CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 019810/S38/S50/S56

Trade Name: PRILOSEC DELAYED-RELEASE CAPSULES

Generic Name: OMEPRAZOLE

Sponsor: ASTRA MERCK, INC.

Approval Date: 1/15/98, 1/7/98 and 7/10/98

Indication(s): GASTROGESOPHAGEAL REFLUX DISEASE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: 019810/S38/S50/S56

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tenative Approval Letter				X
Approvable Letter				X
Final Printed Labeling		X		
Medical Review(s)				X
Chemistry Review(s)	X			
EA/FONSI				X
Pharmacology Review(s)				X
Statistical Review(s)	X			
Microbiology Review(s)				X
Clinical Pharmacology Biopharmaceutics Review(s)				X
Bioequivalence Review(s)				X
Administrative Document(s)/ Correspondence	X			

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: 019810/S38/S50/S56

APPROVAL LETTER

NDA 19-810

Astra Merck Inc.
Attention: Gary P. Horowitz, Ph.D.
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

JAN 15 1998

Dear Dr. Horowitz:

Please refer to your supplemental new drug application dated February 26, 1996, received February 26, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec (omeprazole) Delayed-Release Capsules.

We acknowledge receipt of your submissions dated July 12, August 14, October 10, November 11, and December 3 and 18, 1996 and June 26 and November 21, 1997.

The supplemental application provides for a 40 mg dosage strength.

We have completed the review of this supplemental application, including the submitted draft labeling, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the labeling in the submission dated November 11, 1996. Accordingly, the supplemental application is approved, effective on the date of this letter, with an 18 month expiration date for each package type (Hospital Unit Dose Blister, 30, 100, and 1000 count bottles, and 7 count physician's sample) and with intermediate hold times of 30 days for _____. 60 days for _____ and 90 days for _____ as proposed in your June 26, 1997 submission. Please be advised that the first three batches of 40 mg capsules in each packaging configuration must be placed on stability and the data reported in the annual report.

Please submit 20 copies of the final printed labeling (FPL) as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved supplemental NDA 19-810/S-038. Approval of this submission by FDA is not required before the labeling is used.

The FPL must be identical in content to the labeling submitted on November 11, 1996. In addition, all previous revisions as reflected in the most recently approved package insert must be included.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications, HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Should a letter communicating important information about this drug product (i.e., a "Dear Doctor" letter) be issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20852-9787

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

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

Sincerely yours,

/S/ 1-14-98

APPEARS THIS WAY
ON ORIGINAL

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Original NDA 19-810/S-038
HFD-180/Div. files
HFD-180/CSO/M.Walsh
HFD-180/A.Shaw
E.Duffy
DISTRICT OFFICE
HF-2/Medwatch (with labeling)
HFD-92/DDM-DIAB (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFI-20/Press Office (with labeling)

APPEARS THIS WAY
ON ORIGINAL

Drafted by: M.Walsh 1/13/98
Initialed by: A.Shaw 1/13/98
E.Duffy 1/13/98
L.Talarico 1/13/98
revised: M.Walsh 1/14/98
final: M.Walsh 1/14/98
filename: 19810S38.AP

APPROVAL (AP)

APPEARS THIS WAY
ON ORIGINAL

NDA 19-810/S-050

JAN - 7 1998

Astra Merck Inc.
Attention: Gary P. Horowitz, Ph.D.
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Dear Dr. Horowitz:

Please refer to your supplemental new drug application dated April 28, 1997, received April 30, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec(R) (omeprazole) Delayed-Release Capsules.

We acknowledge receipt of your submissions dated October 30 and December 2, 1997.

The supplemental application provides for packaging the physician's samples in a new alternate secondary package_____

We have completed the review of this supplemental application and it is approved. Your proposal for revising the patient education material, submitted on December 2, 1997 in response to our recommendation, which was communicated to you in a November 25, 1997 telephone conversation between you and Ms. Maria Walsh of this Divison, is acceptable. Specifically, the revision should be made as follows.

From: "While some foods and activities may aggravate GERD symptoms - and are best avoided - changes in diet and lifestyle are not enough to provide adequate symptom relief."

To: " While some foods and activities may aggravate GERD symptoms - and are best avoided - changes in diet and lifestyle may not be enough to provide adequate symptom relief."

