

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-032

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

**Paragraph IV Patent Certification
Omeprazole Tablets
20 mg**

In accordance with Section 505(b)(2)(A)(iv) of the Federal, Food, Drug and Cosmetic Act (21 U.S.C. 355), 21 CFR § 314.50(i)(1)(i)(A)(4) and based on the patent data in the Electronic Orange Book "Approved Drug Products with Therapeutic Equivalence Evaluations" current through December 2005, patent and generic drug data last updated January 13, 2006, Dexcel Pharma Technologies Ltd. certifies that, in its opinion and to the best of its knowledge, the following mentioned patents are invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of omeprazole tablets, 20 mg, for which this application is submitted:

Patents Listed for NDA No. 021229

Appl. No.	Prod. No.	Patent No.	Patent Expiration	Patent Use Code
021229	001	4738974	Apr 19, 2005	
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	

Patents Listed for NDA No. 019810

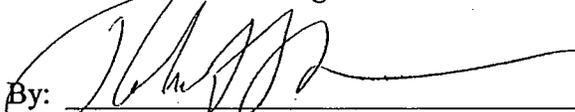
Appl. No.	Prod. No.	Patent No.	Patent Expiration	Patent Use Code
019810	001	4786505	Apr 20, 2007	U-108
019810	001	4786505*PED	Oct 20, 2007	U-108
019810	001	4853230	Apr 20, 2007	U-108
019810	001	4853230*PED	Oct 20, 2007	U-108
019810	001	6147103	Oct 09, 2018	
019810	001	6147103*PED	Apr 09, 2019	
019810	001	6150380	Nov 10, 2018	
019810	001	6150380*PED	May 10, 2019	
019810	001	6166213	Oct 09, 2018	
019810	001	6166213*PED	Apr 09, 2019	
019810	001	6191148	Oct 09, 2018	
019810	001	6191148*PED	Apr 09, 2019	

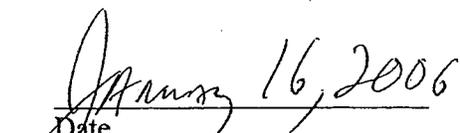
Dexcel Pharma Technologies Ltd. further states that, upon receipt of acknowledgement from the FDA concerning acceptance for review of this submission, appropriate notice regarding this Paragraph IV certification, as required under 21 CFR § 314.52 (a) and (c) and Section 505(b)(3)(A)-(D), will be provided to:

- (I) each owner of each patent which is the subject of the certification or the representative designated by the owner to receive such notice, and
- (II) the holder of the approved applications under section 505(b) of the Act for the listed drug or the representative of such holder designated to receive such notice for which the applicant is seeking approval.

At such time, this application will be amended to certify that such notice requirements have been met as required under 21 CFR § 314.52(b).

Dexcel Pharma Technologies Ltd.

By: 
Robert F. Green, Esq.
Attorney for Dexcel Pharma Technologies Ltd.


Date January 16, 2006



Attachment A – Exclusivity Statement

Marketing Exclusivity Statement

According to information published in the Electronic Orange Book, *Approved Drug Products with Therapeutic Equivalence Evaluations*, current through December 2005, there are no unexpired exclusivities for NDA 19-810 for Prilosec® (Omeprazole) Delayed Release Capsules, 20 mg.

According to information published in the Electronic Orange Book, *Approved Drug Products with Therapeutic Equivalence Evaluations*, current through December 2005, there is one unexpired exclusivity for NDA 21-229 for Prilosec OTC® (Omeprazole Magnesium) Delayed Release Tablets, 20 mg:

Appl. No	Prod No	Exclusivity Code	Exclusivity Expiration
<u>021229</u>	001	<u>RTO</u>	JUN 20, 2006

Dexcel Pharma Technologies Inc. does not intend to introduce its product, Omeprazole Delayed Release Tablets, 20 mg, subject to this 505(b)(2) NDA, to the market prior to the expiration of the above marketing exclusivity period.



Avi Avramoff
 Vice President Research and Development
 Dexcel Pharma Technologies, Inc.

2.2.06
 Date

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 22-032 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: February 10, 2006 PDUFA Goal Date: December 4, 2007

HFD _____ Trade and generic names/dosage form: omeprazole 20 mg delayed-release tablets

Applicant: Dexcel Pharmaceuticals, Inc Therapeutic Class: 8030100 Antacids

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

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

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): _____

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: Treatment of Frequent Heartburn

Is this an orphan indication?

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

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

Yes: Please proceed to Section A.

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

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Other: _____

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

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

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

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

Reason(s) for deferral:

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

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

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. 0 Tanner Stage _____
 Max _____ kg _____ mo. _____ yr. 18 Tanner Stage _____

Comments:

This drug product is appropriately labeled for use in ages less than 18 years for this indication. Therefore, no additional pediatric studies are needed in this age group.

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

NDA 22-032

Page 3

This page was completed by:

{See appended electronic signature page}

Keith Olin

Regulatory Project Manager

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH
STAFF at 301-796-0700**

(Revised: 10/10/2006)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is this an orphan indication?

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

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

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

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

Reason(s) for partial waiver:

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

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

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below)::

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

Reason(s) for deferral:

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

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

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

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

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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/s/

Geraldine Smith
12/14/2007 11:13:02 AM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 22-032 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: February 10, 2006 PDUFA Goal Date: December 10, 2006

HFD _____ Trade and generic names/dosage form: omeprazole 20 mg delayed-release tablets

Applicant: Dexcel Pharmaceuticals, Inc Therapeutic Class: 8030100 Antacids

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

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

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): _____

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: Treatment of Frequent Heartburn

Is this an orphan indication?

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

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

- Yes: Please proceed to Section A.
- No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

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

Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

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

Reason(s) for deferral:

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

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

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

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

Comments:

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

NDA 22-032

Page 3

This page was completed by:

{See appended electronic signature page}

Keith Olin

Regulatory Project Manager

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH
STAFF at 301-796-0700**

(Revised: 10/10/2006)

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is this an orphan indication?

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

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

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed

NOTE: More than one may apply

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

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

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

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
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- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

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

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below)::

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

Reason(s) for deferral:

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

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

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

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

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

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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/s/

Keith Olin
12/8/2006 05:26:53 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-032

Dexcel Pharma Technologies Limited
Attention: John D. Franolic, Ph.D.
Manager, Lachman Consultant Services, Inc
US Agent
1600 Stewart Ave
Westbury, NY 11590

Dear Dr. Franolic:

Please refer to your submission dated February 8, 2006, requesting a waiver for pediatric studies for omeprazole 20mg delayed-release tablets.

We have reviewed the submission and agree that a waiver is justified for omeprazole 20 mg delayed-release tablets for the treatment of frequent heartburn for children under 18 years of age because this product will not represent a meaningful therapeutic benefit over existing therapies for the pediatric patients.

Accordingly, at this time, a waiver for pediatric studies for your application is granted under section 2 of the Pediatric Research Equity Act.

If you have questions, contact LCDR Keith Olin, Regulatory Project Manager, at 301-796-0962.

Sincerely,

{See appended electronic signature page}

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

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/s/

Andrea Segal
12/8/2006 10:45:24 AM

Generic Drug Enforcement Act of 1992 Certification

Dexcel Pharma Technologies LTD debarment certification and certification of compliance with the Generic Drug Enforcement Act of 1992 Certification follows:

Section 306(k) (1) Requirement

Dexcel Pharma Technologies LTD hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application for Omeprazole Delayed Release Tablets, 20 mg submitted under 505 (b) (2) NDA.

Section 306(k) (2) Requirement

Dexcel Pharma Technologies LTD further certifies that there have been no convictions, as described in Sections 306(a) and 306(b) of the Generic Drug Enforcement Act of 1992, of any affiliated persons (including corporations, partnerships, associations or individuals) responsible for the development of data or other information used to support this application.

Jack Yanai
Name: Jack Yanai
Title: Vice President - Operations
Company: Dexcel Pharma Technologies LTD.

18th Dec. 2001
Date

Olin, Keith

From: J.Franolic@Lachmanconsultants.com
Sent: Monday, November 06, 2006 2:35 PM
To: Olin, Keith
Cc: Shetty, Daiva; Lopez, Lolita
Subject: Re: NDA 22032 - Question

Follow Up Flag: Follow up
Flag Status: Red

Keith:

Here is Dexcel's explanation regarding your query below. Please let me know if I need to submit a hardcopy to the NDA.

John

In your safety amendment letter dated Oct. 23, 2006 (no pagination), you stated that a bioequivalence study was conducted for two omeprazole formulations and was submitted on July 2000 in Israel under the application Ompradex 20 mg caplets 12019304800 and was approved in October 2000. However, in your NDA submission and safety summary, you stated that Dexcel has been marketing omeprazole in Israel since 1998. Clarify this inconsistency in the dates of approval/marketing.

In the safety amendment letter dated October 23, 2006, information was submitted for omeprazole tablets and caplets. In Israel the product name is Ompradex 20 mg Caplets while in the UK the product name is Omeprazole 20 mg Gastro Resistant Tablets. Both these names refer to the tablet dosage form.

Since the NDA 22-032 is for Omeprazole Delayed Release Tablets, 20 mg, information for the capsule formulation was not included. The capsule formulation was first introduced in Israel in 1998. Due to patent litigation in Israel only _____ each containing 30 capsules were marketed until the interlocutory injunction obtained in October, 1999. In 2006 an agreement was signed but the hard gelatin capsules dosage form was not remarketed. No ADRs/AEs reports were received for the capsule formulation.

