CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-308

CORRESPONDENCE

Personal Products
COMPANY
DIVISION OF McNEIL-PPC, INC.
199 Grandview Road
Skillman, NJ 08558-9418

new name

new, correct, address

Received Sept 1, 2000.
NDA due date: July 1, 2001.

∴ No new name + address correction notification was sent to this NDA.

August 31, 2000

Dr. Renata Albrecht
Acting Director, Division of Special Pathogen and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockvillle, MD 20850

SUBJECT: ORIGINAL NDA 21-308
Rx to OTC Switch
MONISTAT® 1 COMBINATION PACK
(miconazole nitrate 1200mg soft gel insert and miconazole nitrate 2% external cream)

Dear Dr. Albrecht,

In accordance with the provisions of section 505(b)(1) of the Federal Food, Drug and Cosmetic Act and Title 21 of the Code of Federal Regulations, 21 CFR§314.50, Personal Products Company (PPC) herewith submits a New Drug Application for Miconazole Nitrate 1200mg Soft Gel Vaginal Insert and Miconazole Nitrate 2% External cream. While the application is eligible for submission as an efficacy supplement, we are submitting it as a new NDA for the administrative convenience of the FDA review division. This application has been preassigned NDA # 21-308.

We propose to market this product Over-the-Counter (OTC) under the tradename MONISTAT® 1 Combination Pack. It is indicated as a 1-day treatment of vaginal yeast infections (candidias) and includes a topical cream for relief of associated external symptoms, as needed.

The efficacy of miconazole nitrate (1200mg) soft gel vaginal insert and miconazole nitrate 2% external cream has been established in two pivotal clinical trials that demonstrated equivalence to Monistat® 7 Vaginal Cream in the treatment of vulvovaginal candidiasis. The results of these trials can be found in MONISTAT® DUAL-PAK®, NDA# 20-968 and by reference are incorporated into this submission

This application presents the results of an Actual Use Study (Protocol 98-006-P, "A Single Blind, Observational Study to Evaluate the Safety Profile of a 1,200 mg Miconazole Nitrate Ovule Combination Pack on the Treatment of Vaginal Yeast Infection"). The study was designed to evaluate the safety profile of the combination pack among medically unsupervised consumers who self-selected to use the study medication. The protocol and safety and actual-use measurements were developed with the Food and Drug Administration as a result of the meeting of March 3, 1999 between FDA and Personal Products Company.

Please refer to the Overall Reviewer's Guide located in the first volume (Vol. 1.1) of this NDA for information regarding the organization of this application.

Additionally, the required user fee of [redacted] was sent under separate cover to the FDA, Philadelphia, PA address on August, 31, 2000 (User Fee ID# 4016).

Please contact me directly with any questions you may have related to this submission. I can be reached at (732) 524-1515 or fax (732) 524-1344. After September 11, 2000, the numbers will be changed to (908)904-3745 and (908)904-3746 respectively.

Sincerely,
PERSONAL PRODUCTS COMPANY

Lynn Pawelski
Director, Regulatory Affairs

cc. Daniel Keravich, Project Manager (HFD-560)
Christina Chi, Ph.D., Project Manager (HFD 590)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 Grandview Road
Skillman, NJ 08558

August 31, 2000

Food and Drug Administration
P.O. Box 360909
Pittsburgh, PA 15251-6909

Re: Miconazole Nitrate 1200 mg Vaginal Insert and 2% External Vulvar Cream, OTC
NDA 21-308
FDA User Fee #4016

Dear Sir/Madam:

Enclosed please find a check in the amount of [redacted] covering the full payment of the User Fee (clinical data only) on the above referenced drug. The following information is provided as requested.

1. **Company Name and Address**

   Personal Products Company
   199 Grandview Road
   Skillman, NJ 08558

2. **Contact Person/Phone Number**

   Lynn Pawelski, SF 409
   Director, Regulatory Affairs
   732-524-1515 (until 9/8)
   908-904-3745 (as of 9/11)

3. **Application Number**

   NDA 21-308

4. **Statement whether the application contains clinical data, and whether or not it is a supplement.**

   Contains clinical data (actual use study) only and it is not a supplement.

