding this submission.

Sincerely,

Luana Staiger

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Corcept THERAPEUTICS

December 7, 2011

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 – Korlym™ (mifepristone) 300 mg Tablets**
Amendment to a Pending Application: Chemistry, Manufacturing & Controls

Dear Ms. Weber:

Reference is made to the telephone conversation with Dr. Xavier Ysern on November 7, 2011. Dr. Ysern requested information on the section location in the (b) (4) File (DMF) for information on the film coating (b) (4) (b) (4) used in the manufacturing of Korlym 300 mg Tablets.

(b) (4) the supplier of the film coating (b) (4), has indicated that the information (b) (4) is located in **Section I** of **DMF** (b) (4)

For reference, attached here is a copy of the cross reference letter authorizing FDA to utilize the data in the DMF in support of the NDA for Korlym. This letter was included in Module 1 of the initial NDA.

Please let me know if you have any questions regarding this submission.

Sincerely,

Luana Staiger

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Weber, Jena M

From: Luana Staiger [lstaiger@corcept.com]
nt: Thursday, December 08, 2011 1:01 PM
: Weber, Jena M
Subject: NDA 202107 CMC Amendment

Attachments: NDA 202107_7Dec2011_DMF Ref.pdf

NDA 7Dec2011_DMF

Dear Jena,
Attached here is a copy of the amendment that Corcept sent yesterday in response to the question from Dr. Ysern regarding the DMF for one of the excipients used in the manufacture of Korlym 300 mg Tablets.

Please let me know if you have any questions on the amendment.
Kind regards,
Luana

Regulatory Affairs
Corcept Therapeutics
(650) 678-7230

November 21, 2011

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) Tablets
Amendment to a Pending Application: Chemistry, Manufacturing & Controls (Sections 3.2.P.5 and 3.2.P.8)

Dear Ms. Weber:

Reference is made to the teleconference held on September 26, 2011 with the FDA Biopharmaceutics and Chemistry reviewers to discuss the dissolution methodology for Korlym™ (mifepristone) Tablets, 300 mg and to the previous amendment of October 19, 2011 that provided the dissolution method, validation report, and dissolution profile data. Submitted here are the proposed dissolution specification and justification and follow-up supporting data.

Dissolution profile data are presented using method SMA.COR.007 for the registration stability lots and supportive stability lots. An analysis of combined data supports a proposed dissolution specification of Not Less Than (b) (4) (Q = (b) (4)) at 30 minutes. A (b) (4) dissolution sample point was considered; however, due to higher variation at this time point, a 30-minute sample point is proposed.

This submission completes the response that was requested in the teleconference. Please let me know if you have any questions on this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Corcept
THERAPEUTICS

To CLN 11/21/11

November 18, 2011

Division of Metabolism and Endocrinology Products
CDER - Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Subject: **NDA 202107 Korlym™ (mifepristone) 300 mg Tablets**
Response to FDA Request for Information

Dear Reviewers:

Submitted here is Corcept response to the request received via e-mail on November 15, 2011 for information on the C-DM cohort in study C1073-400. The full text of the FDA request is provided below followed by Corcept's response.

FDA comment:

Please submit the following information about the patients enrolled in the C-DM cohort in study C-1073-400:

1. For each patient who had improvement in AUC glucose (by any percent) and discontinued temporarily mifepristone treatment during the study:
   - The oGTT AUC glucose values before mifepristone treatment discontinuation, off medication, and after resumption of treatment;
   - Specify how long each of these patients was treated with mifepristone prior to drug discontinuation, the time interval the patient was off study medication, and how the treatment changes related temporarily to the AUC glucose assessments.

   Present this information also as a graph.
2. For each patient who had improvement in HbA1C (by any percent) and had treatment with the study drug interrupted during the study:
   - The HbA1c values before mifepristone treatment discontinuation, off medication and after resumption of treatment;
   - Specify how long each of these patients was treated with mifepristone prior to the drug discontinuation, the time interval the patient was off study medication, and how the treatment changes related temporarily to the HbA1c assessments.

   Present this information also as a graph.

Corcept response:

Shown in Table 1 is a list of all 29 subjects in the C-DM cohort in study C1073-400. Twelve of these subjects (shaded in gray) had a dosing interruption at some time during the study. All 12 of these subjects had a decrease in $AUC_{glucose}$ and/or a decrease in HbA1c at the time of their last visit in Study 400, as indicated in the table.

For each subject who had a dosing interruption, details of dosing and $AUC_{glucose}$ and HbA1c levels are provided in individual graphs and tables in the pages following Table 1. These displays show the temporal relationship between treatment and $AUC_{glucose}$ and HbA1c assessments for each subject. The page immediately following Table 1 provides an annotated example of the individual data pages.

Please note that none of the subjects had measurements of $AUC_{glucose}$ and HbA1c taken during the period off medication, except for subject 24-001, whose Week 6 $AUC_{glucose}$ measurement occurred on the day of dosing resumption following a 3-day interruption.

There are two subjects, 01-001 and 03-004, whose dose of mifepristone was administered every other day (QOD) for a significant period of time during the study. This was the prescribed dose regimen for these subjects, so the alternate days on which they did not take drug during that period are not considered to be dose interruptions.

Please let me know if you have any questions on the data provided here.

Sincerely,

Bonnie Harer
for

Luana Staiger
Regulatory Affairs
(650) 678-7230
lstaiger@corcept.com

Meeting Date: November 3, 2011
Time: 8 am – 9 am
Location: Room 6335 (bldg 51)

Attendees: Janet Woodcock, Jane Axelrad, Terry Toigo, John Jenkins, Gerald DalPan, Claudia Karwoski, Mwango Kashoki, Cynthia LaCivita, Kristin Everett, Carla Cartwright, Amy Egan, Lee Lemley, Marina Zemskova, Curt Rosebraugh, Suzanne Robottom, Mary Gross

Subject: REMS with ETASU for Korlym (Mifepristone) to Treat Cushing's Syndrome – Meeting Summary

Background

The purpose of the meeting was to discuss whether it is necessary to require a REMS with ETASU for approval of Korlym (whose indication is to treat endogenous Cushing's syndrome) in order to maintain the integrity of the current Mifeprex REMS program. By approving Korlym without an ETASU, we discussed that Korlym might be used off-label to terminate a pregnancy or misused or diverted in order to terminate a pregnancy without proper healthcare provider supervision. The PDUFA date for this drug is February 17, 2012.

Endogenous Cushing's syndrome is a serious multisystem disorder that results from overproduction of cortisol by the adrenal glands. Treatment requires highly specialized care in tertiary care centers. The disease is associated with a decreased quality of life and increased mortality. Orphan designation was granted on July 5, 2007 for the treatment of signs and symptoms of endogenous Cushing's syndrome.

The prevalence of Cushing's syndrome in the U.S. is ~20,000 patients, one-quarter of whom, or ~5,000 patients, would qualify for treatment with Korlym. The number of prescribers who would prescribe Korlym is also limited; there are only 35 endocrinologists in the U.S. who are recommended by the Cushing's Support and Research Foundation for the treatment and care of Cushing's syndrome patients. The starting dose for Korlym is 300 mg once daily by mouth with a maximum dose of 1200 mg daily. It is packaged in bottles containing 28 or 280 tablets. DMEP and DRISK agreed that a REMS is not necessary to ensure that the benefits of Korlym outweigh the risks for the treatment of patients with Cushing's syndrome.