The capsule formulation is different from the NDA 22-032 Omeprazole Delayed Release Tablets, 20 mg, _____

b(4)

b(4)

Herein below is the table with information for the two applications in Israel

Application #	Approval Date	Dosage Form	Difference from NDA 22-032 Formulation
111882934700	08.1998	Capsules	_____
120193004800	10.2000	Caplets	_____

b(4)

We trust that the information is fully responsive to your question.

John Franolic, Ph.D.
Manager
Lachman Consultant Services, Inc.
1600 Stewart Avenue, Westbury, NY 11590 (USA)
Telephone: 516-222-6222 Fax: 516-683-1887
J.Franolic@Lachmanconsultants.com

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"Olin, Keith"
<keith.olin@fda.h
hs.gov>

10/31/2006 03:51
PM

To
J.Franolic@Lachmanconsultants.com
cc
"Shetty, Daiva"
<daiva.shetty@fda.hhs.gov>, "Lopez,
Lolita" <lolita.lopez@fda.hhs.gov>
Subject
NDA 22032 - Question

John,

Please address the following concerns from the medical reviewer:

1) In your safety amendment letter dated Oct. 23, 2006 (no pagination), you stated that a bioequivalence study was conducted for two omeprazole formulations and was submitted on July 2000 in Israel under the application Ompradex 20 mg caplets 120193004800 and was approved in October 2000. However, in your NDA submission and safety summary, you stated that Dexcel has been marketing omeprazole in Israel since 1998. Clarify this inconsistency in the dates of approval/marketing.

LCDR Keith Olin
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
301-796-0962
Keith.Olin@fda.hhs.gov

Mail:

Food and Drug Administration
Center of Drug Evaluation and Research
Office of Nonprescription Products
590I-B Ammendale Road
Beltsville, MD 20705-1266

APPEARS THIS WAY ON ORIGINAL

APPEARS THIS WAY ON ORIGINAL

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/s/

Keith Olin
11/27/2007 03:08:30 PM
CSO

Olin, Keith

From: J.Franolic@Lachmanconsultants.com
Sent: Tuesday, May 01, 2007 9:15 AM
To: Olin, Keith
Subject: Re: NDA 22-032
Follow Up Flag: Follow up
Flag Status: Red

Hi keith

I will call Dexcel to find out. Please confirm that you received our patent amendment.

John

John Franolic, Ph.D Director

Lachman Consultant Services, Inc.

LCS Office: 516-222-6222 / Fax: 516-683-1887 / Cell: 516-369-7743

J.Franolic@LachmanConsultants.com

Sent Via Blackberry Handheld

----- Original Message -----

From: "Olin, Keith" [keith.olin@fda.hhs.gov]

Sent: 05/01/2007 09:11 AM AST

To: John Franolic

Subject: NDA 22-032

John,

Can you give me an update on the court ruling. You mentioned that you thought the 30 month stay would be lifted on April 19, 2007.

Dexcel is responsible for keeping the FDA up to date on this issue. If not we are going to assume that Dexcel is still under a 30 month stay.

Thanks,

LCDR Keith Olin

Regulatory Project Manager

Division of Nonprescription Clinical Evaluation

301-796-0962

Keith.Olin@fda.hhs.gov

Mail:

Food and Drug Administration

Center of Drug Evaluation and Research

Office of Nonprescription Products

5901-B Ammendale Road

Beltsville, MD 20705-1266

11/27/2007

Olin, Keith

From: Olin, Keith
Sent: Friday, July 06, 2007 5:15 PM
To: 'J.Franolic@Lachmanconsultants.com'
Subject: NDA 22-032

John,

Since you did not call me in regards to the CMC information for NDAD 22-032. I just wanted to let you know that the information for the CMC amendment is considered a major amendment (based on the information that you provided to me) and would be under a 6 month review clock.

LCDR Keith Olin
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
301-796-0962
Keith.Olin@fda.hhs.gov

Mail:
Food and Drug Administration
Center of Drug Evaluation and Research
Office of Nonprescription Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

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/s/

Keith Olin
11/26/2007 04:12:13 PM
CSO

DUPLICATE

LACHMAN CONSULTANT SERVICES, INC.
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

1600 STEWART AVENUE, WESTBURY, NY 11590
(516) 222-6222 • FAX (516) 683-1887

September 24, 2007

(OVERNIGHT COURIER: 9/24/07)

RECEIVED

SEP 25 2007

Charles Ganley, M.D.
Division of Nonprescription Clinical Evaluation
Office of Nonprescription Products
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville, Maryland 20705-1266

RECEIVED

CDER CDR

SEP 27 2007

CDER/WHITE OAK/DRI

**SUBJECT: AMENDMENT: Settlement of Patent Litigation
NDA 22-032 (Omeprazole Delayed Release Tablets, 20 mg)**

NEW CORRESPONDENCE

Dear Dr. Ganley:

N(C)

Reference is made to Dexcel Pharma Technologies Limited's NDA 22-032 for Omeprazole Delayed Release Tablets, 20 mg, which was tentatively approved on June 14, 2007.

Lachman Consultant Services, Inc., as United States Agent, is herewith submitting a statement from Dexcel indicating that the patent litigation with AstraZeneca US has been settled and that an agreement between Dexcel and AstraZeneca US was signed on September 21, 2007. This agreement permits Dexcel to launch its Omeprazole Delayed Release Tablets, 20 mg, on October 21, 2007, dependent upon final approval of NDA 22-032.

If you should have any questions regarding this submission, please do not hesitate to contact the undersigned at 516-222-6222.

Sincerely,

Mary-Anne D'Esposito

Mary-Anne D'Esposito, M.Sc.
Manager

Attachment: Statement regarding settlement of patent litigation

D18E7267

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: September 30, 2008
See OMB Statement on page 2.

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

FOR FDA USE ONLY

APPLICATION NUMBER

SEP 25 2007

CDER CD

APPLICANT INFORMATION

NAME OF APPLICANT Dexcel Pharma Technologies Limited	DATE OF SUBMISSION 09/24/2007
TELEPHONE NO. (Include Area Code) 011-972-4-636-4000	FACSIMILE (FAX) Number (Include Area Code) 011-972-4-636-4004
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Southern Industrial Zone Or Akiva 30600 Israel	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Lachman Consultant Services, Inc. 1600 Stewart Avenue Phone: 516-222-6222 Westbury, New York 11590 Fax: 516-683-1887

RECEIVED

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)	NDA 22-032	
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) Omeprazole Delayed Release Tablets	PROPRIETARY NAME (trade name) IF ANY CDER/WHITE OAK	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 5-methoxy-2-(((4-methoxy-3,5-dimethyl-2-pyridinyl)methyl)sulfonyl)-1H-benzimidazole	CODE NAME (If any)	
DOSAGE FORM: Tablets	STRENGTHS: 20 mg	ROUTE OF ADMINISTRATION: Oral
(PROPOSED) INDICATION(S) FOR USE: For frequent heartburn (occurring 2 or more days a week).		

SEP 27 2007

APPLICATION DESCRIPTION

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

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

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

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

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

CERTIFICATION

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

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

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

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

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

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT <i>Mary-Anne D'Esposito</i>	TYPED NAME AND TITLE Mary-Anne D'Esposito, M.Sc., Manager	DATE 09/24/2007
ADDRESS (Street, City, State, and ZIP Code) Lachman Consultant Services, Inc., 1600 Stewart Ave., Westbury, NY 11590	Telephone Number 516-222-6222	

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

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

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

September 23, 2007

US Food and Drug Administration
5600 Fishers Lane,
Rockville, Maryland 20857, USA

RECEIVED

SEP 27 2007

To Whom It May Concern, US Food and Drug Administration ("FDA"),

NDA 22-032 for Omeprazole Delayed Release Tablets, 20 mg

CDER/WHITE OAK/DRI

Settlement Agreement between AstraZeneca and Dexcel

Dexcel Pharma Technologies, Ltd. ("Dexcel") is pleased to inform the FDA that, on Friday, September 21, 2007 the Dexcel Parties and AstraZeneca US signed a settlement agreement ("Agreement") to conclude the litigation relating to Dexcel's above NDA.

The US District Court for the District of Delaware was informed by AZ's Counsel that the remaining AZ Parties will sign the Agreement this week (commencing September 24, 2007), when it will also be filed with the Court, together with a stipulation of dismissal signed by both parties. In accordance with the Agreement, the AstraZeneca Parties will submit an appropriate notice to the FDA within 5 business days.

The Agreement permits Dexcel to launch its NDA product on October 21, 2007. It will be the first alternative omeprazole product to Prilosec OTC and will significantly reduce costs to the American consumer. Dexcel respectfully requests, therefore, that the FDA utilize its best endeavors to:

- i. **grant a revised tentative approval** (in lieu of the one given on June 14, 2007), and
- ii. **finalize Dexcel's Chemistry and Manufacturing Controls Amendment** (submitted to the FDA on July 19, 2007),

both as soon as possible, to enable Dexcel to launch its product on October 21, 2007.

Should the FDA require any further information, it should not hesitate to get in contact.

Yours faithfully,
Dexcel Pharma Technologies, Ltd.