Sincerely,

Lynn A. Pawelski

Lynn A. Pawelski
Director, Regulatory Affairs

Enclosure (Check)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 Grandview Road
Skillman, New Jersey 08558

October 11, 2000

Ms. Jane Axelrad
Associate Director for Policy (HFD-005)
Food and Drug Administration
Woodmont Office Complex 2
1451 Rockville Pike
Rockville, MD 20852

SUBJECT: REQUEST FOR REFUND
ORIGINAL NDA 21-308, Rx to OTC Switch
MONISTAT® 1 COMBINATION PACK

Dear Ms. Axelrad,

As the result of a conversation with Ms. Beverly Friedman on September 10, 2000, Personal Products Company (PPC) is requesting a User Fee refund for the above referenced submission. On August 31, 2000, as first directed by FDA, PPC submitted a check for [redacted] to the FDA Pittsburgh address (see attached letter), under FDA User Fee # 4016. It has since been determined by Ms. Friedman that the fee is not required.

The above referenced NDA is an application for an Rx to OTC Switch. While the application was eligible for submission as an efficacy supplement, it was submitted as a new NDA for the administrative convenience of the FDA review division. The submission does not contain any clinical data rather it contains an Actual Use Study as requested by the agency.

If you have any questions regarding this request, please contact me at (908) 904-3745 or in my absence, Barbara Popek at (908) 904-3708.

Sincerely,

Lynn A. Pawelski

Lynn Pawelski
Director, Regulatory Affairs

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 Grandview Road
Skillman, New Jersey 08558

October 24, 2000

Dr. Renata Albrecht
Acting Director, Division of Special Pathogen and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockvillle, MD 20850

SUBJECT: **Amendment to NDA 21-308**
Rx to OTC Switch
MONISTAT® 1 COMBINATION PACK
(miconazole nitrate 1200mg soft gel insert and miconazole nitrate 2% external cream)

Dear Dr. Albrecht,

In accordance with 21 CFR § 54.4(a)(1) and 314.50(k), Personal Products Company (PPC) is hereby submitting an amendment to NDA 21-308 for MONISTAT® 1 Combination Pack. Enclosed is a completed form FDA 3454 attesting to the absence of financial interests for the named clinical investigators involved in the Actual Use Study entitled "A Single Blind Observational Study to Evaluate the Safety Profile of a 1200mg Miconazole Nitrate Vaginal Ovule Combination Pack in the Treatment of Vaginal yeast Infection".

[redacted]

If you have any questions regarding this submission, please feel free to contact the undersigned at (908) 904-3745 or in my absence, Barbara Popek at (908) 904-3708.

Sincerely,

Lynn Pawelski
Director, Regulatory Affairs

cc: Daniel Keravich, Project Manger, DOTCDP (HFD-560)
Christina Chi, Project Manager, DSPIDP (HFD-590)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 Grandview Road
Skillman, New Jersey 08558

October 26, 2000

Dr. Renata Albrecht
Acting Director, Division of Special Pathogen and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockvillle, MD 20850

SUBJECT: **Amendment NDA 21-308**
Environmental Assessment (EA)/Switch
MONISTAT® 1 COMBINATION PACK
(miconazole nitrate 1200mg soft gel insert and miconazole nitrate 2% external cream)

Dear Dr. Albrecht,

Reference is made to a telephone request for information from the agency on October 19, 2000 regarding the Environmental Assessment (EA) for the above subject product. The expected Introduction Concentrations (EIC) have been calculated for all dosage forms and strengths included in the application or related applications. The EIC (based on the entire product line) is also used to determine of the application qualifies for a Tier 0 EA. Reference is also made to the final rule regarding the National Environmental Policy Act published July 29, 1997 and more specifically to the categorical exclusions provided in 21 CFR §25.31 as a result of that final rule.

Personal Products Company (PPC) has calculated the EIC for the ovule product line and has found that the application qualifies for a [redacted] A copy of the EIC calculation is attached to this letter.

At this time, Personal Products Company (PPC) is claiming a categorical exclusion for the subject new drug application. Per §25.31, the subject NDA qualifies for a categorical exclusion as the action increases the use of the active moiety, but the estimated concentration at the point of entry into the aquatic environment will be less than 1 part per billion. PPC has no knowledge of extraordinary circumstances that would affect this concentration calculation.

