CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-958

CORRESPONDENCE

Merck & Co., Inc.
West Point, PA 19486

April 13, 2000

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OFFICIAL FDA Copies
not desk copies

MERCK
Research Laboratories

Kerry Rothschild, Esq.
Division of Over-the-Counter Drug Products
HFD-560, Room S-254
Office of Drug Evaluation V (CDER)
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

Dear Mr. Rothschild:

NDA 20-958: PEPCID™ —— Tablets
(Famotidine/Antacid Combination)

Response to Request for Information

Reference is made to the NDA cited above, submitted on February 20, 1998 and to the Amendment to Pending New Drug Application, Response to Not Approvable Letter submitted on December 17, 1999. Reference is also made to a February 22, 2000 submission providing a hard copy of the labeling information of the December 17, 1999 Response. Final reference is made to a telephone conversation between Mr. Paul Levine (FDA) and Mr. George Latyszonek (JJMCP) on March 24, 2000 in which Mr. Levine indicated that the labeling information sent on February 22, 2000 could not be located.

With this submission, we are resending one copy of the labeling information in hard copy. If you have any questions or need additional information please contact George Latyszonek 215-273-7152, or in his absence, Edwin L. Hemwall, Ph.D. 610-397-2306.

Sincerely,

George Latyszonek
Director Regulatory Affairs
Johnson & Johnson ◦ Merck
Consumer Pharmaceuticals Co.
Sumneytown Pike, BLA-33
West Point, PA 19486

Attachment
Federal Express
Desk Copy (letter only): Mr. Paul Levine Jr., HFD-180, Room 6B-45

Q:\carnal\pepcid\letters\20-958req7

MAR 8 2000

NDA 20-958

Merck Research Laboratories
Attention: George Latyszonek
Director, Regulatory Affairs
P.O. Box 4, BLA-20
West Point, PA 19486-0004

Dear Mr. Latyszonek:

We acknowledge receipt on December 20, 1999 of your December 17, 1999 resubmission to your new drug application (NDA) for Pepcid . —— (famotidine/antacid) Chewable Tablets.

This resubmission contains Clinical; Chemistry, Manufacturing, and Controls (CMC) information in response to our February 19,1999, action letter.

We also note that you have requested that the trade name be revised from Pepcid —— to Pepcid Complete. Your request is currently being reviewed.

We consider this a complete class 2 response to our action letter. Therefore, the user fee goal date is June 20, 2000.

If you have any questions, call me at (301) 827-7310.

Sincerely,

/S/

Paul E. Levine, Jr., R.Ph.
Regulatory Project Manager
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDA 20-958
HFD-180/Div. Files
HFD-180/P.Levine

DISTRICT OFFICE

Drafted by: PEL/February 14, 2000
Initialed by: K.Johnson 02/28/00
final: 03/08/00
filename: Pepcid NDA 20958 CH-Ack Ltr.doc

/S/ 3/8/00

CLASS 2 RESUBMISSION ACKNOWLEDGEMENT (AC)

Levine

NDA 20-958

Merck Research Laboratories
Attention: George Latyszonek
Director, Regulatory Affairs
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486-0004

AUG 25 2000

Dear Mr. Latyszonek:

We acknowledge receipt on August 3, 2000, of your August 2, 2000, resubmission to your new drug application (NDA) for Pepcid Complete [famotidine 10mg/antacid (calcium carbonate 800mg, and magnesium hydroxide 165mg)] Chewable Tablets.

This resubmission contains additional labeling, chemistry, manufacturing and controls, and statistical information submitted in response to our June 20, 2000, action letter.

We consider this a complete class 2 response to our action letter. Therefore, the user fee goal date is February 3, 2000.

If you have any questions, call me at (301) 827-7310.

