

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-028

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

PATENT AND EXCLUSIVITY CERTIFICATION

Name of Applicant: Sandoz Canada Inc.
Address of Applicant: 145 Jules-Leger Street, Boucherville, QC CANADA J4B 7K8
Drug: Cosyntropin Injection

(1) PATENT CERTIFICATION STATEMENT

Sandoz Inc. ("Sandoz"), by this ANDA, is requesting approval for COSYNTROPIN INJECTION, 0.25 mg/vial (the "Sandoz Products"). Upon information and belief, Sandoz believes that Amphastar is the holder of the NDA for the listed drug product identified above.

Paragraph I Certification

In accordance with 21 U.S.C. §355(j)(2)(A)(vii)(I), Sandoz hereby certifies, upon information and belief, that patent information has not been listed in Approved Drug Products as covering Amphastar's CORTROSYN® brand cosyntropin injection, 0.25 mg/vial.

(2) EXCLUSIVITY STATEMENT

Sandoz hereby certifies that to the best of its knowledge, there are no unexpired exclusivities associated with the Approved Listed Drug Product, CORTROSYN® brand cosyntropin injection, 0.25 mg/vial.

Beth Brannan

Beth Brannan, US Agent for Sandoz Canada Inc.
Director Regulatory Affairs
Sandoz Inc.

EXCLUSIVITY SUMMARY

NDA # 22-028

SUPPL # N/A

HFD # 510 (DMEP)

Trade Name Cosyntropin Injection 0.25 mg/mL

Generic Name alpha 1-24 corticotropin

Applicant Name Sandoz Inc.

Approval Date, If Known February 21, 2008

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.

BE study entitled, "A Randomized, Open-Label, 2-Way Crossover, Bioequivalence, Pharmacodynamic Endpoint Study of Cosyntropin 0.25 mg/mL Injection and Cortrosyn (reference) Following a 0.25 mg IV Dose in Healthy Subjects."

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?

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

YES

NO

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

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

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

YES

NO

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES

NO

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

NDA# 16-750

Cortrosyn Injection

NDA#

NDA#

2. Combination product.

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

YES NO

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

NDA#

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

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

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

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

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

Investigation #1

YES NO

Investigation #2

YES NO

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

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

Investigation #1

YES NO

Investigation #2

YES NO

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

YES
Explain:

!
! NO
! Explain:

Investigation #2

YES
Explain:

!
!
! NO
! Explain:

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

YES NO

If yes, explain:

=====
Name of person completing form: Jena Weber
Title: Project Manager
Date: 2/19/08

Name of Office/Division Director signing form: Mary Parks, M.D.
Title: Division Director, HFD-510

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/

Mary Parks
2/21/2008 10:10:15 AM

PEDIATRIC PAGE

NDA 22-028

Supplement Type: N/A

Supplement Number: N/A

Stamp Date: February 6, 2006

UFGD: February 21, 2008

AE: December 6, 2006

HFD-510

Trade and generic names/dosage form: cosyntropin Injection 0.25 mg/mL

Applicant: Sandoz Inc.

Therapeutic Class: 5S

Indication previously approved:

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application: 1

Indication: Diagnostic agent in the screening of patients presumed to have adrenocortical insufficiency.

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

Products in this class for this indication have been studied/labeled for pediatric population

Disease/condition does not exist in children

Too few children with disease to study

There are safety concerns

Adult studies ready for approval

Formulation needed

Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 22-028
HFD-960/ Grace Carmouze

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

/s/

Jena Weber

2/1/2008 07:17:49 AM

Pediatric Research and Equity Act Waivers

Product name and active ingredient/ dosage form: Cosyntropin Injection 0.25 mg/mL

NDA 22-028

HFD-510

Sponsor: Sandoz

Indication: This new drug application provides for the use of Cosyntropin Injection as a diagnostic agent in the screening of patients presumed to have adrenocortical insufficiency

1. Pediatric age group to be waived – all.*
2. Reason for waiving pediatric assessment requirements (choose all that apply and provide justification):
 - a. Studies are impossible or highly impractical (e.g. the number of pediatric patients is so small or is geographically dispersed).
 - b. The product would be ineffective or unsafe in one or more of the pediatric group(s) for which a waiver is being requested.
 - c. The product fails to represent a meaningful therapeutic benefit over existing therapies for pediatric patients **and** is unlikely to be used in a substantial number of all pediatric age groups or the pediatric age group(s) for which a waiver is being requested.
 - d. Reasonable attempts to produce a pediatric formulation for one or more of the pediatric age group(s) for which the waiver is being requested have failed.

***Note: As specified in Pediatric Page for this NDA, studies have been fully waived because products in this class (specifically, this product) have been studied and labeled for the pediatric population.**



DEBARMENT CERTIFICATION

Sandoz Canada Inc. hereby certifies that it has not and will not use in any capacity the services of any person debarred under Section 306 (a) or (b) of the Federal Food, Drug and Cosmetic Act, in connection with this application. In addition, Sandoz Canada Inc. states that neither Sandoz Canada Inc. nor any individuals, partnerships, corporations, or associations responsible for the development or submission of this application have been convicted as described in Section 306 (a) and (b) of the Federal Food, Drug and Cosmetic Act.

Sandoz Canada Inc.



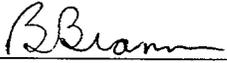
Peggy Levy
Manager, Development Regulatory Centre

2005-12-05
Date

DEBARMENT CERTIFICATION

Sandoz Inc. hereby certifies that it has not and will not use in any capacity the services of any person debarred under Section 306 (a) or (b) of the Federal Food, Drug and Cosmetic Act, in connection with this application. In addition, Sandoz Inc. states that neither Sandoz Inc. nor any individuals, partnerships, corporations, or associations responsible for the development or submission of this application have been convicted as described in Section 306 (a) and (b) of the Federal Food, Drug and Cosmetic Act.

Sandoz Inc.



Beth Brannan
Director, Regulatory Affairs
Sandoz Inc.