Reference is also made to a telephone conversation of October 26, 2000. Please be advised that the request for an Rx to OTC Switch for the above captioned product is for a full switch; the current MONISTAT® DUAL-PAK™ will cease to be available by prescription and would become the proposed over-the-counter, MONISTAT® 1 Combination Pack.

Should you have any questions regarding this amendment, please contact me directly at (908) 904-3745. Or in my absence, please contact Barbara Popek at (908) 904-3708.

Sincerely,

Lynn A. Pawelski
Director, Regulatory Affairs

cc: Christina Chi, Project Manager, DSPIDP (HFD-590)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

OCT 2 6 2000

NDA 21-308

Personal Products Company
Attention: Lynn A. Pawelski
Director, Regulatory Affairs
Division of McNeil-PPC, INC.
199 Grandview Road
Skillman, NJ 08558-9418

Dear Ms. Pawelski:

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: MONISTAT® 1 COMBINATION PACK containing miconazole nitrate 1200 mg soft gel vaginal insert and miconazole nitrate 2% external vulvar cream, for a one-day treatment of vaginal yeast infection (candidiasis) and a topical cream for the relief of associated external symptoms, as needed.

Review Priority Classification: Standard (S)

Date of Application: August 31, 2000

Date of Receipt: September 1, 2000

Our Reference Number: NDA 21-308

Unless we notify you within 60 days of the 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 October 31, 2000 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be July 1, 2001, and the secondary user fee goal date will be September 1, 2001.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal Service:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Special Pathogen and
Immunologic Drug Products, HFD-590
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Special Pathogen and
Immunologic Drug Products, HFD-590
Attention: Mega Document Room
9201 Corporate Blvd.
Rockville, Maryland 20850-3202

If you have any questions, please call Christina H. Chi, Ph.D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

/S/

Ellen C. Frank, R.Ph.
Chief, Project Management Staff
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-308

OCT 30 2000

Personal Products Company
Attention: Lynn A. Pawelski
Director, Regulatory Affairs
Division of McNeil-PPC, INC.
199 Grandview Road
Skillman, NJ 08558-9418

Dear Ms. Pawelski:

Please refer to your August 31, 2000 new drug application (NDA), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for MONISTAT® 1 COMBINATION PACK containing miconazole nitrate 1200 mg soft gel vaginal insert and miconazole nitrate 2% external vulvar cream, for a one-day treatment of vaginal yeast infection (candidiasis) and a topical cream for the relief of associated external symptoms, as needed.

We are reviewing the labeling section of your submission and have the following comment:

You are currently marketing tioconazole under the trade name MONISTAT 1 (in the Over-the-Counter market). The proposed trade name for this NDA 21-308, MONISTAT® 1 COMBINATION PACK (miconazole nitrate 1200 mg soft gel vaginal insert and miconazole nitrate 2% external vulvar cream), will confuse consumers and is therefore not acceptable. The use of the word "MONISTAT" as part of the trade name for this NDA 21-308 is acceptable, however, "MONISTAT 1" is associated with a different active ingredient (tioconazole).

We request your prompt written response (for example, a proposal for a new trade name for this product) as part of our evaluation of your NDA.

If you have any questions, please call Christina H. Chi, Ph.D., Regulatory Project Manager, at (301) 827-2127.

Sincerely,

/S/

Renata Albrecht, M.D.
Acting Director
Division of Special Pathogen and
Immunologic Drug Products (DSPIDP)
HFD-590
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

/S/

Charles Ganley, M.D.
Director
Division of Over-the-Counter
Drug Products (DOTCDP)
HFD-560
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Department of Health and Human Services | Public Health Service

Food and Drug Administration
Rockville, MD 20857

NOV 13 2000

Lynn Pawelski
Director, Regulatory Affairs
Personal Products Company
199 Grandview Road
Skillman, NJ 08558

RE: Personal Products Company NDA 21-308 Miconazole Nitrate 1200 mg Vaginal Insert and 2% External Vulvar Cream

Dear Ms. Pawelski:

This responds to your October 11, 2000, letter requesting a refund of the fiscal year (FY) 2000 application fee for new drug application (NDA) 21-308 paid under the Federal Food, Drug, and Cosmetic Act (the Act).[1] You state that Personal Products Company (PPC) submitted a check for [redacted] for the application on August 31, 2000. You also state that NDA 21-308 is an application for an Rx to OTC switch. You note that the application was eligible for submission as an efficacy supplement, but it was submitted as a new NDA for the administrative convenience of the FDA review division. You also state that the application does not contain any clinical data [for user fee purposes]; rather it contains an actual use study as requested by the Agency.

