CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 078878Orig1s000

Name: Omeprazole Magnesium Delayed-Release Capsules
20 mg

Sponsor: Dr. Reddy's Laboratories Inc.

Approval Date: June 5, 2009

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078878

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078878

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-878

Dr. Reddy's Laboratories Inc.
U.S. Agent for: Dr. Reddy's Laboratories Limited
Attention: Kumara Sekar, Ph.D.
Senior Director, Global Regulatory Affairs
200 Somerset Corporate Boulevard, 7th Floor
Bridgewater, NJ 08807

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated March 16, 2007, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Omeprazole Magnesium Delayed-release Capsules, 20 mg (base) (OTC).

Reference is also made to your amendments dated July 25, and September 18, 2008; March 11, March 25, April 10, April 20, April 22, May 14, and June 2, 2009. Reference is also made to the ANDA suitability petition submitted under section 505(j)(2)(c) of the Act. This petition, approved on July 5, 2005, permitted the agency to file this ANDA for a drug product that differs in dosage form from that of the listed drug product i.e., from Delayed-release Tablet to Delayed-release Capsule.

We have completed the review of this ANDA and have concluded that the drug is safe and effective for use as recommended in the submitted over-the-counter (OTC) labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Omeprazole Magnesium Delayed-release Capsules, 20 mg (base) (OTC) to be bioequivalent to the reference listed drug (RLD), Prilosec OTC Delayed-release Tablets, 20 mg (base), of AstraZeneca.

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your ANDA. The "interim" dissolution specifications are as follows:

Dissolution Testing should first be conducted in Acid Stage:

Medium:	0.1N HCl at 37°C
Volume:	300 mL
Apparatus:	USP II (Paddle)
Rotation Speed:	100 rpm
Specifications:	NMT (b) (4) of the labeled amount of Omeprazole is dissolved in 120 minutes

Dissolution Testing should then be conducted in Buffer Stage:

Medium:	0.05 M Phosphate buffer at pH 6.8 at 37°C
Volume:	1000 mL
Apparatus:	USP II (Paddle)
Rotation Speed:	100 rpm
Specifications:	NLT (b) (4) is dissolved in 30 minutes

Each dosage unit is subjected to acid stage conditions for 2 hours. At the end of the acid stage, 0.1N HCl is drained from the vessel and 1000 mL of 0.05M phosphate buffer is added to begin the buffer stage testing.

These "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement – Changes Being Effected" if there are no revisions to be made to these "interim" specifications, or if the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The RLD upon which you have based your ANDA, Prilosec OTC Delayed-release Tablets, 20 mg, of AstraZeneca, is subject to periods of patent protection. The following patents with their expiration dates are currently listed in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

U.S. Patent Number	Expiration Date
5,690,960 (the '960 patent)	November 25, 2014
5,753,265 (the '265 patent)	June 7, 2015
5,817,338 (the '338 patent)	October 6, 2015
5,900,424 (the '424 patent)	May 4, 2016
6,403,616 (the '616 patent)	November 15, 2019
6,428,810 (the '810 patent)	November 3, 2019

With respect to each of these patents, your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Omeprazole Magnesium Delayed-release Capsules, 20 mg (base) (OTC), under this ANDA. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action was brought against Dr. Reddy's Laboratories Limited (DRL) for infringement of one or more of these patents that were the subjects of the paragraph IV certifications. You have notified the agency that DRL complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation was initiated against DRL for infringement of the '960 and '424 patents in the United States District Court for the Southern District of New York [AstraZeneca v. Dr. Reddy's Laboratories Limited, Civil Action No. CA 07-6790]. You have also notified the agency that the court granted your motion for summary judgment; therefore, under section 505(j)(5)(B)(iii) your ANDA is eligible for approval.[1]

With respect to 180-day generic drug exclusivity, we note that DRL was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification to the '960, '265, '338, '424, '616, and '810 patents. Therefore, with this approval, DRL is eligible for 180-days of generic drug exclusivity for Omeprazole Magnesium Delayed-release Capsules, 20 mg (base) (OTC). This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.

[1]Because information on the '960, '265, '338, '424, '616, and '810 patents was submitted to FDA before August 18, 2003, this reference to section 505(j)(5)(B)(iii) is to that section of the Act as in effect prior to December 8, 2003, when the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) was enacted. See MMA § 1101(c)(3).

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Robert L. West
6/5/2009 11:41:28 AM
Deputy Director, for Gary Buehler

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

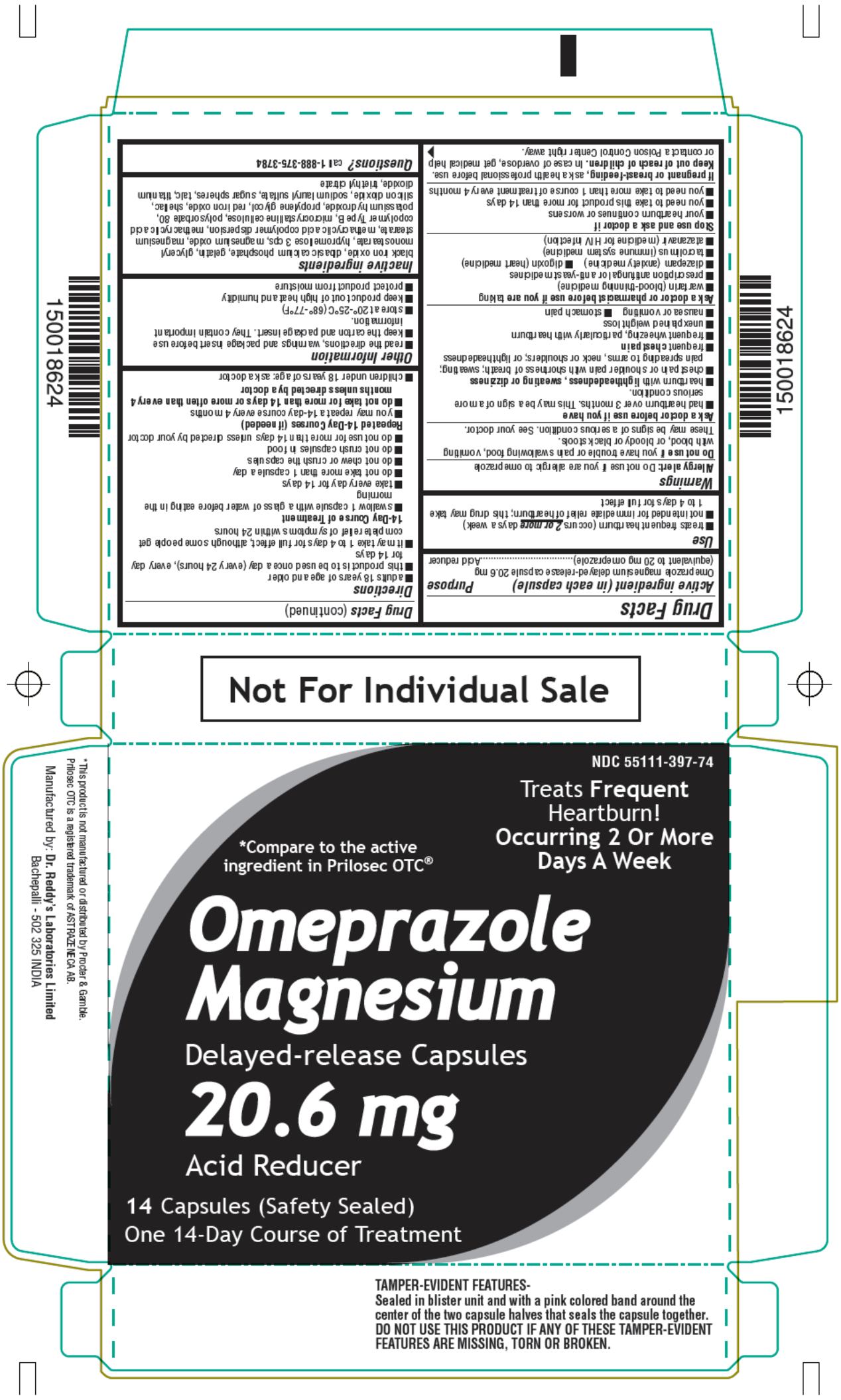
ANDA 078878

LABELING

Revised Blister Card Label

Blister Card label for Omeprazole Magnesium Delayed-release Capsule 20.6 mg

Actual Size 117.5mm x 100mm



LABELING FORMAT INFORMATION

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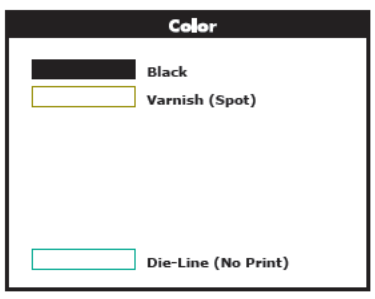
Drug facts cont.	helvetica condensed bold oblique	8 pt.
Headings	helvetica condensed bold oblique	8 pt.
Subheadings	helvetica condensed bold	6 pt.
Body Text	helvetica condensed medium	6 pt.
Leading	N/A	6.5 pt
Bullets	zapf dingbats	6 pt.
Barline	N/A	2.5 pt
Hairlines	N/A	.5 pt.



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Drug facts cont.	helvetica condensed bold oblique	8 pt.
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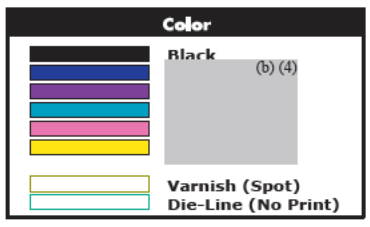
Bullets	zapf dingbats	6 pt.
Barline	N/A	2.5 pt
Hairlines	N/A	.5 pt.



DIE DRR8100060
6.406 x 10.531 Flat
4.094 x .859 x 4.875

THIS IS AN UNAPPROVED DIE

LABELING FORMAT INFORMATION

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Drug facts cont.	helvetica condensed bold oblique	8 pt.
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Bullets	zapf dingbats	6 pt.
Barline	N/A	2.5 pt
Hairlines	N/A	.5 pt.

Color

Black (b) (4)

Varnish (Spot)

Die-Line (No Print)

Lot

Exp

TAMPER-EVIDENT FEATURES-
Sealed in blister unit and with a pink colored band around the center of the two capsule halves that seals the capsule together. DO NOT USE THIS PRODUCT IF ANY OF THESE TAMPER-EVIDENT FEATURES ARE MISSING, TORN OR BROKEN.

NDC 55111-397-28

Treats Frequent Heartburn! Occurring 2 Or More Days A Week

NEW

*Compare to the active ingredient in Prilosec OTC®

Omeprazole Magnesium

Delayed-release Capsules

20.6 mg

Acid Reducer

28 Capsules (Safety Sealed)

Two 14-Day Courses of Treatment

*This product is not manufactured or distributed by Procter & Gamble. Prilosec OTC® is a registered trademark of ASTRAZENECA AB CORPORATION.

Manufactured by: **Dr. Reddy's Laboratories Limited**
Bachepalli - 502 325 INDIA

Drug Facts

Active ingredient (in each capsule) — Purpose

Omeprazole magnesium delayed-release capsule 20.6 mg (equivalent to 20 mg omeprazole) ..... Acid reducer

Use

- treats frequent heartburn (occurs ***2 or more*** days a week)
- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Warnings

Allergy alert: Do not use if you are allergic to omeprazole

Do not use if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools.
These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have

- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting ■ stomach pain

Ask a doctor or pharmacist before use if you are taking

- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- diazepam (anxiety medicine) ■ digoxin (heart medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if

- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Drug Facts (continued)

Directions

- adults 18 years of age and older
- this product is to be used once a day (every 24 hours), every day for 14 days
- it may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours

14-Day Course of Treatment

- swallow 1 capsule with a glass of water before eating in the morning
- take every day for 14 days
- do not take more than 1 capsule a day
- do not chew or crush the capsules
- do not crush capsules in food
- do not use for more than 14 days unless directed by your doctor

Repeated 14-Day Courses (if needed)

- you may repeat a 14-day course every 4 months
- **do not take for more than 14 days or more often than every 4 months unless directed by a doctor**

- children under 18 years of age: ask a doctor

Other Information

- read the directions, warnings and package insert before use
- keep the carton and package insert. They contain important information.
- store at 20°-25°C (68°-77°F)
- keep product out of high heat and humidity
- protect product from moisture

Inactive ingredients

black iron oxide, dibasic calcium phosphate, gelatin, glyceryl monostearate, hypromellose 3 cps, magnesium oxide, magnesium stearate, methacrylic acid copolymer dispersion, methacrylic acid copolymer Type B, microcrystalline cellulose, polysorbate 80, potassium hydroxide, propylene glycol, red iron oxide, shellac, silicon dioxide, sodium lauryl sulfate, sugar spheres, talc, titanium dioxide, triethyl citrate

Questions? call 1-888-375-3784

LABELING FORMAT INFORMATION

	Font	Size
Drug facts:	helvetica condensed bold oblique	12 pt.
Drug facts cont.	helvetica condensed bold oblique	8 pt.
Headings	helvetica condensed bold oblique	8 pt.
Subheadings	helvetica condensed bold	6 pt.
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Hairlines	N/A	.5 pt.

Color

Black (b) (4)

Varnish (Spot)

Die-Line (No Print)

Lot No.

Exp. Date:

*This product is not manufactured or distributed by Procter & Gamble. Prilosec OTC® is a registered trademark of ASTRAZENECA AB CORPORATION.

Manufactured by: **Dr. Reddy's Laboratories Limited**
Bachepalli - 502 325 INDIA

TAMPER-EVIDENT FEATURES-
Sealed in blister unit and with a pink colored band around the center of the two capsule halves that seals the capsule together. DO NOT USE THIS PRODUCT IF ANY OF THESE TAMPER-EVIDENT FEATURES ARE MISSING, TORN OR BROKEN.

Drug Facts

Active ingredient (in each capsule) **Purpose**

Omeprazole magnesium delayed-release capsule 20.6 mg (equivalent to 20 mg omeprazole)..... Acid reducer

Use

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- not intended for immediate relief of heartburn; this drug may take 1 to 4 days for full effect

Warnings

Allergy alert: Do not use if you are allergic to omeprazole

Do not use if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools.
These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have

- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting ■ stomach pain

Ask a doctor or pharmacist before use if you are taking

- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- diazepam (anxiety medicine) ■ digoxin (heart medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if

- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Drug Facts (continued)

Directions

- adults 18 years of age and older
- this product is to be used once a day (every 24 hours), every day for 14 days
- it may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours

14-Day Course of Treatment

- swallow 1 capsule with a glass of water before eating in the morning
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- do not use for more than 14 days unless directed by your doctor

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- you may repeat a 14-day course every 4 months
- **do not take for more than 14 days or more often than every 4 months unless directed by a doctor**

- children under 18 years of age: ask a doctor

Other Information

- read the directions, warnings and package insert before use
- keep the carton and package insert. They contain important information.
- store at 20°-25°C (68°-77°F)
- keep product out of high heat and humidity
- protect product from moisture

Inactive ingredients

black iron oxide, dibasic calcium phosphate, gelatin, glyceryl monostearate, hypromellose 3 cps, magnesium oxide, magnesium stearate, methacrylic acid copolymer dispersion, methacrylic acid copolymer Type B, microcrystalline cellulose, polysorbate 80, potassium hydroxide, propylene glycol, red iron oxide, shellac, silicon dioxide, sodium lauryl sulfate, sugar spheres, talc, titanium dioxide, triethyl citrate

Questions? call 1-888-375-3784

Omeprazole Magnesium Delayed-release Capsules 20.6 mg

Acid Reducer

Please read all of this package insert before taking Omeprazole Magnesium Delayed-release Capsules. Save this to read, as you need.

How Omeprazole Magnesium Delayed-release Capsules Works For Your Frequent Heartburn

Omeprazole Magnesium Delayed-release Capsules works differently from other OTC heartburn products, such as antacids and other acid reducers. Omeprazole Magnesium Delayed-release Capsules stops acid production at the source - the **acid pump** that produces stomach acid. Omeprazole Magnesium Delayed-release Capsules is to be used once a day (every 24 hours), every day for 14 days.

What to Expect When Using Omeprazole Magnesium Delayed-release Capsules

Omeprazole Magnesium Delayed-release Capsules is a different type of medicine from antacids and other acid reducers. Omeprazole Magnesium Delayed-release Capsules may take 1 to 4 days for full effect, although some people get complete relief of symptoms within 24 hours. Make sure you take the entire 14 days of dosing to treat your frequent heartburn.

Safety Record

For years, doctors have prescribed Omeprazole Magnesium Delayed-release Capsules to treat acid-related conditions in millions of people safely.

Who Should Take Omeprazole Magnesium Delayed-release Capsules

This product is for adults (18 years and older) with **frequent heartburn**-when you have heartburn 2 or more days a week.

- Omeprazole Magnesium Delayed-release Capsules is **not** intended for those who have heartburn infrequently, one episode of heartburn a week or less, or for those who want immediate relief of heartburn.

How to Take Omeprazole Magnesium Delayed-release Capsules

14-DAY Course of Treatment

- Swallow 1 capsule with a glass of water before eating in the morning.
- Take every day for 14 days.
- Do not take more than 1 capsule a day.
- Do not chew or crush the capsules.
- Do not crush capsules in food.
- Do not use for more than 14 days unless directed by your doctor.

It is important not to chew or crush these capsules, or crush the capsules in food. This decreases how well Omeprazole Magnesium Delayed-release Capsules works.

When to Take Omeprazole Magnesium Delayed-release Capsules Again

You may repeat a 14-day course of therapy every 4 months.

When to Talk to Your Doctor

Do not take for more than 14 days or more often than every 4 months unless directed by a doctor.

Warnings and When to Ask Your Doctor

Allergy alert: Do not use if you are allergic to omeprazole

Do not use if you have trouble or pain swallowing food, vomiting with blood, or bloody or black stools. These may be signs of a serious condition. See your doctor.

Ask a doctor before use if you have

- had heartburn over 3 months. This may be a sign of a more serious condition.
- heartburn with **lightheadedness, sweating or dizziness**
- chest pain or shoulder pain with shortness of breath; sweating; pain spreading to arms, neck or shoulders; or lightheadedness
- frequent **chest pain**
- frequent wheezing, particularly with heartburn
- unexplained weight loss
- nausea or vomiting
- stomach pain

Ask a doctor or pharmacist before use if you are taking

- warfarin (blood-thinning medicine)
- prescription antifungal or anti-yeast medicines
- diazepam (anxiety medicine)
- digoxin (heart medicine)
- tacrolimus (immune system medicine)
- atazanavir (medicine for HIV infection)

Stop use and ask a doctor if

- your heartburn continues or worsens
- you need to take this product for more than 14 days
- you need to take more than 1 course of treatment every 4 months

If pregnant or breast-feeding,
ask a health professional before use.

Keep out of reach of children.
In case of overdose, get medical help or contact a Poison Control Center right away.

Tips for Managing Heartburn

- Do not lie flat or bend over soon after eating.
- Do not eat late at night or just before bedtime.
- Certain foods or drinks are more likely to cause heartburn, such as rich, spicy, fatty and fried foods, chocolate, caffeine, alcohol and even some fruits and vegetables.
- Eat slowly and do not eat big meals.
- If you are overweight, lose weight.
- If you smoke, quit smoking.
- Raise the head of your bed.
- Wear loose-fitting clothing around your stomach.

How is Omeprazole Magnesium Delayed-release Capsules Sold

Omeprazole Magnesium Delayed-release Capsules is available in 14 capsule, 28 capsule and 42 capsule sizes. These sizes contain one, two, and three 14-day courses of treatment, respectively. Do not use for more than 14 days in a row unless directed by your doctor. For the 28 count (two 14-day courses) and the 42 count (three 14-day courses), you may repeat a 14-day course every 4 months.

For Questions or Comments About Omeprazole Magnesium Delayed-release Capsules

Call 1-888-375-3784

DR. REDDY'S

Made in India

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078878

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number:	78-878
Date of Submission:	March 16, 2007 (Original); July 25, 2008 (Amendment); and September 18, 2008 (Amendment)
Applicant's Name:	Dr. Reddy's Laboratories Limited
Established Name:	Omeprazole Magnesium Delayed-release Capsules, 20 mg (OTC)

Labeling Deficiencies:

1. GENERAL COMMENTS

   a. Please clarify which package sizes utilize child-resistant packaging. Please comply with requirements of 15 U.S.C. 1473(a) and 16 CFR 1700.5.

   b. The image of the capsule on the principal display panels of the carton labeling state "FPO". However, the drug product specifications in your application state that the capsules are "imprinted "OMP2O" on cap with black ink". Please comment.

   c. Please delete the image of the capsule from all labels and labeling.

   d. The listings of inactive ingredients on the carton labeling and container labels are inconsistent with the listing of inactive ingredients found in the statement of components and composition. Please clarify and revise.

2. (b) (4)

3. BLISTER (blister card of 7)

    a. Replace the name [redacted] with the established name "Omeprazole Magnesium Delayed-release Capsule".

    b. Increase the prominence of the expression of strength, "20.6 mg".

4. CARTON (unit dose capsules of 14, 28 and 42)

    a. Replace the name [redacted] with the established name "Omeprazole Magnesium Delayed-release Capsules".

    b. Increase the prominence of the expression of strength, "20.6 mg".

    c. Delete "New" appearing on the top left corner of the principle display panel.

    d. Un-italicize and un-bold "(continued)" in the title "Drug Facts (continued)".

    e. "Warnings" heading – "Keep out of reach of children…" [correct spelling of "out"]

5. [redacted]

6. INSERT

    a. Title line: Replace the name [redacted] with the established name "Omeprazole Magnesium Delayed-release Capsules, 20.6 mg".

    b. Replace the name [redacted] throughout the insert with the established name "Omeprazole Magnesium Delayed-release Capsules".

Please revise your labels and labeling, as instructed above, and submit final printed labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission, please provide a side-by- side comparison of your proposed labeling with your last submission with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

NOTES/QUESTIONS TO THE CHEMIST: None

FOR THE RECORD:
(Part of this review came from Chemistry Review #4)
*****NOTE: This is the first generic*****

1. MODEL LABELING: Prilosec OTC® (20 mg omeprazole magnesium) delayed-release **tablets**:
NDA 21-229/S-010 approved June 18, 2008 (drug facts and labels)
NDA 21-229/S-008 approved January 18, 2008 (consumer insert)

   ANDA suitability petition DOCKET NO. 2004P-0373/CP1, dated 7/5/2005 (change in dosage form from DR TABLET to DR CAPSULE)

   Related applications:
   Dr. Reddy's ANDA 75-576 Omeprazole Delayed-release Capsules USP, 10 mg, 20 mg and 40 mg
   Dr. Reddy's ANDA 78-490 Omeprazole Delayed-release Capsules USP, 40 mg
   Dr. Reddy's ANDA 78-693 Omeprazole Delayed-release Capsules USP, 10 mg and 20 mg
   (ANDA's 78-490 and 78-693 have the same formulation; they have separate inserts.
   ANDA 75-576 has a different formulation.)

2. INACTIVE INGREDIENTS: The listing of inactive ingredients on the carton labeling is ***inconsistent*** with the listing of inactive ingredients found in the statement of components and composition. **Firm is asked to clarify and revise.**

   Chemistry Review #4 states: "The firm has changed the composition in the September 17, 2008 amendment where they have added banding for the capsules."

   Elemental iron content per Chemistry Review #4: "The daily iron uptake was recalculated for the new formula with the capsule band and was found to be [redacted] (b) (4) per capsule which is within acceptable limits." (Acceptable per 21 CFR 73.1200 - the total daily amount of elemental iron should not exceed 5 mg)

3. PATENTS/EXCLUSIVITIES

Appl No	Prod No	Patent No	Patent Expiration	Certification	Labeling Impact	Patent Use Code
021229	001	5690960	Nov 25, 2014	PIV	None	
021229	001	5753265	Jun 7, 2015	PIV	None	
021229	001	5817338	Oct 6, 2015	PIV	None	
021229	001	5900424	May 4, 2016	PIV	None	
021229	001	6403616	Nov 15, 2019	PIV	None	
021229	001	6428810	Nov 3, 2019	PIV	None	

   Exclusivity Data

   There is no unexpired exclusivity for this product.

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON
   - USP: No
   - NDA: Store at 20^0-25^0 (68^0-77^0F)
   - ANDA: Store at 20^0-25^0 (68^0-77^0F)

5. DISPENSING STATEMENT COMPARISON
   - NDA: Keep product out of high heat and humidity. Protect product from moisture.
   - ANDA: Keep product out of high heat and humidity. Protect product from moisture.

6. PACKAGE CONFIGURATION
   - NDA: 2-count samples
     unit dose cartons of 14 (2 x 7)
     unit dose cartons of 28 containing 2 inner cartons of 14 (2 x 7)
     unit dose cartons of 42 containing 3 inner cartons of 14 (2 x 7)
   - ANDA: (b) (4)
     unit dose cartons of 14 (2 x 7)
     unit dose cartons of 28 containing 2 inner cartons of 14 (2 x 7)
     unit dose cartons of 42 containing 3 inner cartons of 14 (2 x 7)

7. CONTAINER/CLOSURE

(b) (4)

Unit dose blister packs (7 count blisters)	(b) (4) (14's, 28's and 42's)

(b) (4)

The proposed container/closure systems comply with USP <661> and USP <671> requirements and all components used in these container/closure systems have been used in approved CDER products.

- Packaged in temper-evident packaging. Temper-evident statements are included on the (b) (4) carton labeling.

- Blister label has the statement "Separate at perforation. Peel at arrow. Push capsule through foil."

- Section 4(a) of the Poison Prevention Packaging Act of 1970 (PPPA), allows the manufacture or packer to package an OTC product subject to special packaging standards in one size of non-CR packaging only if the manufacturer (or packer) also supplies the product in a CR package of a popular size, and the non-CR package bears the statement "This Package for Households Without Young Children" conspicuously and in accordance with all of the requirements of 16 CFR 1700.5(a). [Refer to 15 U.S.C. 1473(a), 16 CFR 1700.5 – "…section 4(a) of the act authorizes manufacturers and packers to package such substances in noncomplying packaging of a single size provided that complying packaging is also supplied and the noncomplying packages are conspicuously labeled to indicate that they should not be used in households where young children are present."] **The firm will be asked to clarify which package sizes use CRC packaging and to comply with the act.**

8. FINISHED DOSAGE FORM

20 mg: Off-white to brown colored enteric coated pellets (inclusive of all shades of yellow and pale brown) and a white to off-white, caplet shaped, biconvex, film coated tablet filled in size '0' hard gelatin (banded) capsule with opaque pink colored cap and opaque white colored body imprinted "OMP2O" on cap with black ink.

9. MANUFACTURER:
Dr. Reddy's Laboratories Limited, Bachepalli - 502 325, India.

10. Bioequivalence – Fasting and fed studies on 20 mg

11. Dissolution Test Method

From Division of Bioequivalence Dissolution Review signed on 9/24/2007:

3. The firm uses the following method and specifications:

Acid Stage:
(Acid resistance is measured from the dosage form and not from an aliquot of 0.1N HCl):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.1N HCl @ 37ºC
Volume: 300mL
Time: 2h
Specification: NMT (b) (4) of the labeled amount of omeprazole is dissolved at the end of the acid stage.

Buffer Stage:
(Fresh capsules are assayed and are from the same lot tested for acid resistance. Drug release measured from an aliquot of the phosphate buffer.):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.05M Na3PO4, pH 6.8 @ 37ºC
Volume: 1000mL
Time: 10, 20, 30, and 45 minutes

Specification: NLT (b) (4) (Q) of the labeled amount of omeprazole is dissolved in 30 minutes.

NOTE: Each dosage unit is subjected to acid stage conditions for 2h. At the end of the acid stage, 0.1N HCl is drained from the vessel and 1000mL of 37°C 0.05M Na3PO4 buffer, pH 6.8, is added to begin the buffer stage testing.

4. The method utilized by the firm is essentially the same as the FDA-recommended method for Omeprazole Magnesium Tablets, DR (OTC). The only difference between the two methods is in the approach used for buffer stage testing. Specifically, the firm's method calls for the 300mL of 0.1N HCl to be drained from the vessel at the end of the

acid stage and replaced with 1000mL of 0.05M Na3PO4, pH 6.8. In contrast, the FDA recommended method (OTC DR tablets) calls for 700mL of 0.086M Na2HPO4 to be added to the 300mL of 0.1N HCl already in the vessel at the end of the acid stage to yield 1000mL of pH 6.8 buffer. The firm's proposed method is **acceptable** since it is very similar to the FDA-recommended method for the OTC DR Tablets.

Primary Reviewer: Sarah Park

Team Leader: Koung Lee

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

/s/

Soojung Sarah Park
4/14/2009 06:08:09 PM
LABELING REVIEWER

Koung Lee
4/15/2009 04:40:06 PM
LABELING REVIEWER
For Wm Peter Rickman

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 78-878

Date of Submission: April 22, 2009 and May 14, 2009 (Amendments)

Applicant's Name: Dr. Reddy's Laboratories Limited

Established Name: Omeprazole Magnesium Delayed-release Capsules, 20.6 mg (OTC)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

All labeling pieces submitted electronically in final print.