2/3/06

Date

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	
------------------------	--

b(4)

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).
- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME SUZANNE LEVESQUE	TITLE HEAD, SANDOZ DEVELOPMENT CENTER
FIRM / ORGANIZATION SANDOZ CANADA INC.	
SIGNATURE 	DATE Dec. 20, 2005

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

9 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

Withheld Track Number: Administrative- 1

Weber, Jena M

From: alison.sherwood@sandoz.com
Sent: Friday, February 15, 2008 6:12 PM
To: Weber, Jena M
Cc: beth.brannan@sandoz.com; peggy.nolder@sandoz.com
Subject: NDA 22-028 Revised PI
Attachments: Cosyntropin Injection 0.25 mg mL.pdf.zip; Cosyntropin Injection 0.25 mg mL.doc.zip; 1006414 136x296mm 02-2008 U.pdf.zip; side by side.doc.zip

Dear Jena

Attached please find the current version of the physician insert including the new figure as you previewed earlier today and found acceptable. / _____

b(4)

Please let us know if you need us to submit anything else prior to the approval of the NDA.

As I mentioned, I will be out of the office on Tuesday, therefore please copy Beth Brannan on any emails regarding this application. You can also call her at 303-438-4237.

Thank you and best regards

Alison Sherwood
Senior Regulatory Affairs Associate

Phone: 303-438-4513 (direct)
Fax: 303-438-4600
E-mail: alison.sherwood@sandoz.com

www.sandoz.com

Sandoz Inc.
2555 W. Midway Blvd., P.O. Box 446
Broomfield, CO 80038-0446
USA



Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Tel +1 303 438-4237
Fax +1 303 438-4600
Email:
Beth.Brannan@gx.novartis.com

OVERNIGHT DELIVERY

Mary H. Parks, M.D., Acting Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology
Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

Labeling Amendment
(electronic labeling)

FEB 12 2008

RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
Labeling Amendment: Revised Package Insert per Email Request

Dear Dr. Parks:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting a labeling amendment to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.60.

Reference is made to the email request from Jena Weber on February 1, 2008 and follow up revision requested on February 11, 2008. We are providing the revised package insert electronically.

One CD is provided which includes the content described below. Accordingly, Sandoz confirms that this CD is virus free and that a letter of non repudiation agreement was submitted by Sandoz Inc. on November 30, 2007.

Document	NDA 22-028
356(h) Form (scanned)	356h.pdf
Sandoz Cover Letter (scanned)	cover.pdf
Physician Insert MS Word	Cosyntropin Injection.doc
Physician Insert pdf	Cosyntropin Injection.pdf
SPL Folder	SPL
Physician Insert – final print artwork	Cosyntropin Actual Size.pdf
Side by Side Comparison with Rev. 09-2006	SideBySide.doc

1 Page(s) Withheld

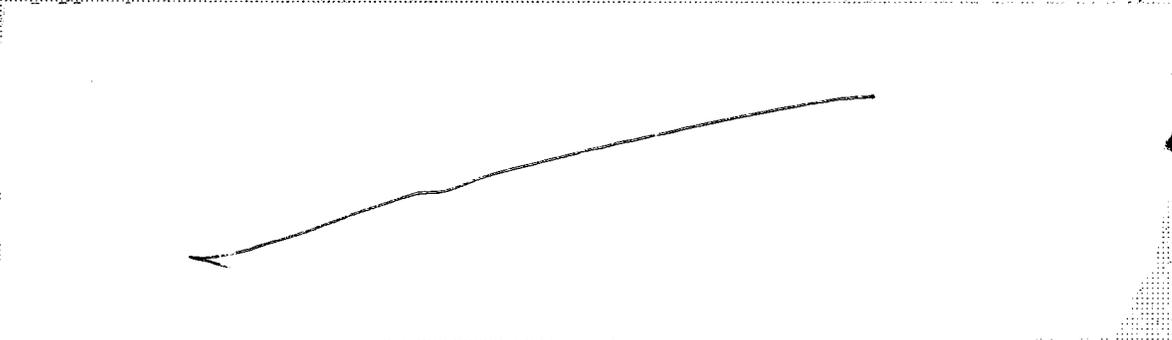
Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

Withheld Track Number: Administrative- 2



b(4)

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,
Sandoz Inc.

Beth Brannan,
Director Regulatory Affairs
US Regulatory Agent

Enclosures
BB/ags

Cc: Maria Garofalo (submission)



Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Tel +1 303 438-4237
Fax +1 303 438-4600
Email:
Beth.Brannan@gx.novartis.com

OVERNIGHT DELIVERY

Mary H. Parks, M.D., Acting Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

**MINOR AMENDMENT
CHEMISTRY**

AGS
12-21-07 21
DEC 20 2007

**RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
Minor Amendment: Chemistry: Response to November 7, 2007 Request**

Dear Dr. Parks:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting a minor amendment to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.70.

Reference is made to the request on November 7, 2007 from Dr. Martin Haber. A copy of this request is included for ease of review. Please find enclosed a complete response prepared by Sandoz Canada Inc.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,
Sandoz Inc.

Beth Brannan,
Director Regulatory Affairs, US Regulatory Agent

Enclosures
BB/ags
Cc: Maria Garofalo (CL)



FIELD CERTIFICATION

Sandoz Inc. hereby certifies that all required information necessary to provide appropriate notification regarding Sandoz Canada Inc.'s correspondence to pending NDA 22-028 for Cosyntropin Injection 0.25mg/mL will be provided to the appropriate field office.

BB

12/21/07

Beth Brannan
Director, Regulatory Affairs

Date

Chemistry comments for Cosyntropin NDA 22-028. Please reply in writing to your NDA file.

Provide information regarding the Eur. Ph. reference standard used for the bioassay (e.g. potency, certificate of analysis, etc.).

Provide an explanation of the calculations used in the bioassay to convert the measured relative potency to the final stated potency in IU/mg substance / _____

b(4)

Reduce the acceptance limits for / _____ and total unspecified impurities in drug product to those proposed for the drug substance (_____, respectively) or provide justification for higher limits. Explain why an unspecified impurity at _____ is present in the drug substance but not the drug product. Attempt to identify all impurities normally found at or above 0.5%.

b(4)

NDA Number: 22-028

Date: 2007-11-07

Applicant's Name: Sandoz Canada Inc.