Our records show that FDA received NDA 21-308 on September 1, 2000, and was notified of the payment of [redacted] for user fee ID # 4016 on September 5, 2000. The Division of Special Pathogen and Immunologic Drug Products (DSPIDP) confirms that the application could have been submitted as a supplement to NDA 20-968. However, for administrative convenience, DSPIDP requested that the Rx to OTC switch be submitted under a new NDA.

DSPIDP also confirms that the supporting data included in the submission are not clinical data for user fee purposes as defined in the Interim Guidance: *Attachment E—Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees Under the Prescription Drug User Fee Act of 1992.*[2] Consequently, because this submission could have been submitted as a supplement that did not require clinical data as defined for user fee purposes, your request for a refund of the application fee is granted.

---

[1] Sections 735 and 736 of the Act (21 U.S.C. 379g and 379h).

[2] FDA, *Attachment E—Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees Under the Prescription Drug User Fee Act of 1992* (July 12, 1993). Available on the Internet at www.fda.gov/cder/pdufa/default.htm under Guidances.

Personal Products Co.
NDA 21-308

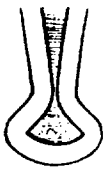
We have asked the FDA Office of Financial Management to refund the [redacted] application fee paid by PPC for NDA 21-308. [redacted] If the refund is not received within 30 days of the date of this letter, please contact Michael Roosevelt, Chief, Systems Accounting Branch, at 301-827-5088.

If you have any further questions concerning these matters or other user fee questions, please contact Michael Jones or Beverly Friedman at 301-594-2041.

Sincerely,

/S/

Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research



Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 Grandview Road
Skillman, New Jersey 08558

November 22, 2000

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products, HFD-590
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
Response to FDA Letter

Dear Dr. Goldberger:

Reference is made to a letter from the agency dated, October 30, 2000. Specifically the FDA noted that the proposed trade name for the subject NDA, "MONISTAT® 1 Combination Pack (miconazole nitrate 1200 mg soft gel vaginal insert and miconazole nitrate 2% external vulvar cream)" would confuse consumers and was therefore unacceptable, since "MONISTAT® 1" is associated with a different active ingredient (tioconazole).

Personal Products Company (PPC) understands the agency's concerns and is committing to address these concerns by changing the name of the tioconazole product. This name change will occur just prior to or concurrent with the over-the-counter launch of the subject NDA product. In no case will a tioconazole product branded as "MONISTAT® 1 (tioconazole)" and a "MONISTAT® 1 Combination Pack (miconazole nitrate)" be shipped concurrently. We would expect that there may be some period of time where both products could be in the marketplace, allowing for normal pull-though. PPC wishes to keep the original proposed tradename associated with the subject NDA, MONISTAT® 1 Combination Pack.

At this time we do not have a specific tradename to which we are ready to commit, for the tioconazole product, but it will not be "MONISTAT®". While the name MONISTAT® may appear somewhere on the product label as a flag or other material (e.g., from the makers of MONISTAT®), it would not intervene with the tradename, statement of identity or intended use.

Please note that the final name change and labeling for the tioconazole product will be submitted via [redacted] closer to its implementation date.

If you have any questions or wish to discuss this issue further, please contact me at (908) 904-3708. We trust that this response will assist in finally resolving this issue.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs

cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 Grandview Road
Skillman, New Jersey 08558

December 1, 2000

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308

MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to a teleconference between the FDA and Personal Products Company (PPC) on November 2, 2000. As a result of that teleconference, PPC is submitting the following information in support of NDA 21-308, MONISTAT® 1 Combination Pack:

1. A literature search on the safety of 1200mg miconazole nitrate ovule. The search resulted in only one article being identified: *"Single-Dose Miconazole Nitrate Vaginal Ovule in the Treatment of Vulvovaginal Candidiasis: Two Single-Blind, Controlled Studies Versus Miconazole Nitrate 100 mg Cream for 7 Days"* David H. Upmalis, M.D., Frederick L. Cone, B. A., Cathleen A. Lamia, M. S., Howard Reisman, M.D., Guillermo Rodriguez-Gomez, M.D., Larry Gilderman, D.O., and Lynn Bradley, M. S., C.R.N.M, J Women's Health & Gender-Based Medicine 9(4): 421-429. A copy of the publication is included as Attachment I.