		Date Submitted	Recommendation
BLISTER	Cards of 7	April 22, 2009	Acceptable for Approval
CARTON - inner	Unit dose capsules of 14	May 14, 2009	Acceptable for Approval
CARTON -outer	Unit dose capsules of 14, 28 and 42	May 14, 2009	Acceptable for Approval
INSERT	Consumer Insert	April 22, 2009	Acceptable for Approval

REVISIONS NEEDED POST-APPROVAL: No

NOTES/QUESTIONS TO THE CHEMIST:

From: Read, Shanaz
Sent: Tuesday, May 12, 2009 9:38 AM
To: Park, Sarah Soojung
Cc: Maldonado, Damaris
Subject: RE: ANDA 78-878 Omeprazole Magnesium DR Caps OTC

Sarah

I have not seen a statement of that kind. However, since there is 20 mg of Omeprazole Magnesium in each capsule and up to (b) (4) magnesium in the Omeprazole Magnesium, that would correspond to about (b) (4) of Mg (b) (4).

(b) (4)

The total as calculated is less than 8 g. However, if you are asking for other info from the firm, you may as well ask them for a statement regarding amount of Mg in each capsule.

Shanaz

From: Park, Sarah Soojung
Sent: Monday, May 11, 2009 3:57 PM
To: Read, Shanaz
Cc: Liu, Theresa
Subject: ANDA 78-878 Omeprazole Magnesium DR Caps OTC

Hi Shanaz,

Would you be able to help me with one question regarding (b) (4) OTC Omeprazole Magnesium DR Capsules, ANDA 78-878? I am trying to determine the total magnesium content per capsule. Did the firm submit calculations of magnesium content or a certification that the magnesium content of a single maximum recommended dose of the product is less than 8 mg?

This ANDA is on the AP matrix. Thanks for your help!

Sarah

FOR THE RECORD:
(Part of this review came from Chemistry Review #4)
*****NOTE: This is the first generic*****

1. MODEL LABELING: Prilosec OTC® (20 mg omeprazole magnesium) delayed-release **tablets**:
   NDA 21-229/S-010 approved June 18, 2008 (drug facts and labels)
   NDA 21-229/S-008 approved January 18, 2008 (consumer insert)

   ANDA suitability petition DOCKET NO. 2004P-0373/CP1, dated 7/5/2005 (change in dosage form from DR TABLET to DR CAPSULE)

   Related applications:
   Dr. Reddy's ANDA 75-576 Omeprazole Delayed-release Capsules USP, 10 mg, 20 mg and 40 mg
   Dr. Reddy's ANDA 78-490 Omeprazole Delayed-release Capsules USP, 40 mg
   Dr. Reddy's ANDA 78-693 Omeprazole Delayed-release Capsules USP, 10 mg and 20 mg
   (ANDA's 78-490 and 78-693 have the same formulation; they have separate inserts.
   ANDA 75-576 has a different formulation.)

2. INACTIVE INGREDIENTS: The listing of inactive ingredients on the carton labeling is consistent with the listing of inactive ingredients found in the statement of components and composition.

   Chemistry Review #4 states: "The firm has changed the composition in the September 17, 2008 amendment where they have added banding for the capsules."

   In the April 22, 2009 amendment, the firm provided a copy of the revised components and composition statement.

   (b) (4)

Elemental iron content per Chemistry Review #4: "The daily iron uptake was recalculated for the new formula with the capsule band and was found to be (b) (4) per capsule which is within acceptable limits." (Acceptable per 21 CFR 73.1200 - the total daily amount of elemental iron should not exceed 5 mg)

Magnesium content per capsule is less than 8 mg, per calculation from the chemist (see NOTES/QUESTIONS TO THE CHEMIST). Since the dose is 1 capsule daily, the magnesium content of a single maximum recommended dose would be less than 8 mg. Therefore, statements regarding magnesium content are not required on the label per 21 CFR 201.71.

3. PATENTS/EXCLUSIVITIES

Appl No	Prod No	Patent No	Patent Expiration	Certification	Labeling Impact	Patent Use Code
021229	001	5690960	Nov 25, 2014	PIV	None	
021229	001	5753265	Jun 7, 2015	PIV	None	
021229	001	5817338	Oct 6, 2015	PIV	None	
021229	001	5900424	May 4, 2016	PIV	None	
021229	001	6403616	Nov 15, 2019	PIV	None	
021229	001	6428810	Nov 3, 2019	PIV	None	

Exclusivity Data

There is no unexpired exclusivity for this product.

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON
   - USP: No
   - NDA: Store at 20^0-25^0 (68^0-77^0F)
   - ANDA: Store at 20^0-25^0 (68^0-77^0F)

5. DISPENSING STATEMENT COMPARISON
   - NDA: Keep product out of high heat and humidity. Protect product from moisture.
   - ANDA: Keep product out of high heat and humidity. Protect product from moisture.

6. PACKAGE CONFIGURATION
   - NDA: 2-count samples
     unit dose cartons of 14
     unit dose cartons of 28 containing 2 inner cartons of 14
     unit dose cartons of 42 containing 3 inner cartons of 14
   - ANDA: unit dose cartons of 14 (2 x 7)
     unit dose cartons of 28 containing 2 inner cartons of 14 (2 x 7)
     unit dose cartons of 42 containing 3 inner cartons of 14 (2 x 7)
   - (b) (4)

7. CONTAINER/CLOSURE

Unit dose blister packs (7 count blisters)	(b) (4) (14's, 28's and 42's) **CRC** (b) (4)

The proposed container/closure systems comply with USP <661> and USP <671> requirements and all components used in these container/closure systems have been used in approved CDER products.

- Packaged in temper-evident packaging. Temper-evident statements are included on the carton labeling.

- Blister label has the statement "Separate at perforation. Peel at arrow. Push capsule through foil."

8. FINISHED DOSAGE FORM
20 mg: Off-white to brown colored enteric coated pellets (inclusive of all shades of yellow and pale brown) and a white to off-white, caplet shaped, biconvex, film coated tablet filled in size '0' hard gelatin (banded) capsule with opaque pink colored cap and opaque white colored body imprinted "OMP2O" on cap with black ink.

9. MANUFACTURER:
Dr. Reddy's Laboratories Limited, Bachepalli - 502 325, India.

10. Bioequivalence – Fasting and fed studies on 20 mg

11. Dissolution Test Method

From Division of Bioequivalence Dissolution Review signed on 9/24/2007:

3. The firm uses the following method and specifications:

Acid Stage:
(Acid resistance is measured from the dosage form and not from an aliquot of 0.1N HCl):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.1N HCl @ 37ºC
Volume: 300mL
Time: 2h
Specification: NMT (b) (4) of the labeled amount of omeprazole is dissolved at the end of the acid stage.

Buffer Stage:
(Fresh capsules are assayed and are from the same lot tested for acid resistance. Drug release measured from an aliquot of the phosphate buffer.):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.05M Na3PO4, pH 6.8 @ 37ºC
Volume: 1000mL
Time: 10, 20, 30, and 45 minutes

Specification: NLT (b) (4) (Q) of the labeled amount of omeprazole is dissolved in 30 minutes.

NOTE: Each dosage unit is subjected to acid stage conditions for 2h. At the end of the acid stage, 0.1N HCl is drained from the vessel and 1000mL of 37°C 0.05M Na3PO4 buffer, pH 6.8, is added to begin the buffer stage testing.

4. The method utilized by the firm is essentially the same as the FDA-recommended method for Omeprazole Magnesium Tablets, DR (OTC). The only difference between the two methods is in the approach used for buffer stage testing. Specifically, the firm's method calls for the 300mL of 0.1N HCl to be drained from the vessel at the end of the acid stage and replaced with 1000mL of 0.05M Na3PO4, pH 6.8. In contrast, the FDA recommended method (OTC DR tablets) calls for 700mL of 0.086M Na2HPO4 to be added to the 300mL of 0.1N HCl already in the vessel at the end of the acid stage to yield 1000mL of pH 6.8 buffer. The firm's proposed method is **acceptable** since it is very similar to the FDA-recommended method for the OTC DR Tablets.

12. The word "New" appears on the carton labeling. In the April 22, 2009 amendment, the firm states the following. "We propose the use of "New" flag for six months duration only…Subsequently the label will be revised to delete the "New" flag." This ANDA is the first generic based on a suitability petition of a change in dosage form from a DR TABLET to DR CAPSULE. No capsule formulations of Omeprazole are in the OTC section of the Orange Book. Therefore, the firm was allowed keep "New" on the carton labeling for 6 months.

Primary Reviewer: Sarah Park

Team Leader: Koung Lee

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

/s/

Soojung Sarah Park
5/19/2009 09:53:30 AM
LABELING REVIEWER

Koung Lee
5/20/2009 05:10:36 PM
LABELING REVIEWER
For Wm Peter Rickman

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078878

CHEMISTRY REVIEWS

ANDA 78-878

Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)

Dr. Reddy's Laboratories Inc.

Damaris Maldonado
Office of Generic Drugs/Division of Chemistry II

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-878

2. REVIEW #: 1

3. REVIEW DATE: June 26, 2007.

4. REVIEWER: Damaris Maldonado

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
N/A	

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original Submission	March 16, 2007.

7. NAME & ADDRESS OF APPLICANT:

Name:	Dr. Reddy's Laboratories Inc. U.S. Agent for: Dr. Reddy's Laboratories, Inc. 200 Somerset Corporate Blvd., 7th floor Bridgewater, NJ 08807
Representative:	Kumara Sekar Ph.D., Director, Global Regulatory Affairs and Compliance
Telephone:	(908)203-4937
Fax	(908)203-4980

8. DRUG PRODUCT NAME/CODE/TYPE:
   a) Proprietary Name: NA
   b) Non-Proprietary Name (USAN): Omeprazole Magnesium Delayed-Release Capsules

9. LEGAL BASIS FOR SUBMISSION:
The basis for Dr. Reddy's proposed Omeprazole Magnesium Delayed Release Capsules is the RLD Prilosec® OTC Tablets, the subject of NDA # 21-229 held by Astra Zeneca. The firm filed a Paragraph III certification for patents 4,786,505 and 4,853,230 that

expire on October 20, 2007. There are no exclusivities for this product. The firm also filed a Paragraph IV certification for six un-expired patents.

In addition, a petition was filed to FDA for a change in the dosage form from that of the listed drug product (from tablets to capsules) and it was approved under the petition docket number 2004P-0373/CP1.

10. PHARMACOL. CATEGORY: Anti-ulcer

11. DOSAGE FORM: Oral Capsule

12. STRENGTH/POTENCY: 20 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _ __Rx _X__OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

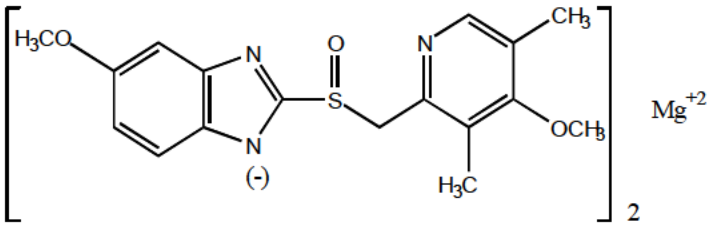
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name: Bis-5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2- pyridinyl) methyl]sulfinyl]-1H-benzimidazole Magnesium

Molecular weight: 713.1 (anhydrous)

Chemical Formula: $(C_{17}H_{18}N_3O_3S)_2Mg$

Chemical structure:



17. RELATED/SUPPORTING DOCUMENTS:

Chemistry Review Data Sheet

A. DMFs

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
17706	II	Dr Reddy	Omeprazole Magnesium	1	Inadequate		
(b) (4)	IV		(b) (4)	4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			
	III			4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
Review	21-229	Prilosec OTC
Review		(b) (4)
Review	78-693	Omeprazole 20 mg & 40 mg

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Acceptable	8-8-06	S. Adams
Methods Validation	N/A		
Labeling			
Bioequivalence			
EA	Exclusion		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

Chemistry Assessment

The Chemistry Review for ANDA 78-878

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not Approvable (MINOR

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, omeprazole magnesium, is non-compendial. The magnesium salt of omeprazole is an off-white to light brown colored powder, slightly soluble in water, methanol and freely soluble in N,N Dimethylformamide. Omeprazole properties are well known; it has two pKas, at ~4 (due to pyridinium ion) and at 8.1 (due to benzimidazole). Half life is highly pH dependent in aqueous solution. According to the information included in NDA (21-229) omeprazole magnesium used in Prilosec® OTC is crystalline in nature. AstraZeneca has a patent on the crystalline form of Omeprazole magnesium, Dr. Reddy will use the (b) (4).

Dr. Reddy currently markets the 10 mg and 20 mg capsules as approved under ANDA 75-576 using a different formulation and trade dress. The firm has submitted (b) (4). The basis for the ANDA submission is the Prilosec® OTC drug product, which is marketed in tablets (enteric coated pellets compressed into a tablet called a MUPS tablet of "multiple unit pellet system"). A suitability petition was approved for the corresponding ANDA change to OTC capsules. Each capsule contains 20.6 mg of omeprazole magnesium which is equivalent to 20 mg of omeprazole.

The drug product contains enteric coated pellets (b) (4) filled into capsules. (b) (4). The drug product will be packaged into (b) (4) (b) (4) aluminum foil blisters. Accelerated and room temperature stability testing support the firm's 24 month expiration dating period.

B. Description of How the Drug Product is Intended to be Used

See Labeling

Following this page, 14 pages withheld in full (b)(4)

(b) (4)

[redacted]

30. MICROBIOLOGY: NA

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS
NA

32. LABELING
Pending

33. ESTABLISHMENT INSPECTION
Acceptable 8-8-06.

34. BIOEQUIVALENCE
Pending

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

Chemistry Assessment

The firm requests a categorical exclusion from the requirement of an Environmental Assessment Statement or Environmental Impact Statement in accord with 21 CFR 25.31(a).

Chemistry Assessment

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-878
APPLICANT: Dr. Reddy's Laboratories Limited
DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. DMF #17706 for Omeprazole Magnesium has been reviewed and found inadequate. The DMF holder has been notified.

2. There seems to be a discrepancy between [redacted] (b) (4) . Please clarify this apparent discrepancy.

3. Omeprazole Magnesium has a known chiral center in the sulfinyl group. No information or specification was provided indicating [redacted] (b) (4) . Please clarify.

4. The specification for [redacted] (b) (4)

5. [redacted] (b) (4)

6. Please note that [redacted] (b) (4)

7. [redacted] (b) (4)

8. Your executed and blank batch records [redacted] (b) (4)

9. Please acknowledg [redacted] (b) (4) .

10. [redacted]

11. Please indicate [redacted].

12. Please note that pages 10005-6 of your ANDA submission list a commercial batch size of [redacted] capsules.

13. It was noted that [redacted] Please clarify.

14. We recommend that you [redacted]

15. Please note that your formulation incorporates [redacted].

16. The physical description of the pellets as described in the in-process information included on pages 11411 and 11413 [redacted] is not in agreement with the description presented on page 10680 (p. 121 of the commercial batch record: [redacted]). Please clarify this apparent discrepancy and provide a physical description of the film coated enteric pellets.

17. We recommend that [redacted]

18. Please address [redacted]

19. It is recommended that [redacted].

20. It is recommended that [redacted].

21. Please provide [redacted].

22. We recommend that [redacted].

23. Please incorporate [redacted]

24. Please clarify (b) (4) Please provide assurance that your policy for expiration dating is in accordance with CDER Guidelines.

25. In addition to the standard USP acid/buffer 2-stage dissolution testing, please provide comparative dissolution profiles of your proposed drug product formulation versus the reference listed drug, Prilosec® OTC, using acid stage testing performed in pH media around the critical solubility pH of the enteric coating. It is suggested that such acid stage testing be conducted over a pH range of 4.0-6.0 (i.e., testing at pH 4.0, 4.5, 5.0, 5.5 and 6.0) for two hours, followed by testing in USP buffer media, pH 6.8. Finally, it is recommended that the amount released during the buffer stage testing at pH 6.8 be determined after 30 minutes and 60 minutes.

B. Additional comments:

1. The labeling and bioequivalence portions of your application are under review. Deficiencies, if any, will be conveyed to you under separate cover.

2. Please provide updated stability data for the exhibit batch.

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 78-878
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-641/DMaldonado/7/09/07

HFD-640/SFurness/7/18/07

HFD-617/TLiu/7/20/07

F/T by:

V:\Firmsnz\reddy\Ltrs&Rev\78-878r1

TYPE OF LETTER: NOT APPROVABLE

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

/s/

Damaris Maldonado
7/24/2007 07:28:53 AM
CHEMIST

Theresa Liu
7/24/2007 09:39:48 AM
CSO

Michael S Furness
7/26/2007 03:14:14 PM
CHEMIST

ANDA 78-878

Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)

Dr. Reddy's Laboratories Inc.

Shahnaz Read
Office of Generic Drugs/Division of Chemistry II

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-878

2. REVIEW #: 2

3. REVIEW DATE: March 10, 2008

4. REVIEWER: Shahnaz Read

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	March 16, 2007
Review #1 (Minor)	June 26, 2007

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor Amendment	December 4, 2007

7. NAME & ADDRESS OF APPLICANT:

Name:	Dr. Reddy's Laboratories Inc. U.S. Agent for: Dr. Reddy's Laboratories, Inc. 200 Somerset Corporate Blvd., 7th floor Bridgewater, NJ 08807
Representative:	Kumara Sekar Ph.D., Director, Global Regulatory Affairs and Compliance
Telephone:	(908)203-4937
Fax	(908)203-4980

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA

b) Non-Proprietary Name (USAN): Omeprazole Magnesium Delayed-Release Capsules

9. LEGAL BASIS FOR SUBMISSION:

The basis for Dr. Reddy's proposed Omeprazole Magnesium Delayed Release Capsules is the RLD Prilosec® OTC Tablets, the subject of NDA # 21-229 held by Astra Zeneca. The firm filed a Paragraph III certification for patents 4,786,505 and 4,853,230 that

expire on October 20, 2007. There are no exclusivities for this product. The firm also filed a Paragraph IV certification for six un-expired patents.

In addition, a petition was filed to FDA for a change in the dosage form from that of the listed drug product (from tablets to capsules) and it was approved under the petition docket number 2004P-0373/CP1.

10. PHARMACOL. CATEGORY: Anti-ulcer

11. DOSAGE FORM: Oral Capsule

12. STRENGTH/POTENCY: 20 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx __X__OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

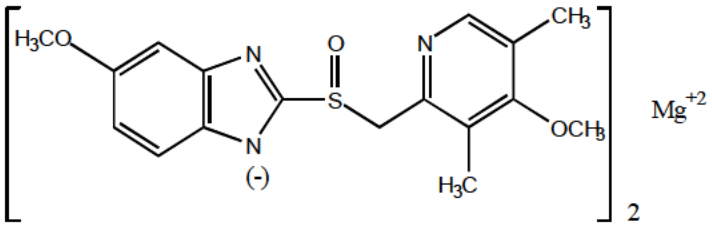
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name: Bis-5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2- pyridinyl) methyl]sulfinyl]-1H-benzimidazole Magnesium

Molecular weight: 713.1 (anhydrous)

Chemical Formula: $(C_{17}H_{18}N_3O_3S)_2Mg$

Chemical structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
17706	II	Dr Reddy	Omeprazole Magnesium	1	adequate	3/6/08	
(b) (4)	IV		(b) (4)	4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Acceptable	6/5/07	S. Adams
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Exclusion		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

Chemistry Assessment

The Chemistry Review for ANDA 78-878

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not Approvable (MINOR)

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, omeprazole magnesium, is non-compendial. The magnesium salt of omeprazole is an off-white to light brown colored powder, slightly soluble in water, methanol and freely soluble in N,N Dimethylformamide. Omeprazole properties are well known; it has two pKas, at ~4 (due to pyridinium ion) and at 8.1 (due to benzimidazole). Half life is highly pH dependent in aqueous solution. According to the information included in NDA (21-229) omeprazole magnesium used in Prilosec® OTC is crystalline in nature. AstraZeneca has a patent on the crystalline form of Omeprazole magnesium, Dr. Reddy will use the (b) (4) form.

Dr. Reddy currently markets the 10 mg and 20 mg capsules as approved under ANDA 75-576 using a different formulation and trade dress. The firm has submitted (b) (4) . The basis for the ANDA submission is the Prilosec® OTC drug product, which is marketed in tablets (enteric coated pellets compressed into a tablet called a MUPS tablet of "multiple unit pellet system"). A suitability petition was approved for the corresponding ANDA change to OTC capsules. Each capsule contains 20.6 mg of omeprazole magnesium which is equivalent to 20 mg of omeprazole.

The drug product contains enteric coated pellets (b) (4) filled into capsules. (b) (4) . The drug product will be packaged into (b) (4) aluminum foil blisters. Accelerated and room temperature stability testing support the firm's 24 month expiration dating period.

B. Description of How the Drug Product is Intended to be Used

According to the product Insert:
How to Take Omeprazole Magnesium Delayed-Release Capsules
14-Day Course of Treatment

- Swallow. 1 capsule with a glass of water before eating in the morning
- Take every day for 14 days
- Do not take more than 1 capsule a day
- Do not chew or crush the capsules
- Do not crush capsules in food
- Do not use for more than 14 days unless directed by your doctor

It is important not to chew or crush these capsules, or crush the capsules in food. A 14-day course of therapy may be repeated every 4 months.

C. Basis for Approvability or Not-Approval Recommendation

Firm needs to resolve issues related to drug product specifications, manufacture, and other deficiencies as noted in the deficiency letter.

Following this page, 17 pages withheld in full (b)(4)

(b) (4)

30. MICROBIOLOGY: NA

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS
NA

32. LABELING
Pending

33. ESTABLISHMENT INSPECTION
Acceptable 6/5/07.

34. BIOEQUIVALENCE
Pending

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
The firm requests a categorical exclusion from the requirement of an Environmental Assessment Statement or Environmental Impact Statement in accord with 21 CFR 25.31(a).

Chemistry Assessment

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-878
APPLICANT: Dr. Reddy's Laboratories Limited
DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. Although your pellets are screened after every step, [redacted] (b) (4) .

2. You have provided results for [redacted] (b) (4) .

3. Your finished product [redacted] (b) (4) .

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 78-878
DIV FILE
Field Copy

Endorsements

HFD-641/SRead/3/10/08

HFD-640/DMaldonado /3/13/08

HFD-617/TLiu/3/13/08

TYPE OF LETTER: NOT APPROVABLE

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

/s/

Shanaz Read
3/14/2008 10:08:04 AM
CHEMIST

Theresa Liu
3/14/2008 10:25:34 AM
CSO

Damaris Maldonado
3/14/2008 12:05:07 PM
CHEMIST

ANDA 78-878

Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)

Dr. Reddy's Laboratories Inc.

Shahnaz Read
Office of Generic Drugs/Division of Chemistry II

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-878

2. REVIEW #: 3

3. REVIEW DATE: June 27, 2008

4. REVIEWER: Shahnaz Read

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	March 16, 2007
Review #1 (Minor)	June 26, 2007
Minor Amendment	December 4, 2007
Review #2	March 10, 2008

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor Amendments	April 30, 2008 and May 20, 2008

7. NAME & ADDRESS OF APPLICANT:

Name:	Dr. Reddy's Laboratories Inc. U.S. Agent for: Dr. Reddy's Laboratories, Inc. 200 Somerset Corporate Blvd., 7th floor Bridgewater, NJ 08807
Representative:	Kumara Sekar Ph.D., Director, Global Regulatory Affairs and Compliance
Telephone:	(908)203-4937
Fax	(908)203-4980

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA

b) Non-Proprietary Name (USAN): Omeprazole Magnesium Delayed-Release Capsules

9. LEGAL BASIS FOR SUBMISSION:

The basis for Dr. Reddy's proposed Omeprazole Magnesium Delayed Release Capsules is the RLD Prilosec® OTC Tablets, the subject of NDA # 21-229 held by Astra Zeneca. The firm filed a Paragraph III certification for patents 4,786,505 and 4,853,230 that expire on October 20, 2007. There are no exclusivities for this product. The firm also filed a Paragraph IV certification for six un-expired patents.

In addition, a petition was filed to FDA for a change in the dosage form from that of the listed drug product (from tablets to capsules) and it was approved under the petition docket number 2004P-0373/CP1.

10. PHARMACOL. CATEGORY: Anti-ulcer

11. DOSAGE FORM: Oral Capsule

12. STRENGTH/POTENCY: 20 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx __X__OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

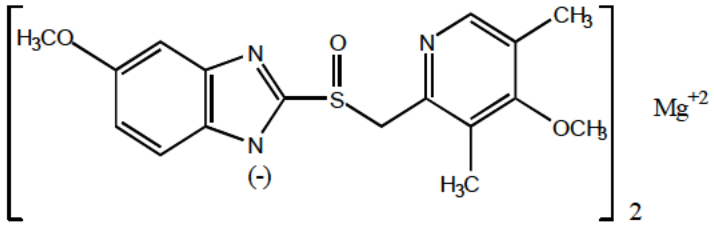
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name: Bis-5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2- pyridinyl) methyl]sulfinyl]-1H-benzimidazole Magnesium

Molecular weight: 713.1 (anhydrous)

Chemical Formula: $(C_{17}H_{18}N_3O_3S)_2Mg$

Chemical structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
17706	II	Dr Reddy	Omeprazole Magnesium	1	adequate	3/6/08	
(b) (4)	IV		(b) (4)	4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Acceptable	6/5/07	S. Adams
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Exclusion		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

Chemistry Assessment

The Chemistry Review for ANDA 78-878

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not Approvable (MINOR)

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, omeprazole magnesium, is non-compendial. The magnesium salt of omeprazole is an off-white to light brown colored powder, slightly soluble in water, methanol and freely soluble in N,N Dimethylformamide. Omeprazole properties are well known; it has two pKas, at ~4 (due to pyridinium ion) and at 8.1 (due to benzimidazole). Half life is highly pH dependent in aqueous solution. According to the information included in NDA (21-229) omeprazole magnesium used in Prilosec® OTC is crystalline in nature. AstraZeneca has a patent on the crystalline form of Omeprazole magnesium, Dr. Reddy will use the (b) (4) form.

Dr. Reddy currently markets the 10 mg and 20 mg capsules as approved under ANDA 75-576 using a different formulation and trade dress. The firm has submitted (b) (4) . The basis for the ANDA submission is the Prilosec® OTC drug product, which is marketed in tablets (enteric coated pellets compressed into a tablet called a MUPS tablet of "multiple unit pellet system"). A suitability petition was approved for the corresponding ANDA change to OTC capsules. Each capsule contains 20.6 mg of omeprazole magnesium which is equivalent to 20 mg of omeprazole.

The drug product contains enteric coated pellets (b) (4) filled into capsules. (b) (4) . The drug product will be packaged into (b) (4) aluminum foil blisters. Accelerated and room temperature stability testing support the firm's 24 month expiration dating period.

B. Description of How the Drug Product is Intended to be Used

According to the product Insert:
How to Take Omeprazole Magnesium Delayed-Release Capsules
14-Day Course of Treatment

- Swallow. 1 capsule with a glass of water before eating in the morning
- Take every day for 14 days
- Do not take more than 1 capsule a day
- Do not chew or crush the capsules
- Do not crush capsules in food
- Do not use for more than 14 days unless directed by your doctor

It is important not to chew or crush these capsules, or crush the capsules in food. A 14-day course of therapy may be repeated every 4 months.

C. Basis for Approvability or Not-Approval Recommendation

Firm needs to provide USP <467> information for drug product.

Following this page, 17 pages withheld in full (b)(4)

(b) (4)

30. MICROBIOLOGY: NA

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS
NA

32. LABELING
Pending

33. ESTABLISHMENT INSPECTION
Acceptable 6/5/07.

34. BIOEQUIVALENCE
Pending

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

The firm requests a categorical exclusion from the requirement of an Environmental Assessment Statement or Environmental Impact Statement in accord with 21 CFR 25.31(a).

Chemistry Assessment

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-878 APPLICANT: Dr. Reddy's Laboratories Limited
DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. We recommend that [redacted] (b) (4) .

2. With USP<467> Residual Solvents going into effect July 1, 2008, please include information to demonstrate compliance with the chapter. A complete submission for this purpose should consist of the following:

   For each excipient in the formulation:
   - manufacturer's statement or COA including solvents
   - applicant's updated COA for the excipient including solvent specification (solvent identity, acceptance criteria and analytical method). Class 3 solvents are also to be named. Loss on drying would be acceptable if only Class 3 solvents are used in the manufacture of an ingredient.
   - applicant's test data for solvents, including data for class 3 solvents, should be submitted for the excipient
   - method validation data if non-USP methods are used
   - upon vendor validation, applicant may accept manufacturer's COA
   - applicant to demonstrate the excipient meets ICH Q3C option 1 or option 2

   If a solvent is used in the manufacturing process, the applicant should have already included a solvent specification in the finished product specification.

   The finished product specification should be updated to state compliance with USP<467>.

3. Please provide updated stability data.

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 78-878
DIV FILE
Field Copy

Endorsements

HFD-641/SRead/6/27/08

HFD-640/DMaldonado /7/17/08

HFD-617/TLiu/7/18/08

TYPE OF LETTER: NOT APPROVABLE

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

/s/

Shanaz Read
7/29/2008 10:15:44 AM
CHEMIST

Theresa Liu
7/29/2008 10:31:59 AM
CSO

Damaris Maldonado
7/29/2008 10:55:06 AM
CHEMIST

ANDA 78-878

Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)

Dr. Reddy's Laboratories Inc.

