

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-327**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

Department of Health and Human Services Food and Drug Administration		Form Approved: OMB No. 0910-0513 Expiration Date: 7/31/10 See OMB Statement on Page 3.	
<b>PATENT INFORMATION SUBMITTED WITH THE FILING          OF AN NDA, AMENDMENT, OR SUPPLEMENT</b>  <i>For Each Patent That Claims a Drug Substance          (Active Ingredient), Drug Product (Formulation and Composition)          and/or Method of Use</i>		NDA NUMBER 22-327	
		NAME OF APPLICANT/NDA HOLDER Novartis Consumer Health, Inc.	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME)			
ACTIVE INGREDIENT(S) Lansoprazole		STRENGTH(S) 15mg	
DOSAGE FORM Capsule, Delayed Release Pellets, Oral			
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the <i>only</i> information relied upon by FDA for listing a patent in the Orange Book.			
<i>For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.</i>			
<i>FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</i>			
<i>For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.</i>			
<b>1. GENERAL</b>			
a. United States Patent Number 4,628,098		b. Issue Date of Patent 12/09/1986	c. Expiration Date of Patent 05/10/2009
d. Name of Patent Owner Takeda Pharmaceutical Company, Limited		Address (of Patent Owner) 1-1, Doshomachi 4-chome Chuo-ku	
		City/State Osaka, Japan	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in t.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input type="checkbox"/> No	

**For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.**

**2. Drug Substance (Active Ingredient)**

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?  Yes  No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?  Yes  No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).  Yes  No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)  Yes  No

2.6 Does the patent claim only an intermediate?  Yes  No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)  Yes  No

**3. Drug Product (Composition/Formulation)**

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?  Yes  No

3.2 Does the patent claim only an intermediate?  Yes  No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)  Yes  No

**4. Method of Use**

**Sponsors must submit the information in section 4 for each method of using the pending drug product for which approval is being sought that is claimed by the patent. For each pending method of use claimed by the patent, provide the following information:**

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2 Patent Claim Number(s) (as listed in the patent) Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes  No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)

**5. No Relevant Patents**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.  Yes

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed

*Diane Furman*

3 June 2008

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Diane Furman

Address

Novartis Consumer Health, Inc. (Legal Dept., 5th Floor)  
200 Kimball Drive

City/State

Parsippany, NJ

ZIP Code

07054

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(973) 503-7050

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(973) 503-8450

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Diane.Furman@Novartis.com

The public reporting burden for this collection of information has been estimated to average 20 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:

Food and Drug Administration  
CDER (HFD-007)  
5600 Fishers Lane  
Rockville, MD 20857

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.

**INFORMATION AND INSTRUCTIONS FOR FORM 3542a**  
**PATENT INFORMATION SUBMITTED WITH THE FILING**  
**OF AN NDA, AMENDMENT OR SUPPLEMENT**

**General Information**

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplement approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. Sending an additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of April 2007) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html>.

**First Section**

Complete all items in this section.

**1. General Section**

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

**2. Drug Substance (Active Ingredient)**

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

**3. Drug Product (Composition/Formulation)**

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

**4. Method of Use**

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement (pending method of use).

- 4.2) For each pending method of use claimed by the patent, identify by number the claim(s) in the patent that claim the pending use of the drug. An applicant may list together multiple patent claim numbers and information for each pending method of use, if applicable. However, each pending method of use must be separately listed within this section of the form.
- 4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

**5. No Relevant Patents**

Complete this section only if applicable.

**6. Declaration Certification**

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

## EXCLUSIVITY SUMMARY

NDA # 22-327

SUPPL #

HFD #

Trade Name Prevacid 24HR

Generic Name 15 mg lansoprazole

Applicant Name Novartis Consumer Health, Inc

Approval Date, If Known

### PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES  NO

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

505(b)(1)

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

YES  NO

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

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

d) Did the applicant request exclusivity?

YES  NO

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

3 years

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

YES  NO

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

Yes - approved in response to a Pediatric Written Request for NDA 20-406, NDA 21-281 and NDA 21-428

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# 20-406	Lansoprazole capsule, 15mg & 30mg
NDA# 21-281	Lansoprazole oral suspension, 15mg & 30mg packet
NDA# 21-428	Lansoprazole orally disintegrating tablet, 15mg & 30mg

2. Combination product.

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

YES  NO

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

NDA#

NDA#

NDA#

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

IF "YES," GO TO PART III.

**PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS**

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a)

is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES  NO

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

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

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

YES  NO

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

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

YES  NO

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

YES  NO

If yes, explain:

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

YES  NO





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:

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Name of person completing form: Mary R. Vienna  
Title: Regulatory Project Manager  
Date: 05-11-09

Name of Office/Division Director signing form:  
Title:

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

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

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Andrea Segal  
5/19/2009 09:06:03 PM

**PEDIATRIC PAGE**

(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 22-327 Supplement Number: \_\_\_\_\_ NDA Supplement Type (e.g. SE5): \_\_\_\_\_

Division Name: DNCE PDUFA Goal Date: 05-16-09 Stamp Date: 07-16-08

Proprietary Name: Prevacid 24HR

Established/Generic Name: Lansoprazole 15mg

Dosage Form: capsule

Applicant/Sponsor: Novartis Consumer Health, Inc.

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):

- (1) \_\_\_\_\_
- (2) \_\_\_\_\_
- (3) \_\_\_\_\_
- (4) \_\_\_\_\_

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 1  
(Attach a completed Pediatric Page for each indication in current application.)

**Indication:** Treats frequent heartburn (occurs 2 or more days per week) OTC.

**Q1:** Is this application in response to a PREA PMC/PMR? Yes  Continue  
No  Please proceed to Question 2.

If Yes, NDA/BLA#: \_\_\_\_\_ Supplement #: \_\_\_\_\_ PMC/PMR #: \_\_\_\_\_

Does the division agree that this is a complete response to the PMC/PMR?

- Yes. Please proceed to Section D.
- No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

**Q2:** Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW  active ingredient(s) (includes new combination);  indication(s);  dosage form;  dosing regimen; or  route of administration?\*

(b)  No. PREA does not apply. **Skip to signature block.**

\* **Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.**

**Q3:** Does this indication have orphan designation?

- Yes. PREA does not apply. **Skip to signature block.**
- No. Please proceed to the next question.

**Q4:** Is there a full waiver for all pediatric age groups for this indication (check one)?

- Yes: (Complete Section A.)
- No: Please check all that apply:
  - Partial Waiver for selected pediatric subpopulations (Complete Sections B)
  - Deferred for some or all pediatric subpopulations (Complete Sections C)
  - Completed for some or all pediatric subpopulations (Complete Sections D)
  - Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
  - Extrapolation in One or More Pediatric Age Groups (Complete Section F)(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

**Section A: Fully Waived Studies (for all pediatric age groups)**

Reason(s) for full waiver: (check, and attach a brief justification for the reason(s) selected)

- Necessary studies would be impossible or highly impracticable because:
  - Disease/condition does not exist in children
  - Too few children with disease/condition to study
  - Other (e.g., patients geographically dispersed): \_\_\_\_\_
- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

Justification: It is clinically inappropriate for Prevacid (lansoprazole) to be available OTC for pediatric patients up to 18 years of age. Pediatric gastroenterologists recommend that children with symptoms of gastroesophageal reflux be examined by physicians for possible complications, and the treatment of frequent heartburn in the pediatric population should be under the direction of a physician. The OTC availability of Prevacid and other proton pump inhibitors (PPI) would be counter to this indication. Currently, omeprazole is the only approved PPI for OTC use, and it is not approved for patients 17 years of age and younger.

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is incomplete and should be signed.*

**Section B: Partially Waived Studies (for selected pediatric subpopulations)**

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

*Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).*

		Reason (see below for further detail):					
		minimum	maximum	Not feasible <sup>#</sup>	Not meaningful therapeutic benefit*	Ineffective or unsafe <sup>†</sup>	Formulation failed <sup>Δ</sup>
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and attach a brief justification):

# Not feasible:

- Necessary studies would be impossible or highly impracticable because:
  - Disease/condition does not exist in children
  - Too few children with disease/condition to study
  - Other (e.g., patients geographically dispersed): \_\_\_\_\_

Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.*)

Justification attached.

*For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.*

**Section C: Deferred Studies (for selected pediatric subpopulations).**

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				Reason for Deferral			Applicant Certification †
Population	minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received	
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
<input type="checkbox"/> All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Date studies are due (mm/dd/yy): _____							

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

\* Other Reason: \_\_\_\_\_

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

**Section D: Completed Studies (for some or all pediatric subpopulations).**

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?.	
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes <input type="checkbox"/>	No <input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):**

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

Population		minimum	maximum
<input type="checkbox"/>	Neonate	__ wk. __ mo.	__ wk. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	Other	__ yr. __ mo.	__ yr. __ mo.
<input type="checkbox"/>	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)**

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as*

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL ([cderpms@fda.hhs.gov](mailto:cderpms@fda.hhs.gov)) OR AT 301-796-0700.

*pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.*

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population	minimum	maximum	Extrapolated from:	
			Adult Studies?	Other Pediatric Studies?
<input type="checkbox"/> Neonate	__ wk. __ mo.	__ wk. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> Other	__ yr. __ mo.	__ yr. __ mo.	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	<input type="checkbox"/>	<input type="checkbox"/>

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.*

*If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.*

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

(Revised: 6/2008)

**NOTE: If you have no other indications for this application, you may delete the attachments from this document.**

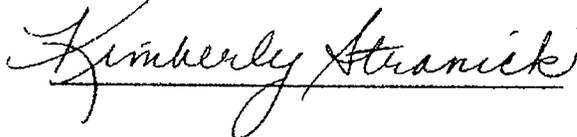
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**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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/s/

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Mary R Vienna  
4/22/2009 12:35:54 PM

**Debarment Certification**

Novartis Consumer Health, Inc. certifies that it did not and will not use in any capacity the services of any person debarred under section 306(a) or 306(b) of the Federal Food, Drug and Cosmetic Act in connection with this application.

  
Kimberly Stranick

Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs

  
23 June 2008

Date

### CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

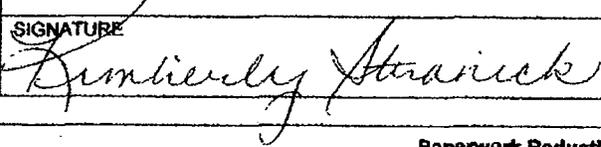
With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the 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	See Module I.3.4	

- (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 Kim Stranick, Ph.D	TITLE Vice President & Head, Global Regulatory Affairs
FIRM / ORGANIZATION Novartis Consumer Health, Inc.	
SIGNATURE 	DATE 13 Jun 2008

#### 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



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

NDA 22-327

**NDA ACKNOWLEDGMENT**

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

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

Name of Drug Product: Prevacid 24 HR (15mg lansoprazole) capsules

Date of Application: July 15, 2008

Date of Receipt: July 16, 2008

Our Reference Number: NDA 22-327

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on September 14, 2008 in accordance with 21 CFR 314.101(a).

The NDA number provided above must 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  
Office of Nonprescription Products  
Division of Nonprescription Clinical Evaluation  
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

NDA 22-327

Page 2

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/cder/ddms/binders.htm>.

If you have any questions, contact Mary Vienna, Regulatory Project Manager, at [mary.vienna@fda.hhs.gov](mailto:mary.vienna@fda.hhs.gov) or (301) 796-4150.

Sincerely,

*{See appended electronic signature page}*

Leah Christl, Ph.D.  
Acting Chief, Project Management Staff  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

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

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Leah Christl  
7/28/2008 01:28:21 PM

## ACTION PACKAGE CHECKLIST

BLA # NDA # 22-327	BLA STN# NDA Supplement #	If NDA, Efficacy Supplement Type
Proprietary Name: Prevacid 24HR Established Name: Lansoprazole Dosage Form: capsules		Applicant: Novartis Consumer Health, Inc.
RPM: Mary Vienna		Division: DNCE      Phone # 301-796-4150
<p>NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)</p> <p>Efficacy Supplement:    <input type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p><b>Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.</b></p> <p><input type="checkbox"/> Confirmed      <input type="checkbox"/> Corrected</p> <p>Date:</p>
❖ User Fee Goal Date		05-16-09
❖ Action Goal Date (if different)		
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions ( <i>specify type and date for each action taken</i> )		<input checked="" type="checkbox"/> None
❖ Advertising ( <i>approvals only</i> ) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed ( <i>indicate dates of reviews</i> )		<input type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 08  NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2  <input type="checkbox"/> Orphan drug designation  NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies  BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies  NDAs and NDA Supplements: <input checked="" type="checkbox"/> OTC drug  Other:  Other comments:	
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• This application is on the AIP	<input type="checkbox"/> Yes <input type="checkbox"/> No
• Exception for review ( <i>file Center Director's memo in Administrative Documents section</i> )	<input type="checkbox"/> Yes <input type="checkbox"/> No
• OC clearance for approval ( <i>file communication in Administrative Documents section</i> )	<input type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Press Office notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other



notice of certification?

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

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

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes  No

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

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

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes  No

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

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

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes  No

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

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

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

Yes  No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced

<p>within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</i></p>	
<p>❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)</p>	<p>DD summary review 05-11-09 DDD memorandum 05-18-09</p>
<p>❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)</p>	
<p>❖ Package Insert</p>	
<ul style="list-style-type: none"> <li>• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	<p>N/A</p>
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	
<ul style="list-style-type: none"> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>	
<p>❖ Patient Package Insert</p>	
<ul style="list-style-type: none"> <li>• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	<p>04-22-09</p>
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	<p>07-15-08</p>
<ul style="list-style-type: none"> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>	
<p>❖ Medication Guide</p>	
<ul style="list-style-type: none"> <li>• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>	<p>N/A</p>
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)</li> </ul>	
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	
<ul style="list-style-type: none"> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling)</li> </ul>	
<p>❖ Labels (full color carton and immediate-container labels)</p>	
<ul style="list-style-type: none"> <li>• Most-recent division-proposed labels (only if generated after latest applicant submission)</li> </ul>	<p>05-18-09</p>
<ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling</li> </ul>	<p>04-22-09 &amp; 04-24-09</p>
<p>❖ Labeling reviews and minutes of any labeling meetings (indicate dates of reviews and meetings)</p>	<ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> DMETS 04-24-09</li> <li><input type="checkbox"/> DSRCS</li> <li><input type="checkbox"/> DDMAC</li> <li><input type="checkbox"/> SEALD</li> <li><input checked="" type="checkbox"/> Other reviews 05-05-09</li> <li><input checked="" type="checkbox"/> Memos of Mtgs 03-17-09</li> </ul>

❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) ( <i>indicate date of each review</i> )	RPR filing review: 10-07-08 DNCE clinical review: 08-26-08 DGP clinical review: 09-21-08 CMC review: 08-27-08 Clin/Pharm review: 08-29-08 Pharm/Tox review: 09-12-08 Labeling review: 09-04-08 Statistics review: 08-28-08
❖ NDA and NDA supplement approvals only: Exclusivity Summary ( <i>signed by Division Director</i> )	<input checked="" type="checkbox"/> Included
❖ AIP-related documents <ul style="list-style-type: none"> <li>Center Director's Exception for Review memo</li> <li>If AP: OC clearance for approval</li> </ul>	
❖ Pediatric Page (all actions)	<input checked="" type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. ( <i>Include certification.</i> )	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Commitment Studies <ul style="list-style-type: none"> <li>Outgoing Agency request for post-marketing commitments (<i>if located elsewhere in package, state where located</i>)</li> <li>Incoming submission documenting commitment</li> </ul>	<input checked="" type="checkbox"/> None
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	See DFS
❖ Internal memoranda, telecons, email, etc.	N/A
❖ Minutes of Meetings <ul style="list-style-type: none"> <li>Pre-Approval Safety Conference (<i>indicate date; approvals only</i>)</li> <li>Pre-NDA/BLA meeting (<i>indicate date</i>)</li> <li>EOP2 meeting (<i>indicate date</i>)</li> <li>Other (e.g., EOP2a, CMC pilot programs)</li> </ul>	<input type="checkbox"/> No mtg 03-17-08 <input checked="" type="checkbox"/> No mtg PIND mtg 04-06-06 ; IND mtg 03-14-07
❖ Advisory Committee Meeting <ul style="list-style-type: none"> <li>Date of Meeting</li> <li>48-hour alert or minutes, if available</li> </ul>	<input checked="" type="checkbox"/> No AC meeting
❖ <u>Federal Register</u> Notices, DESI documents, NAS/NRC reports (if applicable)	N/A
❖ CMC/Product review(s) ( <i>indicate date for each review</i> )	03-25-09; 5-12-09
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Environmental Assessment (check one) (original and supplemental applications) <ul style="list-style-type: none"> <li><input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)</li> <li><input type="checkbox"/> Review &amp; FONSI (<i>indicate date of review</i>)</li> <li><input type="checkbox"/> Review &amp; Environmental Impact Statement (<i>indicate date of each review</i>)</li> </ul>	03-25-09
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> Not a parenteral product
❖ Facilities Review/Inspection	

<ul style="list-style-type: none"> <li>❖ NDAs: Facilities inspections (include EER printout)</li> </ul>	<p>Date completed:</p> <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<ul style="list-style-type: none"> <li>❖ BLAs: Facility-Related Documents             <ul style="list-style-type: none"> <li>• Facility review (<i>indicate date(s)</i>)</li> <li>• Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
<ul style="list-style-type: none"> <li>❖ NDAs: Methods Validation</li> </ul>	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed
<ul style="list-style-type: none"> <li>❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)</li> </ul>	03-24-09
<ul style="list-style-type: none"> <li>❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> No carc
<ul style="list-style-type: none"> <li>❖ ECAC/CAC report/memo of meeting</li> </ul>	N/A
<ul style="list-style-type: none"> <li>❖ Nonclinical inspection review Summary (DSI)</li> </ul>	<input checked="" type="checkbox"/> None requested
<ul style="list-style-type: none"> <li>❖ Clinical review(s) (<i>indicate date for each review</i>)</li> </ul>	DNCE: 03-16-09 DGP: 04-14-09
<ul style="list-style-type: none"> <li>❖ Financial Disclosure reviews(s) or location/date if addressed in another review</li> </ul>	03-16-09
<ul style="list-style-type: none"> <li>❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)</li> </ul>	<input checked="" type="checkbox"/> Not needed
<ul style="list-style-type: none"> <li>❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)</li> </ul>	03-16-09
<ul style="list-style-type: none"> <li>❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)</li> </ul>	N/A
<ul style="list-style-type: none"> <li>❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)</li> </ul>	<input checked="" type="checkbox"/> Not needed
<ul style="list-style-type: none"> <li>❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)</li> </ul>	<input type="checkbox"/> None requested
<ul style="list-style-type: none"> <li>• Clinical Studies</li> </ul>	03-11-09
<ul style="list-style-type: none"> <li>• Bioequivalence Studies</li> </ul>	N/A
<ul style="list-style-type: none"> <li>• Clin Pharm Studies</li> </ul>	N/A
<ul style="list-style-type: none"> <li>❖ Statistical Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None      04-06-09
<ul style="list-style-type: none"> <li>❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None      03-16-09

## Appendix A to Action Package Checklist

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

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

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

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

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

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

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

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

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

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/s/

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Mary R Vienna  
5/19/2009 09:20:46 AM



NDA 22-327

**NDA APPROVAL**

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

Please refer to your new drug application (NDA) dated July 15, 2008, received July 16, 2008, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Prevacid 24 HR (15mg lansoprazole) capsules.

We acknowledge receipt of your submissions dated November 7 and 13, and December 12, 2008 and January 9, 16 and 19, February 20, March 4, 6, 11, and 20, April 6, 22, 24 and 27, 2009.

This new drug application provides for the use of Prevacid 24 HR (15 mg lansoprazole) capsules for the treatment of frequent heartburn (occurs 2 or more days per week).

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

Submit final printed labeling as soon as they are available, but no more than 30 days after they are printed. The final printed labeling (FPL) must be identical to the enclosed labeling (consumer information leaflet, 14-count bottle label and 14-count carton label submitted April 22, 2009, 14-count carton with hangtag, 28- and 42-count carton labels submitted April 24, 2009, and the 42-count "Club" SKU carton label submitted April 22, 2009), and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Labeling for approved NDA 22-327.**" Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

NDA 22-327

Page 2

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 are waiving the pediatric study requirement for this application.

We remind you of your postmarketing agreement in your submission dated March 11, 2009. In that submission you agreed not to distribute physician and consumer samples of Prevacid 24 HR until the chemistry, manufacturing and control information, including stability data, is provided through a supplement to the approved NDA and found to be adequate.

Please submit one market package of the drug product when it is available.

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch  
Food and Drug Administration  
Suite 12B05  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Mary Vienna, Regulatory Project Manager, at (301) 786-4150.

Sincerely,

*{See appended electronic signature page}*

Andrea Leonard Segal, M.D.  
Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

Enclosure

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/s/

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Andrea Segal  
5/13/2009 09:54:13 AM

The following comments are in response to your April 7, 2009 submission of revised labeling for Prevacid 24 HR submitted in follow up to our March 30, 2009 comments. These comments are preliminary in nature and should not be considered a complete evaluation of your proposed labeling.

**Principal Display Panel (PDP)**

The contrast and font size of the statement of identity “Lansoprazole delayed release capsules 15mg/acid reducer” is not compliant with 21 CFR 201.61. Increase the size and contrast of this statement.

**Drug Facts**

Revise the last bullet under the heading “Directions” to read as follows:

- Children under 18 years of age: ask a doctor before use. Heartburn in children may sometimes be caused by a serious condition.

The Pediatric Research and Equity Act (PREA) of 2007 changed the Federal Food, Drug and Cosmetic Act to state at 505(a)(4)(D) that if FDA grants a waiver “because there is evidence that a drug...would be ineffective or unsafe in pediatric populations, the information shall be included in the labeling for the drug...” In order for the labeling to be considered sufficient under PREA, “information” should refer to some safety or efficacy concern in the pediatric population; “ask a doctor” does not adequately convey the concern.

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On Original**

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/s/  
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Mary R Vienna  
4/21/2009 09:56:24 AM

The following comments are in response to your March 20, 2009 submission of revised labeling for Prevacid 24 HR submitted in follow up to our March 17, 2009 discussion. These comments are preliminary in nature and should not be considered a complete evaluation of your proposed labeling.

**Principal Display Panel (PDP)**

T

b(4)

T

2 Page(s) Withheld

       Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

*Withheld Track Number: Administrative - 1*

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/s/

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Mary R Vienna  
3/30/2009 03:05:39 PM

## MEMORANDUM OF TELECON

DATE: March 17, 2009

APPLICATION NUMBER: NDA 22-327

**BETWEEN:**

Name: Suzanne LoGalbo, R. Ph., J.D., Head, North American Region, Global Regulatory Affairs  
Evren Atillasoy, M.D., Global Head, Digestive Health  
Donna Coughlin, Associate Director, North American Liaison, Digestive Health, Global Regulatory Affairs  
Walter Lehneis, Marketing Director  
Todd Adrian, Associate Director, Global Market Research  
Phone: (866) 866-5110  
Representing: Novartis Consumer Health, Inc.

**AND**

Name: Andrea Leonard-Segal, M.D., Division of Nonprescription Clinical Evaluation (DNCE)  
Joel Schiffenbauer, M.D., DNCE  
Leah Christl, Office of Nonprescription Drugs  
Leslie Furlong, M.D., DNCE  
Lolita Lopez, M.D., DNCE  
Melissa Furness, DNCE  
Mary Vienna, DNCE  
Debbie Lumpkins, Div. of Nonprescription Regulation Development (DNRD)  
Mary Robinson, DNRD  
Ruyi He, M.D., Division of Gastroenterology Products (DGP)  
Ali Niak, M.D., DGP  
Carol Holquist, Division of Medication Error and Prevention Analysis (DMEPA)  
Kellie Taylor, DMEPA

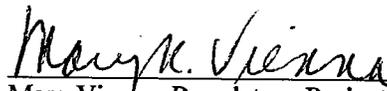
SUBJECT: Trade name for NDA 22-327

BACKGROUND: Novartis Consumer Health, Inc. submitted NDA 22-327 for lansoprazole 15mg capsule on July 16, 2008 and has proposed the tradename Prevacid 24HR for this product. FDA requested a meeting to discuss this request.

DISCUSSION: FDA expressed the concern that the Prevacid 24HR trade name may imply that the drug starts working in 24 hours, which is not supported by efficacy data. If this trade name is to be accepted, Novartis needs to place an asterisk next to the 24HR and put “\*may take 1 to 4 days for effect” on the PDP. If Novartis doesn’t want to make

such a change and chooses to propose a new trade name, that would affect FDA action on the application. Novartis asked if a new trade name request would constitute a major amendment to the application, and FDA stated it would not. Novartis asked if the format, placement and other characteristics of the tradename were acceptable, and FDA replied that the review was not complete and they would have additional comments. Novartis asked how an additional trade name request would affect the PDUFA date, and FDA stated that the PDUFA date would not be affected; either the application's labeling could not be approved and subsequent amendments to the application would be necessary, or labeling could be approved without a trade name. Novartis asked if FDA had feedback on other tradenames in the marketing study, and FDA replied that the "OTC" modifier would not need the explanation of benefit language, as there was no implied onset of action in the name. Modifiers such as [ ] would present the same issues as Prevacid 24HR, and need a comprehensive review, while removing the modifier entirely could present a safety issue in distinguishing between the Rx and OTC medication with different dosages and indications. Novartis stated their understanding of FDA's rationale for the asterisk request. FDA and Novartis agreed that Novartis would respond to the FDA request by March 20, 2009.

b(4)

  
Mary Vienna, Regulatory Project Manager

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/s/

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Mary R Vienna  
3/30/2009 07:41:13 AM  
CSO

MEMORANDUM

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

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CLINICAL INSPECTION SUMMARY

DATE: March 10, 2009

TO: Mary Vienna, Regulatory Project Manager  
Lolita Lopez M.D., Medical Officer  
Division of Nonprescription Products  
Ali Niak, M.D., Medical Officer  
Division of Gastroenterology Products

FROM: Susan Leibenhaut, M.D.  
Good Clinical Practice Branch I  
Division of Scientific Investigations

THROUGH: Constance Lewin, M.D., M.P.H.  
Branch Chief  
Good Clinical Practice Branch I  
Division of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections.

NDA: #22-327

APPLICANT: Novartis Consumer Health

DRUG: Lansoprazole (Prevacid 24HR)

NME: No

THERAPEUTIC CLASSIFICATION: Standard

INDICATION: treatment of frequent heartburn (2 or more days/week).

CONSULTATION REQUEST DATE: October 1, 2008

DIVISION ACTION GOAL DATE: April 24, 2009

PDUFA DATE: May 16, 2009

## **I. BACKGROUND:**

Novartis Consumer Health, Inc. (NCH) submitted NDA 22-327 under the provisions of 505(b)(1) of the FD&C Act for over-the-counter (OTC) marketing of lansoprazole delayed release capsules 15mg for the indication of treatment of frequent heartburn (2 or more days/week). An audit was requested to assess data integrity in support of the pending application.

The innovator product for this NDA, Prevacid (lansoprazole) Delayed-Release Capsules, belongs to a class of drugs known as proton-pump inhibitors and was approved for prescription use in the US on May 10, 1995 for the indication of short-term treatment of active duodenal ulcer. On July 31, 2002 it was approved for the indication of short-term treatment of symptomatic gastroesophageal reflux disease (GERD). Adverse effects (AEs) are infrequent (all AEs<5%). Dosage form is one capsule every day for 14 days. For the OTC product, it is advised that the course of treatment be repeated no more often than every 4 months.

The study consisted of a one week screening and heartburn medication washout period and a one week placebo run-in period to assess the frequency and severity of heartburn, Interactive Voice Response System (IVRS) diary completion compliance, and visit schedule compliance. At Visit 3 after the run-in period subjects were randomized 1:1 to either lansoprazole 15mg or placebo. Subjects were given instruction on completing the daily IVRS diary and sites were instructed to contact subjects by telephone if diary completion was delayed. Subjects were seen on Day 16 after 2 weeks of test article treatment. The data entered into the IVRS by the subjects were sent directly to a contract research organization (CRO) and the sites did not have access to this data.

Clinical sites were selected based on the large number of subjects enrolled and previous inspectional history.

The protocols inspected were:

- A. PRSW-GN-301 entitled "A phase III, multi-center, randomized, double-blind, placebo-controlled, parallel group trial of fourteen day treatment with lansoprazole 15 mg once a day in frequent heartburn"
- B. PRSW-GN-302 entitled "A phase III, multi-center, randomized, double-blind, placebo-controlled, parallel group trial of fourteen day treatment with lansoprazole 15 mg once a day in frequent heartburn"
- C. PRSW-GN-305 entitled "A phase III, multi-center, randomized, double-blind, placebo-controlled, parallel group trial of fourteen day treatment with lansoprazole 15 mg or 30 mg once a day in frequent nighttime heartburn"

**II. RESULTS (by Site):**

Name of Clinical Investigator (CI) or Contract Research Organization (CRO) and Location	Protocol # and # of Subjects:	Inspection Dates	Final Classification
Terence Hart, M.D. 203 West Avalon Ave. Suite 390 Muscle Shoals, AL 35661	Protocol #305 39 subjects	December 9 to 11, 2008	NAI
Steven Bowman, M.D. Tampa Bay Medical Research, Inc. 3251 McMullen Booth Rd., Suite 301 Clearwater, FL 33761	Protocol #302 39 subjects	January 16 to 30, 2009	VAI
Ronald Surowitz, M.D. Health Awareness Inc. 210 Jupiter Lakes Blvd., Suite 4102 Jupiter, FL 33458	Protocol #301 40 subjects	February 9 to 12, 2009	Pending (Preliminary classification NAI)
	Protocol #301/ 40 subjects Protocol #302/ 39 subjects Protocol #305/39 subjects	January 21 to 23, 2009	NAI

b(4)

Key to Classifications

NAI = No deviation from regulations.

VAI = Deviation(s) from regulations.

OAI = Significant deviations from regulations.

Pending = Preliminary classification based on information in 483 or preliminary communication with the field; EIR has not been received from the field and complete review of EIR is pending.

1. Terence Hart, M.D.  
203 West Avalon Ave., Suite 390  
Muscle Shoals, AL 35661

- a. **What was inspected:** At this site, 61 subjects were screened, 39 subjects were randomized, 15 subjects were screen failures determined by IVRS, 3 subjects were terminated because of proton-pump inhibitor use, 2 subjects had adverse events and 2 subjects withdrew consent after being enrolled. An audit of 39 subjects' records was conducted.