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

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

Sincerely yours,

/S/ 1-6-98

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Original NDA 19-810/S-050
HFD-180/Div. Files
HFD-180/M.Walsh
HFD-180/A.Shaw
E.Duffy
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: M.Walsh 12/16/97
Initialed by: A.Shaw 12/17/97
E.Duffy 12/30/97
L.Talarico 1/5/98
final: M.Walsh 1/5/98
filename: 19810S50.AP

APPROVAL (AP)

NDA 19-810/S-056

JUL 10 1998

Astra Merck Inc.
Attention: Gary P. Horowitz, Ph.D.
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

Dear Dr. Horowitz:

Please refer to your supplemental new drug application dated May 28, 1998, received May 29, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prilosec (omeprazole) Delayed-Release Capsules

The user fee goal date for this application is November 29, 1998.

This supplemental new drug application provides for an alternate lidding stock for the Hospital Unit Dose (HUD) package for the 10 mg and 20 mg capsules.

We have completed the review of this supplemental application and it is approved with an expiration date of six months

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

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

Sincerely,

/S/ 7/9/98

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

cc:
Archival NDA 19-810
HFD-180/Div. Files
HFD-180/M.Walsh
HFD-95/DDMS (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: M.Walsh 7/8/98
Initialed by: E.Duffy 7/8/98
final: M.Walsh 7/8/98
filename: 19810S56807.ap.doc

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 019810/S38/S50/S56

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW 3	1. Organization: HFD-180	2. NDA Number: 19-810
3. Name and Address of Applicant (City & State): Astra Merck Inc. 725 Chesterbrook Blvd. Wayne, PA 19087		4. AF Number: JAN 13 1998 5. Supplement(s)
6. Name of Drug: PRILOSEC® Delayed Release Capsule	7. Nonproprietary Name: Omeprazole	Numbers: SCF-038 Dates: Feb 26, 1996
8. Supplement Provides for: a new dosage strength, 40 mg capsule.		9. Amendments and Other (Reports, etc.) Dates: BC Jul 7, 1996 BC Oct 10, 1996 BC June 26, 1997 C August 27, 1997 AC Nov 21, 1997
10. Pharmacological Category: H+/K+ ATPase enzyme inhibitor (H+ pump inhibitor)	11. How Dispensed: RX X OTC	12. Related IND/NDA/DMF(s):
13. Dosage Form: capsule	14. Potency: 10 mg, 20 mg and 40 mg	
15. Chemical Name and Structure: 5-methoxy-2-[((4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl)sulfinyl]-1H-benzimidazole		16. Records and Reports: Current X Yes ___ No Reviewed ___ Yes X No

17. Comments:

cc: NDA 19-810
HFD-180/Div File
HFD-181/MWalsh
HFD-180/LTalarico 1-13-98
HFD-180/EDuffy
HFD-180/AShaw
R/D init by:EDuffy/1-12-98 /S/ 1/13/98
ABS/dob **F/T 1-13-97**\WP: c:\wpfiles\chem\S\19810038.4AS

18. Conclusions and Recommendations: AP. The application may be approved with an 18 month expiration date for each package type (Hospital Unit Dose Blisters, 30 count bottle, 100 count bottle, 1000 count bottle, 7 count physician's sample), with intermediate hold times of 30 days _____, 60 days _____ and 90 days _____ proposed in the June 26, 1997 submission. The applicant should be advised that they must place the first three batches of 40 mg capsules in each packaging configuration on stability and report the data in the Annual Report.

19. Reviewer

Name:	Signature	Date Completed:
Arthur B. Shaw, Ph.D.	1/13/98 /S/	December 9, 1997

Form FDH 2266 (7/75) ALT R

3. Name and Address of Applicant (City & State): Astra Merck Inc. 725 Chesterbrook Blvd. Wayne, PA 19087		4. AF Number: OCT 14 1997 5. Supplement(s)	
6. Name of Drug: PRILOSEC® Delayed Release Capsule	7. Nonproprietary Name: Omeprazole	Numbers SCF-038	Dates Feb 26, 1996
8. Supplement Provides for: a new dosage strength, 40 mg capsule.		9. Amendments and Other (Reports, etc.) Dates: BC Jul 7, 1996 BC Oct 10, 1996 BC June 26, 1997 C August 27, 1997	
10. Pharmacological Category: H+/K+ ATPase enzyme inhibitor (H+ pump inhibitor)	11. How Dispensed: RX X OTC___	12. Related IND/NDA/DMF(s):	
13. Dosage Form: capsule	14. Potency: 10 mg, 20 mg and 40 mg		
15. Chemical Name and Structure: 5-methoxy-2-[((4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl)sulfinyl]-1H-benzimidazole		16. Records and Reports: Current ___X__ Yes ___ No Reviewed _____ Yes __X__ No	