Shahnaz Read
Office of Generic Drugs/Division of Chemistry II

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-878

2. REVIEW #: 4

3. REVIEW DATE: February 2, 2009

4. REVIEWER: Shahnaz Read

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	March 16, 2007
Review #1 (Minor)	June 26, 2007
Minor Amendment	December 4, 2007
Review #2	March 10, 2008
Minor Amendments	April 30, 2008 and May 20, 2008
Review #3	June 27, 2008

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor Amendments	July 21 and September 17, 2008

7. NAME & ADDRESS OF APPLICANT:

Name:	Dr. Reddy's Laboratories Inc. U.S. Agent for: Dr. Reddy's Laboratories, Inc. 200 Somerset Corporate Blvd., 7th floor Bridgewater, NJ 08807
Representative:	Kumara Sekar Ph.D., Director, Global Regulatory Affairs and Compliance
Telephone:	(908)203-4937
Fax	(908)203-4980

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA

b) Non-Proprietary Name (USAN): Omeprazole Magnesium Delayed-Release Capsules

9. LEGAL BASIS FOR SUBMISSION:

The basis for Dr. Reddy's proposed Omeprazole Magnesium Delayed Release Capsules is the RLD Prilosec® OTC Tablets, the subject of NDA # 21-229 held by Astra Zeneca. The firm filed a Paragraph III certification for patents 4,786,505 and 4,853,230 that expire on October 20, 2007. There are no exclusivities for this product. The firm also filed a Paragraph IV certification for six un-expired patents.

In addition, a petition was filed to FDA for a change in the dosage form from that of the listed drug product (from tablets to capsules) and it was approved under the petition docket number 2004P-0373/CP1.

10. PHARMACOL. CATEGORY: Anti-ulcer

11. DOSAGE FORM: Oral Capsule

12. STRENGTH/POTENCY: 20 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx __X__OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

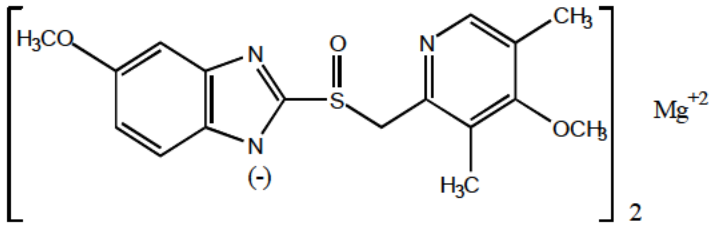
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name: Bis-5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2- pyridinyl) methyl]sulfinyl]-1H-benzimidazole Magnesium

Molecular weight: 713.1 (anhydrous)

Chemical Formula: $(C_{17}H_{18}N_3O_3S)_2Mg$

Chemical structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
17706	II	Dr Reddy	Omeprazole Magnesium	1	adequate	3/6/08	
(b) (4)	IV		(b) (4)	4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Acceptable	9/2908	S. Adams
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Acceptable	8/19/08	
EA	Categorical Exclusion		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

Chemistry Assessment

The Chemistry Review for ANDA 78-878

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Not Approvable (MINOR)

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, omeprazole magnesium, is non-compendial. The magnesium salt of omeprazole is an off-white to light brown colored powder, slightly soluble in water, methanol and freely soluble in N,N Dimethylformamide. Omeprazole properties are well known; it has two pKas, at ~4 (due to pyridinium ion) and at 8.1 (due to benzimidazole). Half life is highly pH dependent in aqueous solution. According to the information included in NDA (21-229) omeprazole magnesium used in Prilosec® OTC is crystalline in nature. AstraZeneca has a patent on the crystalline form of Omeprazole magnesium, Dr. Reddy will use the (b) (4) form.

Dr. Reddy currently markets the 10 mg and 20 mg capsules as approved under ANDA 75-576 using a different formulation and trade dress. (b) (4) . The basis for the ANDA submission is the Prilosec® OTC drug product, which is marketed in tablets (enteric coated pellets compressed into a tablet called a MUPS tablet of "multiple unit pellet system"). A suitability petition was approved for the corresponding ANDA change to OTC capsules. Each capsule contains 20.6 mg of omeprazole magnesium which is equivalent to 20 mg of omeprazole.

The drug product contains enteric coated pellets (b) (4) filled into capsules. (b) (4) . The drug product will be packaged into (b) (4) aluminum foil blisters. Accelerated and room temperature stability testing support the firm's 24 month expiration dating period.

B. Description of How the Drug Product is Intended to be Used

According to the product Insert:
How to Take Omeprazole Magnesium Delayed-Release Capsules
14-Day Course of Treatment

- Swallow. 1 capsule with a glass of water before eating in the morning
- Take every day for 14 days
- Do not take more than 1 capsule a day
- Do not chew or crush the capsules
- Do not crush capsules in food
- Do not use for more than 14 days unless directed by your doctor

It is important not to chew or crush these capsules, or crush the capsules in food. A 14-day course of therapy may be repeated every 4 months.

C. Basis for Approvability or Not-Approval Recommendation

Firm needs to provide USP <467> information for drug product.

Following this page, 21 pages withheld in full (b)(4)

(b) (4)

[redacted]

30. MICROBIOLOGY: NA

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS
NA

32. LABELING
Pending

33. ESTABLISHMENT INSPECTION
Acceptable 9/2/08.

34. BIOEQUIVALENCE
Acceptable 8/19/08

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
The firm requests a categorical exclusion from the requirement of an Environmental Assessment Statement or Environmental Impact Statement in accord with 21 CFR 25.31(a).

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-878 **APPLICANT:** Dr. Reddy's Laboratories Limited

DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. For excipients [redacted] (b) (4)
2. Please set specifications for [redacted] (b) (4)
3. Please provide the methods used for the analysis of residual solvents in the excipients along with verification for USP methods and validation for non USP methods.
4. It is recommended that identification of finished product should include [redacted] (b) (4)
5. Please provide f_2 for dissolution results of [redacted] (b) (4)
6. Please provide updated stability data for [redacted] (b) (4)

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 78-878
DIV FILE
Field Copy

Endorsements

HFD-641/SRead/2/2/09

HFD-640/DMaldonado/3/2/09

HFD-617/TLiu/3/16/09

TYPE OF LETTER: NOT APPROVABLE

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

/s/

Shanaz Read
3/16/2009 02:45:38 PM
CHEMIST

Theresa Liu
3/16/2009 03:16:43 PM
CSO

Damaris Maldonado
3/17/2009 12:33:09 PM
CHEMIST

ANDA 78-878

Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)

Dr. Reddy's Laboratories Inc.

Shahnaz Read
Office of Generic Drugs/Division of Chemistry II

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-878

2. REVIEW #: 5

3. REVIEW DATE: April 15, 2009, revised June 3, 2009

4. REVIEWER: Shahnaz Read

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original Submission	March 16, 2007
Review #1 (Minor)	June 26, 2007
Minor Amendment	December 4, 2007
Review #2	March 10, 2008
Minor Amendments	April 30, 2008 and May 20, 2008
Review #3	June 27, 2008
Minor Amendments	July 21 and September 17, 2008
Review #4	February 2, 2009

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor Amendment	March 25, 2009
Telephone Amendments	April 10, 2009, April 20, 2009 and June 2, 2009

7. NAME & ADDRESS OF APPLICANT:

Name:	Dr. Reddy's Laboratories Inc. U.S. Agent for: Dr. Reddy's Laboratories, Inc. 200 Somerset Corporate Blvd., 7th floor Bridgewater, NJ 08807
Representative:	Kumara Sekar Ph.D., Director, Global Regulatory Affairs and Compliance
Telephone:	(908)203-4937
Fax	(908)203-4980

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA
b) Non-Proprietary Name (USAN): Omeprazole Magnesium Delayed-Release Capsules

9. LEGAL BASIS FOR SUBMISSION:
The basis for Dr. Reddy's proposed Omeprazole Magnesium Delayed Release Capsules is the RLD Prilosec® OTC Tablets, the subject of NDA # 21-229 held by Astra Zeneca. The firm filed a Paragraph III certification for patents 4,786,505 and 4,853,230 that expire on October 20, 2007. There are no exclusivities for this product. The firm also filed a Paragraph IV certification for six un-expired patents.

In addition, a petition was filed to FDA for a change in the dosage form from that of the listed drug product (from tablets to capsules) and it was approved under the petition docket number 2004P-0373/CP1.

10. PHARMACOL. CATEGORY: Anti-ulcer

11. DOSAGE FORM: Delayed Release Capsule

12. STRENGTH/POTENCY: 20 mg

13. ROUTE OF ADMINISTRATION: Oral

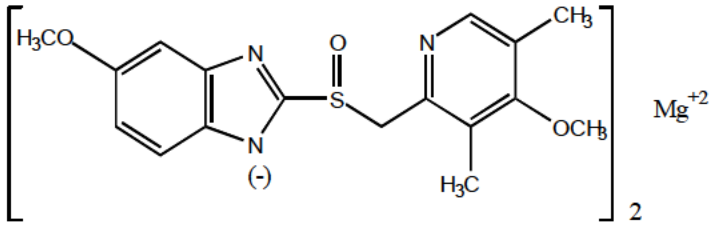
14. Rx/OTC DISPENSED: ___Rx __X__OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
Chemical name: Bis-5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2- pyridinyl) methyl]sulfinyl]-1H-benzimidazole Magnesium
Molecular weight: 713.1 (anhydrous)
Chemical Formula: $(C_{17}H_{18}N_3O_3S)_2Mg$
Chemical structure:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
17706	II	Dr Reddy	Omeprazole Magnesium	1	adequate	4/15/09	
(b) (4)	IV		(b) (4)	4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		
	III			4	NA		

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NA		

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	NA		
EES	Acceptable	9/29/08	S. Adams
Methods Validation	N/A		
Labeling	Acceptable	5/7/09	S. Park
Bioequivalence	Acceptable	8/19/08	
EA	Categorical Exclusion		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

Chemistry Assessment

The Chemistry Review for ANDA 78-878

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable for CMC

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, omeprazole magnesium, is compendial. The magnesium salt of omeprazole is an off-white to light brown colored powder, slightly soluble in water, methanol and freely soluble in N,N Dimethylformamide. Omeprazole properties are well known; it has two pKas, at ~4 (due to pyridinium ion) and at 8.1 (due to benzimidazole). Half life is highly pH dependent in aqueous solution. According to the information included in NDA (21-229) omeprazole magnesium used in Prilosec® OTC is crystalline in nature. AstraZeneca has a patent on the crystalline form of Omeprazole magnesium, Dr. Reddy will use the (b) (4) form.

Dr. Reddy currently markets the 10 mg and 20 mg capsules as approved under ANDA 75-576 using a different formulation and trade dress. (b) (4) . The basis for the ANDA submission is the Prilosec® OTC drug product, which is marketed in tablets (enteric coated pellets compressed into a tablet called a MUPS tablet of "multiple unit pellet system"). A suitability petition was approved for the corresponding ANDA change to OTC capsules. Each capsule contains 20.6 mg of omeprazole magnesium which is equivalent to 20 mg of omeprazole.

The drug product contains enteric coated pellets (b) (4) filled into capsules. (b) (4) . The drug product will be packaged into (b) (4) aluminum foil blisters. Accelerated and room temperature stability testing support the firm's 24 month expiration dating period.

B. Description of How the Drug Product is Intended to be Used

According to the product Insert:
How to Take Omeprazole Magnesium Delayed-Release Capsules
14-Day Course of Treatment

- Swallow. 1 capsule with a glass of water before eating in the morning
- Take every day for 14 days
- Do not take more than 1 capsule a day
- Do not chew or crush the capsules
- Do not crush capsules in food
- Do not use for more than 14 days unless directed by your doctor

It is important not to chew or crush these capsules, or crush the capsules in food. A 14-day course of therapy may be repeated every 4 months.

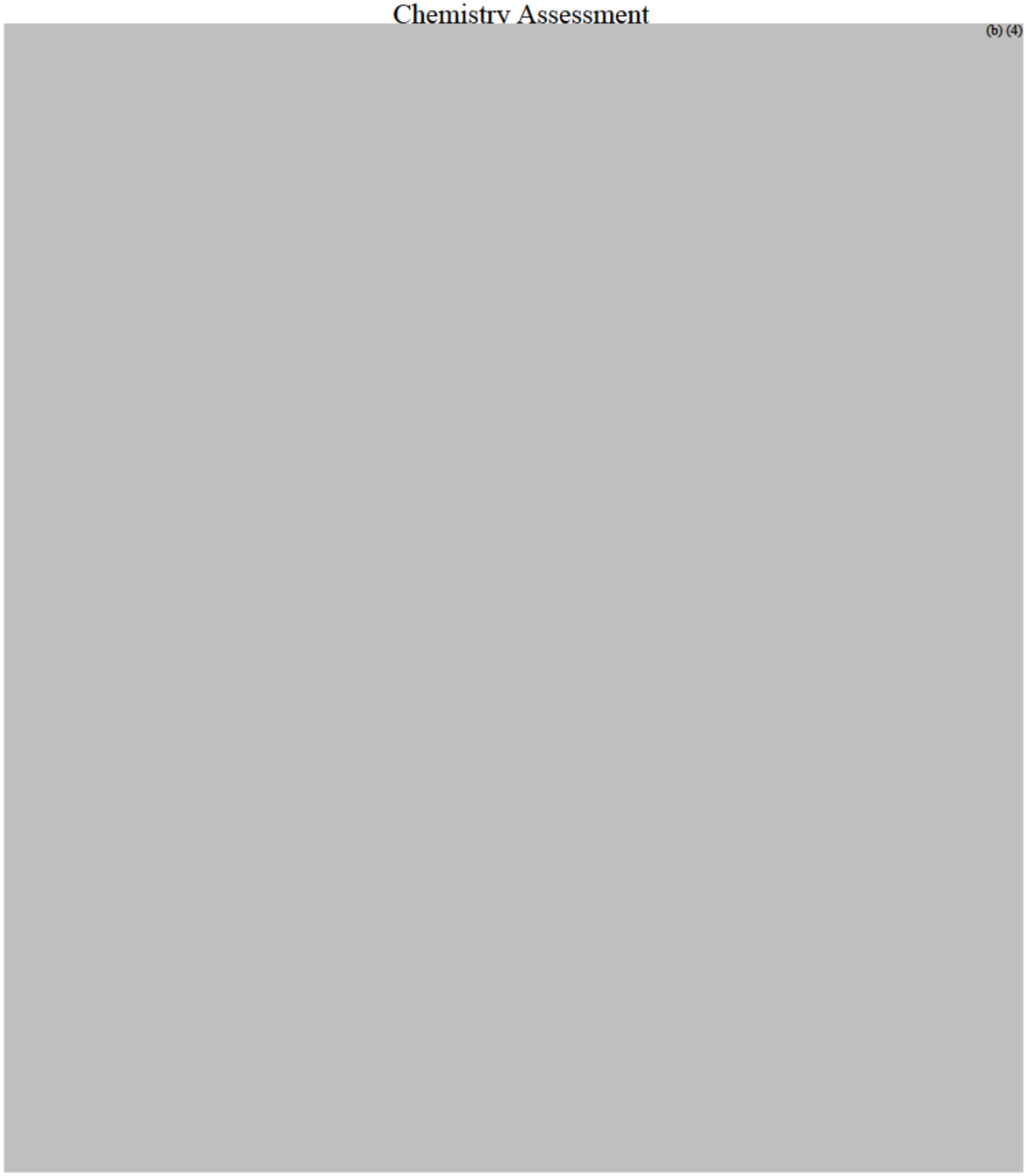
C. Basis for Approvability or Not-Approval Recommendation

All CMC issues have been resolved.

Following this page, 22 pages withheld in full (b)(4)

Chemistry Assessment

(b) (4)



30. MICROBIOLOGY: NA

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS
NA

32. LABELING
Acceptable 5/7/09.

33. ESTABLISHMENT INSPECTION
Acceptable 9/2/08.

34. BIOEQUIVALENCE

Acceptable 8/19/08

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:

The firm requests a categorical exclusion from the requirement of an Environmental Assessment Statement or Environmental Impact Statement in accord with 21 CFR 25.31(a).

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

None

cc: ANDA 78-878
DIV FILE
Field Copy

Endorsements

HFD-641/SRead/4/15/09, 6/3/09

HFD-640/DMaldonado/4/20/09

HFD-617/TLiu/5/7/09

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

/s/

Shanaz Read
6/3/2009 03:08:26 PM
CHEMIST
Updated review

Damaris Maldonado
6/4/2009 02:25:06 PM
CHEMIST

Theresa Liu
6/5/2009 11:24:55 AM
CSO

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078878

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE DISSOLUTION REVIEW

ANDA No.	078878	
Drug Product Name	Omeprazole Magnesium Delayed-Release Capsules	
Strength (s)	eq. to 20mg base	
Applicant Name	Dr. Reddy's Laboratories	
Address	200 Somerset Corporate Boulevard 7th Floor Bridgewater, NJ 08807	
Applicant's Point of Contact	Dr. Kumara Sekar	
Contact's Phone Number	908-203-4937	
Contact's Fax Number	908-203-4980	
Submission Date(s)	March 16, 2007	
First Generic	Yes	
Reviewer	Utpal M. Munshi, Ph.D.	
Study Number (s)	3701/06-07	
Study Type (s)	Fasted	
Strength(s)	20mg	
Clinical Site	Vimta Labs Ltd.	
Clinical Site Address	142, IDA, Phase II, Cherlapally Hyderabad-500 051 India	
Analytical Site	Vimta Labs Ltd.	
Analytical Address	142, IDA, Phase II, Cherlapally Hyderabad-500 051 India	
Study Number (s)	7002/06-07	
Study Type (s)	Fed	
Strength (s)	20mg	
Clinical Site	Wellquest Clinical Research; Clinical Section	
Clinical Address	Wellspring Hospital (4th Floor) Ganpatrao Kadam Marg Lower Parel Mumbai-400 013 (India)	
Analytical Site	(b) (4)	
Analytical Address		

I. EXECUTIVE SUMMARY

This is a review of the dissolution testing data only.

There is no reference product for this OTC DR capsule. However, Astra Zeneca's Prilosec OTC (Omeprazole Magnesium DR TABLET eq 20 mg base NDA 021229) was cited as the reference based on a change in dosage form (DR tablet OTC to DR capsule OTC) approved under Citizen Petition 2004P-0373/CP1. There is no USP or FDA-recommended method for the DR capsule (OTC). However, the public and internal dissolution databases describe a method for Omeprazole Magnesium DR tablets, OTC. The firm submitted dissolution testing data with a method that is essentially the same as that in the databases. As a result, the DBE finds the firm's method acceptable. On the basis of the dissolution data, the DBE also accepts the firm's specification (NMT (b) (4) is dissolved at the end of the acid stage; NLT (b) (4) Q) is dissolved in 30 minutes of the buffer stage). The DBE acknowledges that the firm will conduct dissolution testing with the method and specification given in their application.

As a result of the above, the *in vitro* dissolution studies conducted by the firm are **acceptable.**

The DBE will review the fasted and fed BE studies at a later date.

Table 1: SUBMISSION CONTENT CHECKLIST

Information			YES	NO	N/A
Did the firm use the FDA-recommended dissolution method			☐	☐	X
Did the firm use the USP dissolution method			☐	☐	X
Did the firm use 12 units of both test and reference in dissolution testing			☐	X	☐
Did the firm provide complete dissolution data (all raw data, range, mean, % CV, dates of dissolution testing)			☐	X	☐
Did the firm conduct dissolution testing with its own proposed method			X	☐	☐
Is FDA method in the public dissolution database (on the web)			☐	☐	X
SAS datasets submitted to the electronic document room (edr)	Fasting BE study	PK parameters	X	☐	☐
		Plasma concentrations	X	☐	☐
	Fed BE study	PK parameters	X	☐	☐
		Plasma concentrations	X	☐	☐
	Other study	PK parameters	☐	☐	X
		Plasma concentrations	☐	☐	X
Are all eight electronic summary biotables present			X	☐	☐
Are electronic summary biotables in pdf format			X	☐	☐

Table 2: SUMMARY OF *IN VITRO* DISSOLUTION DATA

Dissolution Conditions	**Apparatus:**	USP Apparatus II (Paddles)
	Speed of Rotation:	100 RPM
	Medium:	Acid Stage : 300 ml of 0.1N HCl (degassed) followed by Buffer Stage : 1000 ml of pH 6.8 Phosphate buffer (degassed)
	Volume:	Acidic Stage : 300 ml Buffer Stage : 1000 ml
	Temperature:	37 ± 0.5 °C
Firm's Proposed Specifications	Acid Stage: Not More than (b) (4) of the labeled amount of Omeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved in 2 hours. Buffer Stage: Not less than (b) (4) (Q) of the labeled amount of Omeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved in 30 minutes.	
Dissolution Testing Site (Name, Address)	Dr. Reddy's Laboratories Limited - Generics, Bachepalli, Post Bag No. 15, Kukatpally P.O., Hyderabad – 500 072, INDIA	

Study Ref No.	**Testing Date**	**Product ID \ Batch No. (Test - Manufacture Date) (Reference – Expiration Date)**	**Dosage Strength & Form**	**No. of Dosage Units**		**Collection Times (minutes)**				**Study Report Location**
						10 Min	**20 Min**	**30 Min**	**45 Min**	
Diss.Study Report No: BM00503	February 21, 2007	Omeprazole Magnesium Delayed-Release Capsules, 20 mg Batch No: EC6319	20 mg Capsule	12	Mean	92	91	90	88	Volume #: 02 Page #: 000110
					Range	(b) (4)				
					%CV	2.2	2.4	2.4	2.4	
Diss.Study Report No: BM00473	February 21, 2007	Prilosec OTC™ (omeprazole magnesium) delayed-release tablets, 20 mg (Batch No: 5338171971)	20 mg Tablet	12	Mean	69	85	93	92	Volume #: 02 Page #: 000111
					Range	(b) (4)				
					%CV	11.7	3.8	1.5	1.4	

Acid Stage Testing Data (provided in the respective Certificates of Analysis)

% of the labeled amount of omeprazole dissolved in 2 hours

Test (Batch #: EC6319)
Date of Analysis: February 21, 2007

	(b) (4)
Capsule 1	
Capsule 2	
Capsule 3	
Capsule 4	
Capsule 5	
Capsule 6	

Reference (Batch #: 5338171971)
Date of Analysis: February 22, 2007

	(b) (4)
Tablet 1	
Tablet 2	
Tablet 3	
Tablet 4	
Tablet 5	
Tablet 6	

II. COMMENTS:

1. The firm did not provide the range of % dissolution data (buffer stage) at each sampling time point in the paper submission of this ANDA. In addition, the firm did not provide %CV for the acid stage testing in neither the paper nor electronic format.

2. The firm provided acid stage dissolution data on six dosage units for the test and reference products instead of the standard twelve dosage units.

3. The firm uses the following method and specifications:

Acid Stage:
(Acid resistance is measured from the dosage form and not from an aliquot of 0.1N HCl):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.1N HCl @ 37ºC
Volume: 300mL
Time: 2h
Specification: NMT (b) (4) of the labeled amount of omeprazole is dissolved at the end of the acid stage.

Buffer Stage:
(Fresh capsules are assayed and are from the same lot tested for acid resistance. Drug release measured from an aliquot of the phosphate buffer.):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.05M Na_3PO_4, pH 6.8 @ 37ºC
Volume: 1000mL
Time: 10, 20, 30, and 45 minutes

Specification: NLT (b) (4) (Q) of the labeled amount of omeprazole is dissolved in 30 minutes.

NOTE: Each dosage unit is subjected to acid stage conditions for 2h. At the end of the acid stage, 0.1N HCl is drained from the vessel and 1000mL of 37°C 0.05M Na_3PO_4 buffer, pH 6.8, is added to begin the buffer stage testing.

4. The method utilized by the firm is essentially the same as the FDA-recommended method for Omeprazole Magnesium Tablets, DR (OTC). The only difference between the two methods is in the approach used for buffer stage testing. Specifically, the firm's method calls for the 300mL of 0.1N HCl to be drained from the vessel at the end of the acid stage and replaced with 1000mL of 0.05M Na_3PO_4, pH 6.8. In contrast, the FDA-recommended method (OTC DR tablets) calls for 700mL of 0.086M Na2HPO4 to be added to the 300mL of 0.1N HCl already in the vessel at the end of the acid stage to yield

1000mL of pH 6.8 buffer. The firm's proposed method is acceptable since it is very similar to the FDA-recommended method for the OTC DR Tablets.

5.. The acid stage dissolution data for the test product pass at the A1 level as defined in USP Acceptance Table 3 in the Dissolution section of USP 30 (6 units tested, no individual value exceeds [redacted] dissolved). The pH 6.8 buffer stage dissolution data for the test product pass at the B1 level as defined in USP Acceptance Table 4 in the Dissolution section of USP 30 (6 units tested, each unit is not less than Q + [redacted]). As a result, the firm's proposed specifications are acceptable.

III. DEFICIENCY COMMENTS:

None.

IV. RECOMMENDATIONS:

The *in vitro* dissolution testing conducted by the firm is **acceptable** but the DBE would like to mention two recommendations for future submissions.

BIOEQUIVALENCE DEFICIENCY

ANDA: 078878

APPLICANT: Dr. Reddy's Laboratories

DRUG PRODUCT: Omeprazole Delayed Release Capsules (OTC), 20mg

The Division of Bioequivalence has completed its review of the dissolution testing portion of your submission acknowledged on the cover sheet. The review of the bioequivalence studies and waiver request will be conducted later. The following deficiency has been identified:

In future submissions, please provide the range of % dissolution data and %CV for each sampling time in both paper and electronic formats. Additionally, in future submissions for delayed-release products, please provide acid stage dissolution data for twelve individual dosage units.

The Division of Bioequivalence acknowledges that you shall conduct dissolution testing with the following method and specifications.

Acid Stage:
(Acid resistance is measured from the dosage form and not from an aliquot of 0.1N HCl):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.1N HCl @ 37°C
Volume: 300mL
Time: 2h
Specification: NMT (b) (4) *of the labeled amount of omeprazole is dissolved at the end of the acid stage.*

Buffer Stage:
(Fresh capsules are assayed and are from the same lot tested for acid resistance. Drug release measured from an aliquot of the phosphate buffer.):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.05M Na_3PO_4, pH 6.8 @ 37°C
Volume: 1000mL
Specification: NLT [redacted] *(Q) of the labeled amount of omeprazole is dissolved in 30 minutes.*

NOTE: Each dosage unit is subjected to acid stage conditions for 2h. At the end of the acid stage, 0.1N HCl is drained from the vessel and 1000mL of 37°C 0.05M Na_3PO_4 buffer, pH 6.8, is added to begin the buffer stage testing.

Sincerely yours,

{See appended electronic signature page}
Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

V. OUTCOME

BIOEQUIVALENCE -**ACCEPTABLE** Submission date: March 16, 2007

[NOTE: The *in vitro* testing is acceptable. The fasting and fed BE studies are pending review.]

1. DISSOLUTION (Dissolution Data)	Strength:	eq. to 20 mg base
	Outcome:	**AC**

Outcome Decisions: **AC-Acceptable**

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

/s/

Utpal Munshi
9/21/2007 09:29:45 AM
BIOPHARMACEUTICS

Shriniwas G. Nerurkar
9/21/2007 05:05:37 PM
BIOPHARMACEUTICS

Barbara Davit
9/24/2007 04:39:24 PM
BIOPHARMACEUTICS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	78-878	
Drug Product Name	Omeprazole Magnesium Delayed-Release (DR) Capsules	
Strength(s)	20 mg (eq. base)	
Applicant Name	Dr. Reddy's Laboratories	
Address	Bachupally, Qutubullapur Mandal Hyderabad. 502 325 INDIA. Tel: +91-40-2304506	
Applicant's Point of Contact	Mr. Indu Bhushan, Sr. Director - R&D, Dr. Reddy's Laboratories, Ltd, Generics, Bachupally, Qutubullapur Mandal, Hyderabad. 502 325 INDIA	
Contact's Telephone Number	91-40-23045063	
Contact's Fax Number	91-40-23045238	
Original Submission Date(s)	16 March 2007	
Submission Date(s) of Amendment(s) Under Review	N/A	
Reviewer	Anitha Palamakula Ph.D., R. Ph.	
Study Number (s)	3701/06-07	
Study Type (s)	Randomized Single-dose two-way Crossover	FASTING
Strength (s)	20 mg	
Clinical Site	Vimta Labs Ltd.	
Clinical Site Address	142, IDA, Phase II, Cherlapally Hyderabad-500 051 India	
Analytical Site	Vimta Labs Ltd.	
Analytical Site Address	Same as clinical site address	
Study Number (s)	7002/06-07	
Study Type (s)	Randomized Single-dose two-way Crossover	FED
Strength (s)	20 mg	
Clinical Site	Wellquest Clinical Research; Clinical Section	
Clinical Site Address	Wellspring Hospital (4th Floor) Ganpatrao Kadam Marg, Lower Parel Mumbai-400 013 India	
Analytical Site	(b) (4)	
Analytical Site Address		
OUTCOME DECISION	**ACCEPTABLE**	

1 EXECUTIVE SUMMARY

The basis for this application for Omeprazole Magnesium Delayed Release **Capsules**, 20 mg, is Prilosec® OTC (Omeprazole Magnesium) Delayed Release **Tablets**, 20 mg (NDA 021229), as established by the Citizen Petition, Docket No. 2004P-0373/CP1, approved on July 5, 2005. This application contains the results of two fasting and fed bioequivalence (BE) studies comparing the test product, Omeprazole Magnesium Delayed Release Capsules, 20 mg to the corresponding reference product, Prilosec® OTC (Omeprazole Magnesium) Delayed Release Tablets, 20 mg, of AstraZeneca. Each of the BE studies was designed as a single-dose, two-way crossover study in healthy male subjects. The firm's fasting and fed BE studies are acceptable. The results are summarized in the tables below.