Action Item

Dr. Woodcock agreed that a REMS with ETASU is not warranted. CDER staff will contact the sponsor to discuss the need to set up a voluntary limited distribution system. A drug utilization study will be required as a PMR in order to ensure the drug is being used in the indicated patient population. Dr. Woodcock will update Dr. Stephen Spielberg in the Commissioner's Office on the CDER plan.

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

/s/

AMY G EGAN
11/15/2011

Weber, Jena M

From: Zemskova, Marina
Sent: Monday, November 14, 2011 5:00 PM
To: Weber, Jena M
bject: Q for Sponsor

+D Concept 11/15/11

Hi, Jena,
Could please send our question to the Sponsor.
Thank you,
Marina

Please submit the following information about the patients enrolled in the C-DM cohort in study C-1073-400 :
1. For each patient who had improvement in AUC glucose (by any percent) and discontinued temporarily mifepristone treatment during the study:
- The oGTT AUC glucose values before mifepristone treatment discontinuation, off medication, and after resumption of treatment;
- Specify how long each of these patients was treated with mifepristone prior to drug discontinuation, the time interval the patient was off study medication, and how the treatment changes related temporarily to the AUC glucose assessments. Present this information also as a graph.
2. For each patient who had improvement in HbA1C (by any percent) and had treatment with the study drug interrupted during the study:
- - The HbA1c values before mifepristone treatment discontinuation, off medication and after resumption of treatment ;
- Specify how long each of these patients was treated with mifepristone prior to the drug discontinuation, the time interval the patient was off study medication, and how the treatment changes related temporarily to the HbA1c assessments. Present this information also as a graph.

rina Zemskova, M.D.
dical Officer
Division of Metabolism and Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Phone 301-796-2463
email: marina.zemskova@fda.hhs.gov

Corcept THERAPEUTICS

NOV 14 2011

November 10, 2011

Division of Metabolism and Endocrinology Products
CDER - Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

SDN 21

Subject: **NDA 202107 Korlym™ (mifepristone) 300 mg Tablets**
Briefing Document for Meeting to Discuss Proposed REMS

Dear Reviewers:

We are pleased to submit the Briefing Document in support of the teleconference scheduled for December 13, 2011, to discuss the proposed Risk Evaluation and Mitigation Strategy for Korlym™ (mifepristone) 300 mg Tablets. Appended to the Briefing Document are the following items:

Attachment 1 – Draft Full Prescribing Information (Package Insert). This is the same version that was previously submitted to the NDA with the 4-month safety update on August 12, 2011.

Attachment 2 – REMS Document

Attachment 3 – REMS Supporting Document

We look forward to talking with you to discuss the proposed REMS for Korlym. Please feel free to contact me should you need any additional information.

Sincerely,

Luana Staiger

Luana Staiger
Regulatory Affairs
(650) 678-7230
lstaiger@corcept.com

cc. Jena Weber, 7 desk copies

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202107

MEETING REQUEST GRANTED

CORCEPT Therapeutics
Attention: Luana Staiger
Regulatory Affairs
149 Commonwealth Drive
Menlo Park, CA 94025

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Korlym (mifepristone) 300 mg Tablets.

We also refer to your October 17, 2011, correspondence requesting a Type B meeting to discuss your proposed REMS (including Medication Guide, communication plan, ETASU, implementation system, and timetable for submission of assessments.) Based on the statement of purpose, objectives, and proposed agenda, we consider this meeting to be a "Type B" meeting.

The teleconference is scheduled as follows:

Date: **Tues December 13, 2011** (EST)
Time: 1 – 2 pm
Phone Arrangements: 1-888-381-9324
Pass code: 1916970

Tentative CDER participants: Mary Parks, M.D. – Division Director
Amy Egan, M.D. – Deputy Director for Safety
John Bishai, Ph.D. – Project Manager, Safety
Dragos Roman, M.D. – Team Leader, Clinical
Marina Zemskova, M.D. – Clinical Reviewer
Cynthia LaCivita, OSE, DRISK
Claudia Karwoski, OSE, DRISK
Suzanne Berkman Robottom, OSE, DRISK
Jena Weber, BS - Project Manager

Please e-mail me any updates to your attendees at Jena.Weber@fda.hha.gov, at least one week prior to the meeting.

Submit background information for the meeting (three paper copies or one electronic copy to the application and **7** desk copies to me) at least **three** weeks prior to the meeting. If the materials presented in the information package are inadequate to prepare for the meeting or if we do not receive the package by **November 30, 2011,** we may cancel or reschedule the meeting.

Submit the 7 desk copies to the following address:

If sending via USPS, please send to:

Jena Weber
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22 Room: 3364
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

If sending via any carrier other than USPS (e.g., UPS, DHL), please send to:

Jena Weber
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 3364
10903 New Hampshire Avenue
Silver Spring, Maryland 20903

If you have any questions, please call me at 301-796-1306.

Sincerely,

{See appended electronic signature page}

Jena M. Weber
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

JENA M WEBER
11/07/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 202107

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Corcept Therapeutics
149 Commonwealth Drive
Menlo Park, CA 94025

Attention: Luana Staiger
Director Regulatory Affairs

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) dated April, 15, 2011, and received April 18, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Mifepristone Tablets, 300 mg.

We also refer to your July 27, 2011, correspondence, received July 28, 2011, requesting review of your proposed proprietary name, Korlym. We have completed our review of the proposed proprietary name, Korlym and have concluded that it is acceptable.

The proposed proprietary name, Korlym, 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.

If **any** of the proposed product characteristics as stated in your July 27, 2011, 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, contact Ermias Zerislassie Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0097. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager Jena Weber at (301) 796-1306.

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

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/s/

CAROL A HOLQUIST
10/21/2011

Weber, Jena M

From: Luana Staiger [lstaiger@corcept.com]
Sent: Wednesday, October 19, 2011 6:50 PM
To: Weber, Jena M
Subject: NDA 202107 Corcept - CMC Amendment

Attachments: NDA202107_CMC-amendmt_19Oct2011.pdf

NDA202107_CM
mendmt_19Oct2(

Dear Jena,

Attached is a copy of an amendment to the NDA that was sent today to the Central Document Room. Included here is the first part of the CMC amendment as discussed in the teleconference of September 26, 2011. Provided in this amendment are the dissolution method, validation summary, and dissolution profile data on batches of mifepristone tablets.

When completed, additional dissolution profile results from analysis of the registration stability lots will be submitted together with a proposed dissolution specification.

Please let me know if you have any questions on this submission.
Kind regards,
Luana

Corcept Therapeutics
(650) 678-7230

Corcept
THERAPEUTICS

October 19, 2011

Ms. Jena Weber
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 – Korlym™ (mifepristone) Tablets**
Amendment to a Pending Application: Chemistry, Manufacturing & Controls (Sections 3.2.P.5 and 3.2.P.8)

Dear Ms. Weber:

This submission is in response to our teleconference held on September 26, 2011 with the FDA Biopharmaceutics and Chemistry reviewers to discuss the dissolution methodology for Korlym™ (mifepristone) Tablets, 300 mg. The reviewers recommended that Corcept convert to (b) (4) method, SMA.COR.007, (b) (4) (b) (4), rather than the dissolution method (b) (4) for dissolution method because it provided more clinical relevance for product testing. As agreed during the call, Corcept is submitting the method and method validation information and currently available dissolution profile data that had been generated with (b) (4) method SMA.COR.007 (b) (4)

Corcept is currently conducting dissolution testing using (b) (4) SMA.COR.007 on the registration stability lots (10C15, 10C16, 10C17, 10C18, 10C19, and 10C20) from the 18 month stability study time point and for supportive stability lots with stability time points scheduled for September 2011. Data from this dissolution testing will be submitted as soon as it is available along with an analysis of all of the dissolution data from the registration and supportive stability lots and a proposed dissolution specification and justification.