Established Name: Cosyntropin Injection 0.25 mg/mL

POINT 1. Provide information regarding the Eur. Ph reference standard used for the bioassay (e.g. potency, certificate of analysis, etc.)

RESPONSE : Please note that for the bioassay, the Novartis reference substance batch 1129 was used. This batch was calibrated against the International Reference Standards (National Institute for Biological Standards and Controls; NIBSC) with a declared potency of \approx IU **b(4)** of _____ per ampoule.

Please find enclosed in Attachment 1, information regarding the standard from the NIBSC and the certificate of analysis for batch 1129.

NDA Number: 22-028

Date: 2007-11-07

Applicant's Name: Sandoz Canada Inc.

Established Name: Cosyntropin Injection 0.25 mg/mL

POINT 2.

Provide an explanation of the calculations used in the bioassay to convert the measured relative potency to the final stated potency in IU/mg substance _____

b(4)

RESPONSE:

In order to obtain the final potency in IU/mg of substance _____ the following calculations are done for the working standard WS2 (COA provided in Attachment 3 of the August 20, 2007 Amendment):

b(4)

b(4)

NDA Number: 22-028

Date: 2007-11-07

Applicant's Name: Sandoz Canada Inc.

Established Name: Cosyntropin Injection 0.25 mg/mL

POINT 3. Reduce the acceptance limits for _____ and total unspecified impurities in the drug product to those proposed for the drug substance (_____, respectively) or provide justification for higher limits. **b(4)**

RESPONSE: As requested, please find enclosed in Attachment 2, the revised drug product specifications where the limits for _____ and the total unspecified impurities are in line with the drug substance specifications. **b(4)**

NDA Number: 22-028

Date: 2007-11-07

Applicant's Name: Sandoz Canada Inc.

Established Name: Cosyntropin Injection 0.25 mg/mL

POINT 4. Explain why an unspecified impurity at _____ is present in the drug substance but not the drug product. Attempt to identify all impurities normally found at or above 0.5%. b(4)

RESPONSE: After investigation, it is suspected that there was a contamination with the packaging when the drug substance lot was received the first time (i.e. first reception). Note that when analyzing subsequent receipts of the lot in question, the peak at _____ was not detected. b(4)

Regarding the second portion of the comment, _____ peaks at _____ were detected with levels above _____ of these peaks were identified and the origin of these peaks determined. Regarding, the peak _____, attempts have been made to identify the peak, however, due to its close proximity to the principal peak (active), it is not possible at the moment to determine its origin. Several avenues are being pursued. Should identification of this peak be made, results will be provided in the annual report. Please refer to Attachment 3, for further details regarding the analytical worked performed to identify the above mentioned peaks. b(4)

In light of the request, a note has been added in the drug substance and drug product specifications to identify any peaks above 0.5%.



Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

ORIGINAL

Tel +1 303 438-4237
Fax +1 303 438-4600
Internet:
Beth.Brannan@sandoz.com

Mary H. Parks, M.D., Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology
Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

CDER/CDR

DEC 07 2007

RECEIVED

ORIGINAL AMENDMENT

N(BC)

DEC 6 2007

**RE: Field Copy of Minor Amendment for NDA 22-028
Cosyntropin Injection 0.25mg/mL**

Dear Director:

On behalf of Sandoz Canada Inc. and pursuant to 21 CFR 314.50(l)(3), we are providing a copy of a minor amendment to NDA 22-028 for Cosyntropin Injection 0.25mg/mL.

As Sandoz Canada Inc. is a foreign applicant, we are submitting the field copy to the CDER Office of New Drug Chemistry.

The required information is provided.

Sincerely,

Sandoz Inc.

Ashwood for
Beth Brannan, Director
Drug Regulatory Affairs

Enclosures

BB/ags



ORIGINAL
pediatric Director
Regulatory Affairs

RECEIVED

OCT 16 2007

CDER CDR

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446
Tel +1 303 438-4237
Fax +1 303 438-4600
Email:
Beth.Brannan@gx.novartis.com

OVERNIGHT DELIVERY

Mary H. Parks, M.D., Acting Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

**GENERAL CORRESPONDENCE
CHEMISTRY**

OCT 15 2007

ORIG AMENDMENT

N-000-(BC)

OCT 17 2007

CDER CDR

**RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
General Correspondence- Submission of Impurity Profile Summary**

Dear Dr. Parks:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting general correspondence to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.70.

Reference is made to the request on October 3, 2007 from Dr. Martin Haber for a summary of the impurity profile of the product with all available lots (API and Drug Product) including identification of method version. A table is provided on the following page.

Additionally, revised stability tables are provided. These stability reports replace the data filed on September 17, 2007. The previous filed reports included an error in the reported impurities at the 24 month time point; the current reports provide the corrected values.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,
Sandoz Inc.

Beth Brannan,
Director Regulatory Affairs, US Regulatory Agent

Enclosures

BB/ags

Cc: Maria Garofalo (CL)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 22-028

9/5/07

Sandoz Inc.
Attention: Beth Brannan
Director, Regulatory Affairs
2555 W. Midway Blvd; P.O. Box 446
Broomfield, CO 80038-0446

Dear Ms. Brannan:

We acknowledge receipt on August 21, 2007, of your August 20, 2007, resubmission to your new drug application for Cosyntropin Injection 0.25 mg/mL.

We consider this a complete, class 2 response to our December 6, 2006, action letter. Therefore, the user fee goal date is **February 21, 2008**.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have submitted pediatric studies with this application. Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this application.

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

Sincerely,

{See appended electronic signature page}

Jena Weber
Regulatory Project Manager
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/

Jena Weber
9/5/2007 10:58:04 AM

REQUEST FOR CONSULTATION

TO (*Division/Office*): OPS, Attention: Robert Mello, Ph.D.
HFD-805

FROM: DEMP
Jena Weber, PM

DATE
9/4/07

IND NO.

