# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

**20988**

# CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-988

MAR 21 2001

Wyeth-Ayerst Laboratories
Attention: Caroline Henesey, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Henesey:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Protonix® I.V. (pantoprazole sodium) for Injection.

We request a letter agreeing to the following post-marketing commitments:

1. To provide a complete physical and chemical characterization of the ___ precipitate, identify the conditions that promote precipitation and identify what other types of substances or combinations of substances in the diluent solutions (other ions, other drugs, etc) can cause precipitation. The time frame for this commitment is 1 year after NDA approval date.

2. To conduct studies comparing commonly used diluents (saline, lactated ringers, D5W) on precipitate formation. The time frame for this commitment is 1 year after NDA approval date.

3. To provide a proposal to eliminate the filtration requirement for the product, i.e. reformulation. The time frame for this commitment is 2 years after NDA approval date.

4. To revise the packaging, i.e. to co-package one vial and one filter per box, after completion of commitments 1 - 3. We note that the investigations of filter stability at 2°C-8°C have been initiated. The time frame for this commitment is 2 years after NDA approval date.

If you have any questions, call Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

*{See appended electronic signature page}*

Liang Zhou, Ph.D.
Chemistry Team Leader for the Division of Gastrointestinal
and Coagulation Drug Products, (HFD-180)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

/s/
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Liang Zhou
3/21/01 10:33:20 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-988

**INFORMATION REQUEST LETTER**

Wyeth-Ayerst Laboratories
Attention: Caroline Henesey, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

FEB 28 2001

Dear Dr. Henesey:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Protonix® I.V. (pantoprazole sodium) for Injection.

We also refer to your submissions dated January 19, and February 21, 22, and 26, 2001.

We are reviewing the Chemistry, Manufacturing, and Controls (CMC) section of your submissions and have the following comments and information requests. We need your prompt written response to continue our evaluation of your NDA.

1. Provide data to demonstrate that the two filters that are being proposed for co-packaging adequately remove particulates from the diluent solutions and yield solutions where particles do not reform on standing. Conduct these experiments with admixtures that contain significant quantities of particulates prior to filtration.

2. Provide all available information on the thermal stability of the two proposed filters, particularly the effects of refrigeration on the physical properties of the filters.

3. Provide a detailed explanation on how the product (with its co-packaged filter) will be transported to ensure that the filter and product will be maintained at the two different recommended storage conditions during transport from the manufacturing site to the intended health care facility(ies).

If you have any questions, call Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7310.

Sincerely,

*{See appended electronic signature page}*

Liang Zhou, Ph.D.
Chemistry Team Leader for the Division of Gastrointestinal
and Coagulation Drug Products, (HFD-180)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

/s/
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Liang Zhou
2/28/01 05:01:40 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-988

JAN 26 2001

Wyeth-Ayerst Laboratories
Attention: Ms. Caroline Henessey
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Ms. Henessey:

We acknowledge receipt on January 22, 2001 of your January 19, 2001 resubmission to your new drug application (NDA) for Protonix® I.V. (pantoprazole sodium) for Injection.

This resubmission contains the following additional information submitted in response to our November 2, 2000 action letter: 1) a modified container proposal including a color mock copy of the proposed labeling for all components of the container; and 2) revised package insert labeling.

We consider this a complete class 1 response to our action letter. Therefore, the primary user fee goal date is March 22, 2001.

If you have any questions, call me at (301) 827-7475.

Sincerely,

*{See appended electronic signature page}*

Cheryl Perry
Regulatory Health Project Manager
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

/s/
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Cheryl Perry
1/26/01 01:52:54 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB - 2 2001

NDA 20-988

**INFORMATION REQUEST LETTER**

Wyeth-Ayerst Laboratories
Attention: Caroline Henesey, PhD
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Henesey:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Protonix® I.V. (pantoprazole sodium) for Injection.

We also refer to your submission dated January 19, 2001 containing revised package insert and carton labels.

We are reviewing the clinical section of your submission. We wish to provide the following comments and recommendations regarding the carton:

1. On the outside carton, revise the "**CONTENTS**" section to read as follows:

2. On the outside carton, wherever the phrase appears, revise the phrase to read:

3. Provide a separate box for the twenty-five (25) in-line filters inside the outer carton. This box should have the same color, font, pattern and background as the outer carton. The filter box label should read Each individual filter package should have an instruction sticker affixed that reads for PROTONIX® I.V."