- b. **General observations/commentary:** No under-reporting of adverse events was detected. Due to the fact that the efficacy data were sent directly from the subject to the CRO, the efficacy data were verified at inspection of the CRO. No regulatory violations were noted.
  - c. **Assessment of data integrity:** The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.
2. Steven Bowman, M.D.  
Tampa Bay Medical Research, Inc.  
3251 McMullen Booth Rd., Suite 301  
Clearwater, FL 33761
- a. **What was inspected:** At this site, 55 subjects were screened, 15 subjects were screen failures, 40 subjects were randomized and 39 subjects completed the study. Consent forms were reviewed for all 55 subjects. An in depth review of 20 subjects' records included review of source documents, case report forms (CRFs), ECGs and laboratory data. There were no deaths or serious adverse events (SAEs) reported.
  - b. **General observations/commentary:** No under-reporting of adverse events was detected. Inspection revealed inadequate records in that there were discrepancies in the reporting of the use of rescue medication for 5 of the subjects at this site. Due to the fact that the efficacy data were sent directly from the subject to the CRO, the efficacy data were verified at inspection of the CRO.
  - c. **Assessment of data integrity:** The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.
3. Ronald Surowitz, M.D.  
Health Awareness Inc.  
210 Jupiter Lakes Blvd., Suite 4102  
Jupiter, FL 33458

**Note:** Observations noted for this site are based on communications with the FDA investigator. An inspection summary addendum will be generated if conclusions change upon receipt and review of the Establishment Inspection Report (EIR).

- a. **What was inspected:** At this site, 48 subjects were screened, 40 subjects were randomized and 36 subjects completed the study. Consent forms were reviewed for all 48 subjects. There were no deaths or SAEs reported. Efficacy data was not available at the site for verification because of the specifics of the protocol.
- b. **General observations/commentary:** There was no under-reporting of adverse events detected. Due to the fact that the efficacy data were sent directly from the subject to the CRO, the efficacy data were verified at inspection of the CRO. No regulatory violations were noted.
- c. **Assessment of data integrity:** The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

4.

**b(4)**

- a. **What was inspected:** The inspection reviewed the following: organization charts, contracts with NDA applicant Novartis, and standard operating procedures (SOPs) concerning development and maintenance of the IVRS systems used to capture the primary endpoint of presence or absence of heartburn. The records related to the IVRS subject diary data included copies of specification documents and approvals, implementation specifications/signoff, validation and change control documents, and data clarification forms.
- b. **General observations/commentary:** The inspection found that IVRS systems had been validated prior to implementation or a deviation was recorded if the validation had not been completed, that access to the database was limited and that audit trails were in place. Comparison of data listings submitted by the sponsor with raw endpoint data on archive compact discs for 11 subjects in protocol 301, 13 subjects for protocol 302 and 20 subjects for protocol 305 did not show discrepancies.
- c. **Assessment of data integrity:** No significant observations of noncompliance were noted. The study appears to have been conducted adequately, and the data submitted by the sponsor may be used in support of the respective indication.

### III. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The inspection of Dr. Bowman showed regulatory violations noted above. All other inspections did not note regulatory violations.

The studies appear to have been conducted adequately, and the data generated by the clinical sites may be used in support of the respective indication.

An addendum to this clinical inspection summary will be forwarded to the review division should there be a change in the final classification or additional observations of clinical and regulatory significance are discovered after reviewing the EIR for Dr. Surowitz's site.

*{See appended electronic signature page}*

Susan Leibenhaut, MD  
Good Clinical Practice Branch I  
Division of Scientific Investigations

#### CONCURRENCE:

*{See appended electronic signature page}*

Constance Lewin, MD, MPH  
Branch Chief  
Good Clinical Practice Branch I  
Division of Scientific Investigations

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/s/

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Susan Leibenhaut  
3/11/2009 12:33:09 PM  
MEDICAL OFFICER

Constance Lewin  
3/11/2009 12:58:33 PM  
MEDICAL OFFICER



INFORMATION REQUEST LETTER

NDA 22-327

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

Please refer to your new drug application (NDA) dated July 15, 2008, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Prevacid 24 HR (15 mg lansoprazole) capsules.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following information request. We request a prompt written response by March 12, 2009 in order to continue our evaluation of your NDA.

1. Submit an amendment to accept an expiration dating period of 24 months, when stored at room temperature, 20-25°C (68-77°F), for the drug product packaged in 7 bottles. The proposed expiration date is not supported by the stability data provided.

b(4)

b(4)

If you have any questions, call Mary Vienna, Regulatory Project Manager, at (301) 796-4150.

Sincerely,

*{See appended electronic signature page}*

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

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/s/

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Moo-Jhong Rhee  
3/10/2009 01:51:04 PM  
Chief, Branch III



INFORMATION REQUEST LETTER

NDA 22-327

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

Please refer to your new drug application (NDA) dated July 15, 2008, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Prevacid 24 HR (15mg lansoprazole) capsules.

We are reviewing the Clinical section of your submission and have the following information request. We request a written response by March 10, 2009 in order to continue our evaluation of your NDA.

1. Please clarify if the Prevacid capsule dosage form was used in the three clinical studies conducted for your proposed frequent heartburn indication. The 'Identity of Investigational products' section of each study makes reference to a lansoprazole 15 mg tablet dosage form.
2. Your application stated at the time of your initial NDA submission that there is an OTC lansoprazole product that is currently approved [ ] in Sweden. Please provide a marketing status update for this Swedish product and an updated OTC label (translated into English) if available.

b(4)

If you have any questions, call Mary Vienna, Regulatory Project Manager, at (301) 796-4150.

Sincerely,

*{See appended electronic signature page}*

Melissa Hancock Furness  
Chief, Project Management Staff  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

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/s/  
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Melissa Furness  
3/5/2009 02:34:46 PM



INFORMATION REQUEST LETTER

NDA 22-327

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

Please refer to your new drug application (NDA) dated July 15, 2008, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Prevacid 24 HR (15 mg lansoprazole) capsules.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following information request. We request a prompt written response by March 2, 2009 in order to continue our evaluation of your NDA.

1. Submit an amendment to accept an expiration dating period of \_\_\_\_\_ when stored at controlled room temperature, 20-25°C (68-77°F), for the drug product packaged in \_\_\_\_\_ bottles. The proposed \_\_\_\_\_ expiration date is not supported by the stability data provided. **b(4)**
2. **b(4)**
3. Submit a letter of commitment to conduct a long-term stability study on the first three production batches of the product produced from each of the associated encapsulation and packaging sites.

If you have any questions, call Mary Vienna, Regulatory Project Manager, at (301) 796-4150.

Sincerely,

*{See appended electronic signature page}*

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

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/s/

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Moo-Jhong Rhee  
2/19/2009 02:24:42 PM  
Chief, Branch III



**General Correspondence  
Electronic Regulatory Submission for Archive**

January 28, 2009

Donna Griebel, MD, Director  
Division of Gastroenterology Products  
Central Document Room  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

**RE: PREVACID<sup>®</sup> (lansoprazole) Delayed-Release Capsules  
NDA 20-406**

Dear Dr. Griebel:

Reference is made to the New Drug Application 20-406 PREVACID<sup>®</sup> (lansoprazole) Delayed-Release Capsules held by Takeda Pharmaceuticals North America, Inc. (Takeda).

Takeda hereby grants to Novartis Consumer Health, Inc. ("Novartis") the full right of reference and FDA authorization to refer to Takeda's NDA 20-406 PREVACID<sup>®</sup> (lansoprazole) Delayed-Release Capsules to support Novartis IND 74,256 and NDA 22-327 in relation to the over-the-counter manufacture, use, and sale of lansoprazole including, but not limited to, all the preclinical and clinical data, chemistry, manufacturing and control data, safety data on lansoprazole, as well as all lansoprazole labeling. This right of reference also applies to the original PREVACID NDA and any and all amendments, supplements, Periodic and Annual Reports. This authorization is retroactive to May 5, 2006.

Please be advised that the material and data in the PREVACID NDA are trade secret and confidential commercial information of Takeda. With the exception of this specific right to reference, please continue to hold the information contained in this application as confidential.

This submission is in electronic Common Technical Document (eCTD) format. Electronic documents are provided in Adobe PDF 1.3 (Adobe 4.05b) format. This submission is approximately 1 MB and is provided on one CD-ROM. It has been checked for viruses using Symantec Endpoint Protection Version 11.0.2010.25, and is virus-free. If you should have any questions concerning the technical aspects of this submission, please contact Lois Householder at 847-582-2682.



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PREVACID<sup>®</sup> (lansoprazole) Delayed-Release Capsules  
January 28, 2009  
Page 2 of 2

Any questions regarding this submission may be directed to my attention.

Sincerely,

A handwritten signature in cursive script that reads "Leslie D. Abelson".

Leslie D. Abelson, BS, RAC  
Manager, Regulatory Affairs  
Takeda Global Research and Development Center, Inc.  
847-582-2631  
847-582-2880 (fax)



**General Correspondence  
Electronic Regulatory Submission for Archive**

January 26, 2009

Donna Griebel, MD, Director  
Division of Gastroenterology Products  
Central Document Room  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

**RE: PREVACID<sup>®</sup> (lansoprazole) Delayed-Release Capsules  
IND 30,159 / Serial No. 0614**

Dear Dr. Griebel:

Reference is made to the Investigational New Drug 30,159 PREVACID<sup>®</sup> (lansoprazole) Delayed-Release Capsules held by Takeda Global Research and Development Center, Inc. ("Takeda").

Takeda hereby grants to Novartis Consumer Health, Inc. ("Novartis") the full right of reference and FDA authorization to refer to Takeda's IND 30,159 PREVACID<sup>®</sup> (lansoprazole) Delayed-Release Capsules to support Novartis IND 74,256 and NDA 22-327 in relation to the over-the-counter manufacture, use, and sale of lansoprazole including, but not limited to, all the preclinical and clinical data, chemistry, manufacturing and control data, as well as all safety data on lansoprazole. This right of reference also applies to the original PREVACID IND and any and all amendments and Annual Reports. This authorization is retroactive to May 5, 2006.

Please be advised that the material and data in the PREVACID IND are trade secret and confidential commercial information of Takeda. With the exception of this specific right to reference, please continue to hold the information contained in this application as confidential.

This submission is in electronic Common Technical Document (eCTD) format. Electronic documents are provided in Adobe PDF 1.3 (Adobe 4.05b) format. This submission is approximately 1 MB and is provided on one CD-ROM. It has been checked for viruses using Symantec Endpoint Protection Version 11.0.2010.25, and is virus-free. If you should have any questions concerning the technical aspects of this submission, please contact Lois Householder at 847-582-2682.



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PREVACID® (lansoprazole) Delayed-Release Capsules  
January 26, 2009  
Page 2 of 2

Any questions regarding this submission may be directed to my attention.

Sincerely,

*Madhavi Uppaluri*

*for* Leslie D. Abelson, BS, RAC  
Manager, Regulatory Affairs  
Takeda Global Research and Development Center, Inc.  
847-582-2631  
847-582-2880 (fax)



INFORMATION REQUEST LETTER

NDA 22-327

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

Please refer to your new drug application (NDA) dated July 15, 2008, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Prevacid 24 HR (15mg lansoprazole) capsules.

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

1. Provide the composition of the ink used to imprint the capsule caps with \_\_\_\_\_
2. Provide document(s) indicating that the gelatin used in the banding kit is in full compliance with US regulatory guidelines regarding BSE/TSE.
3. Provide results of validation on the HPLC method used to determine individual and total impurities present in the drug product including a determination of LOQ of the HPLC method for each of the related substances and response factors for the related substances. The method provided in the application is not equivalent to the current USP method.
4. Add the specification limits for individual and total impurities, specified in the approved prescription drug product (NDA 20-406), to the specification of the proposed OTC drug product.
5. Confirm that the Microbial Limit Tests for Total Aerobic Microbial Count, Total Combined Yeasts/Molds Count and Specified Microorganism(s) are performed according to USP <61>. The acceptance criteria for Microbial Limit Tests (MLT) are recommended in USP <1111>.
6. Commit to perform Microbial Limit Tests on all production batches produced from each manufacturing site over a period of a year. The proposal of reducing MLT frequency can be considered through a post-approval supplement.

b(4)

Appears This Way  
On Original

7. Provide information for handling the bulk capsules before final packaging such as bulk packaging, shipping and storage conditions, and release of bulk capsules. We expect that the expiration dating period starts at the time when the *T*

b(4)

If you have any questions, call Mary Vienna, Regulatory Project Manager, at (301) 796-4150.

Sincerely,

*{See appended electronic signature page}*

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

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

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Moo-Jhong Rhee  
11/12/2008 01:49:06 PM  
Chief, Branch III



**INFORMATION REQUEST LETTER**

NDA 22-327

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

Please refer to your new drug application (NDA) dated July 15, 2008, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Prevacid 24 HR (15mg lansoprazole) capsules.

We are reviewing the Statistical section of your submission and have the following information request. We request a prompt written response in order to continue our evaluation of your NDA.

1. The protocols for studies PRSW-GN-301 and PRSW-GN-302 are labeled as "Amendment 3" in the application. Please clarify whether these protocols are the final version of the study protocols. If not, the final protocols should be submitted as an amendment to the application.
2. Please provide electronic analysis programs (e.g. SAS) for the primary efficacy, secondary efficacy and safety analyses.

In addition to the above statistical comments, we also remind you of the need to submit the 4-month safety update, including the World Health Organization (WHO) post-marketing safety data, by November 16, 2008.

If you have any questions, call Mary Vienna, Regulatory Project Manager, at (301) 796-4150.

Sincerely,

*{See appended electronic signature page}*

Leah Christl, Ph.D.  
Acting Chief, Project Management Staff  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
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.**  
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/s/

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Leah Christl  
10/15/2008 08:48:21 AM

**NDA/BLA REGULATORY FILING REVIEW**  
(Including Memo of Filing Meeting)

Application Information		
NDA # 22-327 BLA#	NDA Supplement #:S- BLA STN #	Efficacy Supplement Type SE-
Proprietary Name: PREVACID®24HR Established/Proper Name: Lansoprazole Dosage Form: Capsule Strengths: 15 mg		
Applicant: Novartis Consumer Health Inc. Agent for Applicant (if applicable): N/A		
Date of Application: 07-15-08 Date of Receipt: 07-16-08 Date clock started after UN: N/A		
PDUFA Goal Date: 05-16-09		Action Goal Date (if different): 05-15-09
Filing Date: 09-14-08 Date of Filing Meeting: 08-26-08		
Chemical Classification: (1,2,3 etc.) (original NDAs only) 8		
Proposed Indication(s): Treats frequent heartburn (occurs 2 or more days per week)		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)
<i>Refer to Appendix A for further information.</i>		
Review Classification:		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority  <input type="checkbox"/> Tropical disease Priority review voucher submitted
<i>If the application includes a complete response to pediatric WR, review classification is Priority.</i>  <i>If a tropical disease Priority review voucher was submitted, review classification defaults to Priority.</i>		
Resubmission after withdrawal? <input type="checkbox"/>		
Resubmission after refuse to file? <input type="checkbox"/>		
Part 3 Combination Product? <input type="checkbox"/>	<input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Drug/Device <input type="checkbox"/> Biologic/Device	
<input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation  <input type="checkbox"/> Rx-to-OTC switch, Full <input checked="" type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC  Other:	<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)	

Collaborative Review Division (if OTC product): Division of Gastroenterology Products (DGP)	
List referenced IND Number(s): INDs 30,159; 58,341; 60,103; 74,256.	
PDUFA and Action Goal dates correct in tracking system? <i>If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are the proprietary, established/proper, and applicant names correct in tracking system? <i>If not, ask the document room staff to make the corrections. Also, ask the document room staff to add the established name to the supporting IND(s) if not already entered into tracking system.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Are all classification codes/flags (e.g. orphan, OTC drug, pediatric data) entered into tracking system? <i>If not, ask the document room staff to make the appropriate entries.</i>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<b>Application Integrity Policy</b>	
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at: <a href="http://www.fda.gov/ora/compliance_ref/aiplist.html">http://www.fda.gov/ora/compliance_ref/aiplist.html</a></i>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
If yes, explain:	
If yes, has OC/DMPQ been notified of the submission?	<input type="checkbox"/> YES <input type="checkbox"/> NO
Comments:	
<b>User Fees</b>	
Form 3397 (User Fee Cover Sheet) submitted	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
User Fee Status	<input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required
<i>Note: 505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. It is expected that all 505(b) applications, whether 505(b)(1) or 505(b)(2), will require user fees unless otherwise waived or exempted (e.g., business waiver, orphan exemption).</i>	
<b>Exclusivity</b>	
Does another product have orphan exclusivity for the same indication? <i>Check the Electronic Orange Book at: <a href="http://www.fda.gov/cder/ob/default.htm">http://www.fda.gov/cder/ob/default.htm</a></i>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
If yes, is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?	<input type="checkbox"/> YES <input type="checkbox"/> NO