NDA NO.
22-028

TYPE OF DOCUMENT: NDA

DATE OF DOCUMENT
8/20/07

NAME OF DRUG
Cosyntropin (α 1-24
corticotropin) for Injection

PRIORITY CONSIDERATION
S

CLASSIFICATION OF DRUG
Diagnostic agent

DESIRED COMPLETION DATE
1/04/08

NAME OF FIRM: Sandoz

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|---|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE--NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input checked="" type="checkbox"/> OTHER (<i>SPECIFY BELOW</i>): |
| <input type="checkbox"/> MEETING PLANNED BY | | |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- | | |
|--|--|
| <input type="checkbox"/> TYPE A OR B NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (<i>SPECIFY BELOW</i>): |
| <input type="checkbox"/> OTHER (<i>SPECIFY BELOW</i>): | |

III. BIOPHARMACEUTICS

- | | |
|--|---|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE IV STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG EXPERIENCE

- | | |
|---|--|
| <input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (<i>List below</i>) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: This is a re-submission in response to our "AE" letter dated 12/6/06. Please review and comment on microbiology controls proposed for the drug substance, drug product, etc, as applicable.

PDUFA DATE: 02/21/08

NAME AND PHONE NUMBER OF REQUESTER
Jena Weber, 301-796-1306

METHOD OF DELIVERY (Check one)

DFS ONLY MAIL HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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/s/

Robert Mello
9/4/2007 08:51:44 AM

ORIGINAL

Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446



R

AUG 21 2007

Tel +1 303 438-4237
Fax +1 303 438-4600
Email:
Beth.Brannan@gx.novartis.com

OVERNIGHT DELIVERY

CDER/WHITE OAK/DRI

Mary H. Parks, M.D., Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

Chemistry
Amendment

RECEIVED

AUG 20 2007

AUG 21 2007

CDR / CDER

ORIG AMENDMENT

N-000-~~BE~~

AC

RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
Chemistry Amendment: Response to Chemistry Deficiencies dated 12-6-06

Dear Dr. Parks:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting a chemistry amendment to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.60.

Reference is made to the FDA letter dated December 6, 2006.
Provided in this submission is a complete response to the listed deficiencies.

Enclosed also please find a copy of the reference communication from FDA.

This response is provided in the following submission binders:

Blue: Archival

Red: Chemistry

White: Microbiology/Sterility Assurance

Maroon: Field

This information is submitted for your review and approval.



Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,

Sandoz Inc.

Beth Brannan, Director Regulatory Affairs
US Regulatory Agent

Enclosures

BB/ags

Cc: Peggy Levy (CL)

MEMO

To: Mary Parks, M.D.
Director, Division of Metabolism and Endocrinology Products
HFD-510

Through: Nora Roselle, Pharm.D., Team Leader
Denise P. Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support, HFD-420

From: Linda M. Wisniewski, RN
Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

Date: December 18, 2006

Re: Cosyntropin Injection, 0.25 mg/mL, NDA# 22-028, OSE Consult 2006-1014

The Division of Metabolism and Endocrinology Products submitted a request on December 11, 2006 for DMETS to assess the container label for Cosyntropin Injection. DMETS previously reviewed the labels submitted on February 3, 2006 by the sponsor in OSE Consults #06-0116 and 2006-479 and provided comments. We note that the sponsor has addressed all of DMETS concerns.

DMETS has no additional comments regarding the container label submitted on December 4, 2006. If you have any other questions or need clarification, please contact Sammie Beam, project manager, at 301-796-0080.

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/s/

Linda Wisniewski
12/20/2006 09:11:38 AM
DRUG SAFETY OFFICE REVIEWER

Nora L. Roselle
12/20/2006 09:54:17 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
12/20/2006 11:29:10 AM
DRUG SAFETY OFFICE REVIEWER



Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Tel +1 303 438-4237
Fax +1 303 438-4600
Email:
Beth.Brannan@gx.novartis.com

DUPLICATE

CDER/CDR

DEC 14 2006

RECEIVED

OVERNIGHT DELIVERY

Mary H. Parks, M.D., Acting Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

Notice of Intent to file
Amendment

NEW CORRESPONDENCE

N-000-C

RECEIVED

DEC 14 2006

December 13, 2006

RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
Response to December 6, 2006 Approvable Letter

OVERNIGHT OAK DA 1

Dear Dr. Orloff:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting a notice of intent to file an amendment to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.110(a)(1).

Reference is made to the December 6, 2006 faxed approvable letter regarding pending NDA 22-028. In response to this letter, Sandoz Canada Inc. is notifying FDA of their intent to provide a complete response to the chemistry and sterility assurance deficiencies noted.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,

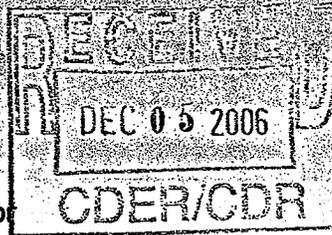
Sandoz Inc.

Beth Brannan,
Director Regulatory Affairs
US Regulatory Agent

Enclosures
BB/ags
Cc: Peggy Levy (submission)



OVERNIGHT DELIVERY



RECEIVED

DEC - 6 2006

Mary H. Parks, M.D., Acting Director
CDER/ Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

CDER White Oak DA 1

Minor Amendment
(including electronic labeling)

ORIG AMENDMENT

DEC 4 2006

ORIGINAL

N-000-BL TV DMETS #3 12/1/06

RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
Minor Amendment: Response to Discipline Review (DMETS) Letter dated
November 3, 2006

Dear Dr. Parks:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting minor amendment to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.60.

Reference is made to the FDA DMETS Discipline Review Letter dated November 3, 2006. Sandoz Canada Inc. is providing the following information in response to the DMETS comments. Provided in this amendment is a copy of the referenced letter for ease of review.

A. General Comments

1). DMETS notes that you have incorporated a warning that includes the statement "For Intravenous Use Only". This statement is qualified on the carton labeling with an asterisk that identifies the statement "Not to be administered by the intramuscular route". However, this statement does not appear on the container label. DMETS recommends that this information also be included on the container label, if space permits.