17. Comments:

cc: NDA 19-810
HFD-180/Div File
HFD-181/MWalsh
HFD-180/LTalarico
HFD-180/EDuffy
HFD-180/AShaw
R/D init by:EDuffy 10/10/97 /S/ 10/14/97
ABS/abs **F/T 10/10/97**\WP: N:\WPFILES\CHEM\FINAL\SUP\19810038.3AS

18. Conclusions and Recommendations: The supplement is Approvable (AE)

19. Reviewer

Name:	Signature	Date Completed:
Arthur B. Shaw, Ph.D.	/S/ 10/10/97	September 24, 1997

Form FDH 2266 (7/75) ALT R

CHEMIST'S REVIEW 2	1. Organization: HFD-180	2. NDA Number: 19-810
3. Name and Address of Applicant (City & State): Astra Merck Inc. 725 Chesterbrook Blvd. Wayne, PA 19087		4. AF Number: APR - 1 1997 5. Supplement(s)
6. Name of Drug: PRILOSEC® Delayed Release Capsule	7. Nonproprietary Name: Omeprazole	Numbers: SCF-038 / Dates: Feb 26, 1996
8. Supplement Provides for: a new dosage strength, 40 mg capsule.		9. Amendments and Other (Reports, etc.) Dates: BC Jul 7, 1996 BC Oct 10, 1996
10. Pharmacological Category: H+/K+ ATPase enzyme inhibitor (H+ pump inhibitor)	11. How Dispensed: RX X OTC__	12. Related IND/NDA/DMF(s):
13. Dosage Form: capsule	14. Potency: 10 mg, 20 mg and 40 mg	
15. Chemical Name and Structure: 5-methoxy-2-[((4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl)sulfinyl]-1H-benzimidazole		16. Records and Reports: Current X Yes __ No Reviewed X Yes __ No

17. Comments:

cc: NDA 19-810
HFD-180/Div File
HFD-181/MWalsh
HFD-180/SFredd
HFD-180/EDuffy
HFD-180/AShaw
R/D init by:EDuffy/3-20-97

/S/ 4/1/97

ABS/dob **F/T 3-26-97**\WP: c:\wpfiles\chem\S\19810038.2AS

18. Conclusions and Recommendations: The application is not approvable (NA).

19. Reviewer

Name:	Signature	Date Completed:
Arthur B. Shaw, Ph.D.	/S/ 3/28/97	March 17, 1997

Form FDH 2266 (7/75) ALT R

CHEMIST'S REVIEW 1	1 Organization: HFD-180	2. NDA Number: 19-810
3. Name and Address of Applicant (City & State): Astra Merck Inc. 725 Chesterbrook Blvd. Wayne, PA 19087		4. AF Number: OCT 28 [illegible] 5. Supplement(s)
6. Name of Drug: PRILOSEC® Delayed Release Capsule	7. Nonproprietary Name: Omeprazole	Numbers: SCP-050 Dates: April 28, 1997
8. Supplement Provides for: alternate secondary packaging of physician's samples by Promex Medical, Inc.		9. Amendments and Other (Reports, etc.) Dates:
10. Pharmacological Category: H+/K+ ATPase enzyme inhibitor (H+ pump inhibitor)	11. How Dispensed: RX X OTC__	12. Related IND/NDA/DMF(s):
13. Dosage Form: capsule	14. Potency: 10 mg and 20 mg	
15. Chemical Name and Structure: 5-methoxy-2-[((4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl)sulfinyl]-1H-benzimidazole		16. Records and Reports: Current __X__ Yes ___ No Reviewed _____ Yes __X No

17. Comments: This supplement actually provides for a new secondary package _____. The secondary packaging will involve placing the currently approved Hospital Unit Dose _____ primary package _____ into _____. The package will also contain personalized physician prescription blanks. The applicant was requested to provide samples of the labeling for review by the Division of Drug Marketing and Advertising _____. This information has not been provided. This establishment was found to be acceptable on August 19, 1997.

