DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-719/S-015

Prometheus Laboratories, Inc.
Attention: David Fulano, Ph.D.
Vice President, Regulatory Affairs
9410 Carroll Park Dr.
San Diego, CA 92121

Dear Dr. Furlano:

Please refer to your supplemental new drug application dated May 19, 2009, received May 20, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for HELIDAC® Therapy (bismuth subsalicylate/metronidazole/tetracycline hydrochloride).

We acknowledge receipt of your submission dated October 1, 2009.

This supplemental new drug application provides for the revisions to the HELIDAC® Therapy package insert (deletions are indicated by ~~strikethrough~~ and additions are indicated by underline) as follows:

PACKAGE INSERT:

1. In the **DESCRIPTION** section, the following revisions were made:

   Metronidazole tablets, USP: Each ~~convex~~, round, white ~~to off-white~~ ~~round~~ tablet contains 250 mg metronidazole. Metronidazole is 2-Methyl-5-nitroimidazole-1-ethanol, with the following structural formula:

   Inactive Ingredients: Each metronidazole tablet contains colloidal silicon dioxide, crospovidone, stearic acid, ~~hydrogenated vegetable oil~~ magnesium stearate and microcrystalline cellulose

   Tetracycline hydrochloride capsules, USP: Each ~~pink and white~~ black and yellow capsule contains 500 mg tetracycline hydrochloride, ~~causing it to appear pale orange and white in color when filled.~~

   Inactive Ingredients: Each tetracycline hydrochloride capsule contains ~~colloidal silicon dioxide, white ink~~ lactose, magnesium stearate and sodium lauryl sulfate; D & C yellow no.10, FD & C ~~Red~~blue No 1, FD & C red no. 40, gelatin~~, pregelatinized starch, stearic acid,~~ and titanium dioxide. It may also contain benzyl alcohol, butylparaben, edetate calcium disodium, FD & C yellow no. 6, methylparaben, propylparaben, silicon dioxide and sodium propionate.

2. In the **PRECAUTIONS/Information for Patients** subsection, the following revisions are made**:**

   Each dose includes 4 pills: 2 pink round chewable tablets (bismuth subsalicylate), 1 white round table (metronidazole), and 1 ~~orange and white~~ black and yellow capsule (tetracycline hydrochloride). Each does (all 4 pills) should be taken 4 times a day, at mealtime and bedtime. Patients should be instructed to chew and swallow the pink round tablets (bismuth subsalicylate

tablets) and to swallow the white round table (hydrochloride capsule) and the ~~pale orange and white~~ black and yellow capsule (tetracycline hydrochloride capsule) whole with a full glass of water (8 ounces). Concomitantly prescribed H 2 antagonist therapy should be taken as directed.

3. In the **ADVERSE REACTIONS** section, the reporting percentage was changed from "=1%" to "≥ 1%". This change is reflected both in the text as well as in the title of the Table describing the incidence of Adverse Reactions reported in Clinical Trials.

4. In the **HOW SUPPLIED** section, the following changes were made:

   4 metronidazole 250-mg tablets~~, each convex~~ are unscored, round, white~~ to off-white tablet with "DAN" imprinted on one side and "5540" imprinted on the other side~~, debossed MP 45.

   4 tetracycline hydrochloride 500-mg capsules, each ~~pale orange and white~~black/yellow capsule ~~printed "PG 12" in white ink~~ imprinted with "barr 010".

We also acknowledge that you have made the following revisions to the Pharmacist Information & Counseling Aid, booklet, and note pad to be consistent with approved labeling.

PHARMACIST INFORMATION & COUNSELING AID, Dosing and Administration subsection, the following revisions are made:

- Each dose includes 4 pills: 2 pink round chewable tablets (bismuth subsalicylate), 1 white round tablet (metronidazole), and 1 ~~orange & white~~ black and yellow capsule (tetracycline hydrochloride).

- Chew and swallow the 2 pink tablets. Then swallow the white tablet and ~~orange and white~~ black and yellow capsule whole with a full glass of water (8 ounces).

BOOKLET

The following revisions are made**:**

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- The therapy contains 14 blister cards, one for each day of your 14-day treatment plan. Each dose includes 4 pills: 2 pink round chewable tablets (bismuth subsalicylate), 1 white round table (metronidazole), and 1 ~~orange & white~~ capsule (tetracycline hydrochloride).

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- Chew and swallow the 2 pink tablets. Then, swallow the white tablet and the ~~orange & white~~ capsule whole with a full glass of water (8 ounces). Remember: Your treatment may not work if even one pill is left out.

NOTE PAD

The following revisions are made:

Day 1
Freedom from your ulcer? Let's get started! Just chew and swallow the two pink tablets. Then, swallow the white tablet- and the ~~orange & white~~ capsule with a glass of water.

We also note that you have updated the package insert and carton label to reflect the new manufacturers of metronidazole (URL Pharma, Inc) and tetracycline (Watson Pharmaceuticals, Inc), which were approved on May 12, 2009 for supplement S-014.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text for the package insert dated October 1, 2009.

If you have any questions, please call Christine Lincoln, RN, M.S., MBA, Regulatory Health Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure- Package Insert for HELIDAC® Therapy

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50719	SUPPL-15	PROMETHEUS LABORATORIES INC	HELIDAC

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

/s/

RENATA ALBRECHT
11/12/2009