SANDOZ RESPONSE: The container label for the - mL size vial has been revised to include the additional statement:

b(4)

For Intravenous Use Only
Not to be Administered
Intramuscularly

In order to make room for this statement, Sandoz has removed the following: "Discard Unused Portion" and "Princeton, NJ 08540"



SANDOZ

Both of these statements are included on the outer carton and on the physician insert. The revised vial label is provided electronically in pdf format.

2. Despite the improved differentiation of this product from Cortrosyn, DMETS continues to encourage you to institute an education campaign to inform practitioners of the differences between these two products.

SANDOZ RESPONSE: Sandoz intends to educate the market as follows:

Sandoz will submit promotional materials to FDA as appropriate.

We are providing the revised labeling electronically, Included in the attached CD are the following files:

Document	File Name on CD
Revised Final Print Vial label in pdf	3052-71 Vial Label. Pdf
Previous filed Draft Vial label in pdf	Cosyntropin Draft Inner Label.pdf

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,

Sandoz Inc.

Beth Brannan, Director Regulatory Affairs
US Regulatory Agent

Enclosures
BB/ags

Cc: Peggy Levy (submission)

b(4)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-028

DISCIPLINE REVIEW LETTER

Sandoz, Inc.
Attention: Beth Brannan
Director, Regulatory Affairs
2555 W. Midway Blvd.; P.O. Box 446
Broomfield, CO 80038-0446

11/3/06

Dear Ms. Brannan:

Please refer to your February 3, 2006, new drug application (NDA) submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for cosyntropin 0.25 mg/mL for Injection.

We also refer to your communication dated September 21, 2006, that was in response to our Discipline Review letter dated August 14, 2006.

In review of the container labels, carton, and package insert labeling, The Division of Medication Errors and Technical Support (DMETS) acknowledges that you have addressed all of the concerns identified in the DMETS review. However, we have identified the following additional concerns with respect to the revised labels and labeling which may minimize potential user error. Please address these deficiencies in writing to your NDA file.

1. DMETS notes that you have incorporated a warning that includes the statement "*For Intravenous Use Only*". This statement is qualified on the carton labeling with an asterisk that identifies the statement "*Not to be administered by the intramuscular route*". However, this statement does not appear on the container label. DMETS recommends that this information also be included on the container label, if space permits.
2. Despite the improved differentiation of this product from Cortrosyn, DMETS continues to encourage you to institute an education campaign to inform practitioners of the differences between these two products.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application.

In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

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 and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Mary Parks

11/3/2006 10:37:26 AM



N-000 BL

Tel +1 303 438-4237
Fax +1 303 438-4600
Email:
Beth.Brannan@gx.novartis.com

ORIG AMENDMENT

OVERNIGHT DELIVERY

DUPLICATE

Mary H. Parks, M.D., Acting Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266**Minor Amendment**
(including electronic labeling)**RECEIVED**

SEP 21 2006

SEP 28 2006

CDER White Oak DR1**RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL**
Minor Amendment: Response to Discipline Review Letter dated August 14, 2006

Dear Dr. Parks:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting minor amendment to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.60.

Reference is made to the FDA Discipline Review Letter dated August 14, 2006. Sandoz Canada Inc. is providing the following information in response to the DMETS comments. Provided in this amendment is a copy of the referenced letter for ease of review.

A. General Comments

- 1). On August 3, 2006, Sandoz Canada submitted the following information regarding the adverse reactions associated with accidental IM administration and the current proposed formulation. We believe this information also addresses DMETS concerns raised in General Comment #1.

A review of all excipients in the Sandoz formulation show that they correlate to other approved IM formulations and in approved concentrations of these excipients in the FDA listing of approved excipients. Further, the active substance concentration is the same as that of the approved cosyntropin product. (i.e. *Cosyntropin Injection is a 1 mL sterile solution in vials containing 0.25 mg of tetracosactide, 0.82 mg trihydrate, 6.4 mg sodium chloride, 10 mg mannitol, 1 mg glacial acetic acid, and water for injection, USP*).

Sandoz has not administered its cosyntropin by the intra-muscular route during its clinical investigations. Although the current package insert and formulation is proposed only for IV administration, neither the excipients nor the active should

cause any undue adverse effects other than that normally shown with an IM dosing route.

2. A boxed warning "For Intravenous Use Only" has been added to the vial label. Although provided labeling has been identified as draft, the text on the vial label has been reformatted and condensed to show the actual layout, font size, and space available for required text. Due to the size limitation, the vial label does not include the statement "not to be administered by the intramuscular route". This statement has been added to the carton label as an asterisk notation. Sandoz does not intend to

b(4)

3. Sandoz has changed "For I.V. Use" to "For Intravenous Use Only". This statement has been boxed to increase its prominence. On the carton label, "not to be administered by the intramuscular route" is also included as an asterisk notation. Sandoz believes the proposed labeling meets FDA's requests regarding both comments (2 and 3).

4. Sandoz color scheme, layout, and format is dissimilar from the Cortrosyn® brand product. Sandoz intends to submit final print labels in the near future. Visual differences will be as described below:

Sandoz Label	Cortrosyn® Label
All Text in dark blue (PMS 541)	All Text in black except the brand name which is light blue
The strength is identified with a green box with white writing	The strength is identified with blue text in a black box
Sandoz includes a "right triangle S" logo in green and blue	Cortrosyn includes a blue and white star

5. Sandoz has decreased the prominence of the logo on the carton. Due to limited space, the logo does not appear on the vial label.

6. Sandoz has added "1 mL single dose vial" to the vial label. Additionally, the net quantity statement "10 x 1 mL single dose vials" has been added to the carton label in accordance with comment C.3.

B. Container Label

See responses A.3.- A.6.

C. Carton Label

1. See responses A.3.- A.6.

2. Sandoz has decreased the point size of the statement "FOR DIAGNOSTIC USE ONLY".

3. Sandoz has revised the statement to "10 x 1 mL single dose vials".

D. Insert Labeling

1) The sentence "_____"

b(4)

2. The paragraph has been revised as requested and now reads as follows:

"A control blood sample of 6 to 7 mL is collected in a heparinized tube. The drug product should be inspected visually for particulate matter and discoloration prior to injection. Inject 1mL of cosyntropin injection. Discard any unused portion."