cc: NDA 19-810
HFD-180/Div File
HFD-181/MWalsh
HFD-180/LTalaric
HFD-180/EDuffy
HFD-180/AShaw
R/D init by:EDuffy/10-28-97
ABS/dob **F/T 10-28-97**\WP: c:\wpfiles\chem\S\19810050.1AS
ATTACHMENTS (2): Telecon, dated 8-18-97
Telecon, dated 10-3-97

/S/ 10/28/97

18. Conclusions and Recommendations: Approvable pending receipt of labeling information

19. Reviewer

Name:	Signature	Date Completed:
Arthur B. Shaw, Ph.D.	/S/ 10/28/97	October 28, 1997

Form FDH 2266 (7/75) ALT R

JUL - 8 1998

DIVISION OF GASTROINTESTINAL AND COAGULATION DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls Supplement

NDA #:19-810 **SUPPLEMENT #:**SCP-056 **CHEM REVIEW #:**1 **REVIEW DATE:**July 7, 1998

DOCUMENT	CDER	ASSIGNED
28-May-98	29-May-98	01-Jun-98

SUPPLEMENT PROVIDES FOR: the use of an alternate _____ stock for the Hospital Unit Dose (HUD) packaging

NAME & ADDRESS OF APPLICANT: Astra Merck
725 Chesterbrook Blvd.
Wayne, PA 19087-5677

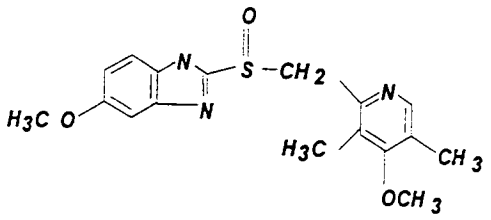
DRUG PRODUCT NAME: Proprietary: Prilosec Nonproprietary/USAN: omeprazole

PHARMACOLOGICAL CATEGORY: proton pump inhibitor **INDICATION:** treatment of ulcers

DOSAGE FORM: CAPSULE, DELAYED RELEASE PELLETS **STRENGTH:** 10 and 20 mg

ROUTE OF ADMINISTRATION: oral **HOW DISPENSED:** X Rx ___OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:
5-methoxy-2-[[()4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl] 1h-benzimidazole



SUPPORTING DOCUMENTS: _____

RELATED DOCUMENTS: N/A **CONSULTS:** N/A

REMARKS/COMMENTS: This supplement resulted from a discovery that the _____ stock supplied by _____ was actually different from the currently approved _____ stock. Further investigation showed that the currently approved _____ stock was introduced in an Annual Report in 1996 but was not flagged as a change. The original application referenced DMF _____ but there was no specific reference and no review.

CONCLUSIONS & RECOMMENDATIONS: The supplement may be approved with an expiration date of six months.

/S/ July 7, 1998
Arthur B. Shaw, Ph.D.,
Review Chemist, HFD-180

/S/ 7/8/98
Eric P.Duffy, Ph.D.
Chemistry Team Leader, HFD-180

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 019810/S38/S50/S56

STATISTICAL REVIEW(S)

STATISTICAL REVIEW - STABILITY STUDIES

NDA#: 19-810 **Date:** MAY 6 1997

Applicant: Astra Merck

Manufacturer: Merck & Co.

Name of Drug: Prilosec Caps (omeprazole, 40mg)

Classification: 1S

Dates: 1/27/1997, Desired 4/12/1997, Goal 5/12/1997

Documents Reviewed: one volume submitted by the sponsor including a floppy disk, dated 10/10/1996

I. INTRODUCTION

In this NDA submission, the sponsor has requested an 18 month expiration dating for their 40mg formulation, as granted for their 10mg and 20 mg formulations.

The reviewing chemist in HFD-180 for this submission is Dr. Art Shaw. He finds chemical reasons for not pooling batches produced at the two sites _____ _____. This leaves only two batches at the first site and one at the second site. Customarily, at least three potentially poolable batches are needed to obtain an expiration date, so no expiration dates can be given.

The first issue addressed is the extent to which pooling across package types is statistically feasible, requested by the reviewing chemist. Based on the assumption that there are no chemical reasons for not pooling package types, this reviewer has reviewed whether there are statistical reasons for not pooling package types.