<p><i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)</i></p> <p><b>Comments:</b></p>	
<p>Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? <i>(NDAs/NDA efficacy supplements only)</i></p> <p><i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i></p> <p><b>Comments:</b></p>	<p><input checked="" type="checkbox"/> YES # years requested: 3 years</p> <p><input type="checkbox"/> NO</p>
<p>If the proposed product is a single enantiomer of a racemic drug previously approved for a different therapeutic use <i>(NDAs only)</i>:</p> <p>Did the applicant (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b) request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?</p> <p><i>If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.</i></p>	<p><input checked="" type="checkbox"/> Not applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<b>505(b)(2) (NDAs/NDA Efficacy Supplements only)</b>	
<p>1. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</p> <p>2. Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (see 21 CFR 314.54(b)(1)).</p> <p>3. Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug (see 21 CFR 314.54(b)(2))?</p> <p><i>Note: If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).</i></p>	<p><input checked="" type="checkbox"/> Not applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>

<p>4. Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? <i>Check the Electronic Orange Book at: <a href="http://www.fda.gov/cder/ob/default.htm">http://www.fda.gov/cder/ob/default.htm</a></i></p>		<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO	
<p>If yes, please list below:</p>			
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration
<p><i>If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 108(b)(2). Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.</i></p>			
<b>Format and Content</b>			
<p><i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i></p> <p>Comments:</p>		<input type="checkbox"/> All paper (except for COL) <input type="checkbox"/> All electronic <input checked="" type="checkbox"/> Mixed (paper/electronic)  <input type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)	
<p><b>If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?</b></p>		<p>All except administrative forms and certifications requiring an original signature</p>	
<p><b>If electronic submission:</b>  <u>paper</u> forms and certifications signed (non-CTD) or <u>electronic</u> forms and certifications signed (scanned or digital signature)(CTD)?</p> <p><i>Forms include: 356h, patent information (3542a), financial disclosure (3454/3455), user fee cover sheet (3542a), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i></p> <p>Comments:</p>		<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	
<p><b>If electronic submission, does it follow the eCTD guidance?</b>  (<a href="http://www.fda.gov/cder/guidance/7087rev.pdf">http://www.fda.gov/cder/guidance/7087rev.pdf</a>)</p> <p>If not, explain (e.g., waiver granted):</p>		<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	

<p><b>Form 356h:</b> Is a signed form 356h included?</p> <p><i>If foreign applicant, both the applicant and the U.S. agent must sign the form.</i></p> <p>Are all establishments and their registration numbers listed on the form?</p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO  <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p><b>Index:</b> Does the submission contain an accurate comprehensive index?</p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including:</p> <p><input checked="" type="checkbox"/> legible  <input checked="" type="checkbox"/> English (or translated into English)  <input checked="" type="checkbox"/> pagination  <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only)</p> <p><b>If no, explain:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p><b>Controlled substance/Product with abuse potential:</b></p> <p>Abuse Liability Assessment, including a proposal for scheduling, submitted?</p> <p>Consult sent to the Controlled Substance Staff?</p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> Not Applicable  <input type="checkbox"/> YES <input type="checkbox"/> NO  <input type="checkbox"/> YES <input type="checkbox"/> NO
<p><b>BLAs/BLA efficacy supplements only:</b></p> <p>Companion application received if a shared or divided manufacturing arrangement?</p> <p><b>If yes, BLA #</b></p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Patent Information (NDAs/NDA efficacy supplements only)</b>	
<p>Patent information submitted on form FDA 3542a?</p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<b>Debarment Certification</b>	
<p>Correctly worded Debarment Certification with authorized signature?</p> <p><i>If foreign applicant, both the applicant and the U.S. Agent must</i></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p><b>sign the certification.</b></p> <p><i>Note: Debarment Certification should use wording in FD&amp;C Act section 306(k)(l) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge..."</i></p> <p><b>Comments:</b></p>	
<p><b>Field Copy Certification (NDAs/NDA efficacy supplements only)</b></p>	
<p>Field Copy Certification: that it is a true copy of the CMC technical section (<i>applies to paper submissions only</i>)</p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>	<p><input checked="" type="checkbox"/> Not Applicable (<i>electronic submission or no CMC technical section</i>)</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p><b>Financial Disclosure</b></p>	
<p>Financial Disclosure forms included with authorized signature?</p> <p><i>Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an Agent.</i></p> <p><i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i></p> <p><b>Comments:</b></p>	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p><b>Pediatrics</b></p>	
<p><b>PREA</b></p> <p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver &amp; deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p>	
<p>Are the required pediatric assessment studies or a full waiver of pediatric studies included?</p> <p>If no, is a request for full waiver of pediatric studies OR a request for partial waiver/deferral and a pediatric plan included?</p> <ul style="list-style-type: none"> <li>• <i>If no, request in 74-day letter.</i></li> <li>• <i>If yes, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3)</i></li> </ul> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> YES</p> <p><input checked="" type="checkbox"/> NO</p> <p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p> <p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>

<b>BPCA (NDAs/NDA efficacy supplements only):</b>	
Is this submission a complete response to a pediatric Written Request?  <i>If yes, contact PMHS (pediatric exclusivity determination by the Pediatric Exclusivity Board is needed).</i>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<b>Comments:</b>	
<b>Prescription Labeling</b>	
Check all types of labeling submitted.  <b>Comments:</b>	<input checked="" type="checkbox"/> <b>Not applicable</b> <input type="checkbox"/> Package Insert (PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use <input type="checkbox"/> MedGuide <input type="checkbox"/> Carton labels <input type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)
Is electronic Content of Labeling submitted in SPL format?  <i>If no, request in 74-day letter.</i>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Comments:</b>	
Package insert (PI) submitted in PLR format?  If no, was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request?  <i>If no, request in 74-day letter.</i>	<input type="checkbox"/> YES <input type="checkbox"/> NO  <input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Comments:</b>	
All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?	<input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Comments:</b>	
MedGuide or PPI (plus PI) consulted to OSE/DRISK? ( <i>send WORD version if available</i> )	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Comments:</b>	
REMS consulted to OSE/DRISK?	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Comments:</b>	
Carton and immediate container labels, PI, PPI, and proprietary name (if any) sent to OSE/DMEDP?	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<b>Comments:</b>	

OTC Labeling	
<p>Check all types of labeling submitted.</p> <p><b>Comments:</b></p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> Outer carton label <input checked="" type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input checked="" type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify)
<p>Is electronic content of labeling submitted?</p> <p><i>If no, request in 74-day letter.</i></p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Are annotated specifications submitted for all stock keeping units (SKUs)?</p> <p><i>If no, request in 74-day letter.</i></p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>If representative labeling is submitted, are all represented SKUs defined?</p> <p><i>If no, request in 74-day letter.</i></p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<p>Proprietary name, all labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEDP?</p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
Meeting Minutes/SPA Agreements	
<p>End-of Phase 2 meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p><b>Comments:</b></p>	<input type="checkbox"/> YES Date(s): <input checked="" type="checkbox"/> NO
<p>Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)?</p> <p><i>If yes, distribute minutes before filing meeting.</i></p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES Date(s): 03-17-08 <input type="checkbox"/> NO
<p>Any Special Protocol Assessment (SPA) agreements?</p> <p><i>If yes, distribute letter and/or relevant minutes before filing meeting.</i></p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> YES Date(s): 09-08-06 <input type="checkbox"/> NO

ATTACHMENT

**MEMO OF FILING MEETING**

**DATE:** August 26, 2008

**NDA/BLA #:** NDA 22-327

**PROPRIETARY/ESTABLISHED NAMES:** PREVACID®24HR/Lansoprazole 15mg

**APPLICANT:** Novartis Consumer Health, Inc.

**BACKGROUND:** This molecular entity is approved as an Rx medication (NDA 20-406), currently submitted as OTC for a frequent heartburn indication at the 15mg dosage level.

**REVIEW TEAM:**

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Mary Vienna	Y
	CPMS/TL:	Leah Christl	Y
Cross-Discipline Team Leader (CDTL)	N/A		
Clinical	Reviewer:	Lolita Lopez Ali Niak (DGP)	Y Y
	TL:	Daiva Shetty Ruyi He (DGP)	Y Y
Social Scientist Review (for OTC products)	Reviewer:	Laura Shay	N
	TL:	N/A	
Labeling Review (for OTC products)	Reviewer:	Mary Robinson	Y
	TL:	Debbie Lumpkins	Y
OSE	Reviewer:	Cathy Miller	N
	TL:	Kellie Taylor	N
Clinical Microbiology (for antimicrobial products)	Reviewer:	N/A	

Clinical Pharmacology	Reviewer:	Insook Kim	Y
	TL:	Sue Chih Lee	N
Biostatistics	Reviewer:	Freda Cooner	Y
	TL:	Mike Welch	Y
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Cindy Li	Y
	TL:	Paul Brown	N
Statistics, carcinogenicity	Reviewer:	N/A	
	TL:		
Product Quality (CMC)	Reviewer:	Yichun Sun	Y
	TL:	Shulin Ding	Y
Facility (for BLAs/BLA supplements)	Reviewer:	N/A	
	TL:		
Microbiology, sterility (for NDAs/NDA efficacy supplements)	Reviewer:	N/A	
	TL:		
Bioresearch Monitoring (DSI)	Reviewer:	N/A	
	TL:		
Other reviewers	N/A		

**OTHER ATTENDEES:** Joel Schiffenbauer, Deputy Director, DNCE.

505(b)(2) filing issues?  If yes, list issues:	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
Per reviewers, are all parts in English or English translation?  If no, explain:	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO

<p><b>Electronic Submission comments</b></p> <p>List comments: None</p>	<input type="checkbox"/> Not Applicable
<p><b>CLINICAL</b></p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> <li>Clinical study site(s) inspections(s) needed?</li> </ul> <p>If no, explain: No clinical studies for this NDA</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> <li>Advisory Committee Meeting needed?</li> </ul> <p>Comments:</p> <p><i>If no, for an original NME or BLA application, include the reason. For example:</i></p> <ul style="list-style-type: none"> <li><i>this drug/biologic is not the first in its class</i></li> <li><i>the clinical study design was acceptable</i></li> <li><i>the application did not raise significant safety or efficacy issues</i></li> <li><i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i></li> </ul>	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> <li>If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?</li> </ul> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p><b>CLINICAL MICROBIOLOGY</b></p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><b>CLINICAL PHARMACOLOGY</b></p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter

<b>Comments:</b>	
<ul style="list-style-type: none"> <li>Clinical pharmacology study site(s) inspections(s) needed?</li> </ul>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<b>BIOSTATISTICS</b>  <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE  <input type="checkbox"/> Review issues for 74-day letter
<b>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</b>  <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE  <input type="checkbox"/> Review issues for 74-day letter
<b>PRODUCT QUALITY (CMC)</b>  <b>Comments:</b> Missing dissolution profile, packaging configurations and contact information for each manufacturing and testing facility.	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE  <input checked="" type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> <li>Categorical exclusion for environmental assessment (EA) requested?</li> </ul> <p>If no, was a complete EA submitted?</p> <p>If EA submitted, consulted to EA officer (OPS)?</p> <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO  <input type="checkbox"/> YES <input type="checkbox"/> NO  <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> <li>Establishment(s) ready for inspection?</li> <li>Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ?</li> </ul> <b>Comments:</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO  <input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> <li>Sterile product?</li> </ul>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO

<p><b>If yes, was Microbiology Team consulted for validation of sterilization? (NDAs/NDA supplements only)</b></p>	<input type="checkbox"/> YES <input type="checkbox"/> NO
<p><b>FACILITY (BLAs only)</b></p> <p><b>Comments:</b></p>	<input type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><b>REGULATORY PROJECT MANAGEMENT</b></p>	
<p><b>Signatory Authority:</b> Director, DNCE</p> <p><b>GRMP Timeline Milestones:</b> Filing Date: 09-14-08; Day 74: 09-28-08; Review Completion Goal Date: 03-16-09; Action Goal Date: 05-15-09; PDUFA Goal Date: 05-16-09</p> <p><b>Comments:</b></p>	
<p><b>REGULATORY CONCLUSIONS/DEFICIENCIES</b></p>	
<input type="checkbox"/>	<p>The application is unsuitable for filing. Explain why:</p>
<input checked="" type="checkbox"/>	<p>The application, on its face, appears to be suitable for filing.</p> <p><input type="checkbox"/> No review issues have been identified for the 74-day letter.</p> <p><input checked="" type="checkbox"/> Review issues have been identified for the 74-day letter. List (optional):</p> <p><input checked="" type="checkbox"/> Standard Review</p> <p><input type="checkbox"/> Priority Review</p>
<p><b>ACTIONS ITEMS</b></p>	
<input type="checkbox"/>	<p>Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into tracking system.</p>
<input type="checkbox"/>	<p>If RTF action, notify everybody who already received a consult request, OSE PM., and Product Quality PM. Cancel EER/TBP-EER.</p>
<input type="checkbox"/>	<p>If filed and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.</p>
<input type="checkbox"/>	<p>If BLA or priority review NDA, send 60-day letter.</p>
<input checked="" type="checkbox"/>	<p>Send review issues/no review issues by day 74</p>
<input type="checkbox"/>	<p>Other</p>

## Appendix A (NDA and NDA Supplements only)

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

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

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

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

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

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

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

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

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

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

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

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/s/

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Mary R Vienna  
10/7/2008 10:25:49 AM  
CSO

## DSI CONSULT: Request for Clinical Inspections

**Date:** October 1, 2008

**To:** Constance Lewin, M.D., M.P.H, Branch Chief, GCP1  
Tejashri Purohit-Sheth, M.D., Branch Chief (Acting), GCP2  
Division of Scientific Investigations, HFD-45  
Office of Compliance/CDER

**From:** Mary Vienna, Regulatory Project Manager, HFD-560

**Subject:** Request for Clinical Site Inspections  
Prevacid 24HR (Lansoprazole 15mg) capsule

### **I. General Information**

Application#: NDA 22-327

Applicant/ Applicant contact information: Donna Coughlin  
Associate Director, Regulatory Affairs  
Novartis Consumer Health, Inc.  
200 Kimball Drive  
Parsippany, NJ 07054  
973-503-7915  
Donna.coughlin@novartis.com

Drug Proprietary Name: Prevacid 24HR

NME or Original BLA: No

Review Priority: Standard

Study Population includes < 17 years of age: No

Is this for Pediatric Exclusivity: No

Proposed New Indication(s): Treatment of frequent heartburn (occurs 2 or more days per week)

PDUFA: May 16, 2009

Action Goal Date: April 24, 2009

Inspection Summary Goal Date: March 2, 2009

**II. Protocol/Site Identification**

*Include the Protocol Title or Protocol Number for all protocols to be audited. Complete the following table.*

<b>Site # (Name,Address, Phone number, email, fax#)</b>	<b>Protocol ID</b>	<b>Number of Subjects</b>	<b>Indication</b>
Health Awareness Inc. 210 Jupiter Lakes Blvd., Suite 4102 Jupiter, FL 33458	301	40	Large study pivotal for approval
University Clinical Research 1150 N. University Drive Pembroke Pines, FL 33024	302	37	Large study pivotal for approval
University Clinical Research 1150 N. University Drive Pembroke Pines, FL 33024	305	40	Large study pivotal for approval

**III. Site Selection/Rationale**

**Domestic Inspections:**

Reasons for inspections (please check all that apply):

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

Should you require any additional information, please contact Mary Vienna at 301-796-4150 or Lolita Lopez at 301-796-0945.