3. The Dosage and Administration section has been revised to include the intravenous fluids, 5% Dextrose Injection USP and 0.9% Sodium Chloride Injection, USP. The recommended volume of these fluids for intravenous injection is the same as the RLD.

4. A statement "**This product should not be given intramuscularly.**" has been added as the first sentence in the Dosage and Administration section.

We are providing the revised labeling electronically, included in the attached CD are the following files:

Document	File Name on CD
Draft Physician insert in MS Word	CosyntropinPI_rev09_2006.doc
Draft Physcian insert in pdf	CosyntropinPI_rev09_2006.pdf
Draft Vial label in pdf	Cosyntropin Draft inner label.pdf
Draft Carton label in pdf	Cosyntropin Draft carton label.pdf

A side by side comparison of the insert with the previous filed version is provided in ATTACHMENT 1.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,

Sandoz Inc.



Beth Brannan, Director Regulatory Affairs
US Regulatory Agent

Enclosures
BB/ags

Cc: Peggy Levy (submission)

RECEIVED

SEP 28 2006

CDER White Oak BR1

RECEIVED

SEP 22 2006

OGD / CDER

OVERNIGHT DELIVERY

Mary H. Parks, M.D., Acting Director,
CDER/ Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

*NDA (BC)
ORIG AMENDMENT*

RECEIVED
SEP 08 2006
CDER/CDR

Minor Amendment

RECEIVED

SEP 11 2006

SEP 7 2006

CDER White Oak DR1

RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
Minor Amendment: Response to Request for Additional Information dated 4-17-06

Dear Dr. Parks:

On behalf of Sandoz Canada Inc, Sandoz Inc. is hereby submitting minor amendment to unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act; 21 CFR Part 314.60.

Reference is made to the FDA request of April 17, 2006 for additional information regarding potential review issues. Provided in this submission is a complete response to the request.

Additionally, we are providing notice of the DMF deficiency response submitted August 3, 2006 in response to deficiencies dated 6-27-06. A copy of _____ cover letter to FDA is provided in ATTACHMENT 6 for reference.

b(4)

This information is submitted for your review and approval.
Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,
Sandoz Inc.



Beth Brannan, Director Regulatory Affairs
US Regulatory Agent

Enclosures
BB/ags
Cc: Peggy Levy (CL)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-028

DISCIPLINE REVIEW LETTER

Sandoz, Inc.
Attention: Beth Brannan
Director, Regulatory Affairs
2555 W. Midway Blvd.; P.O. Box 446
Broomfield, CO 80038-0446

2/14/06

Dear Ms. Brannan:

Please refer to your February 3, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for cosyntropin 0.25 mg/mL for Injection.

In review of the container labels, carton, and package insert labeling, The Division of Medication Errors and Technical Support (DMETS) has identified the following areas of possible improvement, which may minimize potential user error. Please address these deficiencies in writing to your NDA file.

A. GENERAL COMMENTS

1. DMETS has concerns about the potential interchanging of your product, which is only for intravenous administration, with Cortrosyn, which can be administered by both the intramuscular and intravenous routes of administration. We believe there is a distinct possibility that your product may be confused as a generic equivalent to the Organon product since it will be marketed without a proprietary name. Health care practitioners are accustomed to administering Cortrosyn by both routes of administration and may do the same with your product.

It is unknown if a serious local reaction would occur if this product were accidentally injected intramuscularly. If there is a potential for a medically serious adverse reaction after intramuscular injection, DMETS recommends that your product be reformulated so it can be administered by both the intramuscular and intravenous routes of administration. If minimal reaction is expected post intramuscular administration, then an educational campaign relating to the differences between cosyntropin and Cortrosyn should be implemented.

2. To further minimize the risk of inadvertent intramuscular administration as described above, a boxed warning should be added to the container label that states:

Note: For Intravenous Use Only
Not to be administered by the intramuscular route.

3. Because this product can only be given by intravenous administration, it is important to highlight this difference from Cortrosyn. Thus, we request that you revise the route of administration statement to read as described above or, at a minimum, bold the current statement and revise "For IV Use" to read "For Intravenous Use Only", and increase the prominence of this statement by bolding, boxing, or some other means. The rationale to have 'IV' spelled out is that FDA launched a campaign in June 2006, warning healthcare providers and consumers not to use error-prone abbreviations. Thus, we request that abbreviations not be used in labels and labeling as they can be misinterpreted (e.g., the abbreviation 'IV' which can be misinterpreted as the Roman Numeral 4 and contribute to error).

4. The Cortrosyn labels use similar colors with their trade dress (blue on white background). We strongly recommend that you revise your color scheme so your labels and labeling appear entirely different from Organon's Cortrosyn. This visual similarity in conjunction with the fact that your product does not have a proprietary name increases the risk of product interchangeability and selection errors.

5. The presentation of your name and log is more prominent than the established name. Please revise the presentation so that the proprietary and established names are the most prominent information on the primary display panel.

6. Include a net quantity statement on the principal display panel (e.g. 1 mL) and ensure that it is not in close proximity to the strength. We refer you to 21 CFR 201.51 for further guidance.

B. CONTAINER LABEL

See GENERAL COMMENTS A3 through A6.

C. CARTON LABELING

1. See GENERAL COMMENTS A3 through A6.
2. Decrease the size of the 'FOR DIAGNOSTIC USE ONLY' statement.
3. Revise the '10 Single-Dose Vials' statement to read '10 X 1 mL single dose vials'.

D. INSERT LABELING

b(4)

Thus, by including this information it may lead health care practitioners to believe this product can be given by the intramuscular route. Therefore, we request that you delete the adverse reactions generally seen with intramuscular injections.

2. The **DOSAGE AND ADMINISTRATION** section, second paragraph, lists the steps for a 'rapid screening test'. However, these steps appear in reverse order, (e.g. control sample collected, injection of drug, then visual inspection of the drug prior to injection). Revise the directions to provide for a logical flow of activities for the administration of this drug. For example: (1) collect a 6-7 mL sample of blood in a heparinized tube, (2) visually inspect the drug for particulate matter . . . , (3) Inject 1 mL of the cosyntropin).