Sincerely,

/S/ 8/25/00

Paul E. Levine, Jr., R.Ph.
Regulatory Project Manager
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

cc:
Archival NDA 20-958
HFD-180/Div. Files
HFD-180/P.Levine
HFD-180/L.Talarico
S.Aurecchia
H.Gallo-Torres
L.Zhou
M.Adams
HFD-715/T.Permutt
HFD-560/C.Ganley
L.Katz
A.Segal
D.Keravich
H.Cothran
G.Chang
DISTRICT OFFICE

Drafted by: PEL/August 25, 2000
Initialed by: MM 08/25/00
final: 08/25/00
filename: Ack Ltr CR-Pepcid Complete 082500.doc

CLASS 2 RESUBMISSION ACKNOWLEDGEMENT (AC)
(DDR: Update the user fee goal date based on the class of resubmission.)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 20-958

Merck Research Laboratories
Attention: George Latyszonek
Director, Regulatory Affairs
P.O. Box 4, BLA-20
West Point, PA 19486-0004

JUL 16 1999

Dear Mr. Latyszonek:

Please refer to your pending February 20, 1998, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for non-prescription famotidine/antacid (calcium carbonate, 800 mg, & magnesium hydroxide, 165 mg) combination chewable tablet.

We also refer to your submission dated March 18, 1999, received on March 22, 1999, requesting our preliminary comments regarding your proposed labeling.

We have completed our review of the submitted labeling and the actual use study and have the following comments and requests:

A. Concerning your proposed proprietary name "Pepcid ." we are reviewing your January 20, 1999, request to reconsider our determination that the proposed proprietary name, "Pepcid ." is unacceptable. We will notify you as soon as we have completed our review of your request.

B. On March 17, 1999, the final rule titled "Over-the-Counter Human Drugs; Labeling Requirements" [64 FR 13254] was published in the Federal Register requiring reformatting of all labeling for over-the-counter drug products. Because this drug product was not approved on or before May 17, 1999, the applicable parts of all the labeling (i.e., the back panel of the cartons, back panel of the sample pouch dispenser, the second panel bottle over-wrap, and the back panel of the sample pouches) must be revised to comply with the new OTC labeling requirements described in §201.66. For consistency, we also recommend that you also format the label for the 5-panel bottle label as described in this rule.

In addition to the general textual and formatting requirements described in § 201.66 (64 FR 13254), we also have the following revisions which are specific for this drug product (see also Figure 1 below):

4 page(s) of revised draft labeling has been redacted from this portion of the review.

E. Please address the issue of using a peppermint flavored tablet, since peppermint is known to decrease lower esophageal sphincter tone, which may make the heartburn worse. Thus, consideration should be given to including peppermint as a food to avoid in "Tips for Managing Heartburn."

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 and are subject to change as we continue the review of the application. Per the user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed as such. In addition, we may identify other information that must be provided prior to approval of this application. Please include your response to these requests in your response to our February 19, 1999 action letter.

If you have any questions, contact Michael Folkendt, Project Manager, at (301) 827-1602.

Sincerely,

/S/

Maria Rossana R. Cook, M.B.A.
Supervisor, Project Management Staff
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-958

MAR - 3 1998

Merck Research Laboratories
Attention: George Latyszonek
Sumneytown Pike, BLA-20
West Point, PA 19486

Dear Mr. Latyszonek:

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: Non-prescription Pepcid® —— [famotidine, 10 mg/antacid (calcium carbonate, 800 mg; magnesium hydroxide, 165 mg) combination) Chewable Tablet

Therapeutic Classification: Standard

Date of Application: February 20, 1998

Date of Receipt: February 20, 1998

Our Reference Number: 20-958

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 April 21, 1998 in accordance with 21 CFR 314.101(a).

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, please contact me at (301) 443-0487.

Sincerely yours,

/S/ 3/3/98

Michael Folkendt
Project Manager
Division of Gastrointestinal and
Coagulation Drug Products, HFD-180
Office of Drug Evaluation III
Center for Drug Evaluation and Research

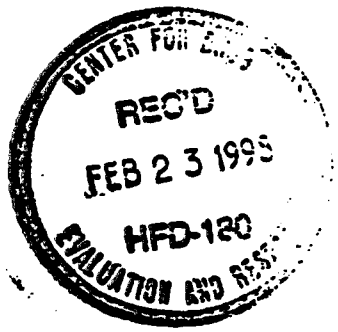
cc: Original NDA 20-958
HFD-180/Div. Files
HFD-180/CSO/M.Folkendt
DISTRICT OFFICE

Drafted by: mf/March 3, 1998
Final: 3/3/98 filename: 20958803.ACK

ACKNOWLEDGEMENT (AC)

Debarment Certification

February 20, 1998



MERCK
Research Laboratories

Lilia Talarico, M.D. - Director
Division of Gastrointestinal and
Coagulation Drug Products
HFD-180, Room 6B-45
Office of Drug Evaluation III (CDER)
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Talarico:

Original New Drug Application
NDA 20-958: Non-Prescription PEPCID® —
(Famotidine/Antacid Combination) Tablets

Pursuant to Section 505(b) of the Federal Food, Drug and Cosmetic Act and in accordance with Title 21 of the Code of Federal Regulations, Merck Research Laboratories (MRL), in collaboration with Johnson & Johnson • Merck Consumer Pharmaceuticals Co. (JJMCPC) is submitting a New Drug Application (NDA) for PEPCID® — (Famotidine/Antacid Combination) Tablets, NDA 20-958.