Concurrence:

Daiva Shetty, Medical Team Leader  
Lolita Lopez, Medical Reviewer

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/s/

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Mary R Vienna  
10/1/2008 08:37:37 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

**FILING COMMUNICATION**

NDA 22-327

Novartis Consumer Health, Inc.  
Attention: Kim Stranick, Ph.D.  
Vice President & Head, Global Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Dr. Stranick:

Please refer to your new drug application (NDA) dated July 15, 2008, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act, for Prevacid 24 HR (15mg lansoprazole) capsules.

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 May 16, 2009.

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

1. The application did not contain a dissolution profile comparison with f2 analysis for the proposed OTC capsules versus the capsules used in the clinical study, and for the proposed OTC capsules versus the approved prescription capsules.
2. The application did not clearly state the to-be-marketed packaging configurations sought for approval.
3. The application did not provide the street address, contact information and CFN/FEI number for each facility involved in the manufacturing and testing of the drug substance and the delayed release granules.

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.

We request that you submit the following information:

1. Dissolution profile comparisons with f2 analysis for the proposed OTC capsules versus the capsules used in the clinical study, and for the proposed OTC capsules versus the

approved prescription capsules. We recommend that you use the dissolution method, NCH 1577-F-5 Tier 1, described in the NDA Module 3.2.P.5.2. Tabulated data for each capsule in both acidic and buffer stages should be submitted, in addition to lot number, manufacturing information (date, site, batch size, etc.), graphic presentations of dissolution profiles and f2 analysis results. We request that you inform us immediately when a significant difference in dissolution profiles between study arms is noted.

2. A clear statement of the to-be-marketed packaging configurations sought for approval.
3. The street address, contact information and CFN/FEI number for each facility involved in the manufacturing and testing of the drug substance and the delayed release granules.

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.

We also remind you of the need to submit the World Health Organization (WHO) post-marketing safety data with your 4-month safety update, as agreed to at the Pre-NDA meeting of March 17, 2008.

#### **REQUIRED PEDIATRIC ASSESSMENTS**

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

We acknowledge receipt of your request for a full waiver of pediatric studies for this application for pediatric patients below 18 years of age. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Mary Vienna, Regulatory Project Manager, at (301) 796-4150.

Sincerely,

*{See appended electronic signature page}*

Joel Schiffenbauer, M.D.  
Deputy Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

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/s/

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Joel Schiffenbauer  
9/19/2008 07:24:09 AM

**REQUEST FOR CONSULTATION**

TO (Division/Office):

**CONSUMER USE CONSULTS**

FROM: Mary Vienna, RPM, ONP/DNCE x64150

DATE  
02-Sept-08

IND NO.

NDA NO.  
22-327

TYPE OF DOCUMENT  
new NDA

DATE OF DOCUMENT  
16-Jul-08

NAME OF DRUG  
Prevacid 24HR

PRIORITY CONSIDERATION  
Standard

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE  
02-Dec-08

NAME OF FIRM: Novartis Consumer Health, Inc.

**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 (SPECIFY BELOW): <b>Trade name review</b> |
| <input type="checkbox"/> MEETING PLANNED BY            |  |   |

**II. BIOMETRICS**

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- TYPE A OR B NDA REVIEW  
 END OF PHASE II MEETING  
 CONTROLLED STUDIES  
 PROTOCOL REVIEW  
 OTHER (SPECIFY BELOW):

- CHEMISTRY REVIEW  
 PHARMACOLOGY  
 BIOPHARMACEUTICS  
 OTHER (SPECIFY BELOW):

**III. BIOPHARMACEUTICS**

- DISSOLUTION  
 BIOAVAILABILITY STUDIES  
 PHASE IV STUDIES

- DEFICIENCY LETTER RESPONSE  
 PROTOCOL-BIOPHARMACEUTICS  
 IN-VIVO WAIVER REQUEST

**IV. DRUG EXPERIENCE**

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL  
 DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES  
 CASE REPORTS OF SPECIFIC REACTIONS (List below)  
 COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP

- REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY  
 SUMMARY OF ADVERSE EXPERIENCE  
 POISON RISK ANALYSIS

**V. SCIENTIFIC INVESTIGATIONS**

CLINICAL

PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Please review the proposed trade name in this NDA.

The DMEPA reviewer, when assigned, will be added to all team and labeling meetings. Please attend as warranted.

**PDUFA DATE: 16-May-09**

**ATTACHMENTS:** Container and Carton Labels, tradename study

**CC:** Archival IND/NDA 22-237

HFD-560/Division File

HFD-560/RPM

60/Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER

Mary Vienna, x64150

METHOD OF DELIVERY (Check one)

DFS ONLY (labels sent to DMEPA via email)  MAIL  HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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Mary R Vienna  
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## NDA 74-Day Fileability Meeting Checklist

NDA#: 22-327

Product Name: Prevacid® 24-HR (lansoprazole 15 mg OTC)

Sponsor: Novartis Consumer Healthcare (NCH)

Reviewer: Lolita A. Lopez, M.D.

Submission Date: July 16, 2008

PDUFA Due Date: May 16, 2008

Filing Meeting Date: August 26, 2008

Item	Yes	No
1. Is the clinical section of the NDA organized in a manner to allow substantive review to begin?	x	
2. Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?	x	
3. Is the clinical section of the NDA legible so that substantive review can begin?	x	
4. If needed, has the sponsor made an appropriate attempt to determine the most appropriate dosage and schedule for this product through appropriately designed dose-ranging studies?	N/A	
5. Do there appear to be the requisite number of adequately and well-controlled studies in the application?	x	
6. Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling?	x	
7. Are all data sets for pivotal efficacy studies complete for all indications requested?	x	
8. Do all pivotal studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	x	
9. Has the applicant submitted line listings in a format to allow reasonable review of the patient data and in the format agreed to previously by the Division?	x	
10. Has the application submitted a rationale for the applicability of foreign data (disease specific, microbiologic specific) in the submission to the U.S. population?	N/A	
11. Has the applicant submitted all additional required case record forms, in addition to deaths and drop-outs, previously requested by the Division?	x	
12. Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division?		x
13. Has the applicant presented the safety assessment based on all current world-wide knowledge regarding this product?	x	
14. Has the applicant submitted adequate and well-controlled actual usage trial(s) within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	N/A	

15. Has the applicant submitted adequate and well-controlled labeling comprehension trial(s) within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	N/A	
16. Has the applicant submitted draft labeling consistent with 201.5 and 201.56, current divisional policies, and the design of the development package?	x	
17. Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?	N/A	
18. Has PREA been addressed?	x	
19. From a clinical perspective, is this NDA file-able? In no, please explain below.	x	

**Reviewer Comments:**

- This application is for the proposed over-the-counter (OTC) marketing of lansoprazole (Prevacid®) delayed release capsules 15 mg for the treatment of frequent heartburn (occurring 2 or more days a week).
- The sponsor of this application, Novartis Consumer Healthcare (NCH), states that it had entered an agreement with TAP Pharmaceuticals, Inc. (TAP), the holder of NDA 20-406 and IND 30,159 (Prevacid®). TAP is granting a full right of reference to NCH to the NDA and IND data in support of all applications related to OTC use. NCH also states that TAP has authorized the Agency, in correspondence dated March 6, 2008, to cross-reference these data in support of NCH's programs.
- The postmarketing safety data submitted is not complete because it does not include safety data obtained from the World Health Organization (WHO) database; however, at the Pre-NDA meeting held on March 17, 2008, the Agency agreed to accept the safety data obtained from the WHO database to be included in their 4-month safety update.

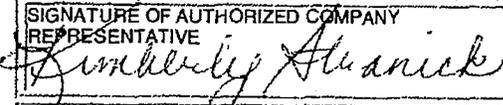
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/s/

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Lolita Lopez  
8/26/2008 01:07:35 PM  
MEDICAL OFFICER

Daiva Shetty  
8/26/2008 01:09:13 PM  
MEDICAL OFFICER

Form Approved: OMB No. 0910 - 0297 Expiration Date: January 31, 2010 See instructions for OMB Statement, below.					
DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		<b>PRESCRIPTION DRUG USER FEE                  COVERSHEET</b>			
A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <a href="http://www.fda.gov/cder/pdufa/default.htm">http://www.fda.gov/cder/pdufa/default.htm</a>					
1. APPLICANT'S NAME AND ADDRESS  NOVARTIS CONSUMER HEALTH INC Donna Coughlin 200 KIMBALL DR PARSIPPANY NJ 070540622 US		4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER  22-327			
2. TELEPHONE NUMBER 973-5037915		5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO  IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:  <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION  <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:			
3. PRODUCT NAME PREVACID24HR ( Lansoprazole )		6. USER FEE I.D. NUMBER PD3008478			
7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION. <input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory) <input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE <input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act <input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY					
8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO					
OMB Statement: Public reporting burden for this collection of information is estimated to average 30 minutes 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:  <table border="0"> <tr> <td>                             Department of Health and Human Services                              Food and Drug Administration                              CBER, HFM-99                              1401 Rockville Pike                              Rockville, MD 20852-1448                         </td> <td>                             Food and Drug Administration                              CDER, HFD-94                              12420 Parklawn Drive, Room 3046                              Rockville, MD 20852                         </td> <td>                             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.                         </td> </tr> </table>			Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 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.
Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 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.			
SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE 		TITLE Vice President			
		DATE 30 June 2008			
9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION \$1,178,000.00					
Form FDA 3397 (03/07)					

Close Print Cover sheet



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

IND 74,256

Novartis Consumer Health, Inc.  
Attention: Donna Coughlin  
Associate Director, Regulatory Affairs  
200 Kimball Drive  
Parsippany, NJ 07054

Dear Ms. Coughlin:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for lansoprazole delayed-release capsules.

We also refer to the meeting between representatives of your firm and the FDA on March 17, 2008. The purpose of the meeting was to discuss your planned NDA submission.

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

If you have any questions, contact Geri Smith, Regulatory Project Manager, at [geri.smith@fda.hhs.gov](mailto:geri.smith@fda.hhs.gov) or (301) 796-2204.

Sincerely,

*{See appended electronic signature page}*

Joel Schiffenbauer, M.D.  
Deputy Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Products  
Center for Drug Evaluation and Research

Enclosure - Meeting Minutes

**MEMORANDUM OF MEETING MINUTES**

**MEETING DATE:** March 17, 2008

**TIME:** 4:00 PM – 5:00 PM

**LOCATION:** White Oak Building 22, Conference Room 1311  
10903 New Hampshire Avenue, Silver Spring, MD 20993

**APPLICATION:** IND 74,256

**DRUG NAME:** lansoprazole delayed-release capsules

**SPONSOR:** Novartis Consumer Health, Inc.

**TYPE OF MEETING:** Pre-NDA (Type B)

**MEETING CHAIR:** Joel Schiffenbauer, M.D., Deputy Director  
Division of Nonprescription Clinical Evaluation (“DNCE”)  
Office of Nonprescription Products

**MEETING RECORDER:** Geri Smith, Regulatory Project Manager

**FDA ATTENDEES:**

*Division of Nonprescription Clinical Evaluation*

Andrea Leonard-Segal, M.D., Director  
Joel Schiffenbauer, M.D., Deputy Director  
Daiva Shetty, M.D., Medical Team Leader  
Lolita Lopez, M.D., Medical Officer  
Wafa Harrouk, Ph.D., Pharmacologist/Toxicologist  
Capt. Laura Shay, R.N., M.S., C-ANP, Social Science Analyst  
Geri Smith, Regulatory Project Manager

*Division of Nonprescription Regulation Development*

Mary Robinson, M.S., Interdisciplinary Scientist

*Division of Gastroenterology Products*

Donna Griebel, M.D., Director  
Joyce Korvick, M.D., Deputy Director  
Ruyi He, M.D., Clinical Team Leader  
Keith St. Amand, M.D., Medical Officer  
Tamara Johnson, M.D., Medical Officer  
Anil Nayyar, M.D., Staff Fellow

Office of New Drug Quality Assessment

Shulin Ding, Ph.D., Chemist, Pharmaceutical Assessment Lead  
Tarun Mehta, Ph.D., Chemistry Reviewer

Office of Clinical Pharmacology and Biopharmaceutics

Sue Chih Lee, Ph.D., Clinical Pharmacology Team Leader  
Jane Bai, Ph.D., Clinical Pharmacology Reviewer

Division of Biometrics III

Mike Welch, Ph.D., Deputy Director

**NOVARTIS ATTENDEES:**

Carola Friedman, M.D., FACC, Vice President, a.i. Global Head, R&D  
Emilia Lonardo, Ph.D., Global Head, Therapeutic Categories, Regulatory Affairs  
Andrew Snoddy, Ph.D., Head, GI & Lifestyle Modification, Clinical Research  
Donna M. Coughlin, Associate Director, Regulatory Affairs  
Stephen Garreffa, Associate Director, Biostatistics  
Ronke Dosunmu, M.D., Deputy Global Head, Drug Safety & Pharmacovigilance  
Rosanne Rotondo, RN, Director, Drug Safety & Pharmacovigilance  
Evren Atillasoy, M.D., Global Head, New Therapeutic Opportunities  
Ravi Chivukula, Associate Director, Regulatory Affairs – CMC  
Denise Goldberg, Associate Director, Global Program Management  
Steve Jurgens, Principal Scientist, Pharmaceutical Development  
Walter Lehneis, Director, Brand Marketing

**1.0 BACKGROUND**

Novartis Consumer Health, Inc. ("Novartis") submitted a meeting request on December 19, 2007 for a pre-NDA meeting to discuss their plans to submit a 505(b)(1) NDA for over-the-counter lansoprazole delayed-release capsules for the treatment of frequent heartburn (defined by Novartis as occurring two or more days per week), T

18 years of age and older.

↓ in adults

**b(4)**

Novartis obtained full right-of-reference to IND 30,159 and NDA 20-406 for Prevacid® from the holder of those applications, TAP Pharmaceuticals, Inc., and will rely on information contained in those applications to support their NDA. Novartis also conducted three clinical studies to evaluate the efficacy and safety of lansoprazole, a label comprehension study, and stability studies to support their NDA.

Novartis plans to submit the NDA during the second quarter of 2008.

## 2.0 DISCUSSION

Preliminary responses to the questions enclosed in the February 14, 2008 meeting package were sent to Novartis via email on March 14, 2008.

On March 17, 2008, Novartis confirmed their acceptance of the FDA responses to Questions 1, 2, 3, 4, 6, 7, 8, 9, 10 and 12, and requested that the meeting focus on Questions 13, 14, 16, 5, 15 and 11, in that order. Following introductions, the agenda focused on further discussion of the preliminary responses from the FDA. The questions from Novartis appear below followed by the preliminary FDA responses in italics. A summary of the discussion that occurred during the meeting follows each question. For questions where no additional discussion is indicated, neither Novartis nor FDA raised any additional issues pertaining to these questions at the meeting.

### 2.1 Question 1

The original NCH IND 74,256 submission included letters from TAP Pharmaceuticals, Inc. granting NCH full right of reference to all information included in IND 30,159 and NDA 20-406. Subsequently, these letters were deemed insufficient to support a 505(b)(1) filing for the switch NDA. NCH obtained updated right of reference letters from TAP Pharmaceuticals, Inc. which were submitted to the IND in Serial No. 0025 on November 14, 2007. Does the Agency agree that these letters are adequate to support a 505(b)(1) filing for the switch NDA and can the Agency confirm that, with these letters of reference as provided, the NDA will be considered for filing as a 505(b)(1) application?