2. Foreign Data:
   a. Canada – Sales and Adverse Experience data, submitted in the original NDA, August 31, 2000, are presented up to and including July 2000. There is no formal reporting requirement in Canada for adverse events. These reports are maintained internally at our Canadian corporate facility.
   b. Europe - The Periodic Safety Update Report (PSUR) in the original submission was for the period covering August 1998-August 1999. We are including two PSUR updates covering the period August 1999–August 2000 (Attachment II), one report is for gynecological formulations and the other for dermatological formulations. The patient exposure was calculated on the basis of the total number of ovules sold from August 1999 to July 2000. This information can be found on page 08-000010.

c. World Health Organization (WHO) – The data reported in the original submission is from October 1998. We have requested an up-dated report. As soon as it becomes available, we will forward it to the agency.
d. Global formulations – The portion of the product that is found inside the ovule is identical worldwide. They only difference in total formulation is in the ovule shell itself. In Europe, the formula includes a preservative since they allow for reprocessing of the material during production. For the U.S., that preservative has been eliminated, since reprocessing is not permitted in our process.
e. Product withdrawals – The subject product has not been withdrawn in any country due to reasons of safety. It has been withdrawn for commercial/business reasons, i.e. lack of sales.

3. U.S. Adverse Experience Reports – we are including, in this submission, copies of five Periodic AE Reports filed to NDA 20 –968, MONISTAT® DUAL-PAK™. They cover the period July, 1999-September, 2000. There were no serious, unexpected/expected ADEs or deaths reported during this period. There were a total of 15 non-serious ADEs from spontaneous, domestic sources reported (Attachment III).

4. The DATA SET and VARIABLE MAPPING, in Excel 97 and SAS Transport version 6.12, for the Actual Use Study (Protocol 98-006-P, "A Single Blind, Observational Study to evaluate the safety Profile of a 1,200 mg Miconazole Nitrate Ovule Combination Pack on the Treatment of Vaginal Yeast Infection") on CD ROM and hard copy (Attachment IV).

If you have any questions regarding this submission, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

cc:. Christina Chi, Ph.D., project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

December 20, 2000

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to a teleconference between the FDA and Personal Products Company (PPC) on November 2, 2000 and to the NDA Amendment submitted on December 1, 2000 to NDA # 21-308.

The following additional information is being submitted in support of NDA 21-308, MONISTAT ® 1 Combination Pack:

1. World Health Organization summary adverse reaction reports on Miconazole dated December 1, 2000.

If you have any questions regarding this submission, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manger, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

Faxed to Bill Nyeholt

January 3, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to a letter from Personal Products Company (PPC) dated November 22, 2000. In that letter, PPC acknowledged FDA's concern over the proposed trade name for the subject NDA, "MONISTAT® 1 Combination Pack (miconazole nitrate 1200 mg soft gel vaginal insert and miconazole nitrate 2% external cream)" and committed to address those concerns by changing the name of the current MONISTAT® 1 (tioconazole) product.

Reference is also made to a teleconference between FDA and PPC on December 7, 2000. During that conversation, PPC was asked to provide some possible timing as to the overlap of both MONISTAT 1 products being in the marketplace at the same time.

The estimated time for product to move through supply chain (warehouse, trade, off shelf) is 18 weeks. If we assume an August 31, 2001 approval of MONISTAT® 1 Combination Pack, NDA 21-308:

1.Cease shipment of current MONISTAT® 1 (tioconazole) packaging	August 31, 2001*
2. Begin to ship tioconazole product with new name	August 31, 2001*
3. Prepare final package copy for new MONISTAT® 1 Combination Pack	September 3, 2001*
4. Begin to ship new MONISTAT 1 Combination Pack	November 5, 2001*
5. New MONISTAT 1 Combination Pack on shelf	December 3, 2001*
6. Target date for current MONISTAT 1 packaging to be off shelf	January 3, 2002*

(*Approximate dates)

Based on expected timings, there could be a one-month overlap when both Monistat 1 products would be on the shelf.