The second issue addressed is how to pool. In both submissions (2/1996 and 1/1997), the sponsor appears to pool when the p-value is above 0.05. However, the custom is to pool only when the p-value is above 0.25, for a target goal of more than 95% of the tablets expiring past the estimated expiration date. If the sponsor wants to use another target goal, they need to tell the FDA what it is, and justify the resulting inference procedure.

II. DESIGN

Number of package types: 6.

HUD Blister	(Hospital Unit Dose)	- all three lots
30 capsule CR	(Child Resistant)	- all three lots
100 capsule CR	(Child Resistant)	- all three lots
1000 capsule nCR	(non-Child Resistant)	- all three lots
7 capsule nCR	(non-Child Resistant)	- lot 214407 only
1000 capsule CR	(Child Resistant)	- lot 214407 only

Tested Parameters:	Specification limits:
Assay	_____
Largest Degradant	_____
Total Degradants	_____

Acid Resistance and Dissolution are not analyzed since these are measured for per-batch quality control, to determine whether to withdraw or continue using a batch, and hence do not need to be considered for stability, unless a substantial number of batches are rejected.

Sampling times: For temperature 30°C, ambient humidity, the observation times and results for each batch analyzed are listed in appendix **Tables 1** to **3**, based on the sponsor's electronically submitted data. Tests were to be conducted at least once every six months to two years.

III. SPONSOR'S ANALYSIS

The sponsor's graphical analysis indicates pooling of all manufacturing sites, lots of drug, and package types. This analysis shows a result for an 18 month expiration. The Largest Degradate appears to be the first parameter to lead to expiration.

IV. REVIEWER'S ANALYSIS OF POOLABILITY

As shown in appendix **Tables 4** to **6**, this reviewer finds only "Largest Degradate" poolable across package types. "Assay" and "Total Degradates" are not poolable in general.

Note that additional data may change these conclusions. The tests for poolability were

conducted at the 0.25 level, matching the analysis which would be used to determine the expiration date if sufficient lots from a single site and manufacturing process were submitted. Substantial increases in data tend to reduce the amount of pooling.

Mock expiration dates and estimated regression lines are included in the appendix **Tables 4** to **6** for completeness and to develop insight into stability. Each expiration date supports the suspicion that an expiration date of at least 18 months would be supported if three lots were tested and submitted, rather than two lots and one lot. None of the regression lines proceed in the reverse of the expected regression.

V. REVIEWER'S COMMENTS, HOW TO POOL

The deviation from 0.05 is considered appropriate based on _____ (*Biometrics* 1964 pp. 427-, "Analysis and Inference for Incompletely Specified Models Involving the use of Preliminary Test(s) of Significance"). Our regulatory decisions concern expiration, not poolability, so the critical value is chosen to make good decisions regarding stability. The choice of 0.25 is shown better than 0.05 or 0.15 in the paper by Chen et al, (*Drug Information Journal* V31#2, May 1997 pp. 573-587, "Shelf-Life Estimation for Multifactor Stability Studies").

Appendix **Tables 4** to **6** are drawn from the output of the _____ SAS program produced by Ng (FDA/CDER). The same runs produce the ANOVA tables in appendix **Tables 7** to **10**, with the key to the tests of hypotheses in appendix **Table 7**. The p-values which are the basis of not pooling are highlighted in bold. Each of these p-values for pooling are between 0.10 and 0.25, consistent with the sponsor's pooling all cases at the 0.05 level.

If the sponsor wants to use another target goal, they need to tell the FDA what it is, and justify the resulting inference procedure.

VI. SUMMARY CONCLUSIONS

Since the number of lots of drug from a single site and manufacturing process is less than three, no expiration date is supported. For the best results, the sponsor needs to submit stability data from at least three lots of drug from each combination of site, manufacturing process, and package for which an expiration date is sought.

The packages appear poolable with respect to the Largest Degradate, but not with respect to Assay nor Total Degradates.

The sponsor needs to test for poolability at the 0.25 level, or tell what their target goal is and justify the resulting inference procedure.

/S/ 5/6/1997

Ferrin Harrison, Ph.D.
Mathematical Statistician

This review consists of 4 pages of text, and 11 pages of appendix tables.