4. Revise the instruction stickers, contained within the box of vials, to read as follows:

5. Provide thirty (30) instruction stickers within the box of vials.

6. Affix an instruction sticker, identical to those provided within, to the outside of the box containing the vials.

7. All instruction sticker fonts should be as large as feasible.

If you have any questions, call Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

*{See appended electronic signature page}*

Julieann DuBeau, R.N., M.S.N.
Chief, Project Management Staff
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

/s/
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Julie DuBeau
2/2/01 04:43:15 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

NDA 20-988

Food and Drug Administration
Rockville MD 20857

**DISCIPLINE REVIEW LETTER** (DRL)

Wyeth-Ayerst Laboratories
Attention: James J. O'Shaughnessy
Associate Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

SEP 15 2000

Dear Mr. O'Shaughnessy:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Protonix I.V.® for Injection (pantoprazole sodium).

We also refer to your submission dated August 30, 2000 containing additional Chemistry, Manufacturing and Controls information in response to our letter dated August 24, 2000.

Our review of the CMC section of your submission is complete, and we have concluded that the proposed ___ specification for the finished product is not satisfactory. Please revise the ___ specification to a level that does not exceed the ___ content in actual production or pilot batches which conform to the visual "Clarity of Reconstituted Solution" test, the USP particulates test, and the ___ assay requirement.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of the issue 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 this issue 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 Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

/S/ 9/15/00

Liang Zhou, Ph.D.
Chemistry Team Leader for the Division of Gastrointestinal and Coagulation Drug Products, (HFD-180)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

NDA 20-988

Food and Drug Administration
Rockville MD 20857

**DISCIPLINE REVIEW LETTER**

Wyeth-Ayerst Laboratories
Attention: James J. O'Shaughnessy
Associate Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

AUG 24 2000

Dear Mr. O'Shaughnessy:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Protonix I.V.® for Injection (pantoprazole sodium).

We also refer to your submissions dated May 2, and 3, 2000.

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

1. On page 22 of the submission, the lyophilized product is dismissed as a significant source of While this is true for the diluent, which contains most of the diluents contain far less For a diluent containing , the contribution from the diluent is only times higher than from the pantoprazole. Consequently, a limit on the amount of in the finished product should be added to the release specification.

2. The USP release test for particulates does not limit the time for complete dissolution of the lyophilized powder. In view of potential insolubility problems due to the presence of in the lyophylized product, the visual test for clarity of reconstituted solution, which requires a clear solution within 30 seconds, should be retained in the release specifications, in addition to the USP test.

In addition, the combined experimental evidence supports the conclusion that are involved in particulate formation. However, additional factors that could result in precipitate formation are not necessarily excluded and the nature of this precipitate has not been adequately characterized. Therefore, we request the following Phase IV, post-approval commitments:

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 Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

/S/

Liang Zhou, Ph.D.
Chemistry Team Leader for the Division of Gastrointestinal and Coagulation Drug Products, (HFD-180)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 20-988

Wyeth-Ayerst Laboratories
Attention: Mr. James J. O'Shaughnessy
Associate Director, Worldwide Regulatory Affairs
P.O. Box 8299
Philadelphia, PA, 19101-8299

JUN 21 2000

ACK

Dear Mr. O'Shaughnessy:

We acknowledge receipt on May 2, 2000 of your May 2, 2000 resubmission to your new drug application (NDA) for PROTONIX I.V. (pantoprazole sodium) for Injection.

This resubmission contains draft labeling, and responses to chemistry, manufacturing and control questions in response to our February 24, 2000 action letter. The submission also contains a safety update.

We consider this a complete class 2 response to our action letter. Therefore, the user fee goal date is November 2, 2000.

If you have any questions, please call me at (301) 827-7475.

Sincerely,

/S/ 6/21/00

Cheryl Perry
Regulatory Health Project Manager
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

WALSH

DEC 16 1999

NDA 20-988

**DISCIPLINE REVIEW LETTER**

Wyeth-Ayerst Laboratories
Attention: Eleanor DeLorme Sullivan, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. DeLorme Sullivan:

Please refer to your July 20, 1998 new drug application for Protonix (pantoprazole sodium sesquihydrate) for Injection.