The Famotidine/Antacid Combination Tablet (FACT) was developed to be an over-the-counter (OTC) drug product for the treatment of heartburn, acid indigestion, and sour stomach. FACT is a chewable tablet that contains famotidine (10 mg), calcium carbonate (800 mg), and magnesium hydroxide (165 mg). The amount of antacid in each tablet provides 21 mEq of acid-neutralizing capacity (ANC), which is within the range of doses typically used in OTC antacid products for the treatment of intermittent heartburn.

This indication is primarily derived from and supported by a clinical program that consisted of nine clinical studies, including three large Phase III clinical trials. These three large, double-blind, placebo-controlled studies, comprising 3645 randomized patients, form the basis for demonstrating the efficacy of PEPCID® — in offering the benefits of more rapid relief of symptoms than famotidine alone, and a longer duration of heartburn relief than antacid alone in a single chewable tablet.

Representatives of MRL and JJMCPC met on July 24, 1996 with FDA personnel to discuss the clinical development program for famotidine/antacid combination. On October 10, 1997 a pre-NDA meeting was held to discuss the presentation and analysis of data in the NDA. The understandings and agreements reached at these meetings have been incorporated into this application and are briefly summarized in the Regulatory Background Information section of this application.

The three components of active ingredients for Famotidine/Antacid Combination Tablets will be purchased from the following vendors:

Manufacturing of Famotidine/Antacid Combination Tablets will occur at the —— —— Merck Manufacturing Division in West Point, Pennsylvania and Johnson & Johnson • Merck Consumer Pharmaceuticals Co. facilities in Lancaster, Pennsylvania.

Merck is requesting a categorical exclusion from the requirements to prepare an Environmental Assessment under 21 CFR §25.31(b). The production of PEPCID® —— (Famotidine/Antacid Combination) Tablets meets the requirements of a categorical exclusion under 21 CFR §25.31(b) because the estimated concentration at the point of entry, referred to as the Expected Introduction Concentration (EIC), into the aquatic environment will be below 1 part per billion (ppb). To the best of the firm's knowledge no extraordinary circumstances. exist in regard to this action.

This application is formatted as required in Title 21, Paragraph 314.50 of the Code of Federal Regulations. Please note this NDA is organized according to the recently revised FDA 356h. It consists of a complete "archival" copy (blue binders), comprising 25 volumes, and review copies for each of the four (4) technical sections (one technical review copy for each Item) as described in the Statement of Organization, which is attached to this letter.

ELECTRONIC SUBMISSION INFORMATION

This NDA is being submitted in the following formats:

FORMAT	INFORMATION INCLUDED	MEDIA FORMAT	DATE OF SUBMISSION
Paper	(all information except CRTs and CRFs)	Paper	February 20, 1998
Electronic Archival Files	NDA Table of Contents, Case Report Tabulations, Case Report Forms	CD	February 20, 1998
Electronic Submission	(all information)	Storage Works Building Block	March 6, 1998 (to Technology Services Support Center)

We are submitting this application in accordance with the Guidance for Industry - Archiving Submissions in Electronic Format - NDAs, published September, 1997.

As noted in the Guidance document, this letter is being included as *cover.pdf* and includes:

- Appropriate regulatory information
- A description of the submission
- A description of which portions of the submission are presented only in paper, only in electronic format, or both paper and electronic format *(see above)*
- A description of the electronic submission including the contents of the media, their number and format, a description of the file types and the total size of the submission
  The electronic archival files for Case Report Tabulations and Case Report Forms are provided on 1 CD. The files are provided in .PDF and .PDF catalogue index format. The total file size is approximately 40 MB.