Omeprazole Magnesium DR Capsules
1 x 20 mg
Fasting Bioequivalence Study No. 3701/06-07, N=39 (Male)
Least-Square Geometric Means, Point Estimates and 90% Confidence Intervals

Parameter (units)	Test	Reference	Ratio	90% C.I.	
AUC0-t (ng*hr/mL)	1362.74	1358.50	1.00	94.97	105.95
AUC∞ (ng*hr/mL)	1394.70	1393.27	1.00	94.83	105.67
Cmax (ng/mL)	688.12	659.96	1.04	97.45	111.56

Omeprazole Magnesium DR Capsules
1 x 20 mg
Fed Bioequivalence Study No. 7002/06-07, N=61 (Male)
Least-Square Geometric Means, Point Estimates and 90% Confidence Intervals

Parameter (units)	Test	Reference	Ratio	90% C.I.	
AUC0-t (ng*hr/mL)	1238.90	1296.11	0.96	89.76	101.79
AUC∞ (ng*hr/mL)	1270.26	1340.28	0.95	89.14	100.77
Cmax (ng/mL)	503.04	500.32	1.01	92.59	109.18

There is no USP- or FDA-recommended dissolution method for the Omeprazole Magnesium DR Capsules. However, the public and internal dissolution databases describe a method for Omeprazole Magnesium DR Tablets, OTC. The firm conducted dissolution testing using the recommended method for Omeprazole Magnesium DR Tablets. The in vitro data submitted meet the recommended specification at the S1 level. The comparative dissolution testing is acceptable.

The clinical site "Wellquest Clinical Research" is pending a Division of Scientific Investigation (DSI) inspection[1]. Therefore the application is incomplete pending a DSI inspection.

[1] ANDA (b) (4) and 78421

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Omeprazole Magnesium Delayed Release Capsules, 20 mg (eq. base)
Reference Product	Prilosec OTC™ (Omeprazole Magnesium) Tablets, 20 mg (eq. base)
RLD Manufacturer	AstraZeneca, Inc.
NDA No.	21-229
RLD Approval Date	20 June 2003
Indication	Prilosec OTC™ is used to treat frequent heartburn (occurring 2 or more days a week). The drug may take 1 to 4 days for full effect and is not intended for immediate relief of heartburn).

3.2 PK/PD Information

Bioavailability	The absolute bioavailability of omeprazole is about 30-40% at doses of 20-40 mg, due in large part to a significant first-pass effect.
Food Effect	The rate, but not the extent, of absorption is affected by food. The time to peak concentration (Tmax) was prolonged when omeprazole was administered after breakfast as compared to fasting conditions (3.5 hours versus 2.21 hours; p = 0.6109).
Tmax	• Tmax = 0.5-3.5 hours. • Absorption of oral omeprazole varies among formulations. Uncoated granules attain peak serum concentrations in about 30 minutes and enteric-coated granules in 2 to 5 hours.
Metabolism	Extensively metabolized by the liver, with four distinct inactive metabolites recovered in the urine. Omeprazole is a substrate for CYP2C19.
Excretion	Following single dose oral administration of a buffered solution of omeprazole, little if any unchanged drug was excreted in urine. The majority of the dose (about 77%) was eliminated in urine as at least six metabolites, which have very little or no anti-secretory activity.
Half-life	0.5 – 1 hours
Drug Specific Issues (if any)	None

3.3 OGD Recommendations for Drug Product

Number of studies recommended:	2, fasting and fed

1.	**Type of study:**	Fasting
	Design:	Single-dose, two-treatment, two-period crossover in-vivo
	Strength:	20 mg
	Subjects:	Normal healthy males and females, general population
	Additional Comments:	Measure only the parent compound, Omeprazole

2.	**Type of study:**	Fed
	Design:	Single-dose, two-treatment, two-period crossover in-vivo
	Strength:	20 mg
	Subjects:	Normal healthy males and females, general population
	Additional Comments:	Measure only the parent compound, omeprazole

Analytes to measure (in plasma/serum/blood):	omeprazole in plasma
Bioequivalence based on:	(90% CI) omeprazole
Waiver request of in-vivo testing:	20 mg
Source of most recent recommendations:	OGD Controls and Protocols
Summary of OGD or DBE History (for details, see Appendix 4.4):	See Appendix 4.4

3.4 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	Yes	1
Single-dose fed	Yes	1
Steady-state		
In vitro dissolution	Yes	1
Waiver requests		
BCS Waivers		
Clinical Endpoints		
Failed Studies		
Amendments		

3.5 Pre-Study Bioanalytical Method Validation

Information Requested	Data
Report Location	**Study Report No.:** 3701/06-07**; Volume – 09 of 23; Section-**16.4; Page No.: 003836 **Study Report No.:** 7002/06-07**; Volume – 16 of 23; Section-**16.4; Page No.: 007548
Analyte	Omeprazole
Internal standard (IS)	(b) (4)
Method description	Refer Method Validation report No. 23/MVR/227 Page No. 19, 20 Analytical method: LC-MS/MS
Limit of Quantitation	10.000 ng/mL
Average recovery of drug (%)	91.78%
Average recovery of IS (%)	86.71%
Standard curve concentrations (ng/mL)	10.000, 20.000, 50.000, 200.000, 500.000, 1500.000, 2999.950 and 3999.950 ng/mL.
QC concentrations (ng/mL)	LQC= 30.050 ng/mL MQC=1601.550 ng/mL HQC= 3203.150 ng/mL
QC Intraday precision range (%)	LQC= 1.03% to 4.66% MQC= 0.92% to 1.66% HQC= 0.91% to 2.26%
QC Intraday accuracy range (%)	LQC= 95.01% to 103.30% MQC= 95.69% to 101.81% HQC= 95.20% to 102.93%
QC Interday precision range (%)	LQC= 4.64% MQC= 2.92% HQC= 3.73%
QC Interday accuracy range (%)	LQC= 99.78% MQC= 98.45% HQC= 98.60%
Bench-top stability (hrs)	12.00 hours at room temperature
Stock stability (days)	19 days @ 2 to 8°C
Processed stability (hrs)	24.00 hours @ 20°C and 24.00 hours @ Room temperature
Freeze-thaw stability (cycles)	Three cycles
Long-term storage stability (days)	92 days @ -20ºC
Dilution integrity	1.8 times of CC8 concentration diluted in 50:50 and 25:75.
Selectivity	No interfering peaks noted in blank plasma samples

3.5.1 Bio-analytical Fasting Method Validation for Omeprazole Magnesium

Information Requested	Data
Report Location	**Study Report No.:** 3701/06-07**; Volume – 09 of 23; Section-**16.4; Page No.: 003836
Analyte	Omeprazole
Internal standard (IS)	(b) (4)
Method description	Refer Partial Method Validation report No. 23/MVR/227/03 Page No.08 Analytical method: LC-MS/MS
Limit of Quantitation	10.000 ng/mL
Standard curve concentrations (ng/mL)	10.000, 20.050, 50.100, 200.400, 500.950, 1001.900 and 2003.850 ng/mL
QC concentrations (ng/mL)	LQC = 30.100 ng/mL GMQC = 155.450 ng/mL MQC = 802.350 ng/mL HQC = 1604.650 ng/mL
QC Intraday precision range (%)	LQC = 4.28% to 4.68% GMQC = 3.44% to 4.92% MQC = 4.85% to 6.62% HQC = 3.78% to 5.18%
QC Intraday accuracy range (%)	LQC = 98.17% to 103.03% GMQC = 94.25% to 98.65% MQC = 87.51% to 101.84% HQC = 86.57% to 105.86%
QC Interday precision range (%)	LQC = 4.96% GMQC = 4.72% MQC = 9.73% HQC = 11.29%
QC Interday accuracy range (%)	LQC = 100.60% GMQC = 96.45% MQC = 94.68% HQC = 96.21%

3.5.2 Bio-analytical Fed Method Validation for Omeprazole Magnesium

Information Requested	Data
Report Location	**Study Report No.:** 7002/06-07; **Volume – 16 of 23; Section**-16.4; Page No.: 007548
Analyte	Omeprazole
Internal standard (IS)	(b) (4)
Method description	Refer Partial Method Validation report No. 23/MVR/227/05 Page No.15 Analytical method: LC-MS/MS
Limit of Quantitation	10.000 ng/mL
Standard curve concentrations (ng/mL)	10.000, 19.950, 49.900, 199.600, 499.000, 997.950 and 1995.900 ng/mL
QC concentrations (ng/mL)	LQC = 30.000 ng/mL GMQC = 155.000 ng/mL MQC = 799.950 ng/mL HQC = 1599.900 ng/mL
QC Intraday precision range (%)	LQC = 0.93% to 1.66% GMQC = 1.50% to 3.49% MQC = 1.24% to 1.94% HQC = 1.03% to 2.40%
QC Intraday accuracy range (%)	LQC = 97.93% to 99.49% GMQC = 88.40% to 98.98% MQC = 94.90% to 98.53% HQC = 97.01% to 99.53%
QC Interday precision range (%)	LQC = 1.52% GMQC = 6.39% MQC = 2.51% HQC = 2.23%
QC Interday accuracy range (%)	LQC = 98.71% GMQC = 93.69% MQC = 96.72% HQC = 98.27%
Bench-top stability (hrs)	12.00_ hours at room temperature
Freeze-thaw stability (cycles)	Three cycles
Selectivity	No interfering peaks noted in blank plasma samples

SOPs submitted	Yes	SOP# 23/MV/227/03 version 1.0
Bioanalytical method is acceptable	Yes	

Comments on the Pre-Study Method Validation: Acceptable.

3.6 In Vivo Studies

Table 1. Summary of all in vivo Bioequivalence Studies

Study Ref. No.	Study Objective	Study Design	Treatments (Dose, Dosage Form, Route) [Product ID]	Subjects No. (M/F) Type Age: mean (Range)	Mean Parameters (+/-SD)						Study Report Location
					C_{max} (ng/mL)	T_{max} (hr)	AUC_{0-t} (units)	AUC_{∞} (units)	$T½$ (hr)	K_{el} (hr-1)	
3701/06-07	An open label balanced randomized, two-treatment, two-period, two-sequence, single dose, crossover oral bioequivalence study to compare Omeprazole Magnesium 20 mg Delayed Release Capsules (Dr. Reddy's Laboratories Ltd.) with Prilosec OTC$_{TM}$ 20 mg (Omeprazole Magnesium Delayed Release Tablets) (Distributed by Procter and Gamble, Cincinnati, Sweden) in 38 healthy, adult, human subjects under fasting conditions.	An Open label, balanced, randomized two-treatment, two-period, two-sequence, analyst-blind, two-way crossover bioequivalence study with at least 14 days washout period between each drug administration under fasting conditions.	**Test** Omeprazole Magnesium 20 mg DR Capsules Single dose of Omeprazole Magnesium 20 mg DR Capsule administered orally with 240mL of water at room temperature under fasting condition. Batch No.: EC6319	40 healthy male subjects Mean age: 25.30 Years Range: 19 - 42	745.404 (40.59)	2.00 (1.00-3.36)	1856.107 (88.64)	1898.529 (88.92)	1.291 (56.61)	0.697 (48.30)	**ANDA Vol. 3 of 23 Page No: 001130 And 001133**
			REFERENCE: Prilosec OTC$_{TM}$ 20 mg DR Tablets Single dose of Prilosec OTC$_{TM}$ 20 mg DR Tablet (Omeprazole Magnesium delayed release Tablet) administered orally with 240mL of water at room temperature under fasting condition. Lot No.: 5338171971		705.566 (36.78)	1.67 (1.00-3.67)	1760.483 (80.96)	1803.868 (81.27)	1.304 (52.26)	0.658 (42.54)	

7002/06-07	An open label, balanced, randomized, two-treatment, two-sequence, two-period, two-way, single-dose, cross-over oral bioequivalence study of Omeprazole Magnesium 20 mg delayed release capsule of Dr. Reddy's Laboratories Limited, Generics, India and Prilosec® OTC$_{TM}$ (Omeprazole Magnesium delayed release) 20 mg tablets distributed by Procter and Gamble, Cincinnati, OH 45202; in healthy human adult subjects, under fed conditions.	An open label, randomized, two-treatment, two-sequence, two-period, two-way, cross-over, single-dose bioequivalence study.	**TEST:** 1 Omeprazole Magnesium 20 mg DR Capsules Single dose of Omeprazole Magnesium 20 mg DR Capsule administered orally with 240mL under fed condition. Batch No.: EC6319	62 healthy male subjects Mean age: 26.50 Years Range: 18 - 40	585.969 (63.74)	3.50 (2.50-5.50)	1875.219 (102.09)	1974.370 (98.67)	1.327 (70.61)	0.741 (47.98)	**ANDA Vol. 10 of 23 Page No: 004450** **And 004454**
			REFERENCE: Prilosec® OTC$_{TM}$ 20 mg DR Tablets Single dose of Prilosec OTC$_{TM}$ (Omeprazole Magnesium delayed release Tablet 20 mg) administered orally with 240mL of water under fed condition`. Lot No.: 5338171971		593.701 (62.96)	3.50 (1.50-5.50)	1873.559 (93.84)	1974.174 (90.85)	1.308 (64.97)	0.739 (52.49)	

Table 2. Statistical Summary of the Comparative Bioavailability Data Calculated by the Reviewer

Omeprazole Magnesium 20mg DR capsules 1 x 20 mg Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals					
Fasting Bioequivalence Study No. 3701/06-07					
Parameter	**Test**	**Reference**	**Ratio**	**90% C.I.**	
AUC0-t (ng*hr/mL)	1362.74	1358.50	1.00	94.97	105.95
AUC∞ (ng*hr/mL)	1394.70	1393.27	1.00	94.83	105.67
Cmax (ng/mL)	688.12	659.96	1.04	97.45	111.56

Omeprazole Magnesium 20mg DR capsules 1 x 20 mg Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals					
Fed Bioequivalence Study No. 7002/06-07					
Parameter	**Test**	**Reference**	**Ratio**	**90% C.I.**	
AUC0-t (ng*hr/mL)	1238.90	1296.11	0.96	89.76	101.79
AUC∞ (ng*hr/mL)	1270.26	1340.28	0.95	89.14	100.77
Cmax (ng/mL)	503.04	500.32	1.01	92.59	109.18

Table 3. Reanalysis of Study Samples

Study No. 3701/06-07 **Location in final report: Volume 09 of 23; Section-16.4; Page No.: 003836**								
Reason why assay was repeated	**Number of samples reanalyzed**				**Number of recalculated values used after reanalysis**			
	Actual Number		**% of total assays**		**Actual number**		**%of total assays**	
	Test	**Reference**	**Test**	**Reference**	**Test**	**Reference**	**Test**	**Reference**
Poor chromatography	13	9	1.80	1.25	13	9	1.80	1.25
Unacceptable calibration curve	76	76	10.53	10.53	76	76	10.53	10.53
Samples were repeated for the reconfirmation of the results	1	-	0.14	0.00	1	-	0.14	0.00
Total	**90**	**85**	**12.47**	**11.78**	**90**	**85**	**12.47**	**11.78**

Total assays Test product: 722
Reference product: 722

Study No. 7002/06-07 **Location in final report: Volume 16 of 23; Section-16.4; Page No.: 007548**								
Reason why assay was repeated	**Number of samples reanalyzed**				**Number of recalculated values used after reanalysis**			
	Actual Number		**% of total assays**		**Actual number**		**%of total assays**	
	Test	**Reference**	**Test**	**Reference**	**Test**	**Reference**	**Test**	**Reference**
QC results were not with in acceptance range	45	45	4.92	4.92	45	45	4.92	4.92
Samples were repeated for the reconfirmation of the results	1	3	0.11	0.33	1	3	0.11	0.33
Total	**46**	**48**	**5.03**	**5.25**	**46**	**48**	**5.03**	**5.25**

Total assays Test product: 915
Reference product: 915

Did use of recalculated plasma concentration data change study outcome? No

Comments from the Reviewer: The in vivo fasting and fed BE studies are acceptable.

3.7 Formulation

Location in appendix	Section 4.2
If a tablet, is the RLD scored?	Not applicable (Capsules)
If a tablet, is the test product biobatch scored	Not applicable (Capsules)
Is the formulation acceptable?	**ACCEPTABLE**
If not acceptable, why?	N\A

3.8 In Vitro Dissolution

Location of DBE Dissolution Review	DFS 078878 Dissolution Review
Source of Method (USP, FDA or Firm)	Firm
Medium	Acid Stage : 300 ml of 0.1N HCl (degassed) followed by Buffer Stage : 1000 ml of pH 6.8 Phosphate buffer (degassed)
Volume (mL)	Acidic Stage : 300 mL Buffer Stage : 1000 mL
USP Apparatus type	USP II (Paddles)
Rotation (rpm)	100
DBE-recommended specifications	Acid Stage: NMT (b) (4) omeprazole dissolved at 2 hours. Buffer Stage: NLT (b) (4) Q) dissolved in 30 min.
If a modified-release tablet, was testing done on ½ tablets?	N/A
F2 metric calculated?	No
If no, reason why F2 not calculated	Rapidly dissolving capsule/tablet
Is method acceptable?	**ACCEPTABLE**
If not then why?	-----

***NOTE:** Each dosage unit is subjected to acid stage conditions for 2h. At the end of the acid stage, 0.1N HCl is drained from the vessel and 1000mL of 37°C 0.05M Na_3PO_4 buffer, pH 6.8, is added to begin the buffer stage testing.

3.9 Waiver Request(s)

Not applicable.

3.10 Deficiency Comments

None.

3.11 Recommendations

- The Division of Bioequivalence (DBE) accepts the fasting BE study # AAI3701/06-07 conducted by Dr. Reddy's Laboratories Ltd., on its Omeprazole Magnesium DR Capsules 20 mg (lot # EC6319) comparing it to Prilosec® OTC (Omeprazole Magnesium) DR Tablets, 20 mg (lot # 5338171971), manufactured by AstraZeneca.

- The DBE also accepts the fed BE study #7002/06-07conducted by Dr. Reddy's Laboratories, on its Omeprazole Magnesium DR Capsules, 20 mg (lot # EC6319) comparing it to Prilosec® OTC (Omeprazole Magnesium) DR Tablets, 20 mg (lot # 5338171971), manufactured by AstraZeneca.

Dissolution recommendation:

The firm's in vitro dissolution testing is acceptable.

The DBE acknowledges that you shall conduct dissolution testing according to the following method and specifications.

Acid Stage:

(Acid resistance is measured from the dosage form and not from an aliquot of 0.1N HCl):

Apparatus:	USP Apparatus II (Paddle)
Speed:	100 rpm
Medium:	0.1N HCl @ 37ºC
Volume:	300 mL
Time:	2h
Specification:	*NMT* (b) (4) *of the labeled amount of omeprazole is dissolved at the end of the 2h acid stage.*

Buffer Stage:

(Fresh capsules are assayed and are from the same lot tested for acid resistance. Drug release measured from an aliquot of the phosphate buffer):

Apparatus:	USP Apparatus II (Paddle)
Speed:	100rpm
Medium:	0.05M Na_3PO_4, pH 6.8 @ 37ºC
Volume:	1000mL
Specification:	*NLT* (b) (4) *Q) of the labeled amount of omeprazole is dissolved in 30 minutes.*

NOTE: Each dosage unit is subjected to acid stage conditions for 2h. At the end of the acid stage, 0.1N HCl is drained from the vessel and 1000mL of 37°C 0.05M Na_3PO_4 buffer, pH 6.8, is added to begin the buffer stage testing.

3.12 Comments for Other OGD Disciplines

Discipline	Comment
DSI	The clinical site Wellquest Clinical Research should be inspected by DSI. Request for inspections sent to DSI for new site inspection (ANDA # (b) (4) and for cause inspection (ANDA #78-421) are still pending.

4 APPENDIX

4.1 Individual Study Reviews

4.1.1 Single-dose Fasting Bioequivalence Study

4.1.1.1 Study Design

Table 4 Study Information

Study Number	3701/06-07
Study Title	An open label balanced randomized, two-treatment, two-period, two-sequence, single dose, crossover oral bioequivalence study to compare Omeprazole Magnesium 20 mg Delayed Release Capsules (Dr. Reddy's Laboratories Ltd.) with Prilosec OTC$_{TM}$ 20 mg (Omeprazole Magnesium Delayed Release Tablets) (Distributed by Procter and Gamble, Cincinnati, Sweden) in 38 healthy, adult, human male subjects under fasting conditions
Clinical Site (Name & Address)	Vimta Labs Ltd. 142, IDA, Phase II, Cherlapally, Hyderabad-500 051, India.
Principal Investigator	Dr. I.S. Gandhi
Dosing Dates	Period-I: 09 Dec 2006 Period-II: 23 Dec 2006
Analytical Site (Name & Address)	Vimta Labs Ltd. 142, IDA, Phase II, Cherlapally, Hyderabad-500 051, India.
Analysis Dates	Analysis Started: 30 Dec 2006 Analysis Completed: 12 Jan 2007
Analytical Director	(b) (6)
Storage Period of Biostudy Samples (no. of days from the first day of sample collection to the last day of sample analysis)	35 Days

Comments: Acceptable.

Table 5. Product information

Product	Test	Reference
Treatment ID	A	B
Product Name	Omeprazole Magnesium DR Capsules	Prilosec OTC ™ (omeprazole magnesium) DR Tablets
Manufacturer	Dr. Reddy's Labs	Astra Zeneca
Batch/Lot No.	Batch No: EC6319	Batch No: 5338171971
Manufacture Date	Oct 2006	
Expiration Date		May 2008
Strength	20 mg	20 mg
Dosage Form	Capsule	Tablet
Bio-Batch Size	(b) (4)	N/A
Production Batch Size		N/A
Potency (Assay)	20 mg	20 mg
Content Uniformity (mean, %CV)	The acceptance value is 5.3	The acceptance value is 6.5
Dose Administered	20 mg	20 mg
Route of Administration	Oral	Oral

Comments: The basis for the ANDA submission is the Prilosec® OTC drug product, which is marketed in tablets. The tablets are comprised of enteric coated pellets compressed into a tablet called a MUPS tablet of "multiple unit pellet system". A suitability petition was approved for the corresponding ANDA change to OTC capsules on July 5, 2005[2]. Each capsule contains 20.6 mg of omeprazole magnesium which is equivalent to 20 mg of omeprazole base. The drug product contains enteric coated pellets (b) (4) (b) (4) filled into capsules. (b) (4)

[2] Docket number 2004P-0373/CP1 approved on 16th May 2005.

Table 6. Study Design, Single-Dose Fasting Bioequivalence Study

Number of Subjects	40 (39 completed)
No. of Sequences	2
No. of Periods	2
No. of Treatments	2
No. of Groups	1
Washout Period	14 days
Randomization Scheme	AB: 1, 3, 6, 7, 9, 11, 13, 15, 17, 19, 22, 23, 26, 27, 30, 31, 33, 36, 38, 40 BA: 2, 4, 5, 8, 10, 12, 14, 16, 18, 20, 21, 24, 25, 28, 29, 32, 34, 35, 37, 39
Blood Sampling Times (hr)	Pre-dose, 0.5, 1, 1.33, 1.67, 2, 2.33, 2.67, 3 .0, 3.33, 3.67, 4, 4.5, 5, 6, 8, 10, 12, and 16.0 hours post-dose.
Blood Volume Collected/Sample	1 x 6 mL per sampling time
Blood Sample Processing/Storage	The samples were collected using pre-labeled Vacutainers® containing potassium-EDTA as the anticoagulant. The blood samples were stored in thermocol box with cool packs before centrifugation and were centrifuged using a refrigerated centrifuge within 30 min at 10 ± 2 °C at 3800 rpm for 10 min. The collected plasma from each tube was aliquotted into pre-cooled labeled polypropylene tubes. The samples were immediately stored frozen at -16°C or colder until assayed. The blood sampling procedure and processing was carried out in a darkened room with a yellow monochromatic light.
IRB Approval	Yes, IEC for study # 3701/06-07 (Dec 8, 2006)
Informed Consent	Yes , submitted a copy
Length of Fasting	From at least 10 hours prior to drug administration until 4 hours post-dose.
Length of Confinement	From the night before dosing until 24 hours pose dosing draw.
Safety Monitoring	Vital signs of subjects were monitored before drug administration and followed up periodically throughout the housing period within 30 min of either side of schedule sampling time. Blood pressure, pulse rate were measured at the time of admission and at each blood sampling time. Temperature recordings were done at the time of admission, prior to dosing and 24 hours post dose. Clinical laboratory data (haematology and serum chemistry) were assessed at the time of admission and study exit.

Comments on Study Design:

The study design is acceptable.

4.1.1.2 Clinical Results

Table 7. Demographics Profile of Subjects Completing the Bioequivalence Study

Study No. 3701/06-07 **Location in final report: Volume 03 of 23; Section-**14.1.2-2; Page No.: 001049		
	Treatment Groups	
	Test Product N =39	**Reference Product N = 39**
Age (Years)		
Mean ± SD	25.03 ± 5.806	25.03 ± 5.806
Range	19 – 42	19 – 42
Groups		
< 18	Nil	Nil
18 – 40	38 (97.44%)	38 (97.44%)
41 – 64	1 (2.56%)	1 (2.56%)
65 – 75	Nil	Nil
> 75	Nil	Nil
Sex		
Female	Nil	Nil
Male	39 (100%)	39 (100%)
Race		
Asian	39 (100%)	39 (100%)
Black	Nil	Nil
Caucasian	Nil	Nil
Hispanic	Nil	Nil
Other	Nil	Nil
BMI		
Mean ± SD	21.56 ± 1.866	21.56 ± 1.866
Range	19 – 25	19 – 25
Other Factors	Nil	Nil

Note:

⇒ Subject number 15 (Sequence AB) dropped from the study due to found positive in urine drugs of abuse in Period - II.

A = Test product

B = Reference product

Table 8. Dropout Information, Fasting Bioequivalence Study

Subject No.	Reason	Period	Replaced?
15	Found positive for UDS	II*	No

* Subject dropped before dosing, hence time and treatment were not provided.

Table 9. Study Adverse Events, Fasting Bioequivalence Study

Body system/Adverse Event	Reported Incidence by Treatment Groups	
	Fasted Bioequivalence Study No.: 3701/06-07	
	Test	Reference
Body as a whole		
Dizziness N (%)	Nil	1 (2.56%)
Cardiovascular N (%)	Nil	Nil
Gastrointestinal N (%)	Nil	Nil
Haemopoetic system*		
Low serum albumin N (%)	5 (12.50%)	
Low HGB/HCT/RBC N (%)	2 (5.00%)	
Low Lymphocytes N (%)	2 (5.00%)	
Elevated Serum Creatinine N (%)	2 (5.00%)	
Elevated Serum Total Bilirubin N (%)	2 (5.00%)	
Low HGB and HCT N (%)	2 (5.00%)	
Low RBC N (%)	1 (2.50%)	
Elevated Serum Total Bilirubin/AST/ALT N (%)	1 (2.50%)	
Low Platelets N (%)	2 (5.00%)	

Note:
N = Number of subjects with incidence of adverse events (AEs).
% = Percentage of total number of subjects treated with the corresponding product.
* = Post clinical laboratory assessment done after completion of Period-II.
Number of subjects dosed with,
Test product 40
Reference product 39
Post clinical assessment 40

Table 10. Protocol Deviations, Fasting Bioequivalence Study

Study No. 3701/06-07 Location in final report: Volume 03 of 23; Section-16.2.2; Page No.: 001416		
Type	**Subject No. (Test)**	**Subject No. (Reference)**
Some subjects were admitted late in the CPU due to delay in UDS reports.	02, 08, 12, 14, 18, 25, 37 and 39	01, 03, 06, 07, 09, 11, 13, 22, 26, 27, 31, 36, 38 and 40
Blood sampling deviation	23 and 28	Nil

Note: * - post clinical sample missing

Comments on Dropouts/Adverse Events/Protocol Deviations:

- No significant protocol deviations occurred during the study.

- There were some blood sampling deviations, but the actual sampling time points were used in the data analysis.

- There were 20 total adverse events (AEs) in 19 subjects, of these 19 were post study abnormal laboratory results and were considered as mild changes.

- Subject #37 reported dizziness during period I which graded as mild in severity and considered as probably related to the study drug.

  Of 20 AEs:
  -Four (4) were considered "Possibly" related to the study drug. Of these four, two (2) AEs occurred after administration of test and two (2) AEs occurred after RLD dosing.
  -Two (2) were considered "Probably" related to the study drug.
  - Nine (9) were unlikely related to either drug treatment.
  - Five (5) were considered "not related" to either drug treatment.

- The AEs were all mild in severity and resolved with no pharmacological action taken.

- Subject #15 was excluded from the study due to positive UDS on period – II.

- Subject #35 was discontinued prior to dosing in Period I due to syncope. This subject was replaced by additional subject #A35.

- The firm's handling of dropouts, adverse events, and protocol deviations are acceptable.