Please let me know if you have any questions on this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

October 17, 2011

Division of Metabolism and Endocrinology Products
CDER - Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Subject: **NDA 202107 Korlym™ (mifepristone) 300 mg Tablets**
Request for Meeting to Discuss Proposed REMS

Dear Reviewers:

Provided here is a request for a meeting to discuss the proposed Risk Evaluation and **Mitigation Strategy for Korlym™ (mifepristone)** 300 mg Tablets. The purpose of the meeting is to discuss the draft REMS and obtain agreement on the key elements of the program.

A draft REMS was submitted with the initial NDA on April 15, 2011. Due to the time frame for setting up and implementing the REMS elements, Corcept has initiated activities with vendors and begun preparing draft materials needed for the program. We would like to obtain Agency input and agreement on the program to be sure we are progressing in the right direction before spending more time and resources to complete these activities.

Although a REMS currently exists for mifepristone that prescribers and patients must adhere to when using the drug to terminate early pregnancy (Mifeprex®), Corcept is proposing that a separate REMS be established for Korlym. (b) (4)

(b) (4)

3. All patients must register in the (b) (4) program prior to receiving drug. Korlym will only be dispensed to patients with documentation of safe use conditions. Female patients of child bearing potential must have had a negative pregnancy test prior to receiving Korlym.

149 Commonwealth Drive • Menlo Park, CA 94025 • Tel 650.327.3270 • Fax 650.327.3218

NDA 202107
Korlym™ (mifepristone) Tablets
Corcept Therapeutics

(b) (4)

Attached here is the meeting request that outlines the purpose and objectives of the meeting, the tentative list of questions for discussion, and the proposed list of participants. We are requesting the meeting for the week of December 5 or 12, and would plan to submit the background information 28 days prior to the meeting.

We look forward to meeting with you to discuss the proposed REMS for Korlym. Please feel free to contact me should you need any additional information.

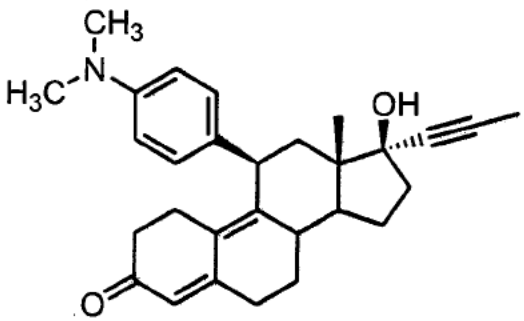
Sincerely,

Luana Staiger
Regulatory Affairs
(650) 678-7230
lstaiger@corcept.com

NDA 202107
Korlym™ (mifepristone) Tablets
Corcept Therapeutics

Request for Meeting

1. **Product name:** Korlym™ (mifepristone) 300 mg Tablets
2. **Chemical name and structure:**
   1. 11β –[p-(dimethylamino)phenyl]-17β–hydroxy-17α -(1-propynyl)estra-4,9-dien-3-one (IUPAC)
   2. (11β,17β)-11-[4-(dimethylamino)phenyl]-17-hydroxy-17-(1-propynyl)estra-4,9-diene-3-one (CAS)
   3. 17β-hydroxy-11β –(4-dimethylaminophenyl)-17α-(1-propynyl)estra-4,9-dien-3-one



3. **Proposed indication:** Korlym (mifepristone) is a cortisol receptor blocker indicated to treat the clinical and metabolic effects of hypercortisolism in patients with endogenous Cushing's syndrome, including:
   - Patients with Cushing's disease who have not adequately responded to or relapsed after surgery
   - Patients with Cushing's disease who are not candidates for surgery

(b) (4)

4. **Type of meeting requested:** Meeting to discuss proposed REMS (Type B)
5. **Purpose of meeting:** To review and discuss the proposed REMS that will be implemented in association with the treatment of patients with Cushing's syndrome with Korlym (mifepristone).
6. **Objectives of meeting:** To obtain agreement from the Agency on the goals and the specific elements of the REMS, including the Medication Guide, communication plan, proposed elements to assure safe use (ETASU), the implementation system, and the timetable for submission of assessments.

7. **Proposed agenda:** We propose that the final list of questions submitted in the background package should serve as the agenda for the meeting. We will not plan any presentation, so that all the meeting time can be devoted to discussion of the questions.

(b) (4)

b. Korlym will be available through a limited number of specialty pharmacies (b) (4)
(b) (4)

c. All patients must be registered into the program and document that they understand the risks of treatment with Korlym. Female patients of child bearing potential must have a negative pregnancy test prior to receiving Korlym.

(b) (4)

[redacted]

9. **List of proposed Corcept attendees:**

Lorene Campbell, Project Director, Commercial Operations
Bernadette DeArmond, M.D., M.P.H., Post-Marketing and Safety Surveillance
Johanna Hunt, Program Director
Steven Lo, Vice President, Commercial Operations
Robert Roe, M.D., President, Corcept Therapeutics
Luana Staiger, Regulatory Affairs

(b) (4)

[redacted]

10. **List of proposed Agency staff:** We request appropriate representatives from the clinical and safety review teams from the Division of Metabolism and Endocrinology Products and the Office of Surveillance and Epidemiology responsible for review and approval of REMS.

11. **Date for submission of background materials:** Background materials will be submitted 28 days prior to the meeting.

12. **Proposed dates for meeting:** Week of December 5 or 12, 2011

Corcept
THERAPEUTICS

October 4, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) Tablets
Amendment to a Pending Application: Response to Request for Information

Dear Ms. Weber:

This submission is in response to your e-mail request of October 3, 2011 to provide the dataset with the raw concentration data for individual subjects for study C1073-05. The data were part of the SAS dataset submitted on September 21, 2011 and are also provide here in an Excel file on CD.

Please let me know if you have any questions on this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Corcept
THERAPEUTICS

September 21, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) Tablets
Amendment to a Pending Application: General Correspondence

Dear Ms. Weber:

This submission is in response to the letter received by Corcept dated September 13, 2011 requesting that we inform you of any studies submitted to the NDA that were conducted by Cetero Research in Houston, TX.

Corcept has not submitted any studies conducted by Cetero Research, Houston, TX, during the time period of April 1, 2005 to June 15. 2010.

Corcept did use a clinical site for study C1073-400 that was acquired by Cetero Research during the time the study was ongoing. (b) (4) was acquired by Cetero in April 2008. Two patients were treated (b) (4) from August 2008 to April 2009 (b) (4). No patients were treated in Houston nor were any analytical samples sent to Houston for assay. Based on this, no further action is warranted with regard to this study.