#### Novartis Position:

This topic was raised at the April 6, 2006 Pre-IND meeting and required additional clarification after that meeting. The right of reference letters which were included with the Pre-IND meeting request were subsequently considered by the Agency to be not adequate to grant full right of reference. Consequently, in the Agency's preliminary comments on the Briefing Package for the Pre-IND meeting, the Agency indicated the switch NDA would be a 505(b)(2) filing. New authorization letters were obtained from TAP and were included in the original IND submission. Subsequently, the Agency reviewed these letters and determined they were also insufficient to support the desired filing. Consequently, new letters were obtained from TAP Pharmaceuticals, Inc. and submitted to the IND in Serial No. 0025. It is our understanding that the November 5, 2007 letters from TAP are adequate, thereby meeting the requirements for filing under 21 U.S.C. 505(b)(1).

#### FDA Preliminary Response

*The letters from TAP Pharmaceutical Products, Inc. that you submitted on November 14, 2007 provide NCH with full right-of-reference to IND 30,159 and NDA 20-406 for Prevacid (lansoprazole) delayed-release capsules only "to support Novartis IND 74,256..." Similar letters from TAP Pharmaceutical Products, Inc. providing NCH with full right-of-reference to IND 30,159 and NDA 20-406 "to support Novartis' IND and NDA applications..." would enable you to reference IND 30,159 and NDA 20-406 in the 505(b)(1) application for your product. We*

*acknowledge your March 11, 2008 submission providing updated letters in response to this concern. The letters appear to adequately provide NCH with full right-of-reference to IND 30,159 and NDA 20-406 for Prevacid (lansoprazole) delayed-release capsules to support Novartis' IND 74,256 and upcoming NDA for lansoprazole. We will determine whether your NDA is adequate for filing during our preliminary review of the NDA prior to the filing date.*

## 2.2 Question 2

NCH plans to submit the NDA in electronic Common Technical Document (CTD) format. We will be cross-referencing portions of Module 3, all of Module 4, and portions of Module 5 of TAP NDA 20-406, in accordance with the right of reference letters from TAP authorizing NCH to cross reference the approved TAP NDA 20-406 and IND 30,159 for lansoprazole delayed-release capsules. Copies of the letters are on file in NCH IND 74,256 and will be included in the switch NDA. Is this approach acceptable to the Agency?

Novartis Position:

TAP, the sponsor of approved NDA 20-406 and IND 30,159 for lansoprazole delayed-release capsules, has submitted right of reference letters to NDA 20-406 and IND 30,159, authorizing NCH to cross-reference NDA 20-406, including all supplements, annual reports and periodic safety reports and IND 30,159. Copies of these letters were submitted to NCH IND 74,256 on November 14, 2007 in Serial No. 0025. Copies will be included in the switch NDA.

### FDA Preliminary Response

*See our response to Question 1. Additionally, please clarify which portions of Module 5 will be cross-referenced and which will be presented in full.*

## 2.3 Question 3

NCH conducted three adequate and well-controlled clinical studies which will be included in the upcoming NDA to support the use of lansoprazole delayed-release capsules 15 mg for the indication "treats frequent heartburn (occurs 2 or more days a week),"

We believe these studies are essential for approval of the OTC marketing of the 15 mg dose of lansoprazole for the treatment of frequent heartburn, thereby supporting 3 years marketing exclusivity. Recognizing that the Agency does not confer exclusivity prior to approval of the application, NCH plans to request marketing exclusivity in our upcoming NDA submission. Does the Agency agree with this approach?

Novartis Position:

NCH believes the three clinical trials meet the statutory definition of "new clinical trials essential for approval" of lansoprazole 15 mg and support 3 years marketing exclusivity. We will request

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exclusivity in the NDA. We recognize the Agency does not confer exclusivity prior to approval of the application.

FDA Preliminary Response

*We agree that you can request marketing exclusivity in your NDA submission. FDA does not award or grant exclusivity prior to approval of a drug product.*

**2.4 Question 4**

The NDA will include the Drug Facts labeling in Word documents as well as Portable Data Files (PDF) illustrating the layout of the various pieces of labeling. Does the Agency concur with this approach?

Novartis Position:

Based on the most recent information available, NCH believes Agency guidance on the file tagging to be used for Drug Facts labeling will not be available prior to submission of this NDA. Consequently, NCH will provide the Drug Facts labeling electronically in both Word documents and PDF files, which will illustrate the layout of the labeling to the Agency Reviewers.

FDA Preliminary Response

*We agree that electronic submission of draft labeling (e.g., package insert, immediate container labels, and carton labels) with Drug Facts in PDF format and, where applicable, Word format is acceptable. Annotated labeling showing font size and type style should also be included. Refer to the Federal Register of March 17, 1999, OTC Labeling Requirements Final Rule at 51 FR 13254 for the format requirements.*

**2.5 Question 5**

NCH submitted a Special Protocol Assessment request containing the draft protocol and related study instruments for a Label Comprehension Study to IND 74,256 on November 20, 2007 (Serial No. 0026). On December 6, 2007, NCH was informed that the Agency was denying this request.

On December 7, 2007 (Serial No. 0027), NCH submitted a request for a Type A meeting to discuss the Label Comprehension Study protocol and study elements, as the study was critical to completion of the clinical development program for the switch of lansoprazole 15 mg for the treatment of frequent heartburn. In a letter dated December 21, 2007, the Agency denied this request, but committed to providing written feedback on the protocol and study elements.

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NCH then amended the protocol to include a revised copy of the label to correct the font of the bulleting (January 9, 2008, Amendment to Serial No. 0027). The Agency provided written feedback on the Label Comprehension Study in a letter dated February 12, 2008.

NCH, as part of our commitment to the development of this product, initiated the Label Comprehension Study in January 2008. Enrollment has been completed and analyses are in progress. In the February letter, the Agency stated that a Label Comprehension Study may not be required. NCH believes the data from this trial may provide useful adjunctive information about consumer comprehension of the elements of the proposed label NCH deemed significantly different compared to the current OTC PPI label [Proposed OTC lansoprazole Drug Facts label; Prilosec OTC<sup>®</sup> Approved Labeling, March 2007]. We plan to include the results of the study in the NDA for the Agency's consideration. Does the Agency concur?

Novartis Position:

As part of our commitment to the development program for lansoprazole 15 mg, and in accordance with formal feedback received at the April 6, 2006 Pre-IND meeting and March 15, 2007 Type C Guidance Meeting on the lansoprazole 30 mg clinical program, NCH designed a Label Comprehension Study focused on testing communication objectives limited to new elements of the proposed Drug Facts label.

The Agency's minutes of the March 15, 2007 Type C Guidance meeting raised the possibility that a Label Comprehension Study may not be required. NCH considered this option prior to submission of the protocol, but chose to move forward with the study to better understand consumer comprehension of label directions that, irrespective of the time of HB occurrence, OTC lansoprazole 15 mg should be taken in the morning. Further, our intention to market a single product for the treatment of frequent heartburn, ¶ is consistent with this option. We plan to include the study results in the NDA.

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FDA Preliminary Response

*On February 12, 2008, we sent you a letter identifying a number of deficiencies in your proposed Label Comprehension study protocol submitted on December 7, 2007; therefore, data derived from that study may be of limited value. We cannot comment on the study results and its impact on labeling until we review your entire NDA submission. It is important that label comprehension data determine that consumers understand elements in your label that would be new to labeling for the OTC marketplace. ¶*

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*We can not provide final comments and recommendations on your draft label until the results of your efficacy studies have been reviewed, as the content of the label may change based on the outcome of the studies. ¶*

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### Discussion

Novartis requested clarification regarding the need for a label comprehension study since the FDA's February 12, 2008 letter stated that a label comprehension study might not be necessary. The FDA explained that the need for a label comprehension study, and the design of that study, will depend on the indication and labeling of the proposed product. If the proposed label differs from the labels of currently approved over-the-counter (OTC) frequent heartburn treatments [

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] then studying consumer understanding of the additional language will be necessary. If the proposed label is similar to the labels of currently approved OTC frequent heartburn treatments, then consumer studies will not be necessary.

The FDA encouraged Novartis to assess, prior to submitting the NDA, whether the label comprehension study already conducted will support the indication and labeling Novartis plans to seek in the NDA. The FDA cautioned Novartis that data from this label comprehension study may be of limited value, as Novartis chose to conduct the study prior to receiving the FDA's comments on the study design, which FDA found to contain a number of deficiencies.

Novartis inquired as to whether the FDA review goal date for the NDA would be impacted if, while reviewing the NDA, the FDA determines that a new label comprehension study is necessary, and Novartis initiates the study during the review cycle. FDA explained that it is Novartis' responsibility to ensure that all studies necessary to support the NDA are submitted as part of the initial submission of the NDA. An incomplete application at the time of initial submission of the NDA would result in the FDA's inability to approve the application.

Novartis inquired as to whether they could submit the results of a small-scale label comprehension study, assessing the differences between the label they submit with the NDA and the labels already approved for OTC frequent heartburn treatments, with the Safety Update that is submitted during Month 4 of the NDA review cycle. The FDA reiterated that all studies must be submitted with the initial submission of the NDA.

## **2.6 Question 6**

NCH will be requesting a waiver from the conduct of a safety and efficacy assessment of lansoprazole 15 mg for all age groups in the pediatric population (less than 18 years of age) according to the Pediatric Research Equity Act of 2003. Our is position to exclude use in the pediatric population is consistent with the Agency's position that treatment of the pediatric population is not appropriate as an OTC indication for a PPI as previously approved for the OTC PPI product currently marketed in the US. The pediatric indications for the short-term treatment of symptomatic GERD and the short-term treatment of erosive esophagitis will be maintained as prescription indications for PREVACID® and the proposed OTC lansoprazole labeling will recommend use in adults 18 years of age and older. Should the Agency identify a pediatric population for which lansoprazole delayed-release capsules would be appropriate treatment in

the OTC environment, NCH would consider requesting a Written Request for the conduct of a pediatric assessment to gain exclusivity under PREA. Does the Agency agree?

Novartis Position:

The pediatric indications approved for the 15 mg dose of PREVACID® (lansoprazole delayed-release capsules) will be maintained as prescription indications. The proposed OTC lansoprazole labeling will be indicated for adults 18 years of age and older, in accordance with the previously approved OTC PPI label. The proposed OTC indication for lansoprazole differs from the prescription indications

FDA Preliminary Response

*Your request for a waiver of the requirement for pediatric studies in patients less than 18 years of age appears reasonable. However, the Pediatric Research Equity Act of 2007 requires that all requests for waivers be reviewed by an internal pediatric committee before a decision is made whether or not to grant such a request.*

*Your waiver request must be included in the NDA submission and contain the scientific rationale on which it is based. See the Guidance for Industry: How to Comply with the Pediatric Research Equity Act at <http://www.fda.gov/cder/guidance/6215dft.pdf>. Your waiver request will be evaluated during our review of your NDA.*

*With regard to your inquiry about a Written Request, if you believe it is reasonable to conduct studies of your product in a certain pediatric population, please submit that information for our review.*

**2.7 Question 7**

NCH plans to incorporate by reference the CMC section of TAP NDA 20-406, including all supplements and annual reports, for the lansoprazole delayed-release granules. NCH will procure these granules from Takeda, the currently approved source for TAP commercial product under NDA 20-406. Does the Agency agree with this approach?

Novartis Position:

NCH will source the lansoprazole delayed-release granules from TAP's current supplier, Takeda. NCH will then encapsulate the granules into pink and teal gelatin capsules, apply a tamper-evident black-colored band at the seam of each capsule, and package the product. The CMC information to support the Drug Product will consist of the components and composition of the lansoprazole delayed-release capsules, the encapsulation and banding processes, packaging, analytical controls and stability, as performed within NCH. NCH has full right of reference to NDA 20-406, including all supplements and annual reports.

FDA Preliminary Response

*We agree.*

**2.8 Question 8**

NCH plans to incorporate by reference the Chemistry, Manufacturing and Controls (CMC) section of TAP NDA 20-406, including all supplements and annual reports, for the Drug Substance section of Module 3. Does the Agency agree with this approach?

Novartis Position:

NCH has full right of reference to NDA 20-406, including all supplements and annual reports. Manufacture of the OTC lansoprazole product begins with encapsulation of lansoprazole delayed-release granules. Therefore, NCH intends to reference NDA 20-406 for all CMC information related to lansoprazole drug substance.

FDA Preliminary Response

*We agree.*

**2.9 Question 9**

The NDA will include 9 month stability data on product encapsulated and banded at two sites, NCH Lincoln, Nebraska and packaged at two sites, NCH Lincoln, Nebraska. We propose to include as an additional encapsulation, banding, and analytical testing site. In support of this site, we propose to submit initial release data (Certificate of Analysis) for one batch which has been encapsulated and banded at — then amend the NDA with 3 and 6 month stability data from this lot approximately 3 and 6 months following the initial NDA submission. Does the Agency concur that the stability amendments made 3 and 6 months after the initial NDA submission do not affect the PDUFA review clock?

b(4)

Novartis Position:

In order to address long-term product supply requirements, NCH has identified an additional site for encapsulation and banding of the lansoprazole-delayed-release capsules. This site will also be utilized for analytical testing. The will be encapsulating and banding one batch of lansoprazole delayed-release capsules in the near future. Consequently, limited data will be available at the targeted NDA filing time. Therefore, the NDA will be amended to include 3 and 6 month data, which will be available approximately 3 and 6 months after the initial NDA filing. According to Agency Guidance documents on the timing of amendments to a pending NDA, we believe these amendments will not impact the PDUFA review clock. We would appreciate confirmation to this effect.

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In addition, Section 3.2.P.8 of the upcoming switch NDA will cross-reference TAP NDA 20-406 and its supplements in order to establish a link to the significant body of stability data available to support the requested \_\_\_\_\_ expiry date for the OTC lansoprazole product. A significant body of stability data exists in the approved TAP NDA 20-406. In addition, 9 months of stability data on encapsulated and banded capsules manufactured and packaged at NCH and \_\_\_\_\_ facilities will be included in the switch NDA. NCH plans to amend the NDA during the review period with 3 and 6 months stability data on product encapsulated and banded at \_\_\_\_\_

b(4)

FDA Preliminary Response

*We do not concur unless you can commit to the following:*

- (1) *The 6-month stability amendment will be submitted no later than 6 months after the NDA initial submission and the container/closure system to be used by the \_\_\_\_\_ is equivalent to that approved under NDA 20-406.*
- (2) \_\_\_\_\_ *\_\_\_\_\_ must be included in the initial submission of the NDA, and it must be ready for product-specific cGMP inspection at time of submission.*
- (3) *You will withdraw the \_\_\_\_\_ if the site is found during the review to be inadequate or unacceptable for approval for any reason (e.g., cGMP inspection, f<sub>2</sub> analysis, stability).*

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b(4)

b(4)

**2.10 Question 10**

The current approved shelf life in TAP NDA 20-406 is 36 months. NCH proposes that the shelf life of the OTC lansoprazole product \_\_\_\_\_, based on the significant body of stability data that exists in the TAP NDA 20-406 and the comprehensive stability data to be submitted in the NCH NDA and amendments made during the review period. Does the Agency concur?

b(4)

Novartis Position:

Section 3.2.P.8 of the upcoming switch NDA will cross-reference TAP NDA 20-406 and its supplements in order to establish a link to the significant body of stability data available to support the requested \_\_\_\_\_ expiry date for the OTC lansoprazole product. In addition, 9 months of stability data on encapsulated and banded capsules manufactured and packaged at Lincoln and \_\_\_\_\_ facilities will be included in the switch NDA. NCH plans to amend the NDA during the review period with 3 and 6 months stability data on product encapsulated and banded at \_\_\_\_\_ and the 12 month update from the Lincoln and \_\_\_\_\_ facilities.

b(4)

FDA Preliminary Response

*No, we do not concur. The actual expiry period granted is a review issue.*

**2.11 Question 11**

We further propose to amend our NDA to provide for [redacted] as a manufacturing site of lansoprazole delayed-release granules, utilizing the process described in TAP NDA 20-406, and similar equipment and manufacturing controls. The proposed NDA amendment would be submitted in month 7 of the NDA PDUFA Review period, assuming a standard, 10 month review. The amendment would contain 3 months stability data on 3 lots of drug product manufactured at [redacted] and the study report of a single dose crossover bioequivalence study in fasting healthy volunteers, comparing [redacted] product (test product) with the current approved PREVACID® 15 mg commercial product (reference product). Does the Agency concur with this proposal?