4.1.1.3 Bioanalytical Results

Table 11. Assay Validation – Within the Fasting Bioequivalence Study

Bioequivalence Study No.: 3701/06-07 Analyte Name: Omeprazole							
Parameter	**Standard Curve Samples**						
CC Level →	**CC1**	**CC2**	**CC3**	**CC4**	**CC5**	**CC6**	**CC7**
Concentration (ng/mL)	**10.000**	**20.000**	**50.050**	**200.150**	**500.350**	**1000.750**	**2001.450**
Inter day Precision (%CV)	3.19	6.16	5.08	3.45	3.39	4.45	4.88
Inter day Accuracy (%Actual)	101.04	98.66	98.72	97.71	97.61	103.92	102.35
Linearity (r)	0.9948-0.9998						
Linearity Range (ng/mL)	10.000 – 2001.450						
Sensitivity (ng/mL)	10.000						

Bioequivalence Study No.:3701/06-07 Analyte Name: Omeprazole				
Parameter	**Quality Control Samples**			
QC ID →	**LQC**	**GMQC**	**MQC**	**HQC**
Concentration (ng,/mL)	**30.050**	**155.250**	**801.200**	**1602.450**
Inter day Precision (%CV)	11.744	12.153	6.397	9.580
Inter day Accuracy (%Actual)	102.086	95.587	100.690	95.785

Comments on Study Assay Validation: Acceptable

Any interfering peaks in chromatograms?	No
Were 20% of chromatograms included?	Yes
Were chromatograms serially or randomly selected?	Serially (Subject #17 to 23)

Comments on Chromatograms: Acceptable.

Table 12. SOP's Dealing with Bioanalytical Repeats of Study Samples

SOP No.	**Effective Date of SOP**	**SOP Title**
23/13	2006-08-16	Repeat analysis of samples & reintegration of chromatograms

Table 13. Additional Comments on Repeat Assays

Were all SOPs followed?	Yes
Did recalculation of PK parameters change the study outcome?	No
Does the reviewer agree with the outcome of the repeat assays?	Yes
If no, reason for disagreement	N/A

Summary/Conclusions, Study Assays:

- All omeprazole samples were received at the bioanalytical facility in good condition on dry ice (i.e., still frozen).
- There were 24% repeats (175 out of 722 total samples) of which 152 (76 from test and 76 from RLD) were performed due to unacceptable calibration curve.

The bioanalytical methodology is **acceptable**.

4.1.1.4 Pharmacokinetic Results

Table 14. Arithmetic Mean Pharmacokinetic Parameters

Mean plasma concentrations are presented in Table 18 and Figure 1

Fasting Bioequivalence Study, Study No. 3701/06-07									
Parameter (units)	Test				Reference				T/R
	Mean	%CV	Min	Max	Mean	% CV	Min	Max	
AUC0-t (ng*hr/mL)	1856.11	88.64	416.00	6803.74	1760.48	80.96	456.19	6326.13	1.05
AUC∞ (ng*hr/mL)	1898.53	88.92	432.59	7013.48	1803.87	81.27	464.00	6609.82	1.05
Cmax (ng/mL)	745.40	40.59	316.33	1417.35	705.57	36.78	295.41	1338.24	1.06
T_{MAX}(hr)	2.00	.	1.00	3.36	1.67	.	1.00	3.67	1.20
KE(hr-1)	0.70	48.30	0.23	1.66	0.66	42.54	0.21	1.32	1.06
THALF(hr)	1.29	56.61	0.42	3.04	1.30	52.26	0.52	3.28	0.99

*Tmax values are presented as median, range

Table 15. Geometric Means and 90% Confidence Intervals - Firm Calculated

Omeprazole Magnesium DR Capsules 1 x 20 mg Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals				
Fasting Bioequivalence Study No. 3701/06-07				
Parameter (units)	Test	Reference	Ratio	90% C.I.
AUC0-t (ng*hr/mL)	1362.7364	1358.5024	100.31	94.97 -105.95
AUC∞ (ng*hr/mL)	1394.6995	1393.2674	100.10	94.83 – 105.67
Cmax (ng/mL)	688.1198	659.9620	104.27	97.45 – 111.56

Table 16. Geometric Means and 90% Confidence Intervals - Reviewer Calculated

Omeprazole Magnesium DR Capsules 1 x 20 mg Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals					
Fasting Bioequivalence Study No. 3701/06-07					
Parameter (units)	Test	Reference	Ratio	90% C.I.	
AUC0-t (ng*hr/mL)	1362.74	1358.50	1.00	94.97	105.95
AUC∞ (ng*hr/mL)	1394.70	1393.27	1.00	94.83	105.67
Cmax (ng/mL)	688.12	659.96	1.04	97.45	111.56

Table 17. Additional Study Information, Fasting Study No. 3701/06-07

Root mean square error, AUC0-t	0.1412	
Root mean square error, AUC∞	0.1398	
Root mean square error, Cmax	0.1747	
	Test	**Reference**
Kel and AUC∞ determined for how many subjects?	38	38
Do you agree or disagree with firm's decision?	Agree	
Indicate the number of subjects with the following:		
measurable drug concentrations at 0 hr	None	None
first measurable drug concentration as Cmax	0	0
Were the subjects dosed as more than one group?	No	

Ratio of AUC0-t/AUC∞				
Treatment	**n**	**Mean**	**Minimum**	**Maximum**
Test	38	0.98	0.96	0.99
Reference	38	0.98	0.93	0.99

Comments on Pharmacokinetic and Statistical Analysis:

The pharmacokinetic and statistical analysis performed by the reviewer by omitting repeats also meet the 90% CI criteria for BE.

The mean AUCt/AUC∞ ratio >0.80 for both test and reference products indicates that the firm's sampling schedule for omeprazole was carried out for a sufficiently long period of time.

The 90% CI for the least-squares geometric means of lnAUCt, lnAUC∞ and lnCmax calculated by the Reviewer agree with the firm's calculations and meet the 90% CI criteria for BE (80.00-125.00%).

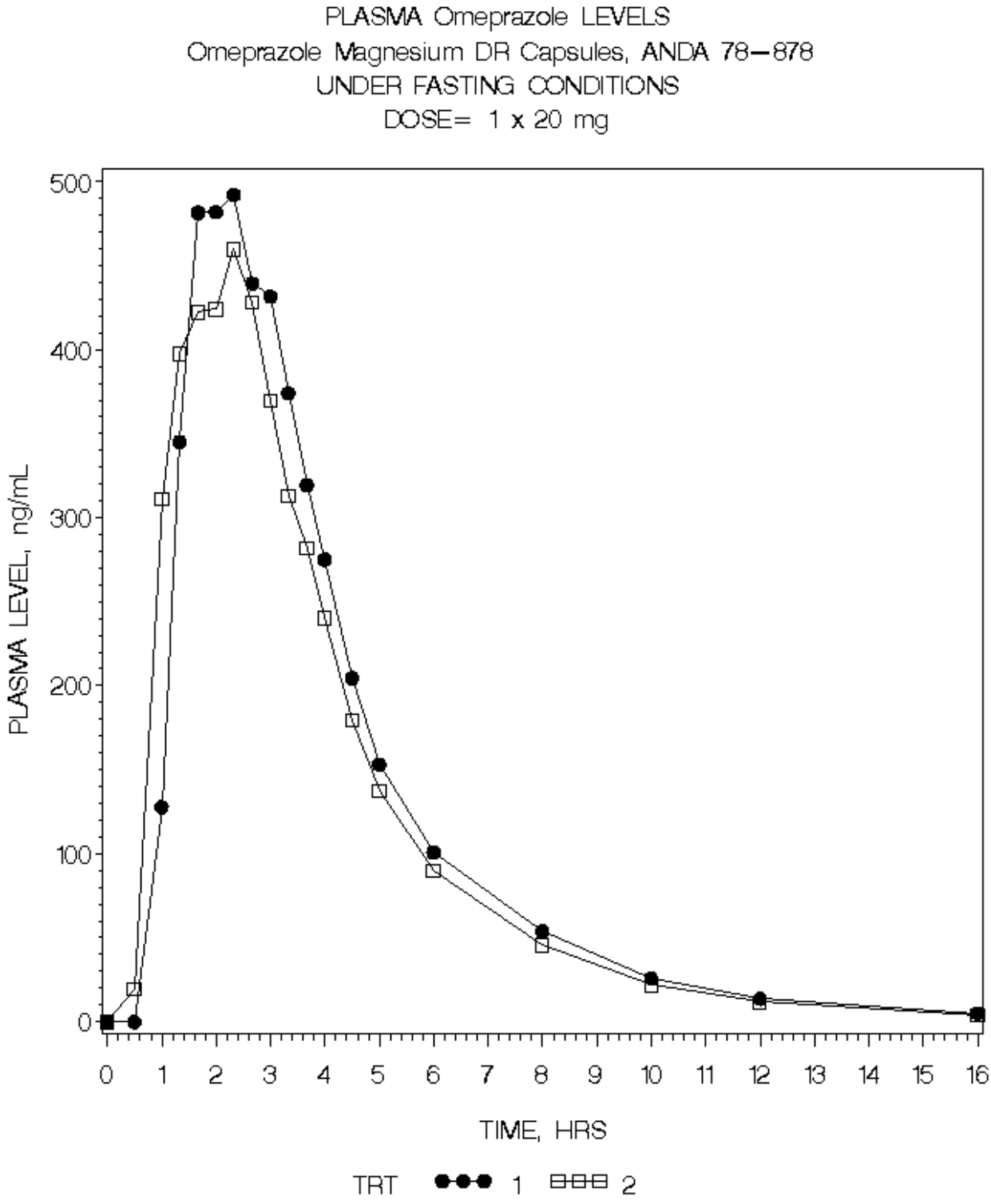
Summary and Conclusions, Single-Dose Fasting Bioequivalence Study:

The in vivo study under fasting conditions is **acceptable**.

Table 18. Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study

Omeprazole					
Time (hr)	Test (n= 39)		Reference (n= 39)		T/R Ratio
	Mean (ng/mL)	% CV	Mean (ng/mL)	% CV	
0.00	0.00	.	0.00	.	.
0.50	0.00	.	19.45	317.79	0.00
1.00	127.87	205.98	311.32	113.68	0.41
1.33	345.35	109.88	397.63	91.98	0.87
1.67	481.80	90.94	422.31	86.62	1.14
2.00	482.05	84.55	424.39	73.81	1.14
2.33	492.39	75.56	459.99	60.86	1.07
2.67	439.59	65.50	428.30	62.94	1.03
3.00	431.77	64.33	369.96	69.82	1.17
3.33	374.22	67.13	313.05	76.12	1.20
3.67	319.47	74.43	281.97	84.55	1.13
4.00	275.22	84.83	240.43	90.27	1.14
4.50	204.63	96.03	179.67	102.29	1.14
5.00	153.25	107.33	137.48	113.84	1.11
6.00	100.85	131.74	89.91	138.08	1.12
8.00	53.94	168.25	45.61	177.42	1.18
10.00	25.85	205.40	21.87	222.91	1.18
12.00	13.77	232.33	11.57	246.98	1.19
16.00	5.10	254.89	3.86	310.15	1.32

Figure 1. Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study



4.1.2 Single-dose Fed Bioequivalence Study

4.1.2.1 Study Design

Table 19. Study Information

Study Number	7002/06-07
Study Title	An open label, balanced, randomized, two-treatment, two-sequence, two-period, two-way, single-dose, cross-over oral bioequivalence study of Omeprazole Magnesium 20 mg delayed release capsule of Dr. Reddy's Laboratories Limited, Generics, India and Prilosec® OTC™ (Omeprazole Magnesium delayed release) 20 mg tablets distributed by Procter and Gamble, Cincinnati, Sweden; in healthy human adult subjects, under fed conditions.
Clinical Site (Name & Address)	Wellquest Clinical Research Clinical Section Wellspring Hospital (4th Floor) Ganpatrao Kadam Marg Lower Parel Mumbai – 400 013 (India) Telephone: +91-22-6660 8566 / 6660 8567 Fax: +91-22-6660 8571
Principal Investigator	Dr. Ghanashyam Rao
Dosing Dates	Period-I: 06 Jan 2007 – 07 Jan 2007 Period-II: 20 Jan 2007 – 21 Jan 2007
Analytical Site (Name & Address)	(b) (4)
Analysis Dates	Analysis Started: 15 Feb 2007 Analysis Completed: 05 Mar 2007
Analytical Director	(b) (6) Group Leader/Bio analytical.
Storage Period of Biostudy Samples (no. of days from the first day of sample collection to the last day of sample analysis)	58 Days

Comments: Acceptable.

Table 20. Product Information

Product	Test	Reference
Treatment ID	A	B
Product Name	Omeprazole Magnesium DR Capsules	Prilosec OTC ™ DR Tablets
Manufacturer	Dr. Reddy's Labs	Astra Zeneca
Batch/Lot No.	Batch No: EC6319	Batch No: 5338171971
Manufacture Date	Oct 2006	

Product	Test	Reference
Expiration Date	[redacted]	May 2008
Strength	20 mg	20 mg
Dosage Form	Capsule	Tablet
Bio-Batch Size	[redacted] (b) (4)	[redacted]
Production Batch Size	[redacted]	[redacted]
Potency (Assay)	20 mg	20 mg
Content Uniformity (mean, %CV)	The acceptance value is 5.3	The acceptance value is 6.5
Dose Administered	20 mg	20 mg
Route of Administration	Oral	Oral

Table 21. Study Design, Single-Dose Fed Bioequivalence Study

No. of Subjects	62 (61 completed)
No. of Sequences	2
No. of Periods	2
No. of Treatments	2
No. of Groups	2
Washout Period	14 days
Randomization Scheme	AB: 1, 2, 3, 5, 7, 10, 11, 14, 15, 16, 17, 19, 21, 22, 23, 24, 25, 28, 30, 34, 35, 39, 40, 42, 45, 46, 50, 54, 56, 58, 60 BA: 4, 6, 8, 9, 12, 13, 18, 20, 26, 27, 29, 31, 32, 33, 36, 37, 38, 41, 44, 47, 48, 49, 51, 52, 53, 55, 57, 59, 61, 62
Blood Sampling Times	Pre-dose, and at 0.50, 1.0, 1.5, 2.5, 3.5, 4.5, 5.5, 6.5, 7.5, 8.5, 10, 12, 16 and 24 hours.
Blood Volume Collected/Sample	1x 6 mL / sample
Blood Sample Processing/Storage	The samples were collected using pre-labeled Vacutainers® containing potassium-EDTA as the anticoagulant. The blood samples were stored in thermocol box with cool packs before centrifugation and were centrifuged at 4°C and 4000 rpm for 10 min. The collected plasma from each tube was aliquotted as 950 µl each, in RIA vials containing 50 µl of 0.5 M Sodium Carbonate buffer and vortexed for 15 seconds. The samples were transferred into a -20°C deep freezer for temporary storage and then maintained at -50°C or colder until assayed. The blood sampling procedure and processing was carried out in a darkened room with a yellow monochromatic light.
IRB Approval	Yes, IRB for protocol # BE-175-OMEP-2006 (Dec 29, 2006)
Informed Consent	Yes , submitted a copy
Length of Fasting Before Meal	Overnight fast of at least 10 hours until high-fat breakfast 30 min prior to dosing.
Length of Confinement	From the night before dosing until after the 24-hour blood draw.

Safety Monitoring	Vital signs of subjects were monitored at the time of check-in, pre-dose and at 2, 6, 12 and 24 hours post dose. Adverse event monitoring was done at 3, 5, and hours post-dose.

Standard FDA Meal Used?	No

Composition of Meal Used in Fed Bioequivalence Study

Composition of Meal Used in Fed Bioequivalence Study		
Composition	**Percent of total Kcal**	**Kcal**
Fat	53.84	458.1
Carbohydrate	14.29	271.2
Protein	31.87	121.6
TOTAL		850.9

Comments on Study Design: The study design is acceptable.

4.1.2.2 Clinical Results

Table 22. Demographics Profile of Subjects Completing the Bioequivalence Study

Study No. 7002/06-07 **Location in final report: Volume 10 of 23; Section**-14.1.2-2; Page No.: 004344		
	Treatment Groups	
	Test Product **N = 61**	**Reference Product** **N = 61**
Age (Years)		
Mean ± SD	26.61 ± 6.222	26.61 ± 6.222
Range	18 – 40	18 – 40
Groups		
< 18	Nil	Nil
18 – 40	61 (100.00%)	61 (100.00%)
41 – 64	Nil	Nil
65 – 75	Nil	Nil
> 75	Nil	Nil
Sex		
Female	Nil	Nil
Male	61 (100%)	61 (100%)
Race		
Asian	61 (100%)	61 (100%)
Black	Nil	Nil
Caucasian	Nil	Nil
Hispanic	Nil	Nil
Other	Nil	Nil
BMI		
Mean ± SD	21.36 ± 2.078	21.36 ± 2.078
Range	19 – 25	19 – 25
Other Factors	Nil	Nil

Note:

⇒ Subject number 43 (Sequence RT) withdrawn from the study before dosing, as he has not consumed high fat, high calorie breakfast completely in Period I.

T = Test product

R = Reference product

Table 23. Dropout Information, Fed Bioequivalence Study

Subject No.	Reason	Period	Replaced?
43*	Not consumed high fat, high calorie breakfast completely	I	No

* = Subject dropped before dosing as he was unable to consume high calorie breakfast, hence time and treatment were not provided.

Table 24. Study Adverse Events, Fed Bioequivalence Study

Body system/Adverse Event	Reported Incidence by Treatment Groups	
	Fed Bioequivalence Study No.: 7002/06-07	
	Test	Reference
Body as a whole N (%)	Nil	Nil
Cardiovascular N (%)	Nil	Nil
Gastrointestinal N (%)	Nil	Nil
Haemopoetic system*		
Elevated WBC N (%)	2 (3.23%)	
Elevated Lymphocytes N (%)	8 (12.90%)	
Elevated SGOT N (%)	3 (4.84%)	
Increased Platelets N (%)	3 (4.84%)	
Low Hemoglobin N (%)	5 (8.06%)	
Decreased Alkaline Phosphatase N (%)	2 (3.23%)	
Increased Eosinophils N (%)	5 (8.06%)	
Decreased Neutrophils N (%)	1 (1.61%)	
Low PCV N (%)	2 (3.23%)	
High ESR N (%)	1 (1.61%)	
Elevated RBC N (%)	1 (1.61%)	
Elevated SGPT N (%)	1 (1.61%)	
Increased Total Bilirubin N (%)	1 (1.61%)	

Note:
N = Number of subjects with incidence of adverse events (AEs).
% = Percentage of total number of subjects treated with the corresponding product.
* = Post clinical laboratory assessment done after completion of Period-II.

Number of subjects dosed with:

Test product	61
Reference product	61
Post clinical assessment	62

Table 25. Protocol Deviations, Fed Bioequivalence Study

Study No. 7002/06-07 **Location in final report: Volume 10 of 23; Section-16.2.2; Page No.: 004704**		
Type	**Subject No. (Test)**	**Subject No. (Reference)**
The Bioanalytical and Statistical facilities were changed to (b) (4) as per sponsor's request	Not applicable	The Bioanalytical and Statistical facilities were changed to (b) (4) (b) (4) as per sponsor's request

Note: * - post clinical sample missing

Comments on Adverse Events/Protocol Deviations:

- A total of 35 AEs in 21 subjects were reported. All AEs were reported during post clinical laboratory assessment. The relationship of AEs to the study drug was considered unlikely to be related to dosing by the investigator.
- All AEs were considered to be mild in severity.
- The firm's handling of dropouts, adverse events, and protocol deviations are acceptable.

4.1.2.3 Bioanalytical Results

Table 26. Assay Validation – Within the Fed Bioequivalence Study

Bioequivalence Study No.: 7002/06-07 Analyte Name: Omeprazole							
Parameter	**Standard Curve Samples**						
CC Level →	**CC1**	**CC2**	**CC3**	**CC4**	**CC5**	**CC6**	**CC7**
Concentration (ng/mL)	10.000	20.050	50.100	200.300	500.800	1001.600	2003.250
Inter day Precision (%CV)	1.90	3.71	3.15	2.89	2.25	2.15	1.74
Inter day Accuracy (%Actual)	101.49	99.74	92.84	100.99	98.83	102.81	103.29
Linearity (r)	0.9973-0.9997						
Linearity Range (ng/mL)	10.000 – 2003.250						
Sensitivity (ng/mL)	10.000						

Bioequivalence Study No.: 7002/06-07 Analyte Name: Omeprazole				
Parameter	**Quality Control Samples**			
QC ID →	**LQC**	**GMQC**	**MQC**	**HQC**
Concentration (ng./mL)	**30.100**	**155.450**	**802.400**	**1604.800**
Inter day Precision (%CV)	0.91	0.91	1.38	1.04
Inter day Accuracy (%Actual)	99.44	99.71	99.89	104.80

Comments on Study Assay Validation: Acceptable.

Any interfering peaks in chromatograms?	None
Were 20% of chromatograms included?	Yes
Were chromatograms serially or randomly selected?	Serially (Subject #22 to 36)

Comments on Chromatograms: Acceptable.

Table 27. SOP's Dealing with Bioanalytical Repeats of Study Samples

SOP No.	Effective Date of SOP	SOP Title
23/13	2006-08-16	Repeat Analysis Of Samples & Reintegration Of Chromatograms

Table 28. Additional Comments on Repeat Assays

Were all SOPs followed?	Yes
Did recalculation of PK parameters change the study outcome?	No
Does the reviewer agree with the outcome of the repeat assays?	Yes
If no, reason for disagreement	N/A

Summary/Conclusions, Study Assays:

- All omeprazole samples were received at the bioanalytical facility in good condition on dry ice (i.e., still frozen).
- There were no reported protocol deviations.
- All sample repeats were performed for analytical reasons of QCs not in acceptable range.
- Four (4) samples for repeated for re-confirmation, these samples were from sample time of 0.0 hrs.

The bioanalytical methodology is **acceptable**.

4.1.2.4 Pharmacokinetic Results

Table 29. Arithmetic Mean Pharmacokinetic Parameters

Mean plasma concentrations are presented in Table 33 and Figure 2

Fed Bioequivalence Study, Study No. 7002/06-07									
Parameter (units)	Test				Reference				T/R
	Mean	%CV	Min	Max	Mean	% CV	Min	Max	
AUC0-t (ng*hr/mL)	1936.59	98.98	244.07	7737.51	1933.40	90.87	168.40	6391.64	1.00
AUC∞ (ng*hr/mL)	1974.37	98.67	253.06	7834.88	2004.72	89.47	288.96	6451.21	0.98
Cmax (ng/mL)	604.44	60.50	116.91	1664.21	611.56	60.00	86.86	1406.53	0.99
T_{MAX}(hr)	3.50	.	2.50	5.50	3.50	.	1.50	5.50	1.00
KE(hr-1)	0.74	47.98	0.17	1.38	0.74	53.06	0.17	2.13	1.01
THALF(hr)	1.33	70.61	0.50	4.18	1.32	64.88	0.33	4.01	1.01

* Tmax values are presented as median, range

Table 30. Geometric Means and 90% Confidence Intervals - Firm Calculated

Omeprazole Magnesium DR capsules 1 x 20 mg Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals				
Fed Bioequivalence Study No. 7002/06-07				
Parameter (units)	Test	Reference	Ratio	90% C.I.
AUC_{last} (ng*hr/mL)	1119.7360	1181.0086	94.81	87.30 - 102.97
AUC_{Inf} (ng*hr/mL)	1232.3389	1299.8792	94.80	89.21 – 100.75
C_{max} (ng/mL)	463.1360	466.9448	99.18	91.10 – 107.99
Omeprazole Magnesium 20mg DR capsules 1 x 20 mg Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals (EXCLUDING Subject # 23)				
Fed Bioequivalence Study No. 7002/06-07				
Parameter (units)	Test	Reference	Ratio	90% C.I
AUC_{last} (ng*hr/mL)	1188.9852	1220.3943	97.43	90.88 – 104.44
AUC_{Inf} (ng*hr/mL)	1232.3389	1299.8792	94.80	89.21 – 100.75
C_{max} (ng/mL)	463.1360	466.9448	99.18	91.10 – 107.99

Comments: Subject # 23 was omitted from PK calculations due to missing samples. Only 2 concentrations are reported in period I and four concentrations in period II. Subject # 8 was also found to have missing

samples, only 2 plasma concentrations are reported in period I and four concentrations in period II. The reviewer has calculated by omitting subjects # 8 and 23.

Table 31. Geometric Means and 90% Confidence Intervals - Reviewer Calculated

Omeprazole Magnesium DR capsules 1 x 20 mg Least Squares Geometric Means, Ratio of Means, and 90% Confidence Intervals					
Fed Bioequivalence Study No. 7002/06-07					
Parameter (units)	**Test**	**Reference**	**Ratio**	**90% C.I.**	
AUC_{last} (ng*hr/mL)	1238.90	1296.11	0.96	89.76	101.79
AUC_{Inf} (ng*hr/mL)	1270.26	1340.28	0.95	89.14	100.77
C_{max} (ng/mL)	503.04	500.32	1.01	92.59	109.18

Table 32. Additional Study Information

Root mean square error, AUC0-t	0.2043	
Root mean square error, AUC∞	0.1957	
Root mean square error, Cmax	0.2676	
	Test	**Reference**
Kel and AUC∞ determined for how many subjects?	58	58
Do you agree or disagree with firm's decision?	Agree	
Indicate the number of subjects with the following:		
measurable drug concentrations at 0 hr	None	None
first measurable drug concentration as Cmax	0	0
Were the subjects dosed as more than one group?	No	

Ratio of AUC0-t/AUC∞				
Treatment	**n**	**Mean**	**Minimum**	**Maximum**
Test	58	0.98	0.92	0.99
Reference	58	0.98	0.92	0.99

Comments on Pharmacokinetic and Statistical Analysis:

The mean AUCt/AUC∞ ratio >0.80 for both test and reference products indicates that the firm's sampling schedule for omeprazole was carried out for a sufficiently long period of time.

The 90% CI for the least-squares geometric means of lnAUCt, lnAUC∞ and lnCmax calculated by the Reviewer agree with the firm's calculations and meet the 90% CI criteria for BE (80.00-125.00%).

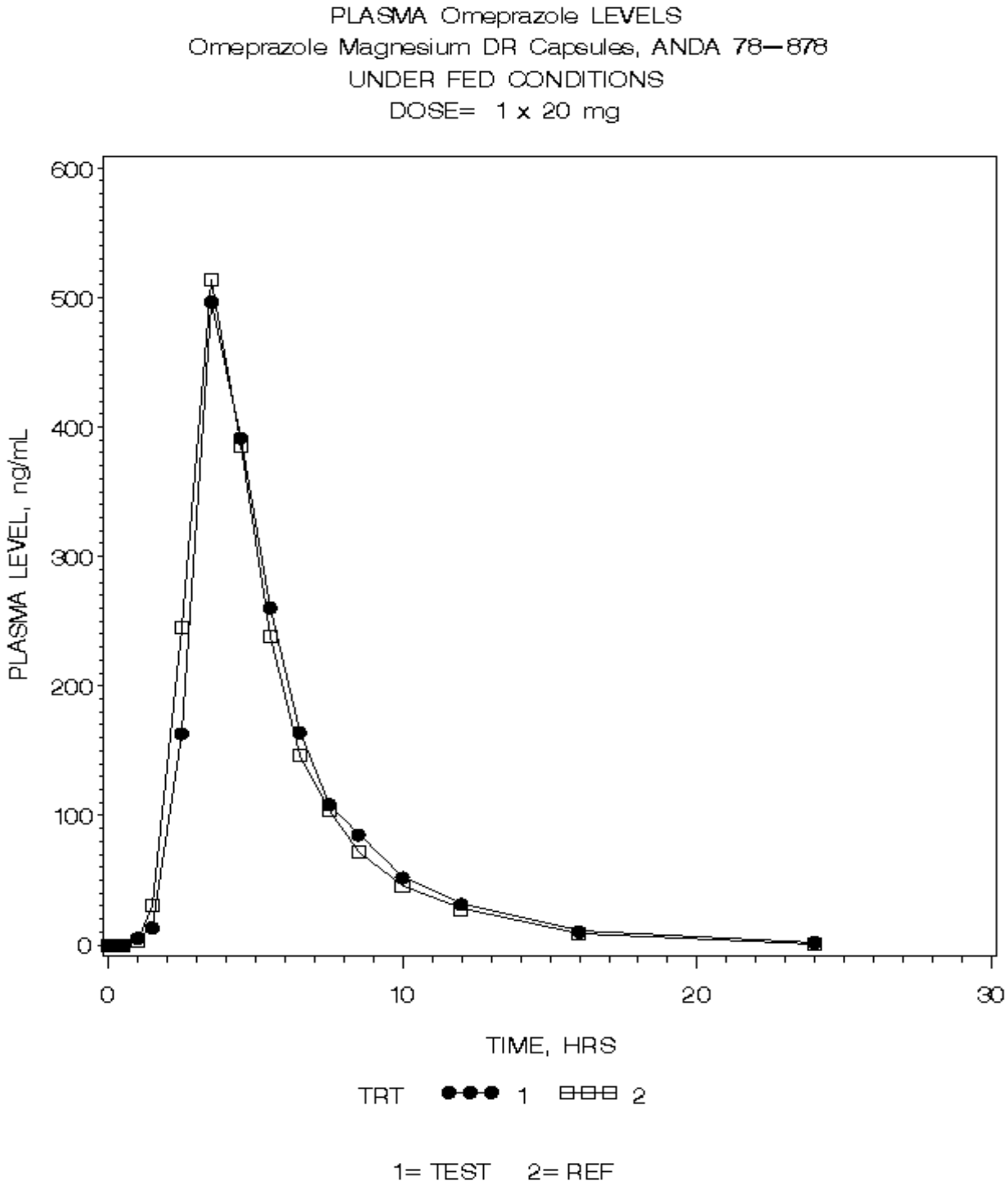
Summary/Conclusions, Single-Dose Fed Bioequivalence Study:

The in vivo BE study under fed conditions is **acceptable**.