Sincerely,

Luana Staiger

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

cc. Office of New Drugs; CDER, 10903 New Hampshire Avenue, Bldg 22, Room 6300

Corcept THERAPEUTICS

September 21, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) Tablets
Amendment to a Pending Application: Response to Request for Information

Dear Ms. Weber:

This submission is in response to your request of September 13, 2011 to provide the datasets used for PK analysis for studies C1073-05 (Hepatic Impairment), C1073-19 (Renal Impairment), C1073-24 (DDI with Alprazolam), and C1073-26 (DDI with Cimetidine). The CD enclosed herein contains the requested files as follows:

Study Number Folder	File	Contents
Study C1073-05	x051904dat_copy.xpt	Raw data sets
	x051904ana_copy.xpt	Analysis data sets
	Study C-1073-05 PK Parameters.xpt	Data set of PK parameters
	Study C-1073-05 Table 14.2.6 and errata.pdf	Corrected Table 14.2.6 from the clinical study report and errata page*
*For study C1073-05, an error was found in the clinical study report Table 14.2.6 whereby the Period 1 C-1073 (mifepristone) AUC0-24 values were mistakenly populated with the values from the analyte RU 42633. A corrected Table 14.2.6 is provided on the CD with the correct values.		
Study C1073-19	PKPC.xpt	Plasma concentration and nominal/actual elapsed time data in CDISC format
	PKPP.xpt	Pharmacokinetic parameters in CDISC format
	EX.xpt	Dose administration information in CDISC format
	C1073_Plasma_20101214.xls	Total mifepristone and metabolite concentrations in plasma
	PF10M-0010 Results12-15-10.xls	% free and % bound drug in plasma

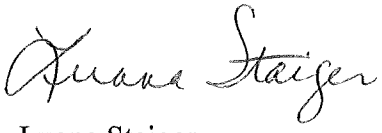
149 Commonwealth Drive • Menlo Park, CA 94025 • Tel 650.327.3270 • Fax 650.327.3218

Study Number Folder	File	Contents
Study C1073-24	PKPC.xpt	Plasma concentration and nominal/actual elapsed time data in CDISC format
	PKPP.xpt	Pharmacokinetic parameters in CDISC format
	EX.xpt	Dose administration information in CDISC format
	C107324_2500301 (2).xls	Alprazolam plasma concentrations
	Final C107324_25MAR10.xls	Total mifepristone and metabolite concentrations in plasma
Study C1073-26	PKPC.xpt	Plasma concentration and nominal/actual elapsed time data in CDISC format
	PKPP.xpt	Pharmacokinetic parameters in CDISC format.
	EX.xpt	Dose administration information in CDISC format
	C_1073_26_Plasma_20100824 (Final).xls	Total mifepristone and metabolite concentrations in plasma
	c107326 urine volume.xls	Urine collection volumes
	C107326_Plasma_20100824.xlsx	Cimetidine plasma concentrations
	C107326_Urine_20101018.xls	Cimetidine urine concentrations

Also provided on the CD is a cross reference table for the Excel file names that are also included in the table above. Different file names were used by the different laboratories that performed the analyses.

Please let me know if you have any questions on this submission.

Sincerely,



Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 0202107 **INFORMATION REQUEST**

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

CORCEPT Therapeutics
Attention: Luana Staiger
Regulatory Affairs
149 Commonwealth Drive
Menlo Park, CA 94025

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mifepristone 300 mg Tablets.

FDA investigators have identified significant violations to the bioavailability and bioequivalence requirements of Title 21, Code of Federal Regulation, Part 320 in bioanalytical studies conducted by Cetero Research in Houston, Texas (Cetero).[1] The pervasiveness and egregious nature of the violative practices by Cetero has led FDA to have significant concerns that the bioanalytical data generated at Cetero from April 1, 2005 to June 15, 2010, as part of studies submitted to FDA in New Drug Applications (NDA) and Supplemental New Drug Applications (sNDA) are unreliable. FDA has reached this conclusion for three reasons: (1) the widespread falsification of dates and times in laboratory records for subject sample extractions, (2) the apparent manipulation of equilibration or "prep" run samples to meet pre-determined acceptance criteria, and (3) lack of documentation regarding equilibration or "prep" runs that prevented Cetero and the Agency from determining the extent and impact of these violations.

Serious questions remain about the validity of any data generated in studies by Cetero Research in Houston, Texas during this time period. In view of these findings, FDA is informing holders of approved and pending NDAs of these issues.

The impact of the data from these studies (which may include bioequivalence, bioavailability, drug-drug interaction, specific population, and others) cannot be assessed without knowing the details regarding the study and how the data in question were considered in the overall development and approval of your drug product. At this time, the Office of New Drugs is searching available documentation to determine which NDAs are impacted by the above findings.

[1] These violations include studies conducted by Bioassay Laboratories and BA Research International specific to the Houston, Texas facility.

To further expedite this process, we ask that you inform us if you have submitted any studies conducted by Cetero Research in Houston, Texas during the time period of concern (April 1, 2005 to June 15, 2010). Please submit information on each of the studies, including supplement number (if appropriate), study name/protocol number, and date of submission. With respect to those studies, you will need to do one of the following: (a) re-assay samples if available and supported by stability data, (b) repeat the studies, or (c) provide a rationale if you feel that no further action is warranted.

Please respond to this query within 30 days from the date of this letter.

This information should be submitted as correspondence to your NDA. In addition, please provide a desk copy to:

Office of New Drugs
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Room 6300
Silver Spring, MD 20993-0002

If you have any questions, please call Jena Weber, Regulatory Project Manager, at 301-796-1306.

Sincerely,

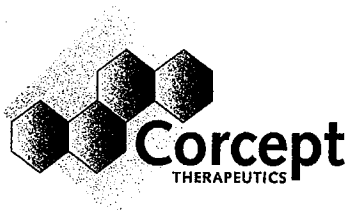
{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

JULIE C MARCHICK
09/13/2011
J. Marchick signing for M. Parks



August 12, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) Tablets
Amendment to a Pending Application: 4-Month Safety Update

Dear Ms. Weber:

In accordance with 21 CRF 315.50(d)(5)(vi)(b), provided here is the 4-month safety update to NDA 202107. Provided in the Reviewer Guide in section 1.6.1 is a summary of the contents of the update, including the details of the information provided on the enclosed CD.

Please contact me at (650) 678-7230 with any questions regarding the enclosed information.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

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Corcept
THERAPEUTICS

August 4, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: NDA 202107 – Korlym™ (mifepristone) Tablets
Amendment to a Pending Application: Response to CMC Requests of June 28, 2011

Dear Ms. Weber:

With regard to your Filing Communication dated June 28, 2011, attached are the responses to the **Chemistry, Manufacturing and Controls** requests.

FDA request:

1. **Please confirm that the formulations coded "E2" in the Clinical Summary (section 2.7.1), and "C2" in the Quality Summary (sec 2.3.P.2), are identical and that they are the final formulation used in the commercial product.**

Corcept response:

The formulation coded "E2" in the Clinical Summary (section 2.7.1) is identical to the formulation coded "C2" in the Quality Summary (sec 2.3.P.2) and represents the formulation proposed for the commercial product. There is one correction to be made to Table A1 in the Clinical Summary (section 2.7.1) for formulation E2; the amount of sodium starch glycolate should be (b) (4). The corrected table is provided as Attachment 1. The corrected table has identical formulation information to Table 13 of the Quality Summary (section 2.3.P.2).

149 Commonwealth Drive · Menlo Park, CA 94025 · Tel 650.327.3270 · Fax 650.327.3218

FDA request:

2. Submit the master batch records for the drug product manufacture per 21 CFR 314.54(a)(1)(i).

Corcept response:

The master batch record for mifepristone tablet product manufacture is provided in Attachment 2. The record is in draft form and will be approved prior to manufacture of drug product validation batches. If there are any changes made to the record, a revised record will be submitted.