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**Novartis Position:**

Per Agency Guidance on the timing of amendments to pending NDAs, major amendments may be submitted up to month 7 for review by the Agency within the 10 month review period defined by PDUFA for an NDA. The NDA will include the [redacted] as a site for encapsulation, banding and analytical testing operations. Addition of granulation operations (manufacture of delayed-release granules) to the activities that will be included in the initial NDA already submitted is considered to be a minor amendment. The granulation process we proposed to transfer from Takeda to [redacted] would be completed with full cooperation and guidance of Takeda. Reference is also made to NDA 20-406, Supplement S-044 submitted on July 13, 2001 and approved December 15, 2001, wherein TAP supplemented the NDA to add Takeda Ireland as a site of manufacture of lansoprazole delayed-release granules. In support of the addition of Takeda Ireland as manufacturer of lansoprazole delayed-release granules, the supplement contained stability data and the study report for a single-dose crossover bioequivalence study in fasting subjects. Consequently, NCH believes this current proposal is sufficient to support the new granulation site.

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FDA Preliminary Response

*We do not concur. The ability to amend an application with a major amendment is not intended to allow the submission of additional, unsolicited material. The application must be complete at the time of submission; therefore, the bioequivalence study data must be submitted at the time of NDA submission. Additionally, ICH Q1A recommends a minimum of 12 months of long term stability data to be provided at the time of NDA submission.*

*We advise you that if you include the [redacted] in the proposed NDA as a site for manufacturing, encapsulation, banding, and analytical testing, this site must be included in the initial submission of the NDA, and it must be ready for product-specific cGMP inspection at the time of submission.*

b(4)

Discussion

Novartis inquired as to whether they could submit the bioequivalence study data during the review cycle. The FDA reiterated that all study data, including the bioequivalence study data, must be included in the initial submission of the NDA.

**2.12 Question 12**

NCH plans to incorporate by cross-reference the Pharmacology and Toxicology information included in NCH IND 74,256, as well as TAP NDA 20-406 and all supplements and annual reports. Does the Agency concur with this approach?

Novartis Position:

NCH has full right of reference to NDA 20-406, including all supplements and annual reports. CTD sections 2.4 and 2.6 will contain summaries extracted from Section 5 of TAP NDA 20-406, approved May 10, 1995 and corresponding supplements. Reports of the key safety studies cited in the non-clinical summaries will be included in Module 4. Reference will be made to NDA 20-406, with links to the corresponding documents in Module 4. Recent publications, identified to be of relevance to the Nonclinical evaluation of lansoprazole, from public databases, will also be included in Module 4 of the NDA. In the event that the Agency would like to review additional references, they will be made available during the Review period.

FDA Preliminary Response

*Yes, we agree with your approach.*

**2.13 Question 13**

NCH plans to submit three adequate and well-controlled clinical studies in the upcoming NDA to support the use of lansoprazole delayed-release capsules 15 mg for the indication "treats frequent heartburn (occurs 2 or more days a week), r"

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Two clinical trials of identical design, Studies PRSW-GN-301 and PRSW-GN-302, "A phase III, multi-center, randomized, double-blind, placebo-controlled, parallel group trial of fourteen day treatment with lansoprazole 15 mg once a day in frequent heartburn," were included in the original IND (Serial No. 0000) submitted on May 6, 2006. Both studies assessed the 15 mg dose of lansoprazole in the described OTC population of frequent heartburn sufferers.

The primary objective of these studies was to demonstrate that repeated daily doses of 15 mg of lansoprazole once a day are effective in increasing the proportion of days with no heartburn

during 14 days (24-hour days) of treatment as compared to placebo in subjects with frequent heartburn.

The secondary objectives were:

- A comparison of treatment groups with regard to the proportion of nighttimes with no heartburn during 14 days of treatment,
- A comparison of treatment groups with regard to the proportion of subjects with no heartburn during Days 1-2, which includes a comparison of treatment groups with regard to the proportion of subjects with no heartburn during Day 1,
- The evaluation of lansoprazole safety.

Study PRSW-GN-305, "A phase III, multi-center, randomized, placebo-controlled, parallel group trial of fourteen day treatment with lansoprazole 15 mg or 30 mg once a day in frequent nighttime heartburn," was filed to the IND in Serial No. 0010 on December 15, 2006.

The primary objective of this study was to demonstrate that repeated daily doses of 15 mg or 30 mg of lansoprazole once a day are effective in increasing the proportion of days (24 hour periods) with no nighttime heartburn as compared to placebo in subjects with frequent heartburn.

The secondary objectives were:

- A comparison of lansoprazole 15 mg and 30 mg to placebo with regard to the proportion of 24-hour days with no heartburn during 14 days of treatment,
- A comparison of lansoprazole 15 mg and 30 mg to placebo with regard to the proportion of subjects with no heartburn during day 1 (the 24 hours following the first dose),
- The evaluation of lansoprazole 15 mg and 30 mg safety.

For the purposes of this NDA, the data for the 15 mg dose relative to placebo will be assessed. The data related to the 30 mg dose are for the initial assessment of the safety and efficacy of this dose in the defined OTC population and, as such, will not be used in support of the NDA submission for the 15 mg dose.

NCH believes these studies, which provide efficacy and safety data to support the use of lansoprazole 15 mg for the treatment of frequent heartburn, are pivotal and adequate for filing and subsequent approval of the NDA. Does the Agency concur?

b(4)

Novartis Position:

NCH believes these studies, which provide efficacy and safety data to support the use of lansoprazole 15 mg for the treatment of frequent heartburn, are pivotal and adequate for filing and subsequent approval of the NDA. The data demonstrate statistically significant and clinically meaningful differences between the active and placebo treatment groups for the primary and secondary endpoints. In addition, the subject assessment of the active treatment demonstrated significant advantage over the placebo treatment. NCH will

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FDA Preliminary Response

*The adequacy of the three studies you conducted to support the filing of an NDA for the OTC use of lansoprazole 15 mg for the treatment of frequent heartburn will be determined during our preliminary review of the NDA prior to the filing date. The adequacy of the efficacy and safety data provided to support approval of the NDA, <sup>1</sup>*

**b(4)**

*will be a review issue. We also refer you to our response to Question 5.*

Discussion

<sup>1</sup>

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**2.14 Question 14**

NCH believes the patient populations in the three clinical studies to be included in the NDA represent a spectrum of symptoms in what is essentially a single OTC population of frequent heartburn sufferers. Does the Agency agree?

## Novartis Position:

In the last decade, additional research has been conducted to better understand the prevalence and clinical significance of nighttime HB. It is important to point out that the majority of sufferers of HB have events occurring both at night and during the day, as seen in multiple Rx and OTC trials in the HB or GERD populations [McQuaid, 2005]. A telephone survey conducted in 1000 heartburn sufferers on behalf of the American Gastroenterologic Association (AGA) demonstrated that 78% of HB sufferers had nighttime HB: Sixty-five percent (65%) had events during both day and night on a 24 hour basis, 13% of subjects had events only during bedtime, and 20% of HB sufferers had daytime events alone [Shaker, 2003]. This survey confirmed other research findings that nighttime HB is associated with diminished quality of life. Two thirds of these participants had poor sleep, which negatively impacted many of these individual's ability to function the following day.

NCH conducted a preliminary review of baseline characteristics of frequent HB sufferers in 2 placebo controlled trials that compared lansoprazole 15mg versus placebo in subjects with GERD. Findings from TAP studies M95-300 ("A Study to Evaluate the Effects of Lansoprazole 15 mg and 30 mg QD versus Placebo on Non-Erosive Gastroesophageal Reflux Disease," N=194) and M96-519 ("A Study to Evaluate the Effects of Lansoprazole 15 mg and 30 mg QD versus Ranitidine 150 mg BID or Placebo on Non-Erosive Gastroesophageal Reflux Disease," N=412) show that 49% of the subjects had an equal incidence of daytime and nighttime events of heartburn. Thirteen percent of the subjects had more nighttime incidents than daytime, while 38% of the subjects had more daytime incidents than nighttime. Only 3% of the subjects did not report nighttime HB incidents during the placebo run-in period. We also divided the population studied into those who suffered nighttime heartburn more often than not ( $\geq 4$  nights during the one week placebo run-in period) and its complement ( $< 4$  nights). The demographic characteristics and the disease states were similar for the two subsets. For example, the proportion of subjects with duodenal ulcer was 10% for the subset with  $\geq 4$  days with nighttime HB events and 11% for the subset with  $< 4$  days with nighttime HB events. The rates for gastric ulcer were 7% and 10% respectively.

An examination of the study populations from studies PRSW-GN-301 and PRSW-GN-302 showed that approximately 74% of the enrolled subjects reported some nighttime HB. This observation is consistent with the AGA survey of HB sufferers. Moreover, the subjects who presented with only nighttime HB during the Run-In phase of the frequent HB studies (PRSW-GN-301 and PRSW-GN-302), were only about 4.5% of the population.

It is the position of NCH that subjects who present with heartburn (HB) symptoms during the nighttime (from the time a subject lies down to sleep until they arise) are a subset of frequent HB sufferers. As part of our development program for the switch of lansoprazole 15 mg from prescription to OTC status, NCH conducted three clinical trials. The first two studies were identical in design and assessed the efficacy and safety of lansoprazole 15 mg for the treatment of frequent HB over 14 days as a primary objective. As a secondary objective, these two studies evaluated the efficacy and safety of lansoprazole 15 mg for the treatment of frequent nighttime HB over 14 days. Based upon discussions with the Agency, NCH conducted a third study to assess efficacy and safety of lansoprazole 15 mg for the treatment of frequent nighttime HB over

14 days as a primary objective, with evaluation of efficacy and safety of lansoprazole 15 mg for the treatment of frequent HB over 14 days as a secondary objective. NCH has assessed the characteristics of the population enrolled in this third study [PRSW-GN-305]. The inclusion criteria for this study stipulated that subjects had to present with a minimum of two nightrightimes with HB during the Run-in period prior to treatment. NCH has compared the characteristics of the enrolled population from Study PRSW-GN-305 to the total population, as well as a subset of those enrolled in the first two studies who, during the Run-in period, reported at least two nightrightimes with HB. Comparisons included: the Demographics of; age, gender, and race. Frequency of HB during the Run-in period and Severity of HB during the Run-in period were evaluated. Relevant Medical History including gastroesophageal reflux disease (GERD) and ulcer and Concomitant medications were compared. Therefore, the population which was enrolled into Study PRSW-GN-305, "the nightrightime study," is the same as those who entered into two separate studies where subjects were recruited to assess the treatment of OTC frequent heartburn.

FDA Preliminary Response

*Based on the demographic and background characteristics presented in your briefing book, we agree that the patient populations in the three clinical studies are similar, and that they are likely representative of the larger OTC population with frequent heartburn.*

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Discussion

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### 2.15 Question 15

In the Rx to OTC switch application for lansoprazole 15 mg, NCH plans to summarize the safety data generated from the lansoprazole 15 mg clinical program and review the TAP post-marketing safety database which contains FDA reportable AE reports since launch of the product. In addition NCH will review and assess data from the FDA SRS/AERs database, the National Poisoning and Exposure Database (formerly called the TESS database), and the Drug Abuse Warning Network (DAWN). We will also provide information on whether lansoprazole has been withdrawn from any foreign markets due to safety or regulatory reasons. Please note that, at present, lansoprazole is only sold as a prescription product worldwide, although it has been approved, [ ] for OTC sale in Sweden. Does the Agency agree with this approach?

b(4)

#### Novartis Position:

NCH met with the Agency on March 15, 2007 to discuss a clinical program for lansoprazole — for the treatment of frequent heartburn. In support of that meeting, NCH submitted a briefing document that outlined the data sources to be used for the safety evaluation of the — for the proposed use. In addition to the sources outlined, the Agency requested data from the Drug Abuse Warning Network (DAWN), a list of countries in which the drug is marketed OTC, English translations of OTC labeling, and a list of countries in which the drug has been withdrawn for safety or regulatory reasons. NCH is utilizing the same data sources, including DAWN for the switch filing. The product is not sold over-the-counter outside the United States and it has not been withdrawn from any country for safety or regulatory reasons. [IND 74,256. FDA Official Minutes, Type C Guidance Meeting]

b(4)

#### FDA Preliminary Response

*Your approach regarding the submission of safety data is acceptable. In addition, please provide:*

1. *A review of safety data from World Health Organization (WHO) databases.*
2. *Information regarding potential interaction(s) between lansoprazole and other drugs. Include information from post-marketing adverse event reporting and the literature.*
3. *A summary of all serious adverse events and case reports of deaths from post-marketing data for all lansoprazole products.*

#### Discussion

Novartis stated that when they originally proposed their clinical program at a March 15, 2007 meeting with FDA, they proposed providing data from specific databases that did not include the WHO database. Novartis stated that the FDA did not request data from the WHO database at that time. Novartis asserted that, even if they request data from the WHO database now, they may not receive it in time to include it in their NDA submission planned for the second quarter of 2008. Novartis requested permission to include the WHO data with their 4-month Safety Update to the NDA, since they had not anticipated the need to supply this data.

The FDA stated that data from the WHO database is a standard component of the global post-marketing safety information that must be submitted with NDAs for OTC marketing, but nonetheless granted the Sponsor permission to supply the data from the WHO database with the 4-month Safety Update. The FDA advised Novartis to include a statement with the NDA submission explaining that the WHO data would be provided with the 4-month Safety Update to ensure that the absence of the WHO data in the original submission is not considered a deficiency. The FDA reiterated the importance of ensuring that the NDA is complete at the time of submission, and Novartis committed to providing the WHO data at that time, if possible.

#### **2.16 Question 16**

Clinical studies PRSW-GN-301 and PRSW-GN-302 are of identical design and were initiated in June 2006. The Statistical Analysis Plan (SAP) for these studies was submitted to IND 74,256 on November 15, 2006 (Serial No. 0008) for review and comment with 2 specific questions. The Last Patient Last Visit for Study 301 was January 29, 2007 and January 24, 2007 for Study 302. Database lock for both studies was March 8, 2007. The Agency's response to the SAP submission was provided on April 6, 2007 and NCH requested clarification of the response to Question 1 in a May 1, 2007 letter (IND 74,256, Serial No. 0014).

Subsequently, this SAP was the topic of discussion during a July 5, 2007 teleconference with the Agency. As a result of this teleconference, two agreements were reached:

1. The protocol for Study PRSW-GN-305 was amended to include the sequential analysis and was submitted with the SAP for review.

2. The final study reports for Studies 301 and 302 include the timing of study initiation, SAP, Last Patient Last Visit (LPLV) and database lock, as well as the rationale for the endpoints and statistical methods.