Table 33. Mean Plasma Concentrations, Single-Dose Fed Bioequivalence Study

Omeprazole					
Time (hr)	Test (n= 59)		Reference (n= 59)		T/R Ratio
	Mean (ng/mL)	% CV	Mean (mcg/mL)	% CV	
0.00	0.00	0.00	.	0.00	.
0.50	0.50	0.17	768.11	0.00	.
1.00	1.00	5.16	608.83	2.95	518.95
1.50	1.50	13.42	308.45	30.30	285.99
2.50	2.50	163.31	100.51	245.16	97.85
3.50	3.50	496.66	82.08	513.66	77.76
4.50	4.50	391.57	88.07	385.76	84.87
5.50	5.50	260.50	111.13	238.22	104.64
6.50	6.50	164.30	137.54	146.23	123.82
7.50	7.50	108.73	147.92	103.84	142.26
8.50	8.50	85.22	173.48	71.73	154.48
10.00	10.00	52.02	180.84	45.57	166.46
12.00	12.00	31.49	192.40	27.71	183.30
16.00	16.00	10.45	219.62	8.58	212.77
24.00	24.00	1.80	320.88	0.89	458.27

Figure 2. Mean Plasma Concentrations, Single-Dose Fed Bioequivalence Study



4.2 Formulation Data

Omeprazole Magnesium Delayed-Release Capsules, 20 mg

S.No	Component	Omeprazole Magnesium Delayed-Release Capsules, 20 mg	
		mg per Capsule	%
			(b) (4)

Total Weight	**735.80**	**100.00**
[redacted] (b) (4)		

Is there an overage of the active pharmaceutical ingredient (API)?	Yes, 20.60 mg equivalent base
If the answer is yes, has the appropriate chemistry division been notified?	N/A
If it is necessary to reformulate to reduce the overage, will bioequivalence be impacted?	N/A
Comments on the drug product formulation:	**ACCEPTABLE**

Comments:

Based on a maximum daily dose of 20 mg, the maximum daily uptake of elemental iron from the 20 mg capsules is [redacted] (b) (4) All the inactive ingredients are USP/NF grade and within the acceptable IIG ranges.

The product formulation is acceptable.

4.3 Dissolution Data

Dissolution Review Path	DFS N078878 Bioequivalence Dissolution Review
Dissolution Conditions	**Apparatus:** USP Apparatus II (Paddles)
	Speed of Rotation: 100 RPM
	Medium: Acid Stage : 300 ml of 0.1N HCl (degassed) followed by Buffer Stage : 1000 ml of pH 6.8 Phosphate buffer (degassed)
	Volume: Acidic Stage : 300 ml Buffer Stage : 1000 ml
	Temperature: 37 ± 0.5 °C
Firm's Proposed Specifications	Acid Stage: Not More than (b) (4) of the labeled amount of Omeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved in 2 hours. Buffer Stage: Not less than (b) (4) Q) of the labeled amount of Omeprazole ($C_{17}H_{19}N_3O_3S$) is dissolved in 30 minutes.
Dissolution Testing Site (Name, Address)	Dr. Reddy's Laboratories Limited - Generics, Bachepalli, Post Bag No. 15, Kukatpally P.O., Hyderabad – 500 072, INDIA

Study Ref No.	**Testing Date**	**Product ID \ Batch No. (Test - Manufacture Date) (Reference – Expiration Date)**	**Dosage Strength & Form**	**No. of Dosage Units**		**Collection Times (minutes)**				**Study Report Location**
						10 Min	**20 Min**	**30 Min**	**45 Min**	
Diss.Study Report No: BM00503	February 21, 2007	Omeprazole Magnesium Delayed-Release Capsules, 20 mg Batch No: EC6319	20 mg Capsule	12	Mean	92	91	90	88	Volume #: 02 Page #: 000110
					Range	(b) (4)				
					%CV	2.2	2.4	2.4	2.4	
Diss.Study Report No: BM00473	February 21, 2007	Prilosec OTC™ (omeprazole magnesium) delayed-release tablets, 20 mg (Batch No: 5338171971)	20 mg Tablet	12	Mean	69	85	93	92	Volume #: 02 Page #: 000111
					Range	(b) (4)				
					%CV	11.7	3.8	1.5	1.4	

Reviewer's Comments: The firm's dissolution testing is the same as that of FDA-recommended method for RLD Tablets. The firm's proposed method is acceptable since it is very similar to the FDA-recommended method for the OTC DR Tablets.

Dissolution testing is **acceptable**.

4.4 Detailed Regulatory History (If Applicable)

The OGD reviewed the following control documents from 2001 to 2008 for Omeprazole Magnesium DR Tablets:

05-0387 for (b) (4) 6/19/2005
05-1035 for 10/15/2005
06-0709 for (b) (4) 7/30/2006

The OGD also reviewed the following protocols from 1998 to 2008 for Omeprazole Magnesium DR Capsules:

06-039, Dr. Reddy; 9/20/2006
03-052, (b) (4) 3/19/2004
97-039, (b) (4) 2/4/1998
98-015, 4/30/1998

4.5 Consult Reviews

None.

4.6 SAS Output

4.6.1 Fasting Study Data

Following this page, 18 pages withheld in full (b)(4)

4.7 Additional Attachments

None.

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-878

APPLICANT: Dr. Reddy's Laboratories Ltd.

DRUG PRODUCT: Omeprazole Magnesium Delayed Release (DR) Capsules, 20 mg (eq. base)

The Division of Bioequivalence (DBE) has completed its review and has no further questions at this time.

We acknowledge that you will perform future dissolution testing using the following dissolution method and specifications:

Acid Stage:

(Acid resistance is measured from the dosage form and not from an aliquot of 0.1N HCl):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.1N HCl @ 37°C
Volume: 300mL
Time: 2h

Specification: NMT (b) (4) *of the labeled amount of omeprazole is dissolved at the end of the acid stage.*

Buffer Stage:

Fresh capsules are assayed and are from the same lot tested for acid resistance. Drug release measured from an aliquot of the phosphate buffer.):

Apparatus: USP Apparatus II (Paddle)
Speed: 100rpm
Medium: 0.05M Na_3PO_4, pH 6.8 @ 37°C
Volume: 1000mL

Specification: NLT (b) (4) *(Q) of the labeled amount of omeprazole is dissolved in 30 minutes.*

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

4.8 Outcome Page

ANDA: 78-878

Completed Assignment for 078878 ID: 4441

Reviewer: Palamakula, Anitha **Date Completed:**

Verifier: Moheb Makary, **Date Verified:**

Division: Division of Bioequivalence

Description: Omeprazole DR Caps Fasting & Fed

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
4441	3/16/2007	Bioequivalence Study	Fasting Study	1	1
4441	3/16/2007	Bioequivalence Study	Fed Study	1	1
				Bean Total:	2

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

/s/

Anitha Palamakula
1/22/2008 10:18:16 AM
BIOPHARMACEUTICS

Moheb H. Makary
1/22/2008 10:22:32 AM
BIOPHARMACEUTICS

Barbara Davit
1/24/2008 05:42:47 PM
BIOPHARMACEUTICS

DIVISION OF BIOEQUIVALENCE ACCEPTABLE DSI INSPECTION REPORT REVIEW

ANDA No.	(b) (4)
Drug Product Name	
Strength	
Applicant Name	Dr. Reddy's Laboratories Limited
Date of Original Submission	June 16, 2006
Date of Report	May 29, 2008
Reviewer	Beth Fabian Fritsch, R.Ph., MBA

EXECUTIVE SUMMARY

The Division of Scientific Investigations (DSI) inspection report of Wellquest Clinical Research, Clinical Section was received by the Division of Bioequivalence and found acceptable. The site inspection was requested for ANDA (b) (4) The following applications contained studies conducted at these sites. Given the acceptable inspection of the site, the applications are now acceptable.

ANDA #	Firm	Drug Product
78-383	Dr. Reddy's Labs	Pioglitazone Hydrochloride
78-878	Dr. Reddy's Labs	Omeprazole
78-493	Dr. Reddy's Labs	Trandolapril

The applications are complete.

COMMENTS:

None

DEFICIENCY COMMENTS:

None

RECOMMENDATIONS:

The Division of Scientific Investigation (DSI) inspection report of Wellquest Clinical Research, Clinical Section was received by the Division of Bioequivalence on May 29, 2008 and found acceptable.

From a bioequivalence point of view, the firm has met the requirements for *in-vivo* bioequivalence and *in-vitro* dissolution testing and the application is approvable.

I. Completed Assignment for (b) (4) ID: 6234

Reviewer: Fritsch, Beth **Date Completed:**

Verifier: , **Date Verified:**

Division: Division of Bioequivalence

Description: Related ANDAs

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
6234	5/29/2008	Other	DSI Inspection Report	1	1
				Bean Total:	1

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

/s/

Beth Fabian-Fritsch
8/14/2008 05:59:28 PM
BIOPHARMACEUTICS

Lizzie Sanchez
8/19/2008 09:07:25 AM
BIOPHARMACEUTICS

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078878

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

DR. REDDY'S
DR. REDDY'S LABORATORIES, INC.

ORIGINAL

90 SOMERSET CORPORATE BOULEVARD
7TH FLOOR
BRIDGEWATER, NJ 08807
TELEPHONE (908) 203-4900
FAX (908) 203-4970

This Letter Contains Confidential, Commercial and Trade Secret Information
Do Not Disclose Under FOI

505(j)(2)(A)
OK 6/4/07

March 16, 2007

78678

Office of Generic Drugs
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re : Omeprazole Magnesium Delayed-Release Capsules, 20 mg
Abbreviated New Drug Application

Dear Sir/ Madam:

Dr. Reddy's Laboratories Inc., U.S. agent to Dr. Reddy's Laboratories Ltd., herewith submits an abbreviated new drug application (ANDA) for Omeprazole Magnesium Delayed-Release Capsules, 20 mg pursuant to Section 505 (j) of the Federal Food, Drug, and Cosmetic Act.

This ANDA refers to the listed drug, PRILOSEC OTC™ (omeprazole magnesium) delayed-release tablets, 20 mg manufactured by Astrazeneca, the holder of the approved application listed in the Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book).

RECEIVED
MAR 19 2007
OGD/ORDER

Reference is made to the petition filed to FDA on August 20, 2004 for a change in the dosage form from that of the listed drug product (i.e., from tablets to capsules) and the same has been approved on July 05, 2005. The petition docket number is 2004P-0373/CP1. A copy of the petition approval letter is enclosed immediately following this cover letter.

Omeprazole Magnesium Delayed-Release Capsules, 20 mg will be manufactured, and supplied by Dr. Reddy's Laboratories Limited, Bachepalli - 502 325, Andhra Pradesh, India, manufacturing facility, in accordance with 21 CFR § 210 and 211.

The manufacturer of the drug substance, Omeprazole Magnesium used to produce Omeprazole Magnesium Delayed-Release Capsules, 20 mg is Dr. Reddy's Laboratories Limited, Active Pharmaceutical Ingredients Unit-III, Plot No. 116, IDA Bollaram, Jinnaram Mandal, Medak District, Andhra Pradesh, India.

Dr. Reddy's Laboratories Limited, Generics division, located at Bachepalli – 502 325, Andhra Pradesh, India provided the purchasing, research and development, production planning, pilot production, as well as the stability testing and other operations.

The bioavailability / bioequivalence study under Fed condition was conducted at Wellquest Clinical Research, Wellspring Hospital (4th floor), Ganpatrao Kadam Marg, Lower Parel, Mumbai - 400 013, India, while the study under Fasting condition was conducted at (b) (4) (b) (4) and these studies support the conclusion that Dr. Reddy's Laboratories Limited's Omeprazole Magnesium Delayed-Release Capsules, 20 mg is bioequivalent to Astrazeneca's PRILOSEC OTC™ (omeprazole magnesium) delayed-release tablets, 20 mg.

The *in vitro* dissolution profiles for Omeprazole Magnesium Delayed-Release Capsules, 20 mg and Astrazeneca's PRILOSEC OTC™ (omeprazole magnesium) delayed-release tablets, 20 mg are comparable. SAS transport files for Fasting and Fed studies are found immediately following this letter in the archival copy of this submission.

Three copies (One Archival and Two Review Copies) of the method validation are also provided. The firm commits to resolve any issues identified in the method validation process post approval.

Omeprazole Magnesium Delayed-Release Capsules, 20 mg are stable and 24 months expiration date is requested. The 24 months expiration dating of this product is supported by one, two and three months accelerated stability data (40°C ± 2°C/ 75% ± 5% Relative Humidity) in the smallest and largest fill size of the container/closure system proposed for marketing. The stability studies were conducted under a stability protocol that is in conformance with the current FDA Stability guidelines.

The route of administration, active ingredient, potency and labeling (except DESCRIPTION & HOW SUPPLIED) for Dr. Reddy's Omeprazole Magnesium Delayed-Release Capsules, 20 mg are same as those for Astrazeneca's PRILOSEC OTC™ (omeprazole magnesium) delayed-release tablets, 20 mg.

Pursuant to Code of Federal Regulations (CFR) Title 21 314.440 (a)(4), a third copy of this application is also enclosed. This is the required field copy. Dr. Reddy's certifies that this is a true copy of the technical section as described in 21 CFR 314.50 (d)(1). The archival copy of this ANDA is submitted in 23 volumes.

A copy of QbR QOS is located immediately behind the cover letter. The pdf rendition of the QbR QOS as well as a MS Word version of the same is being provided in the CD- ROM.

All electronic files included in this submission are located immediately behind the cover letter in the Archival copy of this submission. The electronic submission is approximately 10.9 MB. All files were checked and verified to be free of viruses prior to being written to CD using McAfee® VirusScan® Enterprise, program version 8.0i and scan engine 5100 with a virus definition date of March 15, 2007.

Also included in this submission is an extra copy of our cover letter. Please acknowledge receipt by date stamping the copy and returning it to us in the self-addressed stamped envelope provided for your convenience. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

Kumara Sekar, Ph.D.,
Director, Global Regulatory Affairs & Compliance

M E M O R A N D U M

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

DATE : April 20, 2007

TO : Director
Division of Bioequivalence (HFD-650)

FROM : Chief, Regulatory Support Branch
Office of Generic Drugs (HFD-615)

SUBJECT: Examination of the bioequivalence study submitted with an ANDA 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg to determine if the application is substantially complete for filing and/or granting exclusivity pursuant to 21 USC 355(j)(5)(B)(iv).

Dr Reddy's Laboratories Inc. has submitted ANDA 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg. The ANDA contains a certification pursuant to 21 USC 355(j)(5)(B)(iv) stating that patent(s) for the reference listed drug will not be infringed by the manufacturing or sale of the proposed product. Also it is a first generic. In order to accept an ANDA that contains a first generic, the Agency must formally review and make a determination that the application is substantially complete. Included in this review is a determination that the bioequivalence study is complete, and could establish that the product is bioequivalent.

Please evaluate whether the request for study submitted by Dr Reddy's Laboratories Inc. on March 16, 2007 for its Omeprazole Magnesium Delayed-Release product satisfies the statutory requirements of "completeness" so that the ANDA may be filed.

A "complete" bioavailability or bioequivalence study is defined as one that conforms with an appropriate FDA guidance or is reasonable in design and purports to demonstrate that the proposed drug is bioequivalent to the "listed drug".

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

/s/

Eda Howard
4/23/2007 08:13:55 AM
APPLICATIONS EXA

BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS

ANDA# 078878 **FIRM NAME** **Dr. Reddy's Laboratories, Ltd.**

DRUG NAME Omeprazole Magnesium Capsules, eq 20 mg base

DOSAGE FORM **DR Capsules**
SUBJ: Request for examination of: Bioequivalence Study

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Division of Bioequivalence
☒	**Study meets statutory requirements**
☐	**Study does NOT meet statutory requirements**
	Reason:
☐	**Waiver meets statutory requirements**
☐	**Waiver does NOT meet statutory requirements**
	Reason:

RECOMMENDATION: ☒ **COMPLETE** ☐ **INCOMPLETE**

Reviewed by:

_____ Date: _____

Reviewer

_____ Date: _____

Team Leader

Item Verified:	YES	NO	Required Amount	Amount Sent	Comments
Protocol	☒	☐			fasting, starts p. 164; fed, starts p.209
Assay Methodology	☒	☐			fasting, p.3870-3878; fed, p.7587 to 7595
Procedure SOP	☒	☐			fasting, p.3870-3878; fed, p.7587 to 7595. For reassay: fasting, p.3856 to 3868; fed, p. 7573 to 7585
Methods Validation	☒	☐			fasting, p.3880-3968; fed, p.7597-7684
Study Results Ln/Lin	☒	☐			fasting data starts on p.1076, 1085. Also seen on p.1130, 1133. fasting lin graphs on p.1088, log/lin on p.1089; fed data starts on 4369, 4379. Also seen on p.4450, 4454. fed lin graph on p. 4383, fed log/lin graph on p. 4384
Adverse Events	☒	☐			fasting, p.1181-1182; fed, p.4333-4336
IRB Approval	☒	☐			fasting, p.1283-1284; fed, p. 5029-5036
Dissolution Data	☒	☐			p.105-111,113,114,117
Pre-screening of Patients	☒	☐			fasting, at beginning of case report form for given subject; fasting, p. 5122-5157
Chromatograms	☒	☐			fasting, starts on p. 3971, for subj. 16-23; fed, starts on p. 7687, for subj 22-36
Consent Forms	☒	☐			fasting, starts p.1287,1295; fed, starts p.5038,5047
Composition	☒	☐			fasting, starts on 1029, 1031, 1045,

					1411, 1415; fed p.4341-4345
Summary of Study	☒	☐			fasting, p.1002-1006; fed, p. 4295-4299
Individual Data & Graphs, Linear & Ln	☒	☐			fasting data start on p. 1072,1128,1178;fasting graphs start on p.1090 (lin), p. 1109 (log/lin), and p. 1139 (kel). Fed data start on p. 4347, 4447, 4525. Fed graphs start on p. 4385(lin), p. 4416 (log/lin), and p. 4463 (kel).
PK/PD Data Disk Submitted)	☒	☐			fasting, able to open conc and pk file; fed, able to open conc and pk file
Randomization Schedule	☒	☐			fasting, p.1317-1319; fed, p.5114-5115
Protocol Deviations	☒	☐			fasting, p.1416; fed, p. 4704
Clinical Site	☒	☐			fasting, p. 1015; fed, p. 4295
Analytical Site	☒	☐			fasting, p. 1015; fed, p. 4295
Study Investigators	☒	☐			fasting and fed, p.88
Medical Records	☒	☐			fasting, starts p.1528; fed starts p.5122
Clinical Raw Data	☒	☐			fasting, p. 1435-1483, p. 1490-1522; fed, p. 5122-5258
Test Article Inventory	☒	☐			fasting, p. 1322, fed, p. 5264
BIO Batch Size	☒	☐			p. 113
Assay of Active Content Drug	☒	☐			p.114
Content Uniformity	☒	☐			p.113
Date of Manufacture	☒	☐			p.113
Exp. Date of RLD	☒	☐			p.117
BioStudy Lot Numbers	☒	☐			fasting, p.1003; fed, p.4296

Statistics	☒	☐			fasting, p. 1177; fed, p. 4524, 4528
Summary results provided by the firm indicate studies pass BE criteria	☒	☐			fasting and fed, p.245; fasting, p.1006; fed, p. 4298
Waiver requests for other strengths / supporting data	☒	☐			Not applicable (p. 104)

Additional Comments regarding the ANDA:

1. The reference listed drug (RLD) for this drug product is Astra Zeneca's Omeprazole Magnesium DR TABLET eq 20 mg base.
2. The RLD is an OTC product.
3. This ANDA is for DR CAPSULE and not for a DR TABLET.
4. The firm has not mentioned that its ANDA is for an OTC product. As per communication with Marty Shimer, the firm cannot market this product as a Rx product. The Labeling Division shall tell the firm that it can market this product only as an OTC product and not as a Rx product.
5. The change in dosage form (DR TABLET to DR CAPSULE) is authorized by the approval of Citizen Petititon 2004P-0373/CP1.

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

/s/

Shriniwas G. Nerurkar

5/15/2007 09:46:13 AM

DR. REDDY'S
DR. REDDY'S LABORATORIES, INC.

200 SOMERSET CORPORATE BOULEVARD
7TH FLOOR
BRIDGEWATER, NJ 08807
TELEPHONE (908) 203-4900
FAX (908) 203-4970

ORIGINAL

This Letter Contains Confidential, Commercial and Trade Secret Information Do Not Disclose Under FOI

June 1, 2007

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NJMC

Fax: 301-443-3847

Attention: Peter Chan

Reference: **ANDA # 78-878**
Omeprazole Magnesium Delayed-Release Capsules, 20 mg
Telephone Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Telephone Amendment in response to the telephone discussion with Mr. Peter Chan of the Agency on May 30, 2007.

RECEIVED
JUN 4 2007
OGD

A. Deficiencies:

Mr. Peter Chan called and requested the following:

1. *Signed form 3454 with appropriate checked box.*
2. *Master Batch Record for 14's, 28's and 42's blister pack count.*
3. *Clarification regarding the* [redacted] (b) (4) *information for 7's count blister* [redacted] (b) (4) *one page 011433.*

RESPONSE:

1. The signed for 3454 with appropriate checked box provided in **Exhibit-1.**
2. The Master Batch Record for 14's, 28's and 42's blister pack count are provided in **Exhibit-2.**

3. We would like to inform the Agency that, we have provided the 7's blister strip orientation on page 011433 as 1 x 4 + 1 x 3 (1 row of 4's and 1 row of 3's). We propose the blister packs of 14's, 28's and 42's as market packs. (b) (4) (b) (4) (b) (4). The configuration for blister package of size 14's, 28's and 42's is as follows:

Package Size	Configuration
14's	2 blister strips of 7's (7's blister strip have 1 row of 4 and 1 row of 3) will be packed in a printed carton with one literature.
28's	2 blister package of 14's (each 14's blister package containing 2 blister strips of 7's with one literature) will be packed in a printed carton.
42's	3 blister package of 14's (each 14's blister package containing 2 blister strips of 7's with one literature) will be packed in a printed carton.

Also included in this submission is an extra copy of our cover letter. Please acknowledge receipt by date stamping the copy and returning it to us in the self-addressed stamped envelope provided for your convenience. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

Kumara Sekar, Ph.D.,
Director, Global Regulatory Affairs & Compliance

ANDA CHECKLIST
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION

ANDA Nbr: 78-878 **FIRM NAME**: DR REDDY'S LABORATORIES, INC.

RELATED APPLICATION(S): SEE 78-693 FOR OMEPRAZOLE DELAYED RELEASE CAPSULES USP, 10 MG AND 20 MG FROM DR REDDY'S LABORATORIES, INC. PN 12/21/06 (RLD PRILOSEC)**. SEE 78-490 FOR** OMEPRAZOLE DELAYED RELEASE CAPSULES USP, 40 MG FROM DR REDDY'S LABORATORIES, INC. PN 2/28/07 (RLD PRILOSEC).

Bio Assignments:		**☐ Micro Review (No)**
☒ BPH	**☐ BCE**	
☐ BST	**☒ BDI**	

First Generic Product Received? YES

DRUG NAME: OMEPRAZOLE MAGNESIUM DELAYED RELEASE
DOSAGE FORM: CAPSULES, 20 MG

Random Queue: 7
Chem Team Leader: M. Scott Furness PM: Theresa Liu Labeling Reviewer: Koung Lee

Letter Date: MARCH 16, 2007 **Received Date**: MARCH 19, 2007

Comments: EC - 1 YES **On Cards:** YES
Therapeutic Code: 8030700 ANTI-ULCER

Archival Format: PAPER **Sections** I **(356H Sections per EDR Email)**
Review copy: YES E-Media Disposition: YES SENT TO EDR
Not applicable to electronic sections
Field Copy Certification (Original Signature) YES

Methods Validation Package (3 copies PAPER archive) **YES**
(Required for Non-USP drugs)

Cover Letter YES | **Table of Contents** YES

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Peter Chen	**Recommendation:**
Date 6/4/2007	**☒ FILE** **☐ REFUSE to RECEIVE**
Supervisory Concurrence/Date: ____	**Date: ____**

ADDITIONAL COMMENTS REGARDING THE ANDA:

5/30/2007 Tcon with Sai Prasad

Please provide the following:

1. Please mark the appropriate checkbox on form 3454 and resubmit

(OK per 6/1/2007 correspondence)

2. Please provide master batch packaging record for the 14 ct, 28 ct and 42 ct blisters

(OK per 6/1/2007 correspondence)

3. (b) (4)

Top 200 Drug Product:

ACCEPTABLE

Sec. I	**Signed and Completed Application Form (356h)** YES (Statement regarding Rx/OTC Status) OTC YES	☒
Sec. II	**Basis for Submission** **NDA# : 21-229** Ref Listed Drug: PRILOSEC OTC Firm: ASTRAZENECA ANDA suitability petition required? DOCKET NO. 2004P-0373/CP1 DATED 7/5/05 If Yes, then is change subject to PREA (change in dosage form, route, active ingredient) For products subject to PREA a wavier request must be granted prior to approval of ANDA. Wavier Granted:	☒
Sec. III	**Patent Certification** 1. Paragraph: III and IV 4786505*PED OCT 20,2007 P3 4853230*PED OCT 20,2007 P3 5690960 NOV 25,2014 P4 5753265 JUN 07,2015 P4 5817338 OCT 06,2015 P4 5900424 MAY 04,2016 P4 6403616 NOV 15,2019 P4 6428810 NOV 03,2019 P4 2. Expiration of Patent: Pending consult from general counsel regarding ped extension for the 6 patents. A. Pediatric Exclusivity Submitted? B. Pediatric Exclusivity Tracking System checked? **Exclusivity Statement:** YES	☒
Sec. IV	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use Same as RLD 2. Active ingredients Same as RLD 3. Route of administration Same as RLD 4. Dosage Form Capsule; DOCKET NO. 2004P-0373/CP1 5. Strength Same as RLD	☒
Sec. V	**Labeling** (Mult Copies N/A for E-Submissions) 1. 4 copies of draft (each strength and container) or 12 copies of FPL submitted 2. 1 RLD label and 1 RLD container label submitted 3. 1 side by side labeling comparison with all differences annotated and explained submitted 4. Was a proprietary name request submitted? no (If yes, send email to Labeling Rvwr indicating such.)	☒

Sec. VI

Bioavailability/Bioequivalence **OK per DBE prefiling checklist.** ☒

1. Financial Certification (Form FDA 3454) **and Disclosure Statement** (Form 3455) YES but needs to mark applicable checkbox
(OK per 6/1/2007 correspondence)

2. Request for Waiver of In-Vivo Study(ies): NA

3. Formulation data same? (Comparison of all Strengths) (Ophthalmics, Otics, Topicals Perenterals)

4. Lot Numbers of Products used in BE Study(ies): Test Batch #EC6319

5. Study Type: IN-VIVO PK STUDY(IES) (Continue with the appropriate study type box below)

Study Type

IN-VIVO PK STUDY(IES) (i.e., fasting/fed/sprinkle) FASTING AND FED ON 20 MG ☒

OK per DBE prefiling checklist.

a. Study(ies) meets BE criteria (90% CI or 80-125, Cmax, AUC)

Table 3 Statistical Summary of the Comparative Bioequivalence Data

Study No.: 3701/06-07
Omeprazole Magnesium 20mg DR capsules
Least Squares Geometric Means, Ratio of the Means and 90% Confidence Intervals

Study report location:
Volume 03 of 23; Table 14.2.3-1, Page No.: 001177

Parameter	Test	Reference	Ratio	90% C.I
AUC_{last} (ng*hr/mL)	1362.7364	1358.5024	100.31	94.97 -105.95
AUC_{Inf} (ng*hr/mL)	1394.6995	1393.2674	100.10	94.83 – 105.67
C_{max} (ng/mL)	688.1198	659.9620	104.27	97.45 – 111.56

Study No.: 7002/06-07
Omeprazole Magnesium 20mg DR capsules
Least Squares Geometric Means, Ratio of the Means and 90% Confidence Intervals

Study report location:
Volume 10 of 23; Table 14.2.3-1; Page No.: 004524

Parameter	Test	Reference	Ratio	90% C.I
AUC_{last} (ng*hr/mL)	1119.7360	1181.0086	94.81	87.30 - 102.97
AUC_{Inf} (ng*hr/mL)	1232.3389	1299.8792	94.80	89.21 – 100.75
C_{max} (ng/mL)	463.1360	466.9448	99.18	91.10 – 107.99

Least Squares Geometric Means, Ratio of the Means and 90% Confidence Intervals (Excluding Subject 23)