We also refer to your submission dated August 31, 1999 which constituted a complete response to our July 20, 1999 approvable letter.

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

1. The Drug Master File (DMF) continues to be inadequate. The DMF holder has been notified of the deficiencies.

2. Two sets of specifications are proposed for the drug product, release and shelf life specifications. We recommend that your proposed ____ specifications be the official regulatory specifications.

3. In the proposed revised ____ specifications, total impurities have been reduced from ____ ____%. These limits remain excessively high and should be lowered. The proposed total known, total unknown, and total impurity specifications are considerably more liberal than can be justified by the manufacturing history (stability and clinical batches).

4. The ____ stability data provided in support of the ___% moisture specification do indeed suggest that temperature plays an important role in product stability. However, the data are too limited to make any conclusions regarding the role of moisture in the degradation process with any certainty. In addition, it is FDA policy to base expiration dating on real-time data. As such, since the moisture content did not exceed ___% in the samples on stability testing at ____ moisture specification is considered unreasonably high. It should be lowered to levels at which the real time stability of the product was tested.

5. We note that admixtures of this drug product have been shown to be stable in containers made of polyvinyl chloride and unstable in containers made of ( copolymer. Containers of other chemical composition have not been studied. Studies should be undertaken to

identify the cause of the instability of the drug in ethylene/polypropylene containers as well as the nature of the particulates in that container. The admixture stability studies should be extended to other marketed containers.

6. With regard to the labeling statements that [ and ] we note that according to your submission, admixtures for stability studies were prepared from reconstituted samples within of reconstitution. In view of this experimental design, there is no evidence to support a cumulative solution expiry of hours, from the time of reconstitution to expiry of the admixture.

7. With regard to the labeling statement that neither the reconstituted solution nor the admixed solution needs to be protected from light, the data provided only make use of ambient conditions with ambient lighting. Please provide data from appropriately controlled studies to support the claim that the solutions do not need to be protected from light.

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, contact Maria R. Walsh, M.S., Project Manager, at (301) 443-8017.

Sincerely,

/S/

Liang Zhou, Ph.D.
Acting Chemistry Team Leader for the
Division of Gastrointestinal and Coagulation Drug Products, (HFD-180)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

Walsh

NDA 20-988

MAY - 6 1999

Wyeth-Ayerst Laboratories
Attention: Eleanor DeLorme Sullivan, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. DeLorme Sullivan:

Please refer to your pending July 20, 1998 new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Protonix I.V. (sterile pantoprazole sodium).

We are reviewing the chemistry section of your submission and have identified deficiencies in the Drug Master File (DMF) for the drug substance. We are hereby notifying you that a deficiency letter, dated April 23, 1999, has been issued to ____ regarding DMF___ for pantoprazole sesquihydrate.

Per the user fee reauthorization agreements, the comments issued to the DMF holder do not reflect a final decision on the information reviewed in your application and should not be construed to do so. These comments are preliminary and are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If the DMF holder chooses to respond to the issues raised in the deficiency letter during this review cycle, depending on the timing of their response, as per the user fee reauthorization agreements, we may or may not be able to consider their response prior to taking an action on your application during this review cycle.

If you have any questions, contact Maria R. Walsh, M.S., Regulatory Project Manager, at (301) 443-8017.

Sincerely,

/S/ 5/6/99

Eric P. Duffy, Ph.D.
Chemistry Team Leader for the
Division of Gastrointestinal and Coagulation Drug Products, (HFD-180)
DNDC II, Office of New Drug Chemistry
Center for Drug Evaluation and Research

NDA 20-988

Wyeth-Ayerst Laboratories
Attention: Eleanor DeLorme Sullivan, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

OCT - 6 1998

Dear Dr. DeLorme Sullivan:

Please refer to your July 20, 1998 new drug application for Protonix I.V. (sterile pantoprazole sodium).

Under 21 CFR 314.50(d)(5)(vi)(*b*), we request that you update your NDA by submitting all safety information you have regarding your new drug by April 1, 1999. Please provide updated information as listed below. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.