Dan Oren,
President & CEO

Leonard Segal, Andrea

From: Adebowale, Abimbola O
Sent: Tuesday, June 05, 2007 4:28 PM
To: Leonard Segal, Andrea; Lee, Sue Chih H
Cc: Korvick, Joyce A
Subject: RE: Dexcel omeprazole review NDA 22-032

Andrea,
I would appreciate it if you DFS this e-mail and refer to **this e-mail in your review.**

Thanks,
Abi

-----Original Message-----

From: Leonard Segal, Andrea
Sent: Tuesday, June 05, 2007 3:59 PM
To: Adebowale, Abimbola O; Lee, Sue Chih H
Cc: Korvick, Joyce A
Subject: RE: Dexcel omeprazole review NDA 22-032

Abi,
I can DFS this e-mail instead of asking you to update your memo. I can refer to **this e-mail in the review.** What would you prefer for me to do?
Andrea

Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation
301-796-0940

-----Original Message-----

From: Adebowale, Abimbola O
Sent: Tuesday, June 05, 2007 1:46 PM
To: Leonard Segal, Andrea; Lee, Sue Chih H
Cc: Korvick, Joyce A; Adebowale, Abimbola O
Subject: RE: Dexcel omeprazole review NDA 22-032

Hi Andrea,

You are right, the way I have written the brand name of Prilosec OTC in my review of the amendment is technically incorrect. Basically, the brand name on the label is Prilosec OTC. There is no strength or salt attached to the brand name. The generic name is omeprazole magnesium delayed-release tablets 20.6 mg (equivalent to 20 mg omeprazole). Therefore following discussions with Sue, my suggested revised wording would be as follows:

"Dexcel omeprazole 20 mg was bioequivalent to the Prilosec OTC (omeprazole magnesium delayed-release tablets 20.6 mg)".

Thank-you,
Abi

-----Original Message-----

From: Leonard Segal, Andrea
Sent: Monday, June 04, 2007 3:49 PM
To: Adebowale, Abimbola O; Lee, Sue Chih H
Cc: Korvick, Joyce A
Subject: Dexcel omeprazole review NDA 22-032

Hi Abi and Sue,

I noticed something as I read the Clin Pharm review. I believe on page 2 in the review comments that you meant to say that the Dexcel omeprazole 20 mg was bioequivalent to the Prilosec OTC 20.6 mg omeprazole magnesium (not Prilosec OTC 20 mg). This is what I need to be able to say in my review. What do you think?

Andrea

Andrea Leonard-Segal, M.D.

Director

Division of Nonprescription Clinical Evaluation

301-796-0940

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/s/

Andrea Segal

6/5/2007 04:37:51 PM

MEDICAL OFFICER

This e-mail can serve as a post script to
the Clinical Pharmacology Review dated June 1, 2007.

US Food and Drug Administration
5600 Fishers Lane, Rockville,
Maryland 20857, USA

April 11, 2007

To Whom It May Concern, US Food and Drug Administration,

Re: Litigation Summary

On February 2, 2006, Dexcel Pharma Technologies, Ltd. ("DPT") filed an NDA for its omeprazole OTC generic product. On April 17, DPT then sent Notice Letters to the Orange Book patent holders with respect to the filing, as required under paragraph IV. On May 31, the AstraZeneca and KBI parties ("Plaintiffs") sued DPT under the Hatch-Waxman Act, alleging patent infringement, in the US District Court in Delaware. A day later, Plaintiffs filed an identical suit with the US District Court in Alexandria, Virginia.

In the suits, Plaintiffs argue for the infringement of 3 patents: 2 formulation patents (US 4,853,230 and US 4,786,505) which expire on April 20, 2007 and to which pediatric exclusivity until October 20, 2007 has been granted, and 1 crystalline form patent (US 6,150,380) filed in 1998.

Formulation Patents The subcoating layer in the omeprazole formulation is the claimed invention of the formulation patents, taught by the AstraZeneca formulation patents as providing long-term stability. DPT's product achieves this with a *single* coating layer.

Crystalline Form Patent DPT has good grounds for arguing that US 6,150,380 is invalid due to prior commercial activities in the US.

DPT believes that the suits were filed by Plaintiffs - who had been familiar with DPT's corresponding products, in Israel and the UK, for 7 years - in bad faith. Plaintiffs, for instance, have been offered samples of the NDA product, but have avoided performing any tests to support their claims. Moreover, DPT believes that Plaintiffs' failure to disclose their DMF during the litigation flows from Plaintiffs' desire to conceal information relating to their own prior commercial use of the claimed crystalline form in the US.

DPT thus intends to file an antitrust counterclaim against Plaintiffs next week, a copy of which it will then be served on the US Food and Drug Administration.

Summary of Litigation Status

- US District Court in Delaware assumed exclusive jurisdiction in January 2007.
- According to said Court, April 2, 2007 was the last date for finalizing discovery.
- DPT has recently motioned to lift the 30 month stay of FDA approval for its product.
- The next hearing is expected on April 16 or 18, 2007, at which DPT intends to fix a full trial schedule and to discuss the motion to lift the FDA stay.
- DPT intends to file an antitrust counterclaim against Plaintiffs, for filing the suits in bad faith, next week.

Yours faithfully,
Dexcel Pharma Technologies, Ltd.


Dan Oren,
President & CEO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-032

DISCIPLINE REVIEW LETTER

Lachman Consultant Services, Inc
Attention: John D. Franolic, Ph.D.
Manager
US Agent for Dexcel Pharma Technologies Limited
1600 Stewart Ave
Westbury, NY 11590

Dear Dr. Franolic:

Please refer to your new drug application (NDA) dated February 8, 2006, received February 10, 2006, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for omeprazole 20mg delayed-release tablets.

We also refer to your submission dated April 16, 2007.

Our review of the labeling section of your submission is complete, and we have identified the following deficiencies:

Carton Label - Drug Facts

These revisions apply to the 14-, 28- and 42- count carton label with Drug Facts and the 14-count inner carton label with Drug Facts (for use in the 28- and 42- count package sizes).

- 1) Under the heading "Other information", remove the period after the first statement to read "read the directions, warnings, and package insert before use".

In order to ensure a timely action for this new drug application, we request that you respond to the issues listed above as soon as possible with revised draft labeling as an amendment to your NDA.

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

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

Sincerely,

{See appended electronic signature page}

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

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/s/

Leah Christl

6/1/2007 03:54:38 PM



NDA 22-032

DISCIPLINE REVIEW LETTER

Dexcel Pharma Technologies Limited
Attention: John D. Franolic, Ph.D.
Manager, Lachman Consultant Services, Inc
US Agent
1600 Stewart Ave
Westbury, NY 11590

Dear Dr. Franolic:

Please refer to your new drug application (NDA) dated February 8, 2006, received February 10, 2006, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for omeprazole 20 mg delayed-release tablets.

We also refer to your submission dated December 18, 2006.

Our review of the labeling section of your submission is complete, and we have identified the following deficiencies:

A. Carton Labels – Drug Facts

These revisions apply to the 14-, 28- and 42- count carton label with Drug Facts and the 14-count inner carton label with Drug Facts (for use in the 28- and 42- count package sizes).

- 1) Change the "O" in omeprazole to a lowercase "o", under "Warnings", subheading "Allergy Alert".
- 2) Under the heading "Warnings", add as the last two bullets under the subheading "Ask a doctor or pharmacist before use if you are taking," the following:
 - tacrolimus (immune system medicine)
 - atazanavir (medicine for HIV infection)
- 3) Under "Other information", place a bullet by the first statement in accordance with § 201.66(d)(4) and insert commas as follows:
 - read the directions, warnings, and package insert before use.

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/s/

Leah Christl
4/13/2007 03:33:38 PM

Olin, Keith

From: J.Franolic@Lachmanconsultants.com
Sent: Thursday, December 07, 2006 10:15 AM
To: Olin, Keith
Subject: Re: NDA 22-032 Omeprazole

Attachments: insert.pdf



insert.pdf (77 KB)

Keith:

Thank you. We are working on the amendment, and as agreed we will FEDEX today for tomorrow delivery. I will provide you with an email scanned copy of the whole amendment with:



b(4)

Can we keep this section on the insert as is?

John

John Franolic, Ph.D.
Manager
Lachman Consultant Services, Inc.
1600 Stewart Avenue, Westbury, NY 11590 (USA)
Telephone: 516-222-6222 Fax: 516-683-1887
J.Franolic@Lachmanconsultants.com
(See attached file: insert.pdf)

CONFIDENTIALITY NOTE: This e-mail and any files transmitted are intended only for the use of the individual or entity to whom they are addressed, and may contain information that is privileged, confidential and exempt from disclosure under applicable law. If you are not the intended recipient, you are hereby notified that any disclosure, copying, distribution or use of any of the information is PROHIBITED.

"Olin, Keith"
<keith.olin@fda.hhs.gov>

12/06/2006 05:28 PM

J.Franolic@Lachmanconsultants.com To

"Olin, Keith"
<keith.olin@fda.hhs.gov> cc

NDA 22-032 Omeprazole

Subject

John,

Per our conversation today December 6, 2006 in regards to NDA 22-032 labeling amendment submitted on November 30, 2006, received December 1, 2006.

Please provide a draft label to be reviewed by

December 7, 2006.

Let me know if you have any questions.