Study report location:
Volume 10 of 23; Table 14.2.3-3; Page No.: 004528

Parameter	Test	Reference	Ratio	90% C.I
AUC_{last} (ng*hr/mL)	1188.9852	1220.3943	97.43	90.88 – 104.44
AUC_{Inf} (ng*hr/mL)	1232.3389	1299.8792	94.80	89.21 – 100.75
C_{max} (ng/mL)	463.1360	466.9448	99.18	91.10 – 107.99

b. EDR Email: Data Files Submitted: YES SENT TO EDR

c. In-Vitro Dissolution: YES

test Batch EC6319

Study Type

IN-VIVO BE STUDY with CLINICAL ENDPOINTS NO ☐

a. Properly defined BE endpoints (eval. by Clinical Team)

b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120)

c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team)

d. EDR Email: Data Files Submitted

Study Type

TRANSDERMAL DELIVERY SYSTEMS NO ☐

a. <u>In-Vivo PK Study</u>

1. Study(ies) meet BE Criteria (90% CI or 80-125, Cmax, AUC)
2. In-Vitro Dissolution
3. EDR Email: Data Files Submitted

b. <u>Adhesion Study</u>

c. <u>Skin Irritation/Sensitization Study</u>

Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** NO a. Solutions (Q1/Q2 sameness): 1. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) b. Suspensions (Q1/Q2 sameness): 1. In-Vivo PK Study a. Study(ies) meets BE Criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted 2. In-Vivo BE Study with Clinical EndPoints a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted 3. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	☐
Study Type	**TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES)** NO a. Pilot Study (determination of ED50) b. Pivotal Study (study meets BE criteria 90%CI or 80-125)	☐
Sec. VII	**Components and Composition Statements** 1. Unit composition and batch formulation submitted 2. Inactive ingredients as appropriate YES	☒
Sec. VIII	**Raw Materials Controls** 1. **Active Ingredients** a. Addresses of bulk manufacturers submitted b. Type II DMF authorization letters or synthesis submitted DMF 17706 c. COA(s) specifications and test results from drug substance mfgr(s) submitted Batch MG018G05 d. Applicant certificate of analysis submitted RK0799 e. Testing specifications and data from drug product manufacturer(s) submitted f. Spectra and chromatograms for reference standards and test samples submitted g. CFN numbers 2. **Inactive Ingredients** a. Source of inactive ingredients identified submitted b. Testing specifications (including identification and characterization) submitted c. Suppliers' COA (specifications and test results) submitted d. Applicant certificate of analysis submitted	☒
Sec.IX	**Description of Manufacturing Facility** 1. Full Address(es)of the Facility(ies) submitted 2. CGMP Certification: YES 3. CFN numbers submitted	☒

Sec. X	**Outside Firms Including Contract Testing Laboratories** none used 1. Full Address 2. Functions 3. CGMP Certification/GLP 4. CFN numbers	☒
Sec. XI	**Manufacturing and Processing Instructions** 1. Description of the Manufacturing Process (including Microbiological Validation, if Appropriate) submitted 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified MBR TY (b) (4) capsules Missing 14 ct, 28 ct, and 42 ct master packaging records **(OK per 6/1/2007 correspondence)** 3.If sterile product: Aseptic fill / Terminal sterilization NA 4.Filter validation (if aseptic fill) NA 5. Reprocessing Statement submitted	☒
Sec. XII	**In-Process Controls** 1. Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation Batch # EC6319 TY (b) (4) capsules, AY (b) (4) capsules PY capsules note bracketed (although technically it is not bracketing) 14ct, 28ct, and 42 ct blisters Omeprazole Magnesium Delayed-Release Capsules, 20 mg Section XII – In-Process Information Dr.Reddy's Omeprazole Magnesium delayed-Release capsules, 20 mg Batch # : EC6319 Actual Yield (b) (4) Capsules Batch Size (b) (4) Capsules Quantity Packed (b) (4) Capsules Count / Quantify Packed (Capsules) / Reserve Samples (Capsules) / Stability Samples (Capsules) / R & D Samples (Capsules) / Bio Samples (Capsules) / Quantity transferred to Ware House (Capsules) (b) (4) 2. In-process Controls - Specifications and data submitted	☒

Sec. XIII	**Container** 1. Summary of Container/Closure System (if new resin, provide data) submitted (b) (4) (b) (4) 2. Components Specification and Test Data (Type III DMF References) submitted 3. Packaging Configuration and Sizes (b) (4) 14 ct blister, 28 ct blister, 42 ct blister, (b) (4) (b) (4) 4. Container/Closure Testing submitted 5. Source of supply and suppliers address submitted	☒
Sec. XIV	**Controls for the Finished Dosage Form** 1. Testing Specifications and Data submitted 2. Certificate of Analysis for Finished Dosage Form submitted Batch EC6319	☒
Sec. XV	**Stability of Finished Dosage Form** 1. Protocol submitted submitted 2. Post Approval Commitments submitted 3. Expiration Dating Period 2 yrs 4. Stability Data Submitted Note: no stability data was provided for the 14 ct blister, 28 ct blister, 42 ct blister (b) (4) a. 3 month accelerated stability data submitted b. Batch numbers on stability records the same as the test batch yes	☒
Sec. XVI	**Samples** - Statement of Availability and Identification of: 1. Drug Substance submitted 2. Finished Dosage Form submitted 3. Same lot numbers yes	☒
Sec. XVII	**Environmental Impact Analysis Statement** YES	☒
Sec. XVIII	**GDEA (Generic Drug Enforcement Act)/Other**: 1. Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) submitted 2. Debarment Certification (original signature): YES 3. List of Convictions statement (original signature) none used	☒

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL 05 2005 1892 5 JUL -6 A9:39

Gray Cary Ware & Freidenrich LLP
Attention: David L. Rosen
1625 Massachusetts Avenue NW, Suite 300
Washington, DC 20036-2247

Docket No. 2004P-0373/CP1

Dear Mr. Rosen:

This is in response to your petition filed on August 20, 2004, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug product: Omeprazole Magnesium Delayed-release Capsules, 20 mg. The reference listed drug to which you refer in your petition is Prilosec OTC™ (Omeprazole Magnesium) Delayed-release Tablets, 20 mg, approved under NDA 21-229 held by AstraZeneca.

Your request involves a change in dosage form from that of the listed drug product (i.e., from tablets to capsules). The change you request is the type of change that is authorized under the Federal Food, Drug, and Cosmetic Act (Act).

We have reviewed your petition under Section 505(j) (2) (C) of the Act and have determined that it is approved. This letter represents the Food and Drug Administration's (FDA) determination that an ANDA may be submitted for the above-referenced drug product.

In addition, this petition and your waiver request were evaluated with respect to the "Pediatric Research Equity Act of 2003" (PREA). PREA requires that all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration include an assessment of the safety and effectiveness of the drug for the claimed indication in all relevant pediatric subpopulations unless the requirement is waived or deferred. Your pending ANDA suitability petition is affected by this Act because it is a petition for a change in dosage form. Omeprazole magnesium delayed-release tablets are labeled for over-the-counter use in patients 18 years of age and older. However, the prescription product, omeprazole delayed-release capsules, is adequately labeled for pediatric use. For patients less than 18 years of age it is more appropriate to use the prescription product omeprazole delayed-release capsules because it would require a physician's intervention for proper diagnosis and treatment, and for accurate dosing based upon the child's weight. Therefore, the FDA has determined that your proposed change in dosage form is subject to PREA, but has concluded that the requirements for PREA have already been met.

2004P-0373 PAV 1

BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS

ANDA# 078878 **FIRM NAME** **Dr. Reddy's Laboratories, Ltd.**

DRUG NAME Omeprazole Magnesium Capsules, eq 20 mg base

DOSAGE FORM **DR Capsules**
SUBJ: Request for examination of: Bioequivalence Study

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Division of Bioequivalence
☒	**Study meets statutory requirements**
☐	**Study does NOT meet statutory requirements**
	Reason:
☐	**Waiver meets statutory requirements**
☐	**Waiver does NOT meet statutory requirements**
	Reason:

RECOMMENDATION: ☒ **COMPLETE** ☐ **INCOMPLETE**

Reviewed by:

_____ Date: _____

Reviewer

_____ Date: _____

Team Leader

Active Ingredient Search Results from "OB_OTC" table for query on "omepraz."

Appl No	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
021229	Yes	OMEPRAZOLE MAGNESIUM	TABLET, DELAYED RELEASE; ORAL	EQ 20MG BASE	PRILOSEC OTC	ASTRAZENECA

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through April, 2007
Patent and Generic Drug Product Data Last Updated: May 24, 2007

Search results from the "OB_OTC" table for query on "021229."

Active Ingredient:	OMEPRAZOLE MAGNESIUM
Dosage Form;Route:	TABLET, DELAYED RELEASE; ORAL
Proprietary Name:	PRILOSEC OTC
Applicant:	ASTRAZENECA
Strength:	EQ 20MG BASE
Application Number:	021229
Product Number:	001
Approval Date:	Jun 20, 2003
Reference Listed Drug	Yes
RX/OTC/DISCN:	OTC
Patent and Exclusivity Info for this product:	View

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through April, 2007
Patent and Generic Drug Product Data Last Updated: May 24, 2007

Patent and Exclusivity Search Results from query on Appl No 021229 Product 001 in the OB_OTC list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code
021229	001	4786505	APR 20,2007			
021229	001	4786505*PED	OCT 20,2007			
021229	001	4853230	APR 20,2007			
021229	001	4853230*PED	OCT 20,2007			
021229	001	5690960	NOV 25,2014			
021229	001	5753265	JUN 07,2015			
021229	001	5817338	OCT 06,2015			
021229	001	5900424	MAY 04,2016			
021229	001	6403616	NOV 15,2019			
021229	001	6428810	NOV 03,2019			

Exclusivity Data

There is no unexpired exclusivity for this product.

Following this page, 10 pages withheld in full (b)(4)

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

/s/

Iain Margand
6/7/2007 01:23:48 PM
Signing for Martin Shimer

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-878

Dr. Reddy's Laboratories, Inc.
U.S. Agent for Dr. Reddy's Laboratories Limited
Attention: Kumara Sekar, Ph.D.
200 Somerset Corporate Blvd, 7th Floor
Bridgewater, NJ 08807

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to the telephone conversation dated May 30, 2007 and your correspondence dated June 1, 2007.

NAME OF DRUG: Omeprazole Magnesium Delayed-release Capsules, 20 mg

DATE OF APPLICATION: March 16, 2007

DATE (RECEIVED) ACCEPTABLE FOR FILING: March 19, 2007

You have filed a Paragraph IV patent certification, in accordance with 21 CFR 314.94(a)(12)(i)(A)(4) and Section 505(j)(2)(A)(vii)(IV) of the Act. Please be aware that you need to comply with the notice requirements, as outlined below. In order to facilitate review of this application, we suggest that you follow the outlined procedures below:

CONTENTS OF THE NOTICE

You must cite section 505(j)(2)(B)(ii) of the Act in the notice and should include, but not be limited to, the information as described in 21 CFR 314.95(c).

SENDING THE NOTICE

In accordance with 21 CFR 314.95(a):

- Send notice by U.S. registered or certified mail with return receipt requested to each of the following:

  1) Each owner of the patent or the representative designated by the owner to receive the notice;

2) The holder of the approved application under section 505(b) of the Act for the listed drug claimed by the patent and for which the applicant is seeking approval.

3) An applicant may rely on another form of documentation only if FDA has agreed to such documentation in advance.

DOCUMENTATION OF NOTIFICATION/RECEIPT OF NOTICE

You must submit an amendment to this application with the following:

- In accordance with 21 CFR 314.95(b), provide a statement certifying that the notice has been provided to each person identified under 314.95(a) and that notice met the content requirements under 314.95(c).

- In accordance with 21 CFR 314.95(e), provide documentation of receipt of notice by providing a copy of the return receipt or a letter acknowledging receipt by each person provided the notice.

- A designation on the exterior of the envelope and above the body of the cover letter should clearly state "PATENT AMENDMENT". This amendment should be submitted to your application as soon as documentation of receipt by the patent owner and patent holder is received.

DOCUMENTATION OF LITIGATION/SETTLEMENT OUTCOME

You are requested to submit an amendment to this application that is plainly marked on the cover sheet “PATENT AMENDMENT” with the following:

- If litigation occurs within the 45-day period as provided for in section 505(j)(4)(B)(iii) of the Act, we ask that you provide a copy of the pertinent notification.

- Although 21 CFR 314.95(f) states that the FDA will presume the notice to be complete and sufficient, we ask that if you are not sued within the 45-day period, that you provide a letter immediately after the 45 day period elapses, stating that no legal action was taken by each person provided notice.

- You must submit a copy of a copy of a court order or judgment or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information. We ask that this information be submitted promptly to the application.

If you have further questions you may contact Martin Shimer, Chief, Regulatory Support Branch, at (301)827-0503.

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Theresa Liu
Project Manager
301-827-5791

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Iain Margand
6/7/2007 01:38:09 PM
Signing for Wm. Peter Rickman

MINOR AMENDMENT

ANDA 78-878

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

APPLICANT: Dr. Reddy's Laboratories, Inc. TEL: 908-203-4937

ATTN: Kumara Sekar FAX: 908-203-4980

FROM: Theresa Liu PROJECT MANAGER: (301) 827-5791

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated March 16, 2007, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Omeprazole Magnesium Delayed-Release Capsules, 20 mg.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (__4__ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

See attached chemistry comments.

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-878
APPLICANT: Dr. Reddy's Laboratories Limited
DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. DMF #17706 for Omeprazole Magnesium has been reviewed and found inadequate. The DMF holder has been notified.

2. There seems to be a discrepancy between (b) (4) Please clarify this apparent discrepancy.

3. Omeprazole Magnesium has a known chiral center in the sulfinyl group. No information or specification was provided indicating (b) (4) . Please clarify.

4. The specification for (b) (4) .

5. (b) (4) .

6. Please note that (b) (4) .

7. (b) (4) .

8. Your executed and blank batch records (b) (4) .

9. Please acknowledge (b) (4)

10. (b) (4) .

11. Please indicate (b) (4) .

12. Please note that pages 10005-6 of your ANDA submission list a commercial batch size of (b) (4) capsules.

13. It was noted that (b) (4) Please clarify.

14. We recommend that you [redacted].

15. Please note that your formulation incorporates [redacted].

16. The physical description of the pellets as described in the in-process information included on pages 11411 and 11413 [redacted] is not in agreement with the description presented on page 10680 (p. 121 of the commercial batch record: [redacted]). Please clarify this apparent discrepancy and provide a physical description of the film coated enteric pellets.

17. We recommend that [redacted].

18. Please address [redacted]

19. It is recommended that [redacted].

20. It is recommended that [redacted].

21. Please provide [redacted].

22. We recommend that [redacted].

23. Please incorporate [redacted].

24. Please clarify [redacted] Please provide assurance that your policy for expiration dating is in accordance with CDER Guidelines.

25. In addition to the standard USP acid/buffer 2-stage dissolution testing, please provide comparative dissolution profiles of your proposed drug product formulation versus the reference listed drug, Prilosec® OTC, using acid stage testing performed in pH media around the critical solubility pH of the enteric coating. It is suggested that such acid stage testing be conducted over a pH range of 4.0-6.0 (i.e., testing at pH 4.0, 4.5, 5.0, 5.5 and 6.0) for two hours, followed by testing in USP buffer media, pH 6.8. Finally, it is recommended that the amount released during the buffer stage testing at pH 6.8 be determined after 30 minutes and 60 minutes.

B. Additional comments:

1. The labeling and bioequivalence portions of your application are under review. Deficiencies, if any, will be conveyed to you under separate cover.

2. Please provide updated stability data for the exhibit batch.

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Michael S Furness

7/26/2007 03:16:57 PM

DR. REDDY'S
DR. REDDY'S LABORATORIES, INC.

200 SOMERSET CORPORATE BOULEVARD
7TH FLOOR
BRIDGEWATER, NJ 08807
TELEPHONE (908) 203-4900
FAX (908) 203-4970

This Letter Contains Confidential, Commercial and Trade Secret Information
Do Not Disclose Under FOI

December 04, 2007

N- 000 - AM

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: **ANDA # 78-878**
Omeprazole Magnesium Delayed-Release Capsules, 20 mg
Minor Chemistry Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Minor Chemistry Amendment. This in response to the Agency's deficiency letter dated July 27, 2007 provided as **Exhibit – 1** for your reference.

A. Chemistry Deficiencies:

1. FDA Comment:

DMF # 17706 for Omeprazole Magnesium has been reviewed and found inadequate. The DMF holder has been notified.

RESPONSE:

We would like to inform the Agency that the response to deficiencies in the DMF # 17706 had been submitted by the DMF holder on November 16, 2007. The correspondence from the DMF holder in this reference has been provided as **Exhibit – 2.**

2. FDA Comment:

There seems to be a discrepancy between (b) (4)

Please clarify this apparent discrepancy.

Following this page, 11 pages withheld in full (b)(4)

(b) (4)

25. FDA Comment:

In addition to the standard USP acid/buffer 2-stage dissolution testing, please provide comparative dissolution profiles of your proposed drug product formulation versus the reference listed drug, Prilosec® OTC, using acid stage testing performed in pH media around the critical solubility pH of the enteric coating. It is suggested that such acid stage testing be conducted over a pH range of 4.0-6.0 (i.e., testing at pH 4.0, 4.5, 5.0, 5.5 and 6.0) for two hours, followed by testing in USP buffer media, pH 6.8. Finally, it is recommended that the amount released during the buffer stage testing at pH 6.8 be determined after 30 minutes and 60 minutes.

RESPONSE:

As recommended by the agency, the dissolution data in generated for the proposed drug product formula and reference listed drug (RLD). The dissolution data is provided as **Exhibit – 15.**

B. Additional comments:

1. FDA Comment:

The labeling and bioequivalence portions of your application are under review. Deficiencies, if any, will be conveyed to you under separate cover.

RESPONSE:

We acknowledge agency's comment.

2. FDA Comment:

Please provide updated stability data for the exhibit batch.

Omeprazole Magnesium Delatyed-Release Capsules, 20 mg
ANDA 78-878

RESPONSE:

The updated stability data up to twelve month is provided as **Exhibit – 16.** We would like to inform the agency that Dr. Reddy's (b) (4)

Also included in this submission is an extra copy of our cover letter. Please acknowledge receipt by date stamping the copy and returning it to us in the self-addressed stamped envelope provided for your convenience. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs &B Compliance

MINOR AMENDMENT

ANDA 78-878

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Dr. Reddy's Laboratories, Inc. TEL: 908-203-4937

ATTN: Kumara Sekar FAX: 908-203-4980

FROM: Theresa Liu PROJECT MANAGER: (240) 276-8555

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated March 16, 2007, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Omeprazole Magnesium Delayed-Release Capsules, 20 mg.

Reference is also made to your amendment dated December 4, 2007.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (__**2**__ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-878
APPLICANT: Dr. Reddy's Laboratories Limited
DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. Although your pellets are screened after every step, [redacted] (b) (4) .

2. You have provided results for [redacted] (b) (4) .

3. Your finished product [redacted] (b) (4) .

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Damaris Maldonado

3/14/2008 12:05:43 PM

DR. REDDY'S
Dr. Reddy's Laboratories, Inc.
3600 Arco Corporate Drive, Suite 310
Charlotte, NC 28273-7104
Regulatory Affairs: 704-496-6065
Fax: 704-496-6082

This Letter Contains Confidential, Commercial and Trade Secret Information. Do Not Disclose Under FOI

April 29, 2008

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: ANDA # 78-878
Omeprazole Magnesium Delayed-Release Capsules, 20 mg
Minor Chemistry Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Minor Chemistry Amendment. This in response to the Agency's deficiency letter dated March 14, 2008 provided as **Exhibit – 1** for your reference.

A. Chemistry Deficiencies:

1. FDA Comment:

Although your pellets are screened after every step, [redacted] (b) (4)

RESPONSE:

[redacted] (b) (4)

Following this page, 1 page withheld in full (b)(4)

DR. REDDY'S
DR. REDDY'S LABORATORIES, INC.

Omeprazole Magnesium Delatyed-Release Capsules, 20 mg
ANDA 78-878

(b) (4)

[redacted]

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 704-496-6065 or by fax at 704-496-6082 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

A. Jayalakshmi.

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs

This Letter Contains Confidential, Commercial and Trade Secret Information. Do Not Disclose Under FOI

DR. REDDY'S
Dr. Reddy's Laboratories, Inc.
3600 Arco Corporate Drive, Suite 310
Charlotte, NC 28273-7104
Regulatory Affairs: 704-496-6065
Fax: 704-496-6082

May 20, 2008

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: ANDA # 78-878
Omeprazole Magnesium Delayed-Release Capsules, 20 mg
Gratuitous Chemistry Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Gratuitous Chemistry Amendment.

As committed in our Minor Chemistry Amendment dated April 29, 2008 we are providing microbial data generated on 45-days hold bulk pellets. The microbial data is as follows:

Test	Initial	15 Days	30 Days	45 Days
				(b) (4)

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 704-496-6065 or by fax at 704-496-6082 if you have any questions regarding this submission.

Sincerely,
DR. REDDY'S LABORATORIES, INC.

A. Jayalakshmi

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs

DR. REDDY'S

Dr. Reddy's Laboratories, Inc.
Regulatory Affairs

3600 Arco Corporate Drive, Suite 310
Charlotte, NC 28273-7104
(704) 496-6065
Fax: (704) 496-6082

www.drreddys.com

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

July 21, 2008

Reference: **Omeprazole Magnesium Delayed Release Capsules 20 mg (OTC)**
ANDA # 78-878
Gratuitous Amendment – Addition of Alternate Packaging Sites
(b) (4)

Dear Sir/ Madam:

Pursuant to Code of Federal Regulations Title 21 § 314.60, Dr. Reddy's Laboratories, Inc., US. agent for Dr. Reddy's Laboratories Limited, is submitting a Gratuitous Amendment to ANDA 78-878 Omeprazole Magnesium Delayed Release Capsules 20 MG (OTC) to add additional alternate packaging sites for the packaging of the drug product.

Details on the alternate packaging sites are provided in **Exhibit 1**. The debarment certifications are provided in **Exhibit 2**. The cGMP Certifications are provided in **Exhibit 3** and the stability commitment is provided in **Exhibit 4**. These locations were inspected within the last two years and were found to be cGMP satisfactory by the agency.

This submission is provided as an electronic copy only. The PDF version of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 704-496-6065 or by fax at 704-496-6082 if you have any questions regarding this submission.

Sincerely,
DR. REDDY'S LABORATORIES INC.

Kumara Sekar, Ph.D.
Sr. Director, Global Regulatory Affairs & Compliance

DR. REDDY'S

Dr. Reddy's Laboratories, Inc.
Regulatory Affairs

3600 Arco Corporate Drive, Suite 310
Charlotte, NC 28273-7104
(704) 496-6065
Fax: (704) 496-6082

www.drreddys.com

July 25, 2008

This Letter Contains Confidential, Commercial and Trade Secret Information
Do Not Disclose Under FOI

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: **ANDA # 78-878**
Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC)
Gratuitous Labeling Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC), Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Gratuitous Labeling Amendment.

The labeling has been revised to be in accord with the current labeling of the reference product Prilosec OTC® of AstraZeneca AB.

The revised final labeling and its side by side comparison with the previously submitted labeling are provided electronically.

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival

copy of this submission. Please contact the undersigned at 704-496-6065 or by fax at 704-496-6082 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

Kumara Sekar Ph.D.,
Senior Director, Global Regulatory Affairs

MINOR AMENDMENT

ANDA 78-878

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Dr. Reddy's Laboratories Inc. TEL: 704-496-6065

ATTN: Kumara Sekar FAX: 704-496-6082

FROM: Theresa Liu FDA CONTACT PHONE: (240) 276-8555

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated March 16, 2007, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Omeprazole Magnesium Delayed-Release Capsules, 20 mg.

Reference is also made to your amendment dated April 30 and May 20, 2008.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format.
This will improve document availability to review staff.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (__**2**__ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

ANDA: 78-878 APPLICANT: Dr. Reddy's Laboratories Limited
DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. We recommend that [redacted (b) (4)].

2. With USP<467> Residual Solvents going into effect July 1, 2008, please include information to demonstrate compliance with the chapter. A complete submission for this purpose should consist of the following:

   For each excipient in the formulation:
   - manufacturer's statement or COA including solvents
   - applicant's updated COA for the excipient including solvent specification (solvent identity, acceptance criteria and analytical method). Class 3 solvents are also to be named. Loss on drying would be acceptable if only Class 3 solvents are used in the manufacture of an ingredient.
   - applicant's test data for solvents, including data for class 3 solvents, should be submitted for the excipient
   - method validation data if non-USP methods are used
   - upon vendor validation, applicant may accept manufacturer's COA
   - applicant to demonstrate the excipient meets ICH Q3C option 1 or option 2

   If a solvent is used in the manufacturing process, the applicant should have already included a solvent specification in the finished product specification.

   The finished product specification should be updated to state compliance with USP<467>.

3. Please provide updated stability data.

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Damaris Maldonado

7/29/2008 10:55:33 AM

This Letter Contains Confidential, Commercial and Trade Secret Information. Do Not Disclose Under FOI

DR. REDDY'S

Dr. Reddy's Laboratories, Inc.
Regulatory Affairs

3600 Arco Corporate Drive, Suite 310
Charlotte, NC 28273-7104
(704) 496-6065
Fax: (704) 496-6082

www.drreddys.com

September 17, 2008

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: **ANDA # 78-878**
Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)
Minor Chemistry Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules 20 mg, Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Minor Chemistry Amendment. This is in response to the deficiency letter dated July 29, 2008 provided as **Exhibit – 1** for your reference.

A. Chemistry Deficiencies:

FDA Comment:

1. *We recommend that* (b) (4)

RESPONSE:

(b) (4)

Following this page, 1 page withheld in full (b)(4)

RESPONSE:

The updated stability data up to eighteen months is provided in **Exhibit – 7.**

In addition to the above responses we would like to inform the agency that we have included a banding on the capsules as a tamper evident feature as required by CFR 211.132.We have also revised our labeling in accordance to reflect the changes associated with the banding of the capsule .The following information has been provided :

(b) (4)

[redacted]

This submission is provided as an electronic copy only. The PDF version of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 704-496-6065 or by fax at 704-496-6082 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

A. Jayalakshmi.

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs

DR. REDDY'S

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September 18, 2008

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Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: **ANDA # 78-878**
Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC)
Gratuitous Labeling Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC), Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Gratuitous Labeling Amendment.

The gratuitous labeling amendment includes the following changes:

- Labeling information associated with the introduction of tamper evident feature on the capsule in the form of a gelatin band as required by 21 CFR 211.132 is been added. Information regarding the banding of the capsules has been submitted as a minor chemistry amendment dated September 17, 2008.
- Inclusion of an additional inner carton label of 14's count. This carton will be used as an inner carton for the 28's and 42's count packages.
- [redacted] (b) (4)
- Inclusion of a PIL instead of drug facts sheet to be in line with the current labeling of the reference product Prilosec OTC® of AstraZeneca AB.

- Changes in the blister card.
- Changes in the label presentation.

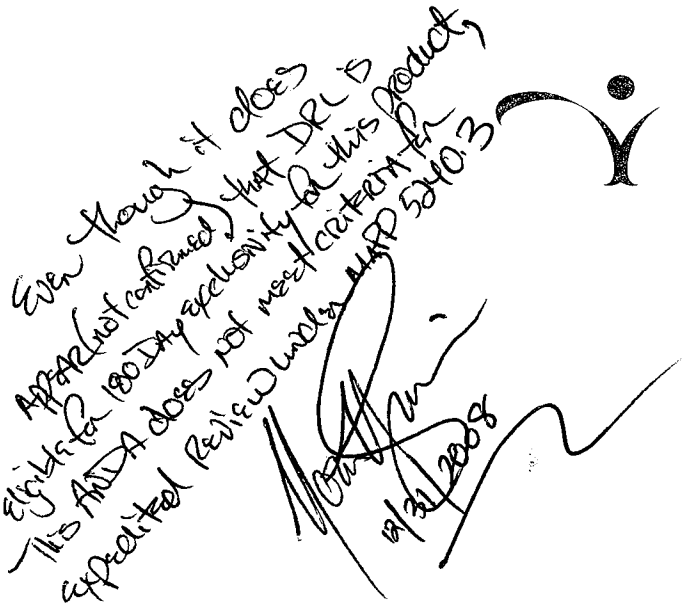
The revised final labeling and its side by side comparison with the previously submitted labeling are provided electronically.

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 704-496-6065 or by fax at 704-496-6082 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

For: **Kumara Sekar Ph.D.,**
Senior Director, Global Regulatory Affairs



DR. REDDY'S

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December 18, 2008

Gary Buehler, Pharm. D.
Director, Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

NEW CORRESP

Reference: **ANDA # 78-878**
Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC)
General Correspondence – Request for Expedited Review and Approval

Dear Sir:

I write on behalf of Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc. (Dr. Reddy's), with respect to the timing of the litigation in the United States District Court for the Southern District of New York concerning the proposed Omeprazole Magnesium Delayed-Release capsules that are the subject of Dr. Reddy's Abbreviated New Drug Application No. 78-878 ("ANDA No. 78-878"). This ANDA corresponds to the branded product Prilosec OTC®. The purpose of this letter is to explain why Dr. Reddy's believes that it will obtain a favorable decision of non-infringement well before the end of the statutory 30 month stay and to ask the United States Food and Drug Administration to expedite its review of ANDA No. 78-878.