The SAP for clinical study PRSW-GN-305 was submitted to IND 74,256 in Serial No. 0020 on July 30, 2007. NCH has completed the data analyses for clinical studies PRSW-GN-301 and PRSW-GN-302 following the SAP discussed with the Agency on July 5, 2007 and the analyses of clinical study PRSW-GN-305 following the SAP for this study which was fundamentally the same as that discussed for PRSW-GN-301 and PRSW-GN-302.

NCH believes that using the SAPs discussed and submitted for the analysis of these studies outline the appropriate analyses needed to support the safety and efficacy of lansoprazole 15 mg for the treatment of frequent heartburn, [redacted] Does the Agency concur? **b(4)**

Novartis Position:

NCH believes that using the SAPs discussed and submitted for the analysis of these studies outline the appropriate analyses needed to support the safety and efficacy of lansoprazole 15 mg for the treatment of frequent heartburn, [redacted] In addition, NCH believes that the data from these studies support the proposed labeling for time to effect and time to full effect. **b(4)**

#### FDA Preliminary Response

*The adequacy of the protocols and statistical analysis plans for Studies PRSW-GN-301, - 302 and - 305 to support efficacy and safety of lansoprazole 15 mg for the treatment of frequent heartburn, [redacted] is a review issue and will be determined during the review process after the NDA is submitted. Secondary endpoints will, in general, not be supportable for labeling purposes unless proper statistical methods were pre-specified to control experiment-wise type I error for the multiple endpoints comparisons. Treatment differences for labeling endpoints would need to be both clinically and statistically significant; it is premature to suggest that specific claim information is supportable prior to review of the data.* **b(4)**

*We have the following additional comments:*

1. *Use a single version of MedDRA for the submission.*
2. *For adverse event datasets, please include all levels of the MedDRA hierarchy as well as verbatim terms.*
3. *Regarding the summaries of AE frequency tables, in addition to the summaries by the primary system organ class and preferred term as proposed in the SAP, evaluations by all levels of the MedDRA hierarchy (high level terms, high level group terms) are necessary so that similar events that may represent the same safety risk can be properly grouped.*

Discussion

The FDA clarified that no formal agreements regarding the acceptability of the analysis plans were made during the referenced July 5, 2007 teleconference. Closed testing (e.g., a “gate-keeping approach”) would, in principle, serve to control type I error. The FDA advised Novartis during the July 5, 2007 teleconference to amend the protocol to include a hierarchical testing procedure, if such a procedure was to be utilized. Novartis confirmed that they had revised the protocol based on the July 5, 2007 discussion. The FDA stated that it will determine the impact of the protocol changes on the integrity of the data during the review of the NDA.

Additional Comments

*CMC:*

1. *We remind you that 16 C.F.R. Section 1700.14(a)(30) requires any over-the-counter (OTC) drug product in a dosage form intended for oral administration that contains any active ingredient that was previously available for oral administration only by prescription to be packaged in child-resistant packaging.*

*Administrative:*

2. *Comments shared with you today are based upon the contents of the briefing package, which is considered to be an informational aid to facilitate the meeting discussion. Review of the information submitted to the NDA might identify additional comments or information requests.*
3. *For applications submitted after February 2, 1999, applicants are required either to certify to the absence of certain financial interests of clinical investigators or disclose those financial interests. For additional information, please refer to 21 CFR 54 and 21 CFR 314.50(k).*

**3.0 SUMMARY**

1. If Novartis chooses to include language (e.g., indications, warnings, directions for use) that differs from the language on labels of approved OTC heartburn medications, this new language must be supported by appropriate studies submitted with the original NDA submission.
2. Novartis will provide data from the WHO database in the original NDA if possible. Otherwise, Novartis will provide this data with the 4-month Safety Update.
3. Novartis accepted the FDA’s responses to their questions and no further discussion took place beyond the discussion reported in these minutes.

Linked Applications

Sponsor Name

Drug Name

IND 74256

NOVARTIS CONS

LANSOPRAZOLE DELAYED RELEASE  
CAPSULES

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

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/s/

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JOEL SCHIFFENBAUER

04/15/2008



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

PIND 74,256

Novartis Consumer Health, Inc.  
Attention: Rich Cuprys  
Global Head, Regulatory Affairs  
200 Kimball Dr  
Parsippany, NJ 07054-0622

Dear Mr. Cuprys:

Please refer to your Pre-Investigational New Drug Application (PIND) file for lansoprazole delayed release capsules, 15 mg.

We also refer to the meeting between representatives of your firm and the FDA on April 6, 2006. The purpose of the meeting was to discuss the proposed clinical program and endpoints to support the Rx-to-OTC switch of lansoprazole.

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

If you have any questions, call Keith Olin, Regulatory Project Manager, at (301) 796-0962.

Sincerely,

*{See appended electronic signature page}*

Andrea Leonard-Segal, M.D.  
Director  
Division of Nonprescription Clinical Evaluation  
Office of Nonprescription Drug Products  
Center for Drug Evaluation and Research

Enclosure

## MEMORANDUM OF MEETING MINUTES

**MEETING DATE:** April 6, 2006  
**TIME:** 9:00 am to 10:00 am EST  
**LOCATION:** White Oak, Room 1315  
**APPLICATION:** PIND 74,256  
**DRUG NAME:** lansoprazole 15 mg delayed release capsule  
**TYPE OF MEETING:** Type B

### FDA ATTENDEES:

#### Division of Nonprescription Clinical Evaluation

Andrea Leonard-Segal, M.D., Director  
Daiva Shetty, M.D., Acting Medical Team Leader  
Steven Osborne, M.D., Medical Officer  
LCDR Keith Olin, Regulatory Project Manager

#### Division of Nonprescription Regulation Development

Helen Cothran, Team Leader, Interdisciplinary Scientist (IDS)  
Mary Robinson, Regulatory Review Chemist

#### Office Of Drug Evaluation III

Julie Beitz, MD, Deputy Director

#### Division of Gastroenterology Products

Ruyi He, M.D., Medical Team Leader  
Eric Brodsky, M.D., Medical Officer  
Jasti Choudary, B.V.Sc., Ph.D., Pharmacologist Team Leader  
Melissa Furness, Regulatory Health Project Manager/Acting Chief Project Manager

#### Office of New Drug Quality Assessment, Division of Pre-Marketing Assessment II

Shulin Ding, Ph.D, Pharmaceutical Assessment Lead

Office of Clinical Pharmacology and Biopharmaceutics,

#### Division of Pharmaceutical Evaluation-III

Dennis Bashaw, Pharm.D., Clinical Pharmacology/Biopharmaceutics Team Leader  
Suliman Al-Fayoumi, Ph.D., Clinical Pharmacology/Biopharmaceutics Reviewer

### EXTERNAL CONSTITUENT ATTENDEES:

#### Novartis Consumer Health, Inc

Carola Friedman, MD	Vice President, New Therapeutic Opportunities & Medical Affairs
Andrew Snoddy, PhD	Director, Clinical Research
Thomas McGraw, PhD	Associate Director, Clinical Research
Rich Cuprys	Global Head, Regulatory Affairs
Gretchen Golikov	Associate Director, Regulatory Affairs
Jean Battikha	Director, Biostatistics

Jacob Zijlstra, PhD  
Evren Atillasoy, MD  
Inna Kissen, PhD  
Jeanne Bennett  
Evren Atillasoy, MD  
Soraya Madani, PhD

Head, Preclinical Development  
Director, New Therapeutic Opportunities  
Director, Regulatory Affairs  
Director, Marketing  
Director, New Therapeutic Opportunities  
Associate Director, Regulatory Affairs

**BACKGROUND:**

Novartis Consumer Health, Inc. (NCH) submitted a request to the FDA for a Pre-IND meeting on February 2, 2006, to discuss their proposed clinical program to support a Rx-to-OTC switch of lansoprazole 15 mg delayed-release capsule for the OTC treatment of frequent heartburn and

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Lansoprazole delayed-release capsules are currently marketed under NDA 20-406 by TAP Pharmaceuticals for many acid-related conditions. NCH has received permission from TAP Pharmaceuticals to cross reference TAP's NDA to support the approval of NCH's NDA.

**MEETING OBJECTIVES:**

To reach an agreement between the FDA and NCH on a development program to support the OTC marketing of a lansoprazole 15 mg delayed-release capsule for treatment of frequent heartburn

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**GENERAL DISCUSSION:**

Following introductions and a brief discussion of the purpose of the meeting, discussion focused on the questions from the March 6, 2006, Briefing Document. **Draft responses** to the questions were sent to NCH on April 5, 2006 (see **bolded text**). These draft responses did not change based on discussions that occurred at the April 6, 2006 meeting. A summary of any *additional discussion* follows (see *bolded italicized text*).

**IND 74,256 Lansoprazole Question:**

1) NCH is seeking labeling for the indication "treats frequent heartburn (occurs 2 or more days a week)

The primary efficacy variable to support "treats frequent heartburn

is the comparison of lansoprazole 15 mg versus placebo in the number of days without heartburn over the course of a 14 day treatment period. *Does the Agency agree that if the primary endpoint is statistically different from placebo, the proposed indication will be supported?*

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**FDA response:**

**No, your proposal is not acceptable.**

For OTC purposes, the term "treatment" is not clear how you will distinguish it from "treatment" of heartburn over 14 days of therapy. It is not clear how you will distinguish it from "treatment" of heartburn over 14 days of therapy.

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Based on your synopses in your briefing package, your three proposed phase 3 trials are your three proposed studies, in

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The label will reflect the design and the results of the phase 3 trials.

The primary efficacy endpoint needs to be statistically significant and clinically meaningful.

***Additional Discussion:***

*In response to NCH's question, the FDA agreed that NCH's proposed endpoints (as outlined in the briefing package) were acceptable for the identical indication granted for Prilosec OTC (the treatment of frequent heartburn). The FDA requested that NCH analyze the frequency of heartburn in their heartburn studies for each day over the 14-day treatment period.*

*Demonstration of statistical significance and a clinically meaningful treatment effect would both be needed.*

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3) The clinical program has been designed to substantiate the proposed labeling. The currently approved Prilosec OTC label has as an indication: "not intended for immediate relief of heartburn; this drug may take 1-4 days for full effect".

┌ The secondary endpoints in the efficacy trials will include comparisons of lansoprazole 15 mg versus placebo with regard to the incidence of no heartburn on days 1 to 4, days 1 to 3, days 1 to 2, and day 1 following the first dose, analyzed sequentially. Does the Agency agree that the secondary endpoints are appropriate measures? Based on the outcome of the clinical program, it may be necessary to modify the consumer expectation of efficacy in the labeling. Does the Agency concur?

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**FDA response:**

Your proposed secondary endpoints (the proportion of days with no heartburn over days 1-4, days 1-3, days 1-2, and day 1) are appropriate measures for heartburn trials.

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**Analysis of multiple secondary endpoints will require the study to be adequately powered for all of these endpoints. The results of the study should be reflected in the label.**

4) Based on the data submitted to NDA 20-406 which supports the current prescription labeling with regard to drug interactions with lansoprazole, NCH proposes including warfarin, digoxin, and prescription antifungal or anti-yeast medicines in the "ask a doctor or pharmacist before using if you are taking" section of the label. Does the Agency agree?

**FDA response:**

**Yes, it is reasonable to include warfarin, digoxin, and antifungal medications in the drug-drug interactions section in a proposed lansoprazole OTC label.**

**In addition, theophylline should be included in this section because individual consumers may require additional titration of their theophylline dosage when lansoprazole is started or stopped to ensure clinically effective blood levels.**

*No additional discussion occurred at the April 6, 2006 meeting.*

5) NCH is proposing a label that is consistent with the labeling approved for Prilosec OTC, but has been modified to better align with consumer expectations that taking Prevacid OTC will treat their initial heartburn episodes and that continuing on the 14 day course of therapy T

Does the Agency agree that label comprehension testing only needs to be conducted on the differentiated use section of the label?

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**FDA response:**

**If the label has the same, and no different, elements from the approved PPI label then an LC study is not needed. If portions of the label are significantly different from the approved PPI label, then an LC study would be needed. Depending upon the label that you submit, you may only need to test the portions of the label that are indeed different from the Prilosec OTC label. However you would need to present your study subjects with the entire label. You should submit a draft of your label comprehension study for our review and comment prior to beginning the study.**

*No additional discussion occurred at the April 6, 2006 meeting.*

6) Since the treatment of frequent heartburn has been established as an OTC category, NCH does not propose conducting actual use studies. Does the Agency concur?

**FDA response:**

**In general, an actual use study would not be needed for the treatment of frequent heartburn if your label does not present new elements that might impact consumer use.**

*No additional discussion occurred at the April 6, 2006 meeting.*

7) NCH does not propose to include a follow-up period in the clinical trials since data from previous studies have not demonstrated acid rebound. Does the Agency agree that this follow-up period is not necessary?

**FDA response:**

**No. We do not agree.**

**A follow-up period is important in your phase 3 heartburn studies to assess heartburn efficacy of study treatments in your proposed OTC frequent heartburn population.**

***Discussion:***

***NCH suggested a 7-day placebo follow-up and the FDA said they would consider it but would need to have further internal discussion.***

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***No additional discussion occurred at the April 6, 2006 meeting.***

9) The safety of the lansoprazole molecule has been extensively demonstrated in clinical studies and post marketing surveillance, and the population in the planned efficacy trials is at no higher risk than that in previous studies. NCH plans to start the double blind placebo controlled clinical efficacy study(ies) soon after the submission of the protocol and waive the 30 day IND wait. Is this acceptable to the Agency?

**FDA response:**

**You may request a waiver of the 30-day IND waiting period when you submit your IND. You need a correspondence from the FDA waiving the 30 day period.**

*No additional discussion occurred at the April 6, 2006 meeting.*

10) NCH plans to submit the data generated from the clinical program described herein along with proposed labeling, updated post-marketing safety data, and potentially updated CMC information via a 505(b)(1) application. All other data will be by reference to NDA 20-406. Does the Agency agree?

**FDA response:**

**Since you were not granted right of reference to the data from TAP Pharmaceuticals, if you cross reference NDA 20-406, your application would be a 505(b)(2) NDA.**

*No additional discussion occurred at the April 6, 2006 meeting.*

11) NCH believes that this clinical program fulfills the requirement of "new clinical trial necessary to the approval" for 3 years marketing exclusivity. Does the Agency agree?

**FDA response:**

**Exclusivity is granted upon approval of a new drug application when new clinical studies, essential for approval, have been conducted or sponsored by the applicant. Whether specific clinical data used to support the Rx-to-OTC switch are essential to the approval of the NDA is a review issue. FDA does not award or grant exclusivity prior to approval of a drug product.**

*No additional discussion occurred at the April 6, 2006 meeting.*

12) NCH will be requesting a waiver from conducting an assessment of the safety and efficacy of lansoprazole in the pediatric population according to the PREA of 2003. The pediatric indications for the short-term treatment of GERD will be maintained as prescription indications and the proposed OTC labeling will be recommended for adults 18 years of age and older. Does the Agency agree?

**FDA response:**

**You may request a pediatric waiver when you submit your NDA. We refer you to FDA's Guidance for Industry: How to Comply with the Pediatric Research Equity Act.**

*No additional discussion occurred at the April 6, 2006 meeting.*

*Additional meeting discussion:*

*Dr. Choudary stated that NCH's pharmacology/toxicology information in their background package may not reflect the approved Prevacid prescription label. NCH acknowledged Dr. Choudary's comments and stated they will correct the pharmacology/toxicology information.*

**AGREEMENTS AND ACTION ITEMS:**

1) The FDA agreed that the proposed 14 day endpoint was acceptable for the identical indication granted for Prilosec OTC and that NCH would analyze the frequency of heartburn each day over the 14 day treatment.

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3) NCH will defer discussion of other new OTC indications that they are considering for future guidance meetings.

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/s/

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Andrea Segal

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