LCDR Keith Olin
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
301-796-0962
Keith.Olin@fda.hhs.gov

Mail:
Food and Drug Administration
Center of Drug Evaluation and Research
Office of Nonprescription Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

b(4)

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/s/

Keith Olin
12/8/2006 11:41:09 AM
CSO



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products

EMAIL TRANSMITTAL SHEET

DATE: December 6, 2006

To: John Franolic	From: Keith Olin, R.Ph. Regulatory Project Manager
Company: Lachman Consultant Services Dexcel Pharma	Division of nonprescription Clinical Evaluation
Email Address: J.Franolic@Lachmanconsultants.com	Fax number: (301)796-9899
Phone number: 516-222-6222	Phone number: (301) 796-0962

Subject: Label comments NDA 22-032

Total no. of pages including cover: 2

Document to be mailed: YES NO

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Please refer to your labeling amendment for NDA 22-032 dated November 30, 2006, received December 1, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for omeprazole 20 mg delayed-release tablets.

John,

Per our conversation yesterday (12/5/06). In response to your November 30, 2006 labeling amendment for NDA 22-032.

Please submit a labeling amendment agreeing to these changes by Thursday, December 7, 2006.

LCDR Keith Olin
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
301-796-0962
Keith.Olin@fda.hhs.gov

Mail:
Food and Drug Administration
Center of Drug Evaluation and Research
Office of Nonprescription Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

b(4)

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/s/

Keith Olin
12/6/2006 05:16:14 PM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-032

DISCIPLINE REVIEW LETTER

Lachman Consultants Services, Inc.
Attention: John D. Franolic, Ph.D.
Manager
Dexcel Pharma Technologies Limited
1600 Stewart Avenue
Westbury, NY 11590

Dear Dr. Franolic:

Please refer to your February 8, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for omeprazole 20 mg delayed-release tablets.

Our review of the labeling section of your submission is complete, and we have identified the following deficiencies:

A. Principal Display Panel:

1. Revise the statement "One 14-day course of treatment" to read: "Two 14-day courses of treatment" on the 28 count.
2. Revise the statement "One 14-day course of treatment" to read: "Three 14-day courses of treatment" on the 42 count.

b(4)

b(4)

b(4)

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

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

Sincerely,

{See appended electronic signature page}

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

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/s/

Leah Christl
11/21/2006 12:51:55 PM



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Nonprescription Products**

EMAIL TRANSMITTAL SHEET

DATE: September 22, 2006

To: John Franolic, Ph.D.	From: Keith Olin, R.Ph. Regulatory Project Manager
Company: Lachman Consultant Group	Division of nonprescription Clinical Evaluation
Email Address: J.Franolic@Lachmanconsultants.com	Fax number: (301)796-9899
Phone number: 516-222-6222	Phone number: (301) 796-0962
Subject: NDA 22-032 Information Request.	

Total no. of pages including cover: 2

Document to be mailed: YES NO

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Please refer to your supplemental new drug application dated February 8, 2006, received February 10, 2006, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for omeprazole 20mg delayed-release tablets. In connection with our review of the clinical section of NDA 22-032, we have the following comments and requests for information:

- 1) Provide a narrative summary and analysis for each of the following safety parameters measured during the PK study (ies):
 - a) Vital signs
 - b) PE
 - c) EKGs
 - d) Laboratory

- 2) Submit a 4-month Safety Update (required under 21 CFR 314.50 (5) vi). It should include new safety data available for omeprazole (postmarketing reports to your company, AERS database, literature, new studies) since the date of your last safety data report. Data should be analyzed separately from the previous submission to assess if there are any new safety issues.

- 3) In the March 23, 2006 Safety Amendment under the heading Postmarketing Data for Omeprazole 10, 20, and 40 mg (p.6), a PSUR submitted for Dexcel's omeprazole product (in the U.K, IL?) from February 2002 to December 2005 is referred to however we do not have a record of this submission. Resubmit this PSUR to the NDA.

- 4) It is also stated in both March 23 and September 1, 2006 Safety Amendments to NDA that during the review interval, there were no adverse drug reactions reported to Dexcel. Is there a safety monitoring system in place for this product in U.K. and Israel? Describe how postmarketing reports are collected in both countries. Clarify if clinical studies were conducted with your formulation prior to marketing in U.K. and Israel. If so, provide any safety data collected during those studies.

We also remind you about our safety data requests conveyed to you in the April 25, 2006 letter and June 8, 2006 e-mail.

In order to ensure a timely action for this new drug application, we request that you respond to the issues listed above by October 6, 2006, as an amendment to your NDA. If you have any questions, contact Keith Olin, Regulatory Project Manager at (301) 796-0962.

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/s/

Keith Olin
9/22/2006 04:10:55 PM
CSO

MEMORANDUM

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

DATE: June 8, 2006

TO: John Franolic, Ph.D.
Lachman Consultant Services, Inc.
Dexcel Pharma

FROM: Keith Olin, Regulatory Project Manager

SUBJECT: **Email Request – Clarification of Safety Request**
NDA 22-032, Omeprazole 20 mg Delayed-Release Tablets

John,

Here are the clarification points:

- A statement that you do not have any adverse events reported is not sufficient to submit. Describe what kind of drug safety monitoring system they have in place in their company. Submit any adverse events in regards to your formulation.
- The safety data should be analyzed for 20 mg omeprazole when used once a day for 2 weeks since this is the proposed dosing regimen. The format you used to summarize AEs is not acceptable and it does not include the dose and duration of use, causality assessment, and outcome. You should analyze AERS, your own data, and literature separately.
- If there are several omeprazole formulations for which AEs are reported into the AERS, you do not need to sort them out by the manufacturer, but you need to provide data for overall safety profile of omeprazole 20 mg when used once a day for 2 weeks. The most important is the safety of your own formulation.

We can discuss this if you have any questions.

LCDR Keith Olin
301-796-0962
Keith.Olin@fda.hhs.gov

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/s/

Keith Olin
8/28/2006 02:50:39 PM
CSO

MEMORANDUM

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

DATE: June 9, 2006

TO: John Franolic, Ph.D.
Lachman Consultant Services, Inc.
Dexcel Pharma

FROM: Keith Olin, Regulatory Project Manager

SUBJECT: **Email Request**
NDA 22-032, Omeprazole 20 mg Delayed-Release Tablets

John,

Here is another request for NDA 22-032:

In order for the reviewer to complete a toxicological assessment of sodium stearate and ethanolamine excipients, hard copies of the references cited in the summary are needed. Provide copies of the references cited on pages 94 and 106 (pages 9 and 12 of the summary).

If you have any questions, let me know.

LCDR Keith Olin
301-796-0962
Keith.Olin@fda.hhs.gov

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/s/

Keith Olin
6/9/2006 05:14:02 PM
CSO



DSI CONSULT

Request for Biopharmaceutical Inspections

DATE: June 2, 2006

TO: Associate Director for Bioequivalence
Division of Scientific Investigations, HFD-48

THROUGH: (Required for international inspections)
Director, Division of Pharmaceutical Evaluation

FROM: Keith Olin, Regulatory Project Manager, HFD-560

SUBJECT: **Request for Biopharmaceutical Inspections**
NDA 22-032
Omeprazole 20mg Delayed –Release Tablet

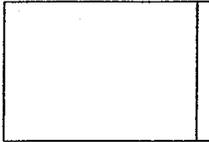
Study/Site Identification:

As discussed with you, the following studies/sites pivotal to approval (OR, raise question regarding the quality or integrity of the data submitted and) have been identified for inspection:

Study #	Analytical Site (name, address, phone, fax, contact person, if available)
AA24171	
AA28531	

b(4)

b(4)



b(4)

International Inspections:

(Please note: International inspections require sign-off by the ORM Division Director or DPE Division Director.)

We have requested an international inspection because:

There is a lack of domestic data that solely supports approval;

Other (please explain):

Goal Date for Completion:

We request that the inspections be conducted and the Inspection Summary Results be provided by **September 27, 2006**. We intend to issue an action letter on this application by **December 10, 2006**.

Should you require any additional information, please contact LCDR Keith Olin at 301-796-0962.

Concurrence:

Abimbola Adebawale, Biopharm Reviewer

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/s/

Keith Olin

6/5/2006 05:36:27 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-032

Lachman Consultant Services, Inc
Attention: John D. Franolic, Ph.D.
Manager
U.S. Agent for Dexcel Pharma Technologies Limited
1600 Stewart Ave
Westbury, NY 11590

Dear Dr. Franolic:

Please refer to your February 8, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for omeprazole delayed release tablets, 20mg.

We also refer to your submission dated March 23, 2006.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on April 11, 2006, in accordance with 21 CFR 314.101(a).

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

- 1) Annotated specifications for the label and labeling were not submitted.
- 2) The patent information is not acceptable.
- 3) The summary of safety information is incomplete.
- 4) The patent certification is not acceptable.

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

We also request that you submit the following information:

- 1) The dissolution method development for your product and dissolution data generated (both individual and average) of your clinical/bioavailability lots using your proposed

dissolution method. In your submission, you stated that your acceptance criteria for your dissolution method was according to the USP. However, we noted that the USP has quite a number of criteria (depending on the method used) for Omeprazole DR capsules and not tablets. Therefore, you need to specify exactly what your proposed acceptance criteria are intended to be for your drug product.

- 2) Adverse events reported for your formulation since marketing worldwide.
- 3) A worldwide literature review for any serious adverse events from 2002 to 2005 for 20mg omeprazole. Provide in an analyzed and summarized format.
- 4) An adverse events summary by dose, duration of use, and by demographics.
- 5) Annotated specifications for the label and labeling.
- 6) Patent information on form FDA 3541a.
- 7) A correctly worded Paragraph IV patent certification statement according to 21 CFR 314.50 (h)(i)(A)(4). Use of the language "to the best of its knowledge" and "in its opinion" is not acceptable.