3. The **DOSAGE AND ADMINISTRATION** section refers to adding Cosyntropin Injection to glucose solutions. Since there are multiple strengths of glucose containing intravenous fluids (e.g. 5% Dextrose, 10% Dextrose, etc.), DMETS recommends that compatible strengths be identified in the package insert. Additionally, this section also refers to 'saline solutions'. The word saline is defined by Dorland's Medical Dictionary as 'salty; of the nature of a salt; containing a salt or salts'. Clearly identify which 'saline' solution and recommended volume is compatible with this product, (for example: 0.9 % Sodium Chloride for Injection, USP).

4. Add a statement to the **DOSAGE AND ADMINISTRATION** section that states that this product should not be given intramuscularly.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

Please note that we have not received a response to our filing letter issued on April 17, 2006, and our communication dated June 27, 2006, regarding deficiencies to DMF file 18963.

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 and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

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this page is the manifestation of the electronic signature.**

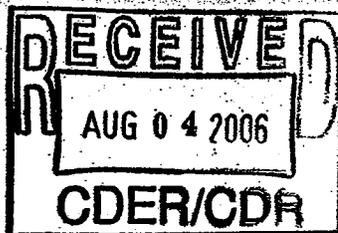
/s/

Eric Colman
8/14/2006 11:28:14 AM
Eric Colman for Mary Parks

Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Tel +1 303 438-4237
Fax +1 303 438-4600
Email:
Beth.Brannan@sandoz.com



N-000 BC

ORIG AMENDMEN

OVERNIGHT DELIVERY

David G. Orloff, M.D., Director,
CDER/Central Document Room
Division of Metabolism and Endocrinology Products
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

TELEPHONE AMENDMENT

RECEIVED

AUG 3 2006

DUPLICATE

AUG 07 2006

CDER White Oak DR 1

RE: NDA 22-028 Cosyntropin Injection 0.25 mg/mL
Telephone Amendment – Request for Additional Information

Dear Dr. Orloff:

On behalf of Sandoz Canada, as their U.S. Authorized Agent, Sandoz Inc. is hereby submitting an amendment to their unapproved New Drug Application 22-028 for Cosyntropin Injection 0.25 mg/mL in accord with Section 505 (j) of the Federal Food, Drug, and Cosmetic Act and with 21 CFR Part 314.96.

Reference is made to the FDA communication (telefax) dated July 17, 2006 from Jena Weber, Project Manager. Provided in the attached documentation is a complete response to the request for additional information.

This information is submitted for your review and approval.

Please acknowledge receipt of this document by signing and dating the enclosed copy of the cover letter and returning it in the self-addressed stamped envelope.

Sincerely,

Sandoz Inc.

Beth Brannan, Director
Regulatory Affairs

Enclosures

BB/lah

cc: Pamela Lewis

Weber, Jena M

From: - Lubas, William (CDER)
Sent: Monday, July 17, 2006 9:41 AM
To: Weber, Jena M
Kehoe, Theresa
Subject: NDA 22028

Hi,

We are concerned that the product which will be labeled for IV use only may accidentally be given IM. Could you contact the sponsor and ask them if they have any information on adverse reactions that may have occurred after the product was given IM, what they might expect the type of reactions to be, and what sort of therapy might be useful to limit the reactions.

Thanks,
Bill

- 1) Do you have any information about accidental IM use of the new IV formulation?
- 2) What would you expect the range of adverse reactions to be if the new formulation was given IM?
- 3) Do you have any suggestions on possible treatments to limit these adverse reactions? Warm soaks? Hyaluronidase? etc.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-028

Sandoz Inc.
Attention: Beth Brannan
Director, Regulatory Affairs
2555 W. Midway Blvd; P.O. Box 446
Broomfield, CO 80038-0446

Dear Ms. Brannan:

Please refer to your February 3, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cosyntropin Injection, 0.25 mg/mL.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on April 7, 2006, in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issues:

1. Please include a bioassay for either the drug substance or drug product specification. Alternatively, add identity testing by peptide mapping to the drug substance specification, and submit data to demonstrate an acceptable direct correlation between the bioassay and the HPLC test method over a range of degradation of the peptide.
Note: A bioassay is critical for this product because it is used as a diagnostic agent. The EP monograph for the drug substance includes a bioassay.
2. Provide the chemical name, structure, molecular formula and mass for the drug substance "cosyntropin acetate," and not "tetracosactide" (INN name), and revise the drug substance specification to state the correct name "cosyntropin (USAN name) acetate."
3. The potency of the peptide reference standards should be verified by a bioassay using an international reference preparation.
4. The composition table of the drug product should include the quantity of the peptide per unit container.
5. Concerning the drug product specification:
 - a. Please include identity testing in the drug product specification as this test is performed on the drug product (results provided in Batch Analyses).
 - b. Revise the specification to include an upper limit in the criteria for Volume (currently having only a limit of \geq mL). USP allows an excess of 0.1 mL for a volume of 1.0 mL.
 - c. Revise the specification to clearly state the criteria for Description (currently the criteria is "Conforms" for test method "Organoleptic").

b(4)

6. The proposed expiry of 24-month under refrigeration is not acceptable given the limited stability data provided (6-months).
7. Labeling (packaging labels and package insert) should include the statement "Each vial contains – mg/mL of cosyntropin acetate to deliver – mg/mL of cosyntropin."

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

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

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.
Acting 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/

Mary Parks
4/17/2006 08:30:03 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-028

NDA ACKNOWLEDGMENT

Sandoz Inc.
Attention: Beth Brannan
Director, Regulatory Affairs
2555 W. Midway Blvd; P.O. Box 446
Broomfield, CO 80038-0446

Dear Ms. Brannan:

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

Name of Drug Product: Cosyntropin Injection, 0.25 mg/mL
Review Priority Classification: Standard
Date of Application: February 3, 2006
Date of Receipt: February 6, 2006
Our Reference Number: NDA 22-028

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 April 7, 2006, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be **December 6, 2006**.