Please let me know if you have any questions on this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

List of Attachments

Attachment 1 Corrected Table A 1 for Section 2.7.1
Attachment 2 Master Batch Record for Mifepristone Tablets, 300 mg

August 4, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 – Korlym™ (mifepristone) Tablets**
Amendment to a Pending Application: Electronic Copy of Module 2 and Module 3

Dear Ms. Weber:

With regard to your request to provide an electronic copy of Module 2 and Module 3 of the NDA, enclosed please find the files on CD.

Please let me know if you have any questions on this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

List of Enclosures

CD containing copy of Module 2 and Module 3

Corcept
THERAPEUTICS

July 27, 2011

Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
Food and Drug Administration
Document and Records Section
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Re: NDA 202107: REQUEST FOR PROPRIETARY NAME REVIEW

Primary Name: Korlym™

Dear Ms. Holquist:

Reference is made to New Drug Application 202107 for mifepristone oral tablets submitted on April 15, 2011, to Corcept's submission of April 19, 2011 requesting review of the proposed proprietary name (b) (4), and to your letter of July 18, 2011 with the finding that the name (b) (4) was unacceptable.

We are requesting a review of the proposed back-up proprietary name Korlym. Following is general information on the respective name:

Korlym	
Intended Pronunciation of the Proposed Proprietary Name	kore' lim
Derivation of Proprietary Name	Blank canvas
Intended Meaning of Proprietary Name Modifier (if applicable)	Not applicable
Pharmacologic/Therapeutic Category	GR-II receptor antagonist

Included with this request are the following attachments:

1. Draft container label and Package Insert revised with the proposed proprietary name
2. *Proprietary Name Safety Summary for Korlym™* for review by the Division of Medication Error Prevention and Analysis (DMEPA), OSE

149 Commonwealth Drive • Menlo Park, CA 94025 • Tel 650.327.3270 • Fax 650.327.3218

Corcept Therapeutics contracted with Drug Safety Institute (DSI) to conduct a nomenclature research study, including an orthographic handwriting analysis, on the candidate name Korlym. The enclosed report discloses the conclusions of that study in detail, and describes the methodology used to conduct the research. The research demonstrated that Korlym is not confusingly similar to existing US drug names or names of related products for review by DMEPA.

Based on these findings, we request that Korlym be considered as the proprietary name.

Please contact me at (650) 678-7230 with any questions regarding the enclosed information.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

July 20, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 – (b) (4) (mifepristone) Tablets**
Amendment to a Pending Application: Response to Biopharmaceutics Requests of June 28, 2011

Dear Ms. Weber:

With regard to your Filing Communication dated June 28, 2011, attached are the responses to the **Biopharmaceutics** requests.

Please let me know if you have any questions on this submission.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 202107

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Corcept Therapeutics
149 Commonwealth Drive
Menlo Park, CA 94025

Attention: Luana Staiger
Director Regulatory Affairs

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) dated April, 15, 2011, and received April 18, 2011, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Mifepristone Tablets, 300 mg.

We also refer to your April 19, 2011, correspondence, received April 21, 2011, requesting review of your proposed proprietary name, (b) (4). We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

We note that you have proposed an alternate proprietary name in your submission dated April 19, 2011. In order to initiate the review of the alternate proprietary name, Korlym, submit a new complete request for proprietary name review. The review of this alternate name will not be initiated until the new submission is received.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Ermias Zerislassie, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0097. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager Jena Weber at (301) 796-1306.

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

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

/s/

CAROL A HOLQUIST
07/18/2011

July 13, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 – [redacted] (b) (4) (mifepristone) Tablets**
Amendment to a Pending Application: Response to Biometrics Requests of June 28, 2011

Dear Ms. Weber:

With regard to your Filing Communication dated June 28, 2011, attached are the responses to the **Biometric** requests. Provided on the enclosed CD is the SAS program referenced in the response.

Please let me know if you have any questions on this submission.

Sincerely,

Luana Staiger

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

July 12, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 – [redacted] (b) (4) (mifepristone) Tablets**
Amendment to a Pending Application: Response to Request Dated June 10, 2011 on TQT Study

Dear Ms. Weber:

Attached here are responses to the request from the TQT group originally sent to Corcept via e-mail on June 10, 2011, with further explanation provided by Devi Kozeli, Regulatory Health Project Manager, QT Interdisciplinary Review Team, in an e-mail dated June 17, 2011. The enclosed CD includes the requested datasets and define file.

Please let me know if you have any questions or need further information with regard to this submission.

Sincerely,

Luana Staiger

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Following are responses to the request for information originally sent on June 10, 2011; supplementary information was received from Devi Kozeli on June 17, 2011. Each FDA request is shown in bold with response from Corcept following.

With regard to this study report, please ask the sponsor to provide the following:

FDA comment:

***ECG raw duplicate dataset**

Only analysis datasets were submitted, the requested ECG raw dataset was not submitted. The original raw dataset should include all duplicates and all ECGs that were submitted to ECG warehouse (small difference of number of observations is allowed), the raw dataset can be like dataset qtci.xpt but be sure to add one more variable ECG time, the ECG time should be up to second. 33353 ECGs were submitted to ECG warehouse, qtci.xpt is analysis dataset and just has 32955 observations.

Corcept response:

Provided on CD is the ECG raw dataset in a SAS transport file (ecg.xpt). All duplicates and all ECGs that were submitted to the ECG warehouse are included.

With regard to the differences in number of observations, when converting from the ECG raw dataset to create the QTCI dataset, sometimes there was more than one ECG raw record for a given replicate because some of the intervals could not be read on one lead, so a second lead was provided to supply the missing interval. For example, if PR interval was missing on Lead II but was available on Lead V5, then the PR interval was taken from Lead V5 and the other intervals from Lead II and condensed into a single record. The algorithm for handling this was specified in the Statistical Analysis Specification (see Corcept clinical study report C-1073_300 A, Module 5.3.4.1.1, Appendix 16.1.9, Statistical Analysis Specification Final 22 February 2011, page 2, Section 1, item 1a-1e.

FDA comment:

***A define file which describes the contents of the electronic dataset**

Normally we need a pdf define file that describe each variable of each dataset. The label information of the dataset didn't give us basic and important information such as concentration unit. We can waive it since by comparing dataset values and a listing file, we could figure out concentration unit should be ng/mL (For some submissions, some time there are concerns between dataset unit and report unit).

Corcept response:

Provided on CD is the updated define file (in pdf format) for the analysis dataset (adpk.xpt) that includes the concentration unit. The define file also addresses the update to the ADSL file to include HEIGHT, WEIGHT, and BMI as noted below.

FDA comment:

***An updated ADSL.xpt dataset with subject baseline HEIGHT, WEIGHT, BMI information if collected.**

Please update the dataset with subject baseline HEIGHT, WEIGHT, BMI information if collected.

Corcept response:

The data on HEIGHT, WEIGHT, and BMI have been merged into the ADSL dataset that is included on the CD.

FDA comment:

***Make sure that ECG raw dataset includes all duplicates and at least the following: subject ID, treatment, ECG date, ECG time up to second, nominal day, nominal time, replicate number, heart rate HR, intervals QT, RR, PR, QRS and QTc (all corrected QT as end points in your report, e.g., QTcB, QTcF, QTcI, QTcN, etc, ECG ID (link to waveform files if applicable)**

See the above answer.

Corcept response:

All duplicates are included in the ECG raw data together with the above variables with the exception of the following:

-Treatment: Because treatment is blinded, this variable is not included in the raw dataset.