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

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

Sincerely,

{See appended electronic signature page}

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

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/s/

Leah Christl

4/25/2006 01:22:49 PM

MEMORANDUM

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

DATE: April 11, 2006

TO: NDA 22-032 File

FROM: Laura Shay, PM, Office of Nonprescription Products

SUBJECT: Permission Granted to Send Paragraph IV Patent Certification via FedEx

At the request of Saumil Mehta, the attorney representing Dexcel Pharma, permission was granted via telephone for them to send the Paragraph IV patent certification to the patent owner of the referenced product via FedEx vs. USPS for NDA 22-032 (omeprazole delayed release tablets).

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/s/

Laura Shay
4/11/2006 03:19:07 PM
CSO



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service*

Food and Drug Administration
Rockville, MD 20857

NDA 22-032

NDA ACKNOWLEDGMENT

Lachman Consultant Services, Inc
Attention: John D. Franolic, Ph.D.
Manager
Dexcel Pharma Technologies Limited
1600 Stewart Ave
Westbury, NY 11590

Dear Dr. Franolic:

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

Name of Drug Product: omeprazole delayed release tablets, 20mg
Review Priority Classification: standard (S)
Date of Application: February 8, 2006
Date of Receipt: February 10, 2006
Our Reference Number: NDA 22-032

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on April 11, 2006, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be December 10, 2006.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application. Once the application has been filed we will notify you whether we have waived the pediatric study requirement for this application.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

NDA 22-032

Page 2

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Nonprescription Clinical Evaluation
5901-B Ammendale Road
Beltsville, MD 20705-1266

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

Sincerely,

{See appended electronic signature page}

Keith Olin, R.Ph.
Regulatory Project Manager
Division of Nonprescription Clinical Evaluation
Office of Drug Nonprescription Products
Center for Drug Evaluation and Research

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/s/

Keith Olin
3/24/2006 11:11:01 AM

Sturgeon, Kathy

From: TrackingUpdates@fedex.com
Sent: Wednesday, April 19, 2006 1:24 PM
To: Sturgeon, Kathy
Subject: FedEx Shipment 790888167504 Delivered

Our records indicate that the following shipment has been delivered:

Tracking number:	790888167504
Reference:	236869
Ship (P/U) date:	Apr 18, 2006
Delivery date:	Apr 19, 2006 12:00 PM
Sign for by:	
Delivered to:	Receptionist/Front Desk
Service type:	FedEx International Priority
Packaging type:	FedEx Envelope
Number of pieces:	1
Weight:	1.0 LB

b(6)

Shipper Information
KATHLEEN STURGEON
LEYDIG, VOIT MAYER, LTD.
180 N. STETSON
SUITE 4900
CHICAGO
IL
US
60601

Recipient Information
ASTRAZENECA AB
PARENT OF AKTIEBOLAGET HASSLE
VASTRA MALARENANMEN 9
SODERTALJE
SE
15185

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Thank you for your business.

Sturgeon, Kathy

From: TrackingUpdates@fedex.com
Sent: Tuesday, April 18, 2006 9:41 AM
To: Sturgeon, Kathy
Subject: FedEx Shipment 792715709487 Delivered

Our records indicate that the following shipment has been delivered:

Tracking number:	792715709487
Reference:	236869
Ship (P/U) date:	Apr 18, 2006
Delivery date:	Apr 18, 2006 09:20 AM
Sign for by:	
Delivered to:	Shipping/Receiving
Service type:	FedEx Priority Overnight
Packaging type:	FedEx Envelope
Number of pieces:	1
Weight:	0.5 LB

b(6)

Shipper Information
 Kathleen Sturgeon
 Leydig, Voit & Mayer, Ltd.
 180 N. Stetson
 Suite 4900
 Chicago
 IL
 US
 60601

Recipient Information
 Philippe L. Durette
 Patent Department
 Merck & Co., Inc.
 126 E. Lincoln Avenue
 Rahway
 NJ
 US
 07065

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Sturgeon, Kathy

From: TrackingUpdates@fedex.com
Sent: Tuesday, April 18, 2006 9:40 AM
To: Sturgeon, Kathy
Subject: FedEx Shipment 792072620935 Delivered

Our records indicate that the following shipment has been delivered:

Tracking number: 792072620935
Reference: 236869
Ship (P/U) date: Apr 18, 2006
Delivery date: Apr 18, 2006 09:20 AM
Sign for by: _____
Delivered to: Shipping/Receiving
Service type: FedEx Priority Overnight
Packaging type: FedEx Envelope
Number of pieces: 1
Weight: 0.5 LB

b(6)

Shipper Information
Kathleen Sturgeon
Leydig, Voit & Mayer, Ltd.
180 N. Stetson
Suite 4900
Chicago
IL
US
60601

Recipient Information
Kenneth C. Frazier
Senior Vice Pres. and Gen. Counsel
Merck & Co., Inc.
126 E. Lincoln Avenue
Rahway
NJ
US
07065

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From: TrackingUpdates@fedex.com
Sent: Tuesday, April 18, 2006 9:26 AM
To: Sturgeon, Kathy
Subject: FedEx Shipment 791917078825 Delivered

Our records indicate that the following shipment has been delivered:

Tracking number:	791917078825
Reference:	236869
Ship (P/U) date:	Apr 18, 2006
Delivery date:	Apr 18, 2006 09:04 AM
Sign for by:	
Delivered to:	Shipping/Receiving
Service type:	FedEx Priority Overnight
Packaging type:	FedEx Envelope
Number of pieces:	1
Weight:	0.5 LB

b(6)

Shipper Information
Kathleen Sturgeon
Leydig, Voit & Mayer, Ltd.
180 N. Stetson
Suite 4900
Chicago
IL
US
60601

Recipient Information
Glenn M. Englemann
Vice President and General Counsel
AstraZeneca Pharmaceuticals
1800 Concord Pike
Wilmington
DE
US
198505437

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Thank you for your business.

Sturgeon, Kathy

From: TrackingUpdates@fedex.com
Sent: Tuesday, April 18, 2006 8:20 AM
To: Sturgeon, Kathy
Subject: FedEx Shipment 791447785696 Delivered

Our records indicate that the following shipment has been delivered:

Tracking number: 791447785696
Reference: 236869
Ship (P/U) date: Apr 18, 2006
Delivery date: Apr 18, 2006 09:10 AM
Sign for by: Receptionist/Front Desk
Delivered to: Receptionist/Front Desk
Service type: FedEx Priority Overnight
Packaging type: FedEx Envelope
Number of pieces: 1
Weight: 0.5 LB

b(6)

Shipper Information
Kathleen Sturgeon
Leydig, Voit & Mayer, Ltd.
180 N. Stetson
Suite 4900
Chicago
IL
US
60601

Recipient Information
Brumbaugh Graves Donohue & Raymond
Agent for Aktiebolaget Hassle,
Molndal, Sweden a Corp. of Sweden
30 Rockefeller Plaza-Suite 44
New York
NY
US
10112

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Sturgeon, Kathy

From: TrackingUpdates@fedex.com
Sent: Tuesday, April 18, 2006 8:19 AM
To: Sturgeon, Kathy
Subject: FedEx Shipment 791447745935 Delivered

Our records indicate that the following shipment has been delivered:

Tracking number:	791447745935
Reference:	236869
Ship (P/U) date:	Apr 18, 2006
Delivery date:	Apr 18, 2006 09:04 AM
Sign for by:	
Delivered to:	Shipping/Receiving
Service type:	FedEx Priority Overnight
Packaging type:	FedEx Envelope
Number of pieces:	1
Weight:	0.5 LB

b(6)

Shipper Information
 Kathleen Sturgeon
 Leydig, Voit & Mayer, Ltd.
 180 N. Stetson
 Suite 4900
 Chicago
 IL
 US
 60601

Recipient Information
 Judy W. Firor
 Regulatory Affairs
 AstraZeneca Pharmaceuticals LP
 1800 Concord Place
 Wilmington
 DE
 US
 198505437

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Sturgeon, Kathy

From: TrackingUpdates@fedex.com
Sent: Tuesday, April 18, 2006 8:12 AM
To: Sturgeon, Kathy
Subject: FedEx Shipment 790396197497 Delivered

Our records indicate that the following shipment has been delivered:

Tracking number:	790396197497
Reference:	236869
Ship (P/U) date:	Apr 18, 2006
Delivery date:	Apr 18, 2006 09:05 AM
Sign for by:	
Delivered to:	Shipping/Receiving
Service type:	FedEx Priority Overnight
Packaging type:	FedEx Envelope
Number of pieces:	1
Weight:	0.5 LB

b(6)

Shipper Information
Kathleen Sturgeon
Leydig, Voit & Mayer, Ltd.
180 N. Stetson
Suite 4900
Chicago
IL
US
60601

Recipient Information
John M. Genova
White & Case LLP
1155 Avenue of the Americas
New York
NY
US
10036

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4/18/2006



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Customer Support Trace
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Module H, 4th Floor
Memphis, TN 38116

U.S. Mail: PO Box 727
Memphis, TN 38194-4643
Telephone: 901-369-3600

November 15, 2006

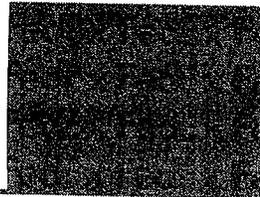
Dear Customer:

The following is the proof of delivery you requested with the tracking number **792089606455**.