Please cite the NDA number listed above 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

NDA 22-028

Page 2

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

Sincerely,

{See appended electronic signature page}

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

**APPEARS THIS WAY
ON ORIGINAL**

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

/s/

Jena Weber
2/21/2006 10:36:23 AM



Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Tel +1 303 438-4237
Fax +1 303 438-4600
Internet:
Beth.Brannan@sandoz.com

ORIGINAL

FEB 03 2006

RECEIVED

RECEIVED FEB - 9 2006

David Orloff, M.D., Director
Division of Metabolism & Endocrinology Products
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

FEB 06 2006 CDER White Oak DR 1

CDER CDR

RE: Original NDA Submission
Cosyntropin Injection 0.25mg/mL

Dear Dr. Orloff:

On behalf of Sandoz Canada Inc. (formerly Sabex 2002, Inc), as their U.S. Authorized Agent, Sandoz Inc. hereby submits an original New Drug Application for Cosyntropin Injection 0.25mg/mL in accord with Section 305(b)(2) of the Federal Food, Drug, and Cosmetic Act.

Reference is made to PIND 69,720 communicated to Sabex 2002, Inc. on August 6, 2004.

In accordance with 21 CFR 314.54, Sandoz Canada Inc. is seeking approval of Cosyntropin Injection 0.25 mg/mL, aqueous solution formulation, based on the listed drug product: Amphastar's CORTROSYN™ for Injection 0.25mg (lyophilized powder). Accordingly, the information required under 21 CFR 314.50(d)(2), (d)(5), (d)(6) and (f) for the listed drug, CORTROSYN™ application (NDA 16-750), is referenced. Please refer to Module 1, section 1.3 for the basis of this submission and a request for therapeutic equivalence to CORTROSYN™.

This NDA in CTD format consists of 18 volumes:

- Module 1- 1 volume
- Module 2- 1 volume
- Module 3- 8 volumes
- Module 4- 1 volume
- Module 5- 7 volumes

Beth Brannan, Director
Regulatory Affairs

Sandoz Inc.
2555 W. Midway Blvd.
P.O. Box 446
Broomfield, CO 80038-0446

Tel +1 303 438-4237
Fax +1 303 438-4600
Internet:
Beth.Brannan@sandoz.com

Sandoz Canada Inc. is filing an archival copy of the ANDA (in blue jackets) with all the required information. Additionally, review copies are provided (red-CMC, white-Sterility Assurance, yellow-Non-clinical, and orange-Bioequivalence jackets) as dictated by the guidelines.

Given that this is a sterile injectable product, the sterility assurance data is included in Module 3 under the Regional Information section with an additional separate review copy of Sections 3.2.R.1-3 provided.

As Sandoz Canada Inc. is a foreign manufacturer, a complete copy of Module 3 is provided as the field copy to the Office of New Drugs (burgundy jackets).

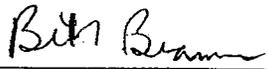
Electronic Media: Immediately following this cover letter, Sandoz is providing one CD entitled "ELECTRONIC LABELING SUBMISSION" which includes the draft physician insert and draft container labels in pdf format.

Additionally, we are providing one separate CD with Module 2 summary tables of in-vivo study data, dissolution data, and formulation data and a SAS Transport File CD provided by Anapharm (the contracted bio lab).

If there are any comments or questions about this application, please contact me at 303-438-4237.

Sincerely,

Sandoz Inc.



Beth Brannan, Director
Regulatory Affairs

BB/ags

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: August 31, 2005
See OMB Statement on page 2.

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT SANDOZ CANADA INC. (formerly Sabex 2002)	DATE OF SUBMISSION FEB 03 2006
TELEPHONE NO. (Include Area Code) 450-641-4903 (US Agent: 303 438-4237)	FACSIMILE (FAX) Number (Include Area Code) (303) 438- 4600
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 145 Jules Leger Street Boucherville (QC) Canada J4B 7K8	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Beth Brannan, Director Regulatory Affairs Sandoz Inc. 2555 W. Midway Blvd. Broomfield, CO 80038-0446

RECEIVED

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)	FEB 06 2006
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Cosyntropin Injection	PROPRIETARY NAME (trade name) IF ANY CDER CDR
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) α 1-24 corticotropin	CODE NAME (If any)
DOSAGE FORM: Injectable	STRENGTHS: 0.25 mg/mL
	ROUTE OF ADMINISTRATION: IV

(PROPOSED) INDICATION(S) FOR USE:
Intended for use as a diagnostic agent in the screening of patients presumed to have adrenocortical insufficiency.

APPLICATION DESCRIPTION

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (NDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug CORTROSYN™ Holder of Approved Application Amphastar Pharmaceuticals, Inc.
TYPE OF SUBMISSION (check one) <input checked="" type="checkbox"/> ORIGINAL APPLICATION <input type="checkbox"/> AMENDMENT TO APENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)
REASON FOR SUBMISSION New Drug Application (505b2)
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED 18 THIS APPLICATION IS <input type="checkbox"/> PAPER <input checked="" type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

See Attached

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)
PIND 69,720
See Attached

This application contains the following items: (Check all that apply)

<input checked="" type="checkbox"/>	1. Index
<input checked="" type="checkbox"/>	2. Labeling (check one) <input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling <input checked="" type="checkbox"/> Electronic Labeling
<input checked="" type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input checked="" type="checkbox"/>	4. Chemistry section
<input checked="" type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input checked="" type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input checked="" type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input checked="" type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input checked="" type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input checked="" type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input checked="" type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input checked="" type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input checked="" type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT

Beth Brannan

TYPED NAME AND TITLE

**Beth Brannan, US Agent
Director, Regulatory Affairs**

DATE:

FEB 03 2006

ADDRESS (Street, City, State, and ZIP Code)

2555 W. Midway Blvd., Broomfield, Colorado 80038-0446

Telephone Number

(303) 438-4237

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CDER, HFD-99
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
12229 Wilkins Avenue
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.