-QTcI: Since QTcI is a derived variable and not a raw variable, it is not included in the raw dataset. This is included in both the QTCI and the ADEG datasets.

-QTcN: This was not a planned variable for the study and is not included in the dataset.

The link to the waveform files is contained in the raw dataset as the variable TRANS NO.

Corcept
THERAPEUTICS

July 11, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

RECEIVED
JUL 12 2011
CDR

ORIGINAL

SDN 7

Subject: **NDA 202107 – [redacted] (b) (4) (mifepristone) Tablets**
Amendment to a Pending Application: Response to Clinical Pharmacology Request of June 28, 2011

Dear Ms. Weber:

With regard to your Filing Communication dated June 28, 2011, following is the response to the Clinical Pharmacology request. This response was originally sent via e-mail on July 7, 2011; this is a hard copy submission to the NDA.

FDA request:

Clinical Pharmacology

Based on study reports for study C-1073-400 and study C-1073-415 it is noted that mifepristone plasma levels were analyzed in patients. Provide the pharmacokinetic datasets from these studies in SAS transport format. Also include data that was used for covariate analysis (e.g., co-medication of ketoconazole). If you have submitted the datasets, please identify the location.

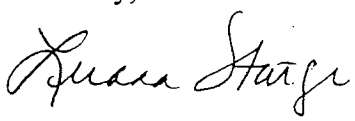
Corcept response:

The datasets for mifepristone trough levels that were collected in studies C-1073-400 and C-1073-415 were submitted in SAS transport format in the NDA. They can be found in EDR folder #6. Within the folder for each respective study, they can be found under tabulations/legacy/trough.xpt.

We would like to request further clarification about the remainder of this request. We did not perform any covariate analysis on data from study C-1073-400 or C-1073-415 exclusively. We did conduct some covariate analyses on data that were pooled across

studies, including data from healthy subjects as well as Cushing's patients. However, these analyses did not include any assessments of concomitant medications. The analyses we conducted are described in the Summary of Clinical Pharmacology in Module 2 (Section 2.7.2) in Section 2.7.2.3 (Comparison and Analysis of Results Across Studies). The discussion of covariate analyses begins on p. 110 under "The Effect of Intrinsic Factors on Mifepristone PK". Can you please provide more information about any additional datasets you would like us to submit.

Sincerely,



Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

June 30, 2011

Susan Leibenhaut, M.D., Medical Officer
FDA/CDER Office of Compliance
Office of Scientific Investigations
Division of Good Clinical Practice Compliance
10903 New Hampshire Avenue
Building 51, Room 5366
Silver Spring, MD 20993

Subject: **NDA 202107 [redacted] (b) (4) (mifepristone) Tablets**
Response to request for information needed for clinical inspection at two investigational sites

Dear Dr. Leibenhaut:

This submission contains Corcept's response to the request received from Ms Jena Weber of the Division of Metabolism and Endocrinology Products on June 28, 2011. The requested information is found on 2 CDs, one labeled "Site 7: Schteingart" and the other labeled "Site 8: Fleseriu". Both CDs contain the information requested in item 1 (original protocol and all amendments) and item 2 (sample annotated CRFs). A separate pdf file on each CD contains the requested listings (a – s) for the labeled site. Two copies of each CD are enclosed.

In response to your question in item 3 about the location and format of source documents, we can confirm that all data are contained at the sites in paper format. However, the oral glucose tolerance test results were laboratory analyses, which were performed at [redacted] (b) (4) [redacted] (b) (4) Reports of the results for each site's patients were sent from [redacted] (b) (4) to that site, and these reports are contained in each site's files in paper format. These results were also sent electronically from [redacted] (b) (4) for entry into the study database. The analysis of this endpoint was conducted based on the direct data transfer from [redacted] (b) (4), not on information received from the sites regarding this endpoint.

There is one explanatory note about the listings on the CDs. Entries within the listings were arranged by site, so data from each site is grouped in consecutive listing entries, with one exception. This is the listing of protocol deviations (item e - 16.2.2.2), in which the entries were arranged chronologically rather than by site, so entries for each site are found non-consecutively across the listing. The column in that listing headed "Date Signed" refers to the date the deviation form was signed by Corcept.

149 Commonwealth Drive • Menlo Park, CA 94025 • Tel 650.327.3270 • 650.327.3218

Please contact me if you need further information.

Sincerely,

Bonnie Horner for

Luana Staiger
Regulatory Affairs
Ph: (650) 678-7230
Fax: (650) 327-3218
e-mail: lstaiger@corcept.com

cc: J. Weber (cover letter only)

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation OODP

FACSIMILE TRANSMITTAL SHEET

DATE: June 28, 2011

To: Luana Staiger Regulatory Affairs	**From:** Jena Weber Project Manager
Company: CORCEPT Therapeutics	Division of Metabolism & Endocrinology Products
Fax number: 650-327-3218	**Fax number:** 301-796-9712
Phone number: 650-678-7230	**Phone number:** 301-796-1306

Subject: Reference NDA 202107, initial submission dated April 15, 2011.

Total no. of pages including cover: 4

Comments: Reference attached pages and request from DSI for additional information to conduct clinical inspections on 2 sites. Please respond in writing to your NDA file as appropriate.

Document to be mailed: ☐ **YES** ☑ **NO**

For C1073-400 entitled “An Open-label Study of the Efficacy and Safety of CORLUX® (mifepristone) in the Treatment of the Signs and Symptoms of Endogenous Cushing’s Syndrome” please provide the following:

1. Original protocol and all amendments
2. A sample annotated Case Report Form
3. Please state the location and format of the source documents containing the primary efficacy (glucose measurements for the oral glucose tolerance tests and blood pressure readings) and safety endpoints. Specifically, are the data available at the clinical site and in what format? If not at the clinical site, please describe the location and format for the primary efficacy data.

Please provide line listings in pdf format for the following two sites.

Site 7: Dr. David Schteingart
University of Michigan Medical Center Division of Endocrinology;
5570 MSRB II Spc 5678
1150 W Medical Center Drive Ann Arbor, MI 48109-0678

Site 8: Dr. Maria Grama Fleseriu
Oregon Health Sciences University
Dept of Endo/Pituitary Unit 3515 SW
US Veterans Hospital Road;
BTE472 Portland, OR 97239

Please provide the listings electronically on CDs. Please provide the listings as one CD and a duplicate for each site, a total of four CDs. For each CD please include a copy of the protocol, amendments and annotated case report form on the CD. This package should be sent directly to:

Susan Leibenhaut, M.D.
Medical Officer
FDA/CDER/Office of Compliance
Office of Scientific Investigations
Division of Good Clinical Practice Compliance
Good Clinical Practice Assessment Branch
10903 New Hampshire Avenue
Building 51, Room 5366
Silver Spring, MD 20993
Phone 301-796-3626 Fax 301-847-8748
susan.leibenhaut@fda.hhs.gov