Delivery Information:

Status:	Delivered	Delivery location:	1155 6TH BSMNT
Signed for by:		Delivery date:	May 5, 2006 09:09 b(6)
Service type:	Standard Overnight		

b(6)



Shipping Information:

Tracking number:	792089606455	Ship date:	May 4, 2006
-------------------------	--------------	-------------------	-------------

Recipient:
M. ANDREA RYAN
AGENT FOR AKTIEBOLAGET HASSLE
WHITE & CASE LLP
1155 AVENUE OF THE AMERICAS
NEW YORK CITY, NY 10036 US
Reference

Shipper:
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CHICAGO, IL 60601 US
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April 17, 2006

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DENNIS R. SCHLEMMER
GORDON R. COONS
JOHN W. KOZAK
MARK E. PHELPS
H. MICHAEL HARTMANN
BRUCE M. GAGALA
CHARLES H. MOTTIER
JOHN KILYK, JR.
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ROGER D. WYLIE***
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NANCY J. GETTEL
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JEFFREY N. TURNER
SUSAN L. STEELE
STEPHANIE M. LAWLEY*
KURT T. BUECHLE
KEVIN C. PARRIS
THOMAS K. McBRIDE, JR.
JENNIFER M. DUK
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JOHN P. SNOW
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DIMITRY KAPMAR
EDWARD M. SIGEL
BRYAN D. MURPHY
BRIAN A. GARCIA

WASHINGTON OFFICE
700 THIRTEENTH STREET, N.W., SUITE 300
WASHINGTON, D.C. 20005-3960
(202) 737-6770
FACSIMILE: (202) 737-6776

ROCKFORD OFFICE
6815 WEAVER ROAD, SUITE 300
ROCKFORD, ILLINOIS 61114-8018
(815) 963-7661
FACSIMILE: (815) 963-7664

SEATTLE OFFICE
1420 FIFTH AVENUE, SUITE 2200
SEATTLE, WASHINGTON 98101-1346
(206) 521-8985
FACSIMILE: (206) 224-3557

OF COUNSEL

C. FREDERICK LEYDIG
THEODORE W. ANDERSON
BERTON SCOTT SHEPPARD

CHARLES S. OSLAKOVIC**
JOHN D. FOSTER*

TECHNICAL ADVISORS

KRISTEN J. HARRELL
MELISSA E. KOLOM
CARYN C. BORG-BREEN
RACHEL J. MEJDRICH
JULIE J. HONG
DEREK W. BARNETT

KATHLEEN M. HELM-BYCHOWSKI
FRANCIS J. KOSZYK
ELIZABETH M. CROMPTON
JASON A. MILLER
ELIZABETH A. LITZINGER

ALL RESIDENT IN CHICAGO EXCEPT AS NOTED
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VIA FEDERAL EXPRESS

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Attn: Glenn M. Engelmann
Vice President Policy, Legal and
Scientific Affairs, General Counsel
Attn: Judy W. Firor
Regulatory Affairs

Re: Omeprazole Delayed Release Tablets, 20 mg
Our reference: 236869

To Whom It May Concern:

We are writing on behalf of Dexcel Pharma Technologies Ltd. ("Dexcel"), pursuant to 21 U.S.C. § 355(b)(3)(C)(i) and (ii), to inform you that Dexcel, in order to obtain approval to engage in the commercial manufacture, use or sale of 20 mg delayed release omeprazole tablets for over-the-counter sale ("Dexcel's Tablets"), submitted to the United States Food and Drug Administration ("FDA") a New Drug Application ("Dexcel's NDA"), under 21 U.S.C. § 355(b)(1)(A-G) and (b)(2)(A), and which has been assigned NDA No. 22-032 ("Dexcel's NDA"). Dexcel's NDA identifies 20 mg tablets of PRILOSEC® OTC (omeprazole magnesium delayed release tablets), approved under NDA No. 021229, and PRILOSEC® 10 mg, 20 mg, and

40 mg capsules (omeprazole delayed release pellets), approved under NDA No. 019810, both of which are the Listed Drugs referenced in the Orange Book for their respective NDAs.

Dexcel's NDA includes a certification pursuant to 21 U.S.C. § 355(b)(2)(A)(iv) with respect to U.S. Patent Nos. 6,150,380 ("the '380 patent"), 6,428,810 ("the '810 patent"), 5,690,960 ("the '960 patent"), 5,900,424 ("the '424 patent"), 6,403,616 ("the '616 patent"), 5,753,265 ("the '265 patent"), and 5,817,338 ("the '338 patent), certifying that, in Dexcel's opinion, said patents are invalid, unenforceable, and/or not infringed by Dexcel's Tablets. Dexcel intends to market its Tablets before the respective expiration dates of the '380, '810, '960, '424, '616, '265 and '338 patents on November 10, 2018, November 3, 2019, November 25, 2014, May 4, 2016, November 15, 2019, June 7, 2015 and October 6, 2015, as extended by pediatric exclusivity extensions as indicated in the Orange Book.

We are writing to AstraZeneca AB, as, upon information and belief, the current owner of the '380, '810, '960, '424, '616, '265 and '338 patents, and to AstraZeneca, as the entity listed with the FDA as the current holder of NDA Nos. 021229 and 019810. This letter represents notice to AstraZeneca AB and AstraZeneca of its contents. As required by 21 U.S.C. § 355(b)(3)(B)(i), a detailed statement of the factual and legal basis upon which Dexcel bases its opinion regarding the '380, '810, '960, '424, '616, '265 and '338 patents is set forth below.

Pursuant to 21 C.F.R. § 314.95(e), Dexcel requested and received permission from the FDA to send this notice by means other than registered or certified mail. Specifically, Dexcel requested that it be allowed to send this notice by Federal Express® courier. The FDA granted Dexcel's request prior to this notice being sent.

I. APPLICABLE LEGAL STANDARDS

A. The Law with Respect to Infringement

There are generally two ways a claim can be directly infringed. A claim can be either (a) literally infringed or (b) infringed under what is known as the "doctrine of equivalents." In order to determine whether a product or process infringes a U.S. patent, the courts apply a two-step test for each invention claimed. First, the court construes or interprets the claim and resolves any dispute as to the meaning of the particular claimed technology. The patented invention, as set forth in the words of the patent claims, must be clearly understood. This is a question of claim interpretation, which is determined by the court as a matter of law. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 116 S.Ct. 1384, 134 LEd.2d 577 (1996) (en banc), aff'd, 517 U.S. 370, 116 S.Ct. 1384, 38 U.S.P.Q.2d 1461 (1996). Next, under the second step of the analysis, the properly construed claim is compared to the accused product to determine whether there is literal infringement or a claim of infringement under the doctrine of equivalents. *Mas-Hamilton Group v. La Gard, Inc.*, 156 F.3d 1206, 1211-12, 48 U.S.P.Q.2d 1010, 1014-15 (Fed.Cir. 1998). If the accused product has every element of a claim, literal infringement is established. *Acco Brands, Inc. v. Micro Sec. Devices, Inc.*, 346 F.3d 1075, 1081 (Fed. Cir. 2003); *Rohm & Haas Co. v. Brotech Corp.*, 127 F.3d 1089, 1092 (Fed. Cir. 1997). All claim elements are material and must be present to find infringement. *Odetics, Inc. v. Storage Tech.*

Corp., 185 F.3d 1259, 1268. ("It is of course axiomatic that '[e]ach element contained in a patent claim is deemed material to determining the scope of the patented invention.'" (quoting *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29 (1997))).

If there is not a literal correspondence between the elements of a claim and the accused product, there may still be infringement under the doctrine of equivalents if the accused product contains the substantial equivalent of each and every one of the elements of the asserted claim. *Eagle Comtronics, Inc. v. Arrow Communication Labs.*, 305 F.3d 1303, 1316 (Fed. Cir. 2002); *Digital Biometrics, Inc. v. Identix, Inc.*, 149 F.3d 1335, 1349 (Fed. Cir. 1998). This doctrine comes into play only when literal infringement is not present. Under the doctrine of equivalents, an accused product that does not literally infringe a claim may be found to infringe if it performs substantially the same function in substantially the same way to obtain the same or substantially the same result as the claimed invention. *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1349 (Fed. Cir. 2001). Importantly, even under the doctrine of equivalents, every claim element or its equivalent must be present in the accused device. *Kustom Signals, Inc. v. Applied Concepts, Inc.*, 264 F.3d 1326, 1333 (Fed. Cir. 2001). "No claimed element, or an equivalent thereof, can be absent if the doctrine of equivalents is invoked." *Id.*

Under the doctrine of "prosecution history estoppel," a patent holder is presumed to have surrendered all equivalents of a claim element under the doctrine of equivalents if, during the course of prosecution, either voluntarily or involuntarily, a narrowing amendment is made to the claim element to satisfy any requirement of the Patent Act. *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 122 S.Ct. 1831, 1838-39 (2002).

B. The Law with Respect to Invalidity

Patents may be held invalid for lack of patentable subject matter, lack of novelty and various statutory bars, obviousness, and deficiencies in the specification disclosure and the claims. 35 U.S.C. §§ 101-103, 112 (2004).