Dr. Reddy's filed ANDA No. 78-878 on March 19, 2007. Dr. Reddy's included in its ANDA a patent certification pursuant to §505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act ("the Act") and § 314.94(a)(12)(i)(A)(4) of the CFR, alleging that the patents listed in the Orange Book for Prilosec OTC® were invalid, unenforceable

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DEC 19 2008
OGD

or not infringed by DRL's proposed product. On June 13, 2007, Dr. Reddy's sent the required Notice of Paragraph IV Certification to the holder of the application under § 505(b) of the Act and the assignee of the Orange Book listed patents (collectively "AstraZeneca"). Dr. Reddy's Notice Letter included an Offer of Confidential Access to portions of Dr. Reddy's ANDA for the purpose of determining whether an infringement action should be filed under 35 U.S.C. § 355

On July 27, 2007, AstraZeneca filed an action for patent infringement against Dr. Reddy's in the United States District Court for the Southern District of New York, Civil Action No. 07-CIV 6790 ("the '6790 Action"). In its complaint, AstraZeneca alleged that Dr. Reddy's Omeprazole Magnesium product infringed only two of the six patents listed in the Orange Book for AstraZeneca's product, U.S. Patent 5,690,960 ("the '960 patent") and U.S. Patent 5,900,424 ("the '424 patent"). In an apparent admission that AstraZeneca was merely speculating that Dr. Reddy's proposed product infringed the two patents, AstraZeneca candidly stated in its complaint that it had brought the action against Dr. Reddy's, in part, "to employ the judicial process and discovery" in order to "confirm" Dr. Reddy's alleged infringement.

On September 19, 2007, trial counsel for Dr. Reddy's sent a letter to the Court in the '6790 Action suggesting that the issues could be narrowed most expeditiously if Dr. Reddy's filed an early motion for summary judgment.

On September 21, 2007, Dr. Reddy's and AstraZeneca participated in the Initial Pretrial Conference. At this Conference the Court directed the parties to assume that Dr. Reddy's had made its motion for summary judgment. The Court ordered Dr. Reddy's to produce samples by September 24, 2007. AstraZeneca was ordered to test these samples by November 1, 2007. AstraZeneca was given leave to file 10 Interrogatories. Dr. Reddy's produced its samples on September 24, 2007 and Dr. Reddy's responded to the Interrogatories on November 1, 2007.

Dr. Reddy's and AstraZeneca attended a second Conference with the Court on November 7, 2007. At this Conference AstraZeneca's counsel reported that it had tested Dr. Reddy's samples and that the test results did not show infringement. From the bench the Court then ordered AstraZeneca to submit to the Court a list detailing the additional discovery that was needed and to include for each-and-every claim an explanation why the additional discovery was needed to show infringement. AstraZeneca submitted its 43 page "Explanation of Infringement Discovery" on November 19, 2007. Dr. Reddy's submitted its "Reply to AstraZeneca's Explanation of Infringement Discovery" on November 28, 2007.

On May 5, 2008 the parties received the Court rulings on AstraZeneca's discovery requests. The Court found that "AstraZeneca's discovery requests smack of a fishing expedition." (emphasis added). The Court also found it obvious that AstraZeneca had no

proof of infringement and that it "it simply hopes to find such proof by engaging in additional discovery." Against this backdrop, the Court ordered Dr. Reddy's to produce certain portions of its ANDA and DMF and a deposition witness who could testify on the process that Dr. Reddy's uses to produce its ANDA product and the Omeprazole Magnesium that is used therein.

The required discovery was ordered to be completed by May 23, 2008. The Court ordered AstraZeneca to decide within 30 days thereafter whether it would withdraw its action. If not, Dr. Reddy's was given 30 days to move for summary judgment. The discovery was completed on time, AstraZeneca did not withdraw its action and Dr. Reddy's moved for summary judgment on July 9, 2008.

The briefing related to Dr. Reddy's summary judgment motion was completed on September 11, 2008. If granted, Dr. Reddy's summary judgment motion will dispose of the entire case and all of the patents which formed the basis of the 30 month stay. Dr. Reddy's expects to receive a favorable decision on its summary judgment motion by the end of December 2008.

Further, Dr. Reddy's believes that this application is the first generic application for the Reference Listed Drug, Prilosec OTC®. Dr. Reddy's also believes that approval of this product would benefit the public with access to an OTC product in direct competition to Prilosec OTC®.

Considering the expected favorable court decision and as a first generic, Dr. Reddy's respectfully asks for an expedited review and approval of its ANDA No. 78-878.

Please contact the undersigned at 704-496-6065 or by fax at 704-496-6082 for additional information or questions.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

Kumara Sekar, PhD
Sr. Director, Global Regulatory Affairs and Compliance.

This Letter Contains Confidential, Commercial
and Trade Secret Information. Do Not Disclose Under FOI

DR. REDDY'S

March 11, 2009

Dr. Reddy's Laboratories, Inc.
Regulatory Affairs

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Gary Buehler, Pharm. D.
Director, Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

AX

Reference: ANDA No. 78-878
Omeprazole Magnesium Delayed Release Capsules, 20mg (OTC)
General Correspondence – Request for Expedited Review and Approval

Dear Sir,

This letter is in reference to ANDA No. 78-878 for Omeprazole Magnesium delayed Release Capsules, 20mg (OTC), which corresponds to the branded product Prilosec OTC®. Please refer to our correspondence dated December 18, 2008 **(Exhibit 1)** wherein we had requested an expedited review and approval for this product. As a follow up to the correspondence, we wish to bring to your attention that on March 10, 2009 the United States District Court for the Southern District of New York granted a motion for summary judgment in favor of Dr. Reddy's Laboratories Inc. and Dr. Reddy's Laboratories Ltd., issuing an Order dismissing AstraZeneca AB's complaint, AstraZeneca v. Dr. Reddy's, No. 07 Civ. 6790 (S.D.N.Y. Mar. 10, 2009) **(Exhibit 2)**.

Dr. Reddy's would like to stress again that we believe our application is a First Generic application to the Reference Listed Drug Prilosec OTC®. Approval of this product would benefit the public with access to a generic OTC product.

In view of the favorable court decision and as a First Generic applicant, Dr. Reddy's respectfully requests an expedited review and approval of its ANDA No. 78-878.

Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 for additional information or questions.

Sincerely,
DR. REDDY'S LABORATORIES, INC.

Kumara Sekar, Ph.D.
Sr. Director, Global Regulatory Affairs and Compliance.

cc: Martin Shimer
Theresa Liu

MAR 1 3 2009

COMPLETE RESPONSE -- MINOR

ANDA 78-878

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Dr. Reddy's Laboratories Inc. TEL: 908-203-4937

ATTN: Kumara Sekar FAX: 908-203-4980

FROM: Theresa Liu FDA CONTACT PHONE: (240) 276-8555

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated March 16, 2007, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Omeprazole Magnesium Delayed-Release Capsules, 20 mg.

Reference is also made to your amendments dated July 21 and September 17, 2008.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

We have completed the review of your ANDA and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues in the following attachments (__**2**__ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. Upon OGD's acceptance for filing of your ANDA, it was determined that an adequate amount of information was submitted to allow for review of your Bioequivalence and Microbiology data. You will be notified in a separate communication of any further deficiencies identified during our review of your Bioequivalence and Microbiology data If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

ANDA: 78-878 **APPLICANT:** Dr. Reddy's Laboratories Limited

DRUG PRODUCT: Omeprazole Magnesium Delayed-release Capsules, 20mg (OTC)

The deficiencies presented below represent MINOR deficiencies.

A. Chemistry Deficiencies:

1. For excipients (b) (4) .

2. Please set specifications for (b) (4) .

3. Please provide the methods used for the analysis of residual solvents in the excipients along with verification for USP methods and validation for non USP methods.

4. It is recommended that identification of finished product should include (b) (4)

5. Please provide f_2 for dissolution results of (b) (4)

6. Please provide updated stability data for (b) (4)

Sincerely yours,

{See appended electronic signature page}

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Damaris Maldonado

3/17/2009 12:33:50 PM

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DR. REDDY'S

Dr. Reddy's Laboratories, Inc.
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March 25, 2009

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: **ANDA # 78-878**
Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)
Minor Chemistry Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Minor Chemistry Amendment. This is in response to the deficiency letter dated March 17, 2009 provided as **Exhibit – 1** for your reference.

A. Chemistry Deficiencies:

(b) (4)

[redacted]

Following this page, 1 page withheld in full (b)(4)

(b) (4)

[redacted]

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h are provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

for:

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs

This Letter Contains Confidential, Commercial and Trade Secret Information
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DR. REDDY'S

April 10, 2009

Dr. Reddy's Laboratories, Inc.
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Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Ref: ANDA # 78-878
Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)
Telephone Chemistry Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg, Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Telephone Chemistry Amendment. This is in response to the Telephonic correspondence (dated April 04, 2009) with Shahnaz Read of the Agency.

1. **FDA Comment:**

Please submit the drug substance specifications as per USP.

RESPONSE:

As recommended by the Agency the drug substance specifications have been revised in accordance with USP. The revised specifications, standard test procedure and analysis report as per the revised specifications has been provided as **Exhibit – 1**.

The test methods for all the tests are as per USP with the exception of Assay and Related Substance. The equivalency report of in-house method against USP method for Assay and Related Substance is provided as **Exhibit – 2**.

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h are provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,
DR. REDDY'S LABORATORIES, INC.

for:

Kumara Sekar, Ph.D.
Senior Director, Global Regulatory Affairs

Telephone Fax

ANDA 78-878

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8995

TO: Dr. Reddy's Laboratories, Inc.
U.S. Agent for Dr. Reddy's Laboratories Limited

TEL: 908-203-4937

FAX: 908-203-4980

ATTN: Kumara Sekar, Ph.D.

FROM: Sarah Park

Dear Madam:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Omeprazole Magnesium Delayed-release Capsules, 20 mg (OTC).

Pages (including cover): 5

SPECIAL INSTRUCTIONS:

Please see attached.

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number:	78-878
Date of Submission:	March 16, 2007 (Original); July 25, 2008 (Amendment); and September 18, 2008 (Amendment)
Applicant's Name:	Dr. Reddy's Laboratories Limited
Established Name:	Omeprazole Magnesium Delayed-release Capsules, 20 mg (OTC)

Labeling Deficiencies:

1. GENERAL COMMENTS

   a. Please clarify which package sizes utilize child-resistant packaging. Please comply with requirements of 15 U.S.C. 1473(a) and 16 CFR 1700.5.

   b. The image of the capsule on the principal display panels of the carton labeling state "FPO". However, the drug product specifications in your application state that the capsules are "imprinted "OMP2O" on cap with black ink". Please comment.

   c. Please delete the image of the capsule from all labels and labeling.

   d. The listings of inactive ingredients on the carton labeling and container labels are inconsistent with the listing of inactive ingredients found in the statement of components and composition. Please clarify and revise.

2. (b) (4)

3. BLISTER (blister card of 7)

    a. Replace the name [redacted] with the established name "Omeprazole Magnesium Delayed-release Capsule".

    b. Increase the prominence of the expression of strength, "20.6 mg".

4. CARTON (unit dose capsules of 14, 28 and 42)

    a. Replace the name [redacted] with the established name "Omeprazole Magnesium Delayed-release Capsules".

    b. Increase the prominence of the expression of strength, "20.6 mg".

    c. Delete "New" appearing on the top left corner of the principle display panel.

    d. Un-italicize and un-bold "(continued)" in the title "Drug Facts (continued)".

    e. "Warnings" heading – "Keep out of reach of children…" [correct spelling of "out"]

5. [redacted]

6. INSERT

    a. Title line: Replace the name [redacted] with the established name "Omeprazole Magnesium Delayed-release Capsules, 20.6 mg".

    b. Replace the name [redacted] throughout the insert with the established name "Omeprazole Magnesium Delayed-release Capsules".

Please revise your labels and labeling, as instructed above, and submit final printed labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission, please provide a side-by- side comparison of your proposed labeling with your last submission with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Koung Lee
4/15/2009 04:40:51 PM
For Wm Peter Rickman

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DR. REDDY'S

April 20, 2009

Dr. Reddy's Laboratories, Inc.
Regulatory Affairs

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Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Ref: ANDA # 78-878
Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)
Telephone Chemistry Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Telephone Chemistry Amendment. This is in response to the Telephone correspondence (dated April 15, 2009) with Shahnaz Read of the Agency.

(b) (4)

[redacted]

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

For

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs

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DR. REDDY'S

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April 22, 2009

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Ref: ANDA # 78-878
Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC)
Labeling Amendment – response to deficiency letter dated April 15, 2009

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC), Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a labeling amendment. This is in response to the deficiency letter dated April 15, 2009 which is provided as Exhibit 1.

A. Labeling Deficiencies

FDA Comments

1. *General Comments:*

   a. *Please clarify which package sizes utilize child-resistant packaging. Please comply with requirements of 15 U.S.C. 1473(a) and 16 CFR 1700.5.*

RESPONSE:

We acknowledge agencies comments. Currently proposed [redacted] (b) (4) 7ct blisters utilize the child-resistant packaging. We would like to confirm that, we will be utilizing the CRC closure for the [redacted] (b) (4).

   b. *The image of the capsule on the principal display panels of the carton labeling state "FPO". However the drug product specifications in your application state that the capsules are imprinted "OMP20" on cap with black ink". Please comment*

RESPONSE:

We acknowledge the agencies comment. We would like to confirm that appropriate changes have been implemented in the carton labeling to display the actual picture of the capsule instead of the image printed with text "FPO". The revised labels and the side by side comparison of the revised labels are provided electronically in the folder titled "Labeling".

c. *Please delete the image of the capsule from all labels and labeling.*

RESPONSE:

We acknowledge the agency's comment. We would like to inform that we propose to keep the image of the capsule on the principle display panel in line with many of the approved OTC product labeling which have the product image on the PDP. Since this is a common practice for OTC products, we request the agency to accept the proposed labeling.

Further we would like to confirm that the image is the actual picture of the capsule. The actual picture of the capsule is provided for reference in the folder titled "Labeling".

d. *The listings of inactive ingredients on the carton labeling and container labels are inconsistent with the listing of inactive ingredients found in the statement of components and composition. Please clarify and revise.*

RESPONSE:

We acknowledge the agencies comment. The inactive ingredients section has been updated to be in accordance with the components and composition information provided as Exhibit 2 for ready reference.

(b) (4)

[redacted]

(b) (4)

FDA Comments

3. *BLISTER (blister card of 7)*

   a. *Replace the name* (b) (4) *with the established name "Omeprazole Magnesium Delayed-release Capsules".*

   b. *Increase the prominence of the expression of strength, "20.6 mg".*

RESPONSE:

We acknowledge the agencies comment. The blister card labeling has been revised accordingly. The revised final blister card labeling and its side by side comparison with the previously submitted labeling is provided electronically in the folder titled "Labeling".

FDA Comments

4. *CARTON (unit dose capsule of 14, 28 and 42)*

   a. *Replace the name* (b) (4) (b) (4) *with the established name "Omeprazole Magnesium Delayed-release Capsules".*
   b. *Increase the prominence of the expression of strength, "20.6 mg".*
   c. *Delete "New" appearing on the top left corner of the principle display panel.*
   d. *Un-italicize and un-bold "(continued)" in the title "Drug Facts (continued)".*
   e. *"Warnings" heading – "Keep out of reach of children..." [correct spelling of 'out"]*

RESPONSE:

We acknowledge the agencies comments. The blister carton labeling has been revised as per comments a, b, d and e. The revised final blister carton labeling and its side by side comparison with the previously submitted labeling are provided electronically in the folder titled "Labeling".

Regarding removal of the "NEW" flag as per comment c, kindly note that the agency has approved the usage of term "New" for various product labels with a condition to remove it after six months post marketing.

In view of the above we propose to retain the "NEW" flag on the PDP for six months post marketing. Subsequently the label will be revised to delete the "New" flag.

(b) (4)

FDA Comments

6. INSERT

a. *Title line: Replace the name* [redacted] (b) (4) *with the established name "Omeprazole Magnesium Delayed-release Capsules, 20.6 mg".*
b. *Replace the name* [redacted] (b) (4) *throughout the insert with the established name "Omeprazole Magnesium Delayed-release Capsules".*

RESPONSE:

We acknowledge the agencies comments. The insert labeling has been revised accordingly to reflect the change in the established name of the product. The revised insert labeling is provided electronically in the folder titled "Labeling".

Please note that the revised Foil pouch labeling with changes in the Established name of the product as per the comments received for blister [redacted] (b) (4) labels is also provided for reference.

This submission is provided as an electronic copy only. The PDF versions of the exhibits along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

For

Kumara Sekar Ph.D.,
Senior Director, Global Regulatory Affairs

This Letter Contains Confidential, Commercial and Trade Secret Information
Do Not Disclose Under FOI

DR. REDDY'S

Dr. Reddy's Laboratories, Inc.
Regulatory Affairs

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Bridgewater, NJ 08807-2862

Tel: (908) 203-4937
Fax: (908) 203-4980

www.drreddys.com

May 14, 2009

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Ref: ANDA # 78-878
Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC)
Labeling Amendment – response to deficiency dated May 13, 2009

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed Release Capsules, 20 mg (OTC), Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a labeling amendment. This is in response to the email deficiency received from Sarah Park on May 13, 2009.

Labeling Deficiencies:

FDA Comments

(b) (4)

2. *Please increase the prominence of the expression of strength on the carton labeling. The established name and strength should be the most prominent information.*

RESPONSE:

We acknowledge agencies comments. We have revised the carton labeling as per the agencies recommendation. The revised labels are provided in the folder titled "Labeling".

This submission is provided as an electronic copy only. The PDF version of the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

For:
Kumara Sekar Ph.D.,
Senior Director, Global Regulatory Affairs

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DR. REDDY'S

June 01, 2009

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Theresa Liu
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N-000-MC

Ref: ANDA # 78-878
Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)
General correspondence – Samples of reference product and test product

Dear Ms Liu:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a sample of the innovator product and the above referenced Dr Reddy's product. This is in response to the Telephone correspondence (dated May 29, 2009) with Shahnaz Read of the Agency.

Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

For:

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs

This Letter Contains Confidential, Commercial and Trade Secret Information
Do Not Disclose Under FOI

DR. REDDY'S

June 02, 2009

Dr. Reddy's Laboratories, Inc.
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Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Reference: ANDA # 78-878
Omeprazole Magnesium Delayed-Release Capsules, 20 mg (OTC)
Telephone Amendment

Dear Sir/ Madam:

With reference to ANDA # 78-878 for Omeprazole Magnesium Delayed-Release Capsules, 20 mg, Dr. Reddy's Laboratories Inc., U.S. agent for Dr. Reddy's Laboratories Limited, herewith submits a Telephone Amendment. This is in response to the Telephone correspondence (dated May 29, 2009) with Shahnaz Read of the Agency.

A. Chemistry Deficiencies:

1. FDA Comment:

Agency has requested to submit revised Certificate of Analysis for the batch # EC8139 showing data for second identification test as per current finished product specification.

Agency has also requested to submit a sample of the reference and test product.

RESPONSE:

We acknowledge the agency's comments. As requested by the agency, revised Certificate of Analysis (Batch # EC8139) which is in-line with current finished product specification has been provided as **Exhibit-1.**

A sample of reference and test product has already been send to the agency on June 01, 2009 to the attention of Ms Theresa Liu.

This submission is provided as an electronic copy only. The PDF version of the exhibit along with the cover letter and Form 356h is provided in a CD ROM which is placed in the archival copy of this submission. Please contact the undersigned at 908-203-4937 or by fax at 908-203-4980 if you have any questions regarding this submission.

Sincerely,

DR. REDDY'S LABORATORIES, INC.

For:

Kumara Sekar, Ph.D.,
Senior Director, Global Regulatory Affairs

OGD APPROVAL ROUTING SUMMARY

ANDA # 78-878 Applicant Dr. Reddy's Laboratories Limited
Drug Omeprazole Mg Delayed-release Capsules Strength(s) 20 mg OTC

APPROVAL ☒ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)** ☐ **OTHER** ☐

REVIEWER: **DRAFT Package** **FINAL Package**

1. **Martin Shimer** Date 5 May 2009 Date 6/5/09
Chief, Reg. Support Branch Initials MHS Initials rlw

Contains GDEA certification: Yes ☒ No ☐ Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92) Pediatric Exclusivity System
RLD = Prilosec OTC NDA# 21-229
Patent/Exclusivity Certification: Yes ☒ No ☐ Date Checked 6/5/09
If Para. IV Certification- did applicant Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☒ No ☐ Written request issued ☐
Was applicant sued w/in 45 days: Yes ☒ No ☐ Study Submitted ☐
Has case been settled: Yes ☒ No ☐ Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☒ No ☐
Date of latest Labeling Review/Approval Summary _____
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒
Type of Letter: Full Approval.

Comments: ANDA submitted on 3/19/2007, BOS=Approved Suitability Petition 2004P-0373 and Prilosec OTC NDA 21-229, PIII to '505 and '230, PIV to the '960, '265, '338, '424, '616 and '810 patents. ANDA ack for filing with PIV on 3/19/2007(LO dated 6/7/2007). Letter dated 12/18/2008-request for expedited review, letter also confirms that CA 07-6790 was filed in the Southern Distric of New York on 7/27/2007 for infringement of the '960 and '424 patents. Also in the 12/18/2008 letter Dr. Reddy's reports that they moved for summary judgement on 9/11/2008. On 3/12/2009 Dr. Reddy's produced an Order from the Southern D of NY 07-6790 in which Dr. Reddy's Motion for Summary Judgment was granted. This Summary Judgment was granted on 3/10/2009 and effectively dismissed CA 07-6790.

Firm was not sued on the '265, '338, '616 and '810 patents. Dr. Reddy's never submitted copies of the RRs which confirm delivery of notice to the appropriate parties. However, because Dr. Reddy's was sued in the Southern D of NY it is obvious that notice was served to the correct parties. Furthermore, Dr. Reddy's admitted in their 12/18/2008 that a 30 month stay was triggered by the lawsuit. Since Dr. Reddy's freely admits that a 30 month stay was in place it is safe to assume that CA 07-6790 was filed within 45 days of the parties receiving notice. This is also supported by the timing of events: Dr. Reddy's could not have provided notice before 6/7/2007(date on which the FDA PIV filing letter was issued) and we know that CA 07-6790 was filed on 7/27/2007. The difference between 6/7/2007 and 7/27/2007 being approximately 50 days. The award of Summary Judgment in favor of Dr. Reddy's effectively removes any remaining patent or legal barriers to the approval of this ANDA.

On 4/9/2009, Proctor and Gamble submitted CP 2009-P-0183 requesting that the Agency impose certain labeling requirements on pending and future ANDAs and NDAs for any OTC PPI product. Even though AstraZeneca is the NDA holder of record for NDA 21-229, the product is actually marketed by Proctor and Gamble. This was confirmed on 5/5/2009 when I looked at the most recent annual report submission for NDA 21-229 which was submitted on 8/8/2008. This annual reports shows that P & G distributed [redacted] (b) (4) of Prilosec OTC between 6/20/2007 and 6/19/2008. Obviously P & G has an interest in delaying generic market entry.

Dr. Reddy's is eligible for 180 day exclusivity for this drug product. From a patent/legal perspective there are no remaining barriers to the Full Approval of this ANDA. The impact of the petition will be discussed in a meeting later today.

Update 5/6/2009-T-con held on 5/5/09 to discuss impact of petition on pending NDAs and ANDAs. The outcome of the discussion was the petition will not block the approval of this ANDA. OGD is free to approve once all review disciplines are

acceptable.

2. Project Manager, Theresa Liu Team 7 Review Support Branch Date4/29/09 Date_____
Initialstcl Initials_____

Original Rec'd date3/16/07
Date Acceptable for Filing3/19/07
Patent Certification (type)pIV
Date Patent/Exclus.expires11/15/2019
Citizens' Petition/Legal Case Yes☐ No ☒
(If YES, attach email from PM to CP coord)
First Generic Yes ☒ No ☐
Priority Approval Yes ☐ No ☒
(If yes, prepare Draft Press Release, Email it to Cecelia Parise)
Acceptable Bio reviews tabbed Yes ☐ No ☒
Bio Review Filed in DFS: Yes ☒ No ☐
Suitability Petition/Pediatric Waiver Yes ☒
Pediatric Waiver Request Accepted ☐ Rejected ☐ Pending ☐
Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def. /NA Minor issued ☐ Date _____
Comments:

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 9/29/08
Date of Office Bio Review 8/19/08
Date of Labeling Approv. Sum 5/20/09
Labeling Acceptable Email Rec'd Yes ☐ No ☐
Labeling Acceptable Email filed Yes ☐ No ☐
Date of Sterility Assur. App. NA
Methods Val. Samples Pending Yes ☐ No ☒
MV Commitment Rcd. from Firm Yes ☐ No ☒
Modified-release dosage form: Yes ☒ No ☐
Interim Dissol. Specs in AP Ltr: Yes ☒

3. Labeling Endorsement
Reviewer:
Date_____
Name/Initials_____

Labeling Team Leader:
Date 6/5/09
Name/Initials rlw/for

Comments:

Final-printed labeling (FPL) found acceptable for approval 5/20/09.

4. David Read **(PP IVs Only)** Pre-MMA Language included ☐ Date 14May09
OGD Regulatory Counsel, Post-MMA Language Included ☐ InitialsDTR
Comments:Changes to AP ltr saved to V drive.

5. Div. Dir./Deputy Dir. Date5/27/09
Chemistry Div. II InitialsRCA

Comments:CMC OK. See attached spredsheet.

6. Frank Holcombe **First Generics Only** Date6/3/09
Assoc. Dir. For Chemistry InitialsRMP Comments: (First generic drug review)
Audited as requested by Robert. CMC is satisfactory as amended on 6/2/09.

7. Vacant Date_____ Deputy Dir., DLPS

Initials_____

RLD = Prilosec OTC Delayed-release Tablets 20 mg (base)
AstraZeneca LP NDA 21-229

8. Peter Rickman Date 6/5/09
Director, DLPS Initials rlw/for

Para.IV Patent Cert: Yes☐ No☐;Pending Legal Action: Yes ☐No ☐;Petition: Yes☐ No☐ Comments:Bioequivalence studies (fasting and non-fasting) found acceptable.
In-vitro dissolution testing also found acceptable. DSI inspection conducted of clinical bio site - Wellquest Clinical Research. Inspection of Wellquest conducted under Dr. Reddy's ANDA (b) (4) Inspection was acceptable - copy of review of inspection filed in DFS. Office-level bio endorsed 1/24/08 and 8/19/08.

Final-printed labeling (FPL) found acceptable dor approval 5/20/09.

CMC found acceptable for approval (Chemistry Review #5).

OR

8. Robert L. West Date 6/5/09
Deputy Director, OGD Initials RLWest
Para.IV Patent Cert: Yes☒ No☐; Pending Legal Action: Yes☐ No☒; Petition: Yes☒ No☐
Press Release Acceptable ☐
Comments: Acceptable EES dated 9/29/08 (Verified 6/5/09). No "OAI" Alerts noted.

This ANDA is based upon approved ANDA Sutiability Petition 2004P-0373/CP1. This petition was approved on July 5, 2005, and provided for a change in dosage form from that if the reference listed drug)i.e., from delayed-relase tablets to delayed-release capsules.

Dr. Reddy submitted paragraph IV certifications to each of the patents listed in the "Orange Book" for AstraZeneca's Prilosec OTC Delayed-release Tablets ('960, '265, '338, '424, '616 and '810). Dr. Reddy's was sued only on the '960 and '424 patents, but the litigation was subsequently dismissed via summary judgement. There are additional patents or exclusivity currently listed in the "Orange Book" for this drug product.

Dr. Reddy is eligible for 180-day generic drug exclusivity for this drug product.

This ANDA is recommended for approval.

9. Gary Buehler Date 6/5/09

Director, OGD Initials rlw/for
Comments:First-generic approval for this OTC drug product.
First Generic Approval ☒ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

10. Project Manager, Theresa Liu Team 7 Date6/5/09
Review Support Branch Initials tcl
_____Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
2 pm Time notified of approval by phone 2 pm Time approval letter faxed

FDA Notification:
6/5/09 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
6/5/09 Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

EER DATA:

EES Data for: 078878

****** Compliance Recommendations ******

App No	Doc Seq No	Date	OC Recommendation
078878	000	9/29/2008	ACCEPTABLE
078878	000	6/5/2007	ACCEPTABLE

****** EER Table ******

CFN	Name	Profile Code	Last Milestone Name	Last Milestone Date	Last Status	Last Status Date	OAI Alert/ Effective Date
(b) (4)							

ORANGE BOOK PRINT OFF:

Patent and Exclusivity Search Results from query on Appl No 021229 Product 001 in the OB_OTC list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
021229	001	5690960	Nov 25, 2014				
021229	001	5753265	Jun 7, 2015				
021229	001	5817338	Oct 6, 2015				
021229	001	5900424	May 4, 2016				
021229	001	6403616	Nov 15, 2019				
021229	001	6428810	Nov 3, 2019				

Exclusivity Data

There is no unexpired exclusivity for this product.

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.

View a list of all patent use codes
View a list of all exclusivity codes
Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support

Update Frequency:

Orange Book Data - **Monthly**

Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through April, 2009

Patent and Generic Drug Product Data Last Updated: June 04, 2009

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

/s/

Theresa Liu

6/5/2009 01:41:54 PM