Concur: Dr. Huque /S/ 5/6/97

Dr. Smith /S/ 5/6/97

APPEARS THIS WAY
ON ORIGINAL

cc: Archival NDA

HFD-180/ Division Files	
HFD-180/ Dr. Talarico	acting medical division director
HFD-180/ Dr. Duffy	chemistry team leader
HFD-180/ Dr. Shaw	reviewing chemist
HFD-180/ Ms. Maria Walsh	CSO/review team administrator
HFD-870/ Dr. Raj Pradhan	consulting biopharmaceutics
HFD-720/ Dr. Smith	statistical division director
HFD-720/ Dr. Huque	statistical team leader
HFD-720/ Dr. Harrison	reviewing stability
HFD-720/ Chron	
HFD-720/ File Copy	

Table 1
Prilosec Stability Data
Lot AET MA-029-94, manufacturing site _____

Package	Study	Time, Months	Assay	Largest Degradate	Total Degradates
blister	X3341	0			
		3			
		6			
		12			
		18			
30caps/ 75cc CR	X3267	0			
		3			
		6			
		11			
		12			
		18			
100caps/120cc CR	X3286	0			
		3			
		6			
		9			
		12			
		18			
1000caps/40cc nCR	X3282	0			
		3			
		6			
		12			
		18			

CR: Child Resistant cap nCR: non-Child Resistant cap

APPEARS THIS WAY
ON ORIGINAL

Table 2
Prilosec Stability Data
Lot AET MA-030-94, manufacturing site_____

Package	Study	Time, Months	Assay	Largest Degradate	Total Degradates
____ blister	X3342	0			
		3			
		6			
		12			
		18			
30caps/ 75cc CR	X3268	0			
		1			
		3			
		6			
		11			
		12			
		18			
100caps/120cc CR	X3287	0			
		3			
		6			
		9			
		12			
		18			
1000caps/40oz nCR	X3283	0			
		3			
		6			
		12			
		18			

CR: Child Resistant cap nCR: non-Child Resistant cap

APPEARS THIS WAY
ON ORIGINAL

Table 3
Prilosec Stability Data
Lot 214407, manufacturing site

Package	Study	Time, Months	Assay	Largest Degradate	Total Degradates
blister	X3343	0			
		3			
		6			
		12			
		18			
30caps/ 75cc CR	X3291	0			
		3			
		6			
		9			
		12			
		18			
100caps/120cc CR	X3290	0			
		3			
		6			
		9			
		12			
		18			
1000caps/40oz nCR	X3300	0			
		3			
		6			
		12			
		18			
7caps/30cc nCR	X3363	0			
		3			
		6			
		12			
1000caps/40oz CR	X3364	0			
		3			
		6			
		12			

CR: Child Resistant cap nCR: non-Child Resistant cap

Table 4
Stability Analysis, Assay

Lot AET MA-029-94
HUD, 30cap CR, 100cap CR, 1000cap nCR
Common Intercept and Common Slope

Fitted Line	Expiration
Y = 97.64 + 0.01149 X	72 months

Lot AET MA-030-94
Separate Intercepts and Common Slope

Package	Study	Fitted Line	Expiration
HUD Blister	X3268	Y = 101.78 - 0.06699 X	71 months
30cap CR	X3283	Y = 99.26 - 0.06699 X	57 months
100cap CR	X3287	Y = 99.94 - 0.06699 X	61 months
1000cap nCR	X3342	Y = 100.16 - 0.06699 X	62 months

Lot 224407
Separate Intercepts and Common Slope

Package	Study	Fitted Line	Expiration
HUD Blister	X3290	Y = 97.57 - 0.15218 X	34 months
30cap CR	X3291	Y = 98.73 - 0.15218 X	39 months
100cap CR	X3300	Y = 99.55 - 0.15218 X	42 months
1000cap nCR	X3343	Y = 97.27 - 0.15218 X	32 months
7cap nCR	X3363	Y = 98.55 - 0.15218 X	37 months
1000cap CR	X3364	Y = 98.77 - 0.15218 X	38 months

Table 5
Stability Analysis of Largest Degradate

HUD, 30cap CR, 100cap CR, 1000cap nCR
Common Intercept and Common Slope

Fitted Line	Expiration	
Y = 0.12642 + 0.008629 X	27 months	**Lot AET MA-029-94**
Y = 0.09511 + 0.010805 X	26 months	**Lot AET MA-030-94**
Y = 0.10999 + 0.009774 X	30 months	**AET MA-029-94+MA-030-94**