1. Prior Art - Anticipation

Validity is often challenged based on the prior art. A patent claim is invalid because of "anticipation" when a single prior art reference contains each and every limitation, or element, of the claim. 35 U.S.C. § 102 (2004); *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 545 (Fed. Cir. 1998); *Union Oil*, 208 F.3d at 995. The prior art reference must describe the patent claim with sufficient clarity and detail to establish that the invention existed. *ATD Corp.*, 159 F.3d at 545. However, the prior art reference may anticipate without explicitly disclosing a limitation if that limitation was necessarily present, or inherent, in the prior art reference. Furthermore, a prior art reference can disclose enough for inherent anticipation even if the inherent teaching was unappreciated by those of ordinary skill at the time. *Toro Co. v. Deere & Co.*, 69 U.S.P.Q.2d 1584, 1589-90 (Fed. Cir. 2004). Thus, the doctrine of inherency protects the public's practice of the prior art even if they did not understand the principles that allow it to operate. *Schering Corp. v. Geneva Pharm., Inc.*, 399 F.3d 1373, 1377-80 (Fed. Cir. 2003).

2. The On Sale Bar Under § 102(b)

A patent is invalid under section 102(b) if "the invention was . . . on sale in this country, more than one year prior to the date of the application for patent in the United States . . .", which is known as the critical date. Before the critical date, the invention must both be the subject of a commercial sale or offer for sale and be "ready for patenting." See *Pfaff v. Wells Electronics Inc.*, 48 U.S.P.Q.2d 1641, 1646-47 (Fed. Cir. 2005). Furthermore, the statutory on-sale bar is not subject to exceptions for sales made by third parties either innocently or fraudulently. See *Evans Cooling Sys., Inc. v. General Motors Corp.*, 125 F.3d 1448, 1453-54, 44 U.S.P.Q.3d 1037, 1040-42 (Fed. Cir. 1997).

3. Public Use Under § 102(b)

"Public use [under 35 U.S.C. § 102(b)] includes any use of the claimed invention by a person other than the inventor who is under no limitation, restriction or obligation of secrecy to the inventor." *Netscape Communications Corp. v. Konrad*, 295 F.3d 1315, 1320 [63 U.S.P.Q.2d 1580] (Fed. Cir. 2002).

4. Obviousness - 35 U.S.C. § 103

A patent claim is invalid if, at the time the invention was made, the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is a legal conclusion based on underlying factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

II. THE '380 PATENT

The '380 patent contains a total of 6 claims with one independent claim. Claim 1 specifies Omeprazole form A which is a non-salt racemate, wherein omeprazole form A provides an X-ray powder diffraction pattern exhibiting substantially the following d-values:

<u>Form A</u>		<u>Form A</u>	
d-value (Å)	Relative intensity	d-value (Å)	Relative intensity
9.5	vs	3.71	s
7.9	s	3.59	m
7.4	w	3.48	m
7.2	vs	3.45	s
6.0	m	3.31	w
5.6	s	3.22	s
5.2	s	3.17	m
5.1	s	3.11	w
4.89	w	3.04	w.
4.64	m	3.00	w
4.60	m	2.91	w
4.53	w	2.86	w
4.49	m	2.85	w
4.31	m	2.75	w
4.19	w	2.67	w
4.15	w	2.45	w
3.95	w	2.41	w

Analysis of the '380 patent

1. Invalidation

Dexcel has obtained evidence related to a sale and shipment of omeprazole by its API supplier in March 1997. Dexcel has further evidence that the omeprazole sold in March 1997 was form A omeprazole: The sale, and hence any "offer for sale" of the omeprazole, occurred more than one year prior to the earliest possible filing date of any application upon which the '380 patent is based. This offer for sale completely anticipates claims 1 and 2 of the '380 patent, that are directed to omeprazole form A, under 35 U.S.C. § 102(b). The prior sale anticipates claims 1 and 2 of the '380 patent.

Claim 3 relates to any composition containing omeprazole of claim 1 and claim 4 relates to the use of form A omeprazole to treat gastrointestinal disorders. At the time of filing the application that resulted in the '380 patent, it was known in the art that omeprazole could be made into finished dosage forms that could be used to treat gastrointestinal disorders (*See*, U.S. Patent No. 4,786,505). Indeed, Prilosec omeprazole was approved as a delayed release capsule for such an indication in the United States on September 14, 1989. Accordingly, claims 3 and 4 should be found to be invalid under 35 U.S.C. § 103.

2. Non-infringement

Claim 5 (and claim 6 which is dependent thereon) relates to a process for making omeprazole form A by a crystallization procedure that requires the crystallization to occur "for at least 2 hours" at a temperature of 15 - 25° C and in accordance with claim 6 the use of certain specific solvents. The process for manufacturing the omeprazole used in Dexcel's Tablets does not make use of a crystallization process that occurs over at least 2 hours, at a temperature of 15-25° C, hence there is no infringement. During prosecution of the '380 patent various amendments were made to the pending claims, including an amendment to pending claim 6 (now claim 5) which *inter alia*, added the time limitation of "for at least 2 hours." Thus, claims 5 and 6 are not infringed literally or under the doctrine of equivalents.

III. THE '810 PATENT

The '810 patent contains a total of 22 claims with one independent claim. Claim 1 specifies an enteric coated oral pharmaceutical formulation comprising (a) a core material which comprises an active ingredient selected from the group consisting of omeprazole, an alkaline salt of omeprazole, one of the single enantiomers of omeprazole and an alkaline salt of one of the single enantiomers of omeprazole; (b) a separating layer; and (c) an enteric coating layer, wherein the separating layer comprises a hydroxypropyl cellulose (HPC) with a cloud point of at least 38° C., and wherein the light transmission at cloud point of a system comprising the HPC dissolved in a concentration of 1.0% (s/s) in a mixed solution of disodium hydrogen phosphate buffer 0.086 M and hydrochloric acid 0.1 M in the proportions 7:3 at a pH of 6.75-6.85 is 96%.

Analysis of the '810 patent

All independent claims of the '810 patent require the presence of a separating layer between the core and the enteric coating. No such separating layer is present in Dexcel's Tablets. Dexcel's Tablets are manufactured using conventional processing steps. The active ingredient, omeprazole, and other excipients are mixed together, compressed into tablets and then coated with an enteric coating. There is no step involving the application or formation of a subcoating or separating layer between the core and the enteric coating. Hence, there is no literal infringement of any of the claims of the '810 patent.

Additionally, the only independent claim of the '810 patent specifically requires that the separating layer be comprised of a hydroxypropyl cellulose ("HPC") having a cloud point of at least 38° C. Dexcel's Tablets contain no HPC of any type and accordingly infringement is also avoided on that basis alone.

Further, there is no structure in the Dexcel Tablets that could provide the basis for arguing infringement under the doctrine of equivalents. There simply is nothing in the Dexcel Tablets that performs the same function as a separating layer, in substantially the same way to achieve substantially the same result. Indeed, no equivalent of such a claim element is present. Accordingly, there can be no infringement of the '810 patent under the doctrine of equivalents.

IV. THE '960, '424, AND '616 PATENTS

The '960 patent

The '960 patent contains a total of 22 claims of which three are independent, claims 1, 10 and 22. Claim 1 specifies a stable oral formulation comprising a core containing a magnesium salt of omeprazole said salt having more than 70% crystallinity as determined by x-ray powder diffraction; a subcoating layer; and an enteric coating layer, whereby the thickness of the enteric coating layer does not effect the release of omeprazole into solution at the pH predominantly present in the small intestine.

Claim 10 specifies a process for preparing an oral formulation as recited in Claim 1.

Claim 22 specifies an improved oral pharmaceutical composition containing a core of omeprazole salt with a subcoating and an enteric coating wherein the improvement comprises magnesium omeprazole salt having more than 70% crystallinity as determined by x-ray powder diffraction.

The '424 patent

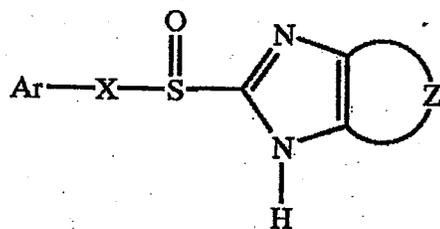
The '424 patent contains a total of 22 claims of which two are independent, claims 1 and 20. Claim 1 specifies an omeprazole magnesium salt having a degree of crystallinity which is higher than 70% as determined by x-ray powder diffraction.

Claim 20 specifies a process for the manufacture of a crystalline magnesium salt comprising, (a) treating omeprazole or a salt thereof with magnesium alcoholate in a solution, (b) crystallizing magnesium omeprazole and (c) isolating the obtained crystalline magnesium omeprazole, wherein the improved process comprises separating inorganic salt from the reaction mixture prior to the crystallization step by the addition of water.

The '616 patent

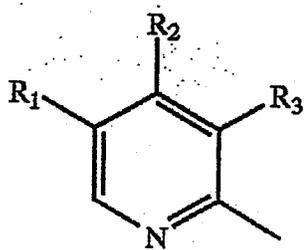
The '616 patent contains a total of 18 claims of which one is independent.