2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.

3. Details of any significant changes or findings.

4. Summary of worldwide experience on the safety of this drug.

5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.

6. English translations of any approved foreign labeling not previously submitted.

7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

If you have any questions, contact Maria R. Walsh, M.S., Project Manager, at (301) 443-0487.

Sincerely,

/S/ 10/5/98

Kati Johnson
Supervisory Consumer Safety Officer
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDA 20-988
HFD-180/Div. Files
HFD-180/M.Walsh
DISTRICT OFFICE

Drafted by: M.Walsh 9/29/98
Initialed by: H.Gallo-Torres 9/30/98
K.Johnson 10/2/98
final: M.Walsh 10/5/98
filename: 20988809.IR2.doc

INFORMATION REQUEST (IR)

NDA 20-988

Wyeth-Ayerst Laboratories
Attention: Eleanor DeLorme Sullivan, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

SEP 18 1998

Dear Dr. DeLorme Sullivan:

Please refer to your pending July 20, 1998 new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Protonix I.V. (sterile pantoprazole sodium).

We are reviewing the clinical statistics section(s) of your submission and have the following comments and information requests:

1. Please create a data set with the following variables:

PROTOCOL - Protocol number.
PATID - Patient identification number.
SEXTXT - F for female; M for male.
Age - Patient age at baseline (unit: years).
Weight (kg)
Height (cm)
RANDNO - Patient randomization number.
INVESTID - Investigator ID.
ITT - Y if patient was intent-to-treat; N otherwise.
MITT - Y if patient was modified intent-to-treat defined in the application; N otherwise.
VFE - Y if patient was valid-to-efficacy analysis defined in the application; N otherwise.
EXCOV - Y if patient was excluded from the analysis of covariance described in Section 6.7.1.2; N otherwise.
TRT - Treatment group code:
1 for Pantoprazole 20 mg oral and Pantoprazole 20 mg IV;
2 for Pantoprazole 20 mg oral and placebo 20 mg IV;
3 for Pantoprazole 40 mg oral and Pantoprazole 40 mg IV;
4 for Pantoprazole 40 mg oral and placebo 40 mg IV.
Antacidu - Antacid use: Yes or No.
Antacidp - Percentage of days antacids used during oral and IV treatment phases.
$MAO_{PO}$ - Maximum acid output (MAO) determined after the last oral dose of Pantoprazole.
$MAO_{LIV}$ - MAO determined after the last IV dose of Pantoprazole or placebo.
$MAO_{FIV}$ - MAO determined after the first IV dose of Pantoprazole or placebo.
$BAO_{PO}$ - Basal acid output (BAO) determined after the last oral dose of Pantoprazole.
$BAO_{LIV}$ - BAO determined after the last IV dose of Pantoprazole or placebo.

$BAO_{FIV}$ - BAO determined after the first IV dose of Pantoprazole or placebo.

Please leave one space between two adjacent variables.

2. Please provide the SAS programs used to perform the efficacy statistical analyses for datasets from the three types of populations (ITT, MITT, and VFE) described in Section 6.7.1.1, comparisons within groups, and Section 6.7.1.2, comparisons across dose groups in Volume 1.177. These programs should be modified to read the data from the file defined by request #1 above.

3. Please provide, in a 3½ floppy diskette, the data set defined in request #1 above and the SAS programs specified in request #2 above.

We would appreciate your prompt written response so we can continue our evaluation of your NDA.

These comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the 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 are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. If you choose to respond to the issues raised in this letter during this review cycle, depending on the timing of your response, as per the user fee reauthorization agreements, we may or may not be able to consider your response prior to taking an action on your application during this review cycle.

If you have any questions, contact me at (301) 443-0487.

Sincerely,

/S/ 9/17/98

Kati Johnson
Supervisory Consumer Safety Officer
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

NDA 20-988

Wyeth-Ayerst Laboratories
Attention: Eleanor DeLorme Sullivan, Ph.D.
P.O. Box 8299
Philadelphia, PA 19101-8299

JUL 30 1998

Dear Dr. DeLorme Sullivan:

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: Protonix I.V. (sterile pantoprazole sodium)

Therapeutic Classification: Standard (S)

Date of Application: July 20, 1998

Date of Receipt: July 20, 1998

Our Reference Number: 20-988

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 18, 1998 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be July 20, 1999.