HUD, 30cap CR, 100cap CR, 1000cap nCR, 7cap nCR, 1000cap CR
Common Intercept and Common Slope

Fitted Line	Expiration	
Y = 0.22292 + 0.003299 X	35 months	**Lot 224407**

APPEARS THIS WAY
ON ORIGINAL

Table 6
Stability Analysis of Total Degradates

Lot AET MA-029-94
Separate Intercepts and Separate Slopes

Package	Study	Fitted Line	Expiration
HUD Blister	X3267	Y = 0.33742 + 0.009509 X	38 months
30cap CR	X3282	Y = 0.14138 + 0.012644 X	72 months
100cap CR	X3286	Y = 0.06286 + 0.033810 X	36 months
1000cap nCR	X3341	Y = 0.12155 + 0.043391 X	30 months

Lot AET MA-030-94
Separate Intercepts and Separate Slopes

Package	Study	Fitted Line	Expiration
HUD Blister	X3268	Y = 0.21247 + 0.017896 X	50 months
30cap CR	X3283	Y = 0.13707 + 0.010632 X	72 months
100cap CR	X3287	Y = 0.02857 + 0.038095 X	33 months
1000cap nCR	X3342	Y = 0.075 + 0.041667 X	34 months

Lot 224407
HUD, 30cap CR, 100cap CR, 1000cap nCR, 7cap nCR, 1000cap CR
Common Intercept and Common Slope

Fitted Line	Expiration
Y = 0.24792 + 0.022975 X	58 months

Table 7
Analysis of Poolability by Package Type
Key to Sources of Variation,
for use with Tables 8-10

Statistical Analysis:
Key to sources of variation

A = separate intercept, separate slope
| common intercept, common slope

B = separate intercept, common slope
| common intercept, common slope

C = separate intercept, separate slope
| separate intercept, common slope

D = Residual

E = Full Model

Explanation: The p-value in line A is used to test whether to use a separate intercept, separate slope model, if $p<.25$, versus a common intercept, common slope model. Similarly for B and C, with a different pair of models in each case.

Table 8
Analysis of Poolability, Assay
_____, 30cap CR, 100cap CR, 1000cap nCR, Lot AET MA-029-94
Common Intercept and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

_____, 30cap CR, 100cap CR, 1000cap nCR, Lot AET MA-030-94
Separate Intercepts and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

____), 30cap CR, 100cap CR, 1000cap nCR, 7cap nCR, 1000cap CR
Lot 224407
Separate Intercepts and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

A = separate intercept, separate slope
| common intercept, common slope

B = separate intercept, common slope
| common intercept, common slope

C = separate intercept, separate slope
| separate intercept, common slope

Table 9
Analysis of Poolability, Largest Degradate
30cap CR, 100cap CR, 1000cap nCR, Lot AET MA-029-94
Common Intercept and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

30cap CR, 100cap CR, 1000cap nCR, Lot AET MA-030-94
Common Intercept and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

30cap CR, 100cap CR, 1000cap nCR
Lots AET MA-029-94, AET MA-030-94
Common Intercept and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

A = separate intercept, separate slope
| common intercept, common slope

B = separate intercept, common slope
| common intercept, common slope

C = separate intercept, separate slope
| separate intercept, common slope

Table 9b
Analysis of Poolability, Largest Degradate

30cap CR, 100cap CR, 1000cap nCR, 7cap nCR, 1000cap CR
Lot 224407
Common Intercept and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

A = separate intercept, separate slope
| common intercept, common slope

B = separate intercept, common slope
| common intercept, common slope

C = separate intercept, separate slope
| separate intercept, common slope

Table 10
Analysis of Poolability, Total Degradates
30cap CR, 100cap CR, 1000cap nCR, Lot AET MA-029-94
Separate Intercepts and Separate Slopes

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

30cap CR, 100cap CR, 1000cap nCR, Lot AET MA-030-94
Separate Intercepts and Separate Slopes

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

30cap CR, 100cap CR, 1000cap nCR, 7cap CR, 1000cap CR
Lot 224407
Common Intercept and Common Slope

SOURCE	SS	DF	MS	F	P
A					
B					
C					
D					
E					

A = separate intercept, separate slope
| common intercept, common slope

B = separate intercept, common slope
| common intercept, common slope

C = separate intercept, separate slope
| separate intercept, common slope