Claim 1 of the '616 patent specifies a process for the manufacturing of slightly soluble or less soluble alkaline salts of substituted sulphinyl heterocycles containing an imidazole moiety with Formula I in the form of a racemate, one of the single enantiomers or an enantiomeric enriched form,

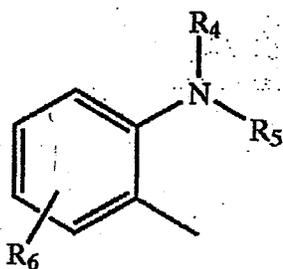


wherein

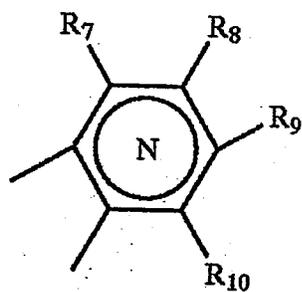
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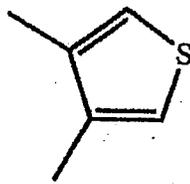
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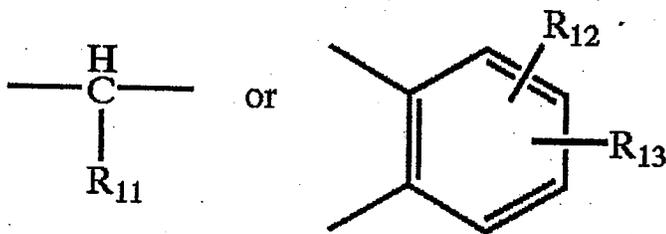
Z is



or



and X is



wherein

N inside the benzene ring of the benzimidazole moiety means that one of the carbon atoms substituted by R₇-R₁₀ optionally may be exchanged for a nitrogen atom without any substituents;

R₁, R₂ and R₃ are the same or different and selected from the group consisting of hydrogen, alkyl, alkylthio, alkoxy, alkoxy substituted by fluorine, alkoxyalkoxy, dialkylamino, piperidino, morpholino, halogen, phenylalkyl and phenylalkoxy;

R₄ and R₅ are the same or different and selected from the group consisting of hydrogen, alkyl and aralkyl;

R₆ is selected from the group consisting of hydrogen, halogen, trifluoromethyl, alkyl and alkoxy;

R₇-R₁₀ are the same or different and selected from the group consisting of hydrogen, alkyl, alkoxy, halogen, haloalkoxy, alkylcarbonyl, alkoxy carbonyl, oxazolyl, and trifluoroalkyl, or adjacent groups R₇-R₁₀ form ring structures which may be further substituted;

R₁₁ is hydrogen or forms an alkylene chain together with R₃ and

R₁₂ and R₁₃ are the same or different and selected from the group consisting of hydrogen and alkyl,

and wherein alkyl groups, alkoxy groups and moieties thereof may be branched and straight C₁-C₉-chains or comprise cyclic alkyl groups, which process comprises the step of reacting the substituted sulphinyl heterocycle of Formula I with a source of the cation in the presence of a base, and a washing step in which the prepared alkaline salt of the substituted sulphinyl compound is washed with a basic aqueous solvent mixture.

Analysis of the '960, '424, and '616 patents

The Dexcel Tablets differ from the inventions claimed in the '960, '424, and '616 patents because Dexcel's Tablets are made using omeprazole base, and not a salt thereof, of any kind. All claims of all three patents are directed to salts of compounds (including omeprazole), formulations containing such salts, the manufacture of such salts, or the use of such salts. No claim is directed to a base (such as omeprazole base) or to any formulation containing a base, such as omeprazole, which is not in the form of a salt. Further, no claim is directed to the use or manufacture of a base, such as omeprazole, as opposed to a salt. Accordingly, there can be no literal infringement of any of the claims of the '960, '424, or '616 patents.

As indicated previously, all independent claims of the '960, '424, and '616 patents require the presence, use or manufacture of a salt, which is not present in Dexcel omeprazole tablets. Indeed, no equivalent of such a claim element is present. The prior art is extensive as it relates to the presence, use or manufacture of omeprazole, *per se*. For example, U.S. Patent No. 4,786,505 teaches the use of omeprazole base in pharmaceutical formulations. Thus, there is no issue of infringement under the doctrine of equivalents as Dexcel is using the prior art omeprazole base in its formulation. Accordingly, there can be no infringement under the doctrine of equivalents.

V. THE '265 AND '338 PATENTS

The '265 patent

The '265 patent contains a total of 23 claims of which one claim is independent. Claim 1 specifies an oral pharmaceutical composition in the form of a multiple unit tablet comprising a tablet excipient; a multiple of a core unit comprising as an active ingredient an acid-labile H^+K^+ -ATPase inhibitor compound in a neutral form or a salt form, a single enantiomer or an alkaline salt of a single enantiomer; the core unit being covered with at least one enteric coating layer having mechanical properties so as not to significantly effect the acid resistance of the enteric coating layered unit by compression during tableting.

The '338 patent

The '338 patent contains a total of 25 claims of which one claim is independent. Claim 1 specifies a pharmaceutical multiple unit tablet composition for oral treatment of gastrointestinal disorder comprising at least one tablet excipient; and a multiple of a pellet or granule, the pellet or granule ranging between 0.1 mm and 2 mm in size and comprising an active ingredient selected from the group consisting of omeprazole, a single enantiomer of omeprazole, an alkaline salt of omeprazole, and an alkaline salt of a single enantiomer of omeprazole; and the pellet or granule being covered with at least one enteric coating layer comprising a plasticizing compound in the amount of more than about 20% to less than about 50% by weight of the enteric coating layer polymer so as to minimize the reduction of acid resistance of the enteric coating layered units upon compression into the tablet form.

Analysis of the '265 and '338 patents

The Dexcel Tablets differ from the inventions claimed in the '265 and '338 patents because Dexcel's Tablets are made using conventional tableting techniques and are not formulated with individual units. The tablets do not contain multiples of beads, particles or the like and, as well, there are no individual enteric-coated beads, particles or the like. Dexcel's Tablets are conventional enteric coated tablets and are not comprised of multiple units as that term is used in the claims of the '265 and '338 patents. There is no formation of separate particles of any type nor a step whereby such particles are separately enteric coated. Hence, the Dexcel Tablets are not "multiple unit tablets". Based on the aforementioned manufacturing procedure used by Dexcel to make its own omeprazole tablets there also is no infringement of any of the claims of the '265 or '338 patents because Dexcel is practicing disclaimed subject matter.

As indicated previously, all independent claims of the '265 and '338 patents require the presence of multiple units that are not present in Dexcel Tablets. Further, there is no indication of any structure in the Dexcel Tablets that could provide the basis for arguing infringement under the doctrine of equivalents. There simply is nothing in the Dexcel Tablets that performs the same function as multiple units, in substantially the same way to achieve substantially the same result. Indeed, no equivalent of such a claim element is present. Accordingly, there can be no infringement under the doctrine of equivalents.

VI. JURISDICTION

Dexcel hereby consents to jurisdiction in the United States District Court for the Eastern District of Virginia, Norfolk Division, solely for purposes of any infringement action based upon its aforementioned NDA. Dexcel maintains an office located at Wainwright Building, 229 West Bute Street, Suite 407, Norfolk, Virginia 23510.

VII. CONCLUSION

For the reasons set forth above, Dexcel's Tablets do not infringe any of the claims of the '810, '960, '424, '616, '265 and '338 patents. Claims 1-4 of the '380 patent are invalid and claims 5 and 6 are not infringed.

To the extent that process claims are discussed above, any such discussion is for informational purposes only. As process claims cannot be listed in the Orange Book, no certification or detailed statement regarding them is required and such claims cannot form the basis of any 30 month statutory prohibition against approval of Dexcel's NDA.

Pursuant to 21 U.S.C. § 355(c)(3)(D)(i)(III), Dexcel hereby extends AstraZeneca AB and AstraZeneca an Offer of Confidential Access to Dexcel's NDA pursuant to a mutually agreeable confidentiality agreement that contains reasonable restrictions as to persons entitled to access and on the use and disposition of any information accessed.

April 17, 2006

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Please be advised that Dexcel intends to obtain final approval of its NDA and proceed to market its Tablets as soon as permitted by applicable statutes and regulations.

Dexcel expressly reserves the right to challenge the validity and enforceability of the '380, '810, '960, '424, '616, '265 and '338 patents and/or any assertion of infringement that AstraZeneca, AstraZeneca AB and/or the current owner of the '380, '810, '960, '424, '616, '265 and '338 patents might make on new, other, or further grounds should such grounds become apparent during any ensuing litigation between the parties.

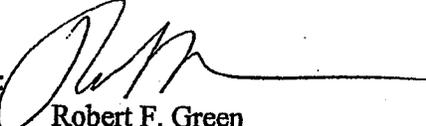
As AstraZeneca AB and AstraZeneca are surely aware, institution of baseless litigation against an applicant seeking approval to market a generic drug product can give rise to antitrust liability. The Federal Trade Commission ("FTC") has in the past strongly condemned such tactics. Suffice it to say, should AstraZeneca AB or AstraZeneca choose the precarious route of filing suit against Dexcel, it is reasonably certain that the FTC will have a great interest in such litigation.

So there is no misunderstanding, Dexcel will not only aggressively defend against any baseless lawsuit filed by AstraZeneca AB or AstraZeneca, Dexcel also will seek all appropriate remedies to redress what could only be viewed as a fraudulent misuse of the '380, '810, '960, '424, '616, '265 and '338 patents, which would harm not only Dexcel but the patients who take Prilosec® OTC tablets, resulting in antitrust liability for AstraZeneca AB and AstraZeneca.

If you have any questions after reviewing this letter, please feel free to contact us to discuss this matter.

Very truly yours,

LEYDIG, VOIT & MAYER, LTD.

By: 

Robert F. Green

RFG/SSM/krs