- Verification that the submission is virus free with a description of the software used to check the files for viruses
  Merck Research Laboratories (MRL) has employed Norton anti-virus (NAV) software and has scanned all files. No viruses were detected.

- A description of any deviation from the specifications in the guidance document
  There are no deviations from the specifications as noted in the guidance document.

MRL will work with FDA to arrange orientation to the electronic submission for all interested Agency reviewers.

In accordance with the Prescription Drug User Fee Act of 1992, and the Food and Drug Administration Modernization Act of 1997, a check for this NDA in the amount of $256,846.00 (Check No. C4485196); User Fee I.D. No. 3399 was sent to the Mellon Bank, Three Mellon Bank Center, 27th Floor (FDA 360909), Pittsburgh, Pennsylvania 15295-0001, on February 6, 1998.

Pursuant to 21 CFR 314.50(k)(3), a complete field copy of the Chemistry, Manufacturing and Controls technical section (Item 4) has been submitted to the FDA Philadelphia District Office. This field copy is a true copy of Item 4 as contained in the archival copy and review copies of this application.

As required by §306(k)(1) of 21 U.S.C. 335a(k)(1), we hereby certify that, in connection with this application, Merck & Co., Inc. did not and will not use in any capacity the services of any person debarred under subsections 306(a) or (b) of the Act.

As provided for in 21 CFR 314.102, MRL would like to meet with the FDA approximately 90 days following receipt of these applications. The purpose of this meeting will be to discuss the general progress and status of the review of this application and to determine if there are any important deficiencies identified at that time. We will contact the FDA to arrange for this meeting.

We consider the filing of this New Drug Application to be a confidential matter and request that the Food and Drug Administration not make its existence public without first obtaining written permission from Merck & Co., Inc.

Please direct questions or need for additional information to George Latyszonek at (215) 233-7152 or, in my absence, Edwin L. Hemwall, Ph.D. at (610) 397-2306.

Sincerely,

/S/

George Latyszonek
Director, Regulatory Affairs
Johnson & Johnson • Merck
Consumer Pharmaceuticals Co.
Sumneytown Pike BLA-20
West Point, Pennsylvania 19486

Attachment
Hand Delivered

Desk Copy: (Item 4) Ms. Debra Pagano
Philadelphia District Office
Food & Drug Administration
U.S. Custom House Room 900
2nd & Chestnut Street
Philadelphia, Pennsylvania 19106-2973
Federal Express #1

Desk Copy: (Letter and Patent Information Only)
Mr. George Scott
Room 218 Chapman Building
1901 Chapman Avenue
Rockville, MD 20852
Federal Express #2

(Letter Only) Ms. Debra Bowen
Bldg. CRP2, Room S205
9201 Corporate Blvd.
HFD-560
Rockville, MD 20850
Federal Express #3

Original New Drug Application: NDA 20-958

PEPCID® —— Tablets
(Famotidine/Antacid Combination)

STATEMENT OF ORGANIZATION

This application is formatted as required in 21 CFR 314.50. It consists of a complete "archival" copy (Blue Binders), comprising 25 volumes, and "review" copies of the four (4) technical sections as follows:

ITEM	DESCRIPTION	BINDER COLOR	TOTAL VOLUMES
4	Chemistry, Manufacturing and Control Documentation	Red	3
6	Human Pharmacokinetics and Bioavailability Documentation	Orange	3
8	Clinical Documentation	Light Brown	9
10	Statistical Documentation	Green	6

In addition to the specific technical item, each review copy also includes, in the appropriate color binder, Volumes 1.1, containing Item 1 (the overall Index to the Contents of the Application) and Item 2 (labeling) and Volume 1.2, containing Item 3 (Synopsis of the Application), which is the overall summary provided for in 21 CFR 314.50(c). Thus, the total number of volumes in this submission is 54 volumes.

Two additional copies of Item 4C, Methods Validation Package, are included with the archival copy for the FDA Labs, but are not included in the total volume count. Items 11 and 12 are provided in electronic format only in accordance with the Guidance for Industry - Archiving Submissions in Electronic Format - NDAs, published Sept. 1997.

Pursuant to 21 CFR 314.50(k)(3), a complete field copy of the revised Chemistry, Manufacturing and Controls technical section (Item 4) has been submitted to the FDA Philadelphia District Office. This copy is a true copy of Item 4 as contained in the archival and review copies of this application.

q\robinson\mchugh\NDA20958