Request for Subject Level Data Listings by Site

For the two sites listed above, please provide the following line listings that have been submitted in paper form in your NDA:

a. Listing 16.2.1.0: Enrolled population
b. Listing 16.2.1.1: Subject Disposition: Safety Population
c. Listing 16.2.2: Listing of Study Completion by Visit: Safety Population
d. Listing 16.2.2.1: Listing of Screen Failure
e. Listing 16.2.2.2: Protocol Deviations
f. Listing 16.2.4.1: Subject Demographic and Baseline Characteristics: Safety Population
g. Listing 16.2.4.2.2: Listing of Past Cushing's Disease History: Safety Population
h. Listing 16.2.4.4.1: Listing of Prior Medications: Safety Population
i. Listing 16.2.4.4.2: Listing of Concomitant Medications: Safety Population
j. Listing 16.2.4.5.1: Listing of Anti -Diabetic Concomitant Medications: Safety Population
k. Listing 16.2.4.5.2: Listing of Anti-Hypertension Concomitant Medications: Safety Population
l. Listing 16.2.5.1: Listing of Drug Administration: Safety Population
m. Listing 16.2.6.1.1: Listing of Plasma Glucose Concentration Data from 2-hour oGTT: C-DM Cohort: ITT/Safety Population
n. Listing 16.2.6.1.3 Listing of Deviation of Plasma Glucose Sampling Time: C-DM Cohort: ITT/Safety Population
o. Listing 16.2.6.2.1: Listing of Individual Blood pressure Data: C-HT and C-DM: ITT/Safety Population
p. Listing 16.2.7.2: Listing of All Adverse Events: Safety Population
q. Listing 16.2.7.3: Listing of Subjects Withdrawn Due to AEs: Safety Population
r. Listing 16.2.7.4: Listing of Deaths or SAEs: Safety Population
s. Listing 16.2.7.5: Listing of Treatment-Emergent Adverse Events by Dose Levels: Safety Population

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

/s/

JENA M WEBER
06/28/2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202107

FILING COMMUNICATION

CORCEPT Therapeutics
Attention: Luana Staiger
Regulatory Affairs
149 Commonwealth Drive
Menlo Park, CA 94025

Dear Ms. Staiger:

Please refer to your New Drug Application (NDA) dated April 15, 2011, received April 18, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for mifepristone 300 mg tablets.

We also refer to your submission dated April 25, 2011.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is **February 17, 2012**.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by January 27, 2012.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

We also request that you address the following comments and requests in writing to your NDA file:

Chemistry, Manufacturing and Controls

1. Please confirm that the formulations coded "E2" in the Clinical Summary (section 2.7.1), and "C2" in the Quality Summary (sec2.3.P.2), are identical and that they are the final formulation used in the commercial product.

2. Submit the master batch records for the drug product manufacture per 21 CFR 314.54(a)(1)(i).

Biopharmaceutics

We acknowledge that you included the dissolution method validation report that was requested in the pre-NDA meeting from October 26, 2010. However, this report includes the validation of the analytical method and the quality testing of the dissolution methodology (i.e., robustness, etc.), but does not contain the dissolution information collected during the development of the proposed dissolution test, and how you concluded that this test is the optimal method for the evaluation of your product. Therefore, please provide the dissolution method development report outlining the experiments performed and all data collected by (b) (4) to support revising the (b) (4) dissolution method. This report should clearly outline the following information:

1. Complete mifepristone pH solubility over the pH range of 1 to 7.5 (both numerical and graphed data), including a description of the buffers and conditions used to determine equilibrium solubility. Solution pH data measured before and after the product should be summarized.

2. Please specify the developmental parameters (i.e., selection of equipment/apparatus, in vitro dissolution/release media, agitation/rotation speed, pH, assay, sink conditions, etc.) used to select the dissolution method. Testing conditions used for each test and complete dissolution profile data (individual, mean, SD, profiles) should be submitted.

3. Testing conducted to demonstrate the discriminating capability of the proposed method to manufacturing changes should be stated.

Clinical Pharmacology

Based on study reports for study C-1073-400 and study C-1074-415 it is noted that mifepristone plasma levels were analyzed in patients. Provide the pharmacokinetic datasets from these studies in SAS transport format. Also include data that was used for covariate analysis (e.g., co-medication of ketoconazole). If you have submitted the datasets, please identify the location.

Biometrics

1. Please submit the parameter code for the Diastolic Blood pressure (SAS variable name for the primary efficacy variable for the C-HT cohort).

2. If you have submitted a subgroup analyses on Age, Gender, and Race, you should identify the location. If not, please provide these results as soon as possible.

Clinical

Submit or indicate where the following information about the patients enrolled in study C-1073-400 can be located:

1. Previous medical treatment of hypercortisolemia in patients with all causes of Cushing's syndrome:
   -how many patients were naïve to medical treatment prior to study enrollment;
   -the number of patients and which patients were treated medically and were subsequently "washed out" of treatment prior to enrollment;
   - if subjects were previously treated medically, indicate what antiglucocorticoid drugs were administered, in general, and by patient indicating the duration of medical treatment;
   - if patients were treated medically in the past, indicate the number of patients and which of them failed drug therapy.

2. Previous radiation treatment of patients with Cushing's disease:

   - specify the time period that elapsed for each patient since the last date of radiation treatment (years/months/days), and the beginning of study drug therapy.

3. Baseline urinary free cortisol information by patient and descriptive statistics for the entire cohort.

If you have not already done so, you must 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. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

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.

If you have any questions, please call Ms. Jena Weber, Regulatory Project Manager, at 301-796-1306.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research.

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

/s/

MARY H PARKS
06/28/2011

June 9, 2011

Division of Metabolism and Endocrinology Products
CDER - Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Subject: **NDA 202107 (b) (4) (mifepristone) Tablets**
Amendment: Updated Investigator Brochure

Reviewers:

We enclose a copy of the updated Investigator Brochure, Mifepristone (C-1073) for Treatment of Cushing's Syndrome, Edition 3. In e-mail correspondence with Ms Jena Weber (March 11, 2011) regarding supporting documentation for the submission of electronic data from a Thorough QT study, it was agreed that we should submit the revised Brochure within 60 days of the NDA submission. This NDA was submitted on April 15, 2011.

We are sending an archival copy and one additional paper copy of this amendment. We are also sending this documentation to Ms Jena Weber as an electronic file (pdf). Please contact me if you need further information.

Sincerely,

Bonnie Horner for

Luana Staiger
Regulatory Affairs

Ph: (650) 678-7230
Fax: (650) 327-3218
e-mail: lstaiger@corcept.com

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202107

NDA ACKNOWLEDGMENT

CORCEPT Therapeutics
Attention: Luana Staiger
Regulatory Affairs
149 Commonwealth Drive
Menlo Park, CA 94025

Dear Ms. Staiger:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Mifepristone 300 mg Tablets

Date of Application: April 15, 2011

Date of Receipt: April 18, 2011

Our Reference Number: NDA 202107

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 **June 17, 2011,** 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 Metabolism and Endocrinology 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.

If you have any questions, please call me at 301-796-1306.

Sincerely,

{See appended electronic signature page}

Jena M. Weber
Regulatory Project Manager
Division of Metabolism & Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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

/s/

JENA M WEBER
05/09/2011

April 25, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107** [redacted] (b) (4) **(mifepristone) Tablets**
Amendment to a Pending Application: Revised NDA Table of Contents

Dear Ms. Weber:

In reference to our teleconference of April 21, 2011, included with this amendment is a revised Table of Contents for NDA 202107. The Table of Contents has been amended to allow cross reference from Corcept assigned module and volume numbers to FDA Archive Volume Number, EDR Folder Number, and Technical Volume Number. Specific notation is provided for each document that was submitted on CD or DVD and reference to the EDR-assigned folder.

A copy of the amended Table of Contents, a copy of this cover letter, and a copy of the Form FDA 356h are also provided on the enclosed CD.