Under 21 CFR 314.102(c) of the new drug regulations, you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

If you have any questions, contact me at (301) 443-0487.

Sincerely,

/S/ 7/28/98

Maria R. Walsh, M.S.
Regulatory Project Manager
Division of Gastrointestinal
and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDA 20-988
HFD-180/Div. Files
HFD-180/PM/M.Walsh
DISTRICT OFFICE

final: M.Walsh 7/28/98
filename: 20988807.ack.doc

ACKNOWLEDGEMENT (AC)

WYETH-AYERST RESEARCH

PO BOX 8299 • PHILADELPHIA, PA 19101-8299

Division of American Home Products Corporation

WORLDWIDE REGULATORY AFFAIRS

March 21, 2001

**NDA No. 20-988**
**PROTONIX® I.V.**
**(pantoprazole sodium) for Injection**

**Amendment to Pending**
**New Drug Application**
Response to FDA Request for
post-marketing commitments

Lilia Talarico, M.D., Director
Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Center for Drug Evaluation and Research
Attn: Document Control Room 6B-24
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-1706

Dear Dr. Talarico:

Reference is made to our pending New Drug Application No. 20-988 for PROTONIX® I.V. (pantoprazole sodium) for Injection. Reference is also made to the Division of Gastrointestinal and Coagulation Drug Products' (DGCDP's) March 20, 2001 letter requesting agreement to post-marketing commitments. Wyeth-Ayerst agrees to comply with the four requests, specifically:

1. To provide a complete physical and chemical characterization of the precipitate, identify the conditions that promote precipitation and identify what other types of substances or combinations of substances in the diluent solutions (other ions, other drugs, etc) can cause precipitation. The time frame for this commitment is 1 year after the NDA approval date.

2. To conduct studies comparing commonly used diluents (saline, lactated ringers, ---- on precipitate formation. The time frame for this commitment is 1 year after the NDA approval date.

3. To provide a proposal to eliminate the filtration requirement for the product, i.e., reformulation. The time frame for this commitment is 2 years after the NDA approval date.

4. To revise the packaging, i.e. to co-package one vial and one filter per box, after completion of commitments 1 – 3. The time frame for this commitment is 2 years after the NDA approval date.

If you have questions regarding this submission, please contact me at (610) 902-7013 or Caroline Henesey, Ph.D. at (610) 902-3729.

Sincerely,

WYETH-AYERST LABORATORIES

John J. Savarese, M.D., Ph.D.
Sr. Director
Worldwide Regulatory Affairs

WYETH-AYERST RESEARCH

P.O. BOX 8299 • PHILADELPHIA, PA 19101-8299

Division of American Home Products Corporation

WORLDWIDE REGULATORY AFFAIRS

February 26, 2001

**NDA No. 20-988**
**PROTONIX® I.V.**
**(pantoprazole sodium) for Injection**

**Amendment to Pending**
**New Drug Application**

Lilia Talarico, M.D., Director
Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Center for Drug Evaluation and Research
Attn: Document Control Room 6B-24
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-1706

Dear Dr. Talarico:

Reference is made to our pending New Drug Application No. 20-988 for PROTONIX® I.V. (pantoprazole sodium) for Injection. Reference is also made to the February 26, 2001 conversation during which we discussed (1) performance of a study after the approval of NDA No. 20-988 to provide assurance that an in-line filter is being used during the administration of this product, and (2) efforts to reformulate PROTONIX® I.V. for Injection.

The purpose of this submission is to respond to that conversation. Wyeth-Ayerst agrees to a Phase 4 commitment to perform a study to provide assurance that an in-line filter is being used during the administration of this product. In addition, we are actively pursuing the development of a PROTONIX® I.V. for Injection formulation that alleviates the need for use of an in-line filter.

If you have any questions regarding this submission, please contact me at (610) 902-3729.

Sincerely,

WYETH-AYERST LABORATORIES

Caroline M. Henesey

Caroline M. Henesey, Ph.D.
Manager, Worldwide Regulatory Affairs

Attachment
CMH/177