Please feel free to contact me at (650) 678-7230 with any further questions.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

April 22, 2011

Ms. Jena Weber
Project Manager
Division of Metabolism & Endocrinology Products
Center for Drug Evaluation and Research
Food and Drug Administration
Central Document Room
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Subject: **NDA 202107 (b) (4) (mifepristone) Tablets**
Amendment to a Pending Application: Electronic Copy of Label and Labeling

Dear Ms. Weber:

In reference to our teleconference of April 21, 2011 for NDA 202107, included with this amendment is an electronic copy of the container label and package insert for (b) (4) (mifepristone). Included on the enclosed disk are the following:

Cover Letter (pdf)
Form FDA 356h (pdf)
Container label (MS Word and pdf)
Package insert (MS Word and pdf)

Please feel free to contact me at (650) 678-7230 with any further questions.

Sincerely,

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

SON-2

DUPLICATE

RECEIVED

APR 21 2011

CDR

April 19, 2011

Carol Holquist, RPh, Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
Food and Drug Administration
Document and Records Section
5901-B Ammendale Rd
Beltsville, MD 20705-1266

Re: NDA 202107: REQUEST FOR PROPRIETARY NAME REVIEW

Primary Name: (b) (4)
Alternate Name: Korlym™

Dear Ms. Holquist:

Reference is made to New Drug Application 202107 for (b) (4) (mifepristone) oral tablets submitted on April 15, 2011.

We are requesting a review of the proposed proprietary name (b) (4). The alternative name, Korlym, is also included here. Should the primary name be found unacceptable, Corcept requests that the alternative name be reviewed. Following is general information on the respective names:

(b) (4)

Korlym	
Intended Pronunciation of the Proposed Proprietary Name	kore' lim
Derivation of Proprietary Name	Blank canvas
Intended Meaning of Proprietary Name Modifier (if applicable)	Not applicable
Pharmacologic/Therapeutic Category	GR-II receptor antagonist

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Included with this request are the following attachments:

1. Draft container label and Package Insert that have been submitted in the NDA
2. *Proprietary Name Safety Summary* [redacted] for review by the Division of Medication Error Prevention and Analysis (DMEPA), OSE
3. *Proprietary Name Safety Summary for Korlym*™ for review by the Division of Medication Error Prevention and Analysis (DMEPA), OSE

Corcept Therapeutics contracted with Drug Safety Institute (DSI) to conduct a nomenclature research study, including an orthographic handwriting analysis, on the primary candidate [redacted] and alternate name Korlym. The enclosed reports disclose the conclusions of that study in detail, and describe the methodology used to conduct the research. The research demonstrated that [redacted] is not confusingly similar to existing US drugs names or names of related products for review by DMEPA. Similar results were obtained with the alternate name Korlym.

Based on these findings, we request that [redacted] be considered as the proprietary name.

Please contact me at (650) 678-7230 with any questions regarding the enclosed information.

Sincerely,

Luana Staiger

Luana Staiger
Regulatory Affairs

Phone: (650) 678-7230
e-mail: lstaiger@corcept.com

Corcept
THERAPEUTICS

April 15, 2011

Division of Metabolism and Endocrinology Products
CDER - Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

Subject: **NDA 202107 (b) (4) (mifepristone) Tablets**
Initial Application with Request for Priority Review

Dear Reviewers:

Corcept is pleased to submit a New Drug Application for (b) (4) (mifepristone) Tablets, under section 505(b)(2) of the Federal Food, Drug, and Cosmetics Act, for the treatment of (b) (4); syndrome. The extent and organization of data submitted in support of the NDA are consistent with agreements that were reached between Corcept and the Division of Metabolic and Endocrine Products at the pre-NDA meeting held on September 14, 2010 and in other correspondence under IND 76,480.

The efficacy of (b) (4) for this indication has been demonstrated in study C1073-400 that was conducted in 50 patients with Cushing's syndrome. Support for the efficacy of mifepristone in Cushing's syndrome is provided in a review of literature reports of the treatment of Cushing's syndrome with mifepristone. The safety of mifepristone is supported by data from study C1073-400 and the long-term extension study, C1073-415. Additional safety data are provided from Corcept-sponsored studies conducted in other indications as well as from its clinical pharmacology program.

Request for Priority Review

Corcept is requesting a priority review designation for this application, as established in the Prescription Drug User Fee Act, as amended. Cushing's syndrome is a disease for which there is no approved drug treatment currently available in the United States. The disease is life-threatening and/or associated with very serious morbidities in the majority of patients. Corcept believes that the data presented in this application demonstrate that (b) (4) offers a major advance in the treatment of Cushing's syndrome.

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Corcept
THERAPEUTICS

Orphan designation has been granted to Corcept Therapeutics for the use of mifepristone in the treatment of clinical manifestations of endogenous Cushing's syndrome (designation 07-2395; July 5, 2007.)

We look forward to working with the Division on this application for approval of a new treatment for patients with endogenous Cushing's syndrome.

Sincerely,

Luana Staiger
Regulatory Affairs

Ph: (650) 678-7230
Fax: (650) 327-3218
e-mail: lstaiger@corcept.com

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

IND 076480

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Corcept Therapeutics
149 Commonwealth Drive
Menlo Park, CA 94025

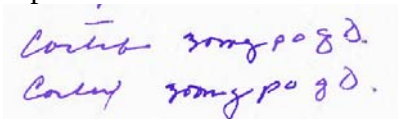
Attention: Bonnie Horner
Director Regulatory Affairs

Dear Ms. Horner:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Mifepristone Tablets, 300 mg.

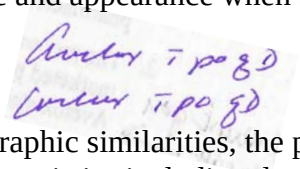
We also refer to your August 5, 2010, correspondence, received August 6, 2010, requesting review of your proposed proprietary name, Corlux. We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons.

1. The proposed proprietary name Corlux is orthographically similar to the currently marketed product Cortef. The orthographic similarity between the names, Corlux and Cortef stems from the fact that both names begin with the letters "Cor," share an upstroke letter in the fourth position and the remaining letters appear similar when scripted. Additionally, both names have 6 letters which gives them a similar shape and appearance when scripted.



In addition to their orthographic similarities, the proposed product and Cortef share overlapping product characteristics including dosage form, route of administration, numerical overlap in dose (30 mg vs. 300 mg), and frequency of administration. The overlapping product characteristics provide little means to prevent a medication error should the names Corlux and Cortef be confused by a pharmacist or other healthcare provider a written prescription or medication order.

2. The proposed proprietary name Corlux is orthographically similar to the currently marketed product Avelox. The orthographic similarity between the names Corlux and Avelox stems from the fact that the beginning letters 'A' and 'C' and ending letters 'lox' and 'lux' appear similar when scripted. Additionally, both names have 6 letters which gives them a similar shape and appearance when scripted.



In addition to their orthographic similarities, the proposed product and Avelox share overlapping product characteristics including dosage form, route of administration, overlapping dose, frequency of administration and are available in a single strength. When writing prescriptions, prescribers may often omit the strength of products that are only available in a single strength. The overlaps in product characteristics provide little means to prevent a medication error should the names Avelox and Corlux be confused by a pharmacist or other healthcare provider reading a written prescription or medication order.

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

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Margarita Tossa, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4053. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager Jena Weber at (301) 796-1306.

Sincerely,

{See appended electronic signature page}

Denise P. Toyer, PharmD.
Deputy Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

DENISE P TOYER
01/04/2011