If you have any questions regarding this information, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

March 19, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to teleconferences dated Jan. 25, Feb.15 and Feb. 27, 2001 between FDA and Personal Products Company (PPC). As the result of these teleconferences, PPC is submitting the following information in support of NDA 21-308, MONISTAT® 1 Combination Pack:

1. The Annotated Physician Contact Sheets for Actual Use Study (Protocol 98-006P, "A Single Blind, Observational Study to Evaluate the Safety Profile of a 1,200 mg. Miconazole Nitrate Ovule Combination Pack on the Treatment of Vaginal Yeast Infection").
2. A Modified Data Set, on CD – ROM, for the above mentioned Actual Use Study providing one record for each subject for thirty previously sent SAS data sets. Two additional copies were sent to Dr. Linda Hu's attention on March 15, 2001.

If you have any questions regarding this submission, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

cc. Christina Chi, Ph.D., Project Manger, DSPIDP (HFD-590)
Daniel Keravich, Project Manger, DOTCDP (HFD-560)
Linda Hu, M.D., Medical Officer, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

March 23, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to teleconferences dated Jan. 25, Feb.15 and Feb. 27, 2001 between FDA and Personal Products Company (PPC). Reference is also made to letters from PPC to FDA dated November 22, 2000 and February 12, 2001 and from FDA to PPC dated October 30, 2000. As a result of these teleconferences and letters, we are providing additional information on two issues. These issues are the name change for the Tioconazole product and the timing of the possible overlap in the marketplace.

1.NAME FOR TIOCONAZOLE PRODUCT:

Due to the agency's concern of consumer confusion over having two products, with different active ingredients, named MONISTAT® 1, PPC agreed to change the name of the product containing Tioconazole. Based on two consumer studies conducted and fielded by contracted 3rd parties, consisting of a "Shopping Simulation Study" and a "Pre-BASES Concept Test", PPC has chosen to call the Tioconazole product "1-DAY™".The

"Shopping Simulation Study" creates a typical shelf setting that a consumer would see in a grocery store, drug store or a mass market. The shelves are stocked with actual labeled product, including graphics, from different competitors (named brands and store brands) within the VVC category. Several different shelf sets were created incorporating new, proposed and existing products. The consumer is only exposed to the labeled package of the product and a price for the item. They are then asked to choose the product that they would purchase if they had a vaginal yeast infection. The results of the study show that a consumer understood that the 1-DAY™ package conveyed a Vaginal Treatment for yeast infections identical to products such as VAGISTAT®1 or MONISTAT®3.

The "Pre-BASES Concept Test" exposed consumers to a photograph of a product along with copy that described the product. The consumers were then asked various questions regarding their possible product purchase intent, including how likely they were to purchase the product, and how much they liked the product and it's positioning. The results of this study showed that their purchase intent and number of annual purchase occasions for a product labeled "1-DAY™" was consistent with any other VVC Treatment. Further, consumers did not feel that this product was "new and different" from other VVC topical treatments.

The agency has raised the concern that consumers might confuse our product with ONE A DAY® vitamins and supplements. While we understand the agency's concern around pharmacists dispensing drugs with similar names, the circumstances surrounding the consumer purchase of an OTC Drug Product is different.

In the Prescription arena, the pharmacist dispenses each product as needed from bulk stock bottles, i.e. 500 or more tablets per bottle. The similarity in name can cause the pharmacist to pick up and dispense the wrong medication.

In the consumer OTC Drug arena, products are individually packaged in accordance with their respective NDA or in the compliance with a Final Monograph. In each case, the principal display panel clearly states the name of the product with the corresponding Statement of Identity. In the case of VVC products, they are all clearly labeled as "Vaginal Antifungals". Vitamins and supplements are also clearly labeled as to their purpose, can be positioned for use by either men or women, people over 50, and in the case of supplements, the structure/function area that the product is intended for.

When you look at all of the current OTC Vaginal Antifungal products available in the marketplace, the outward appearance of the products are all presented in similar cartons, i.e. the shape of the box is rectangular. The contents, depending on the treatment duration, are: a tube of cream with an applicator, pre-filled applicators, or suppositories. For ONE A DAY® vitamins and supplements, their packaging is a vertical carton with their primary packaging being a sealed plastic bottle. The contents of the bottle are either tablets or softgels with the smallest count size available of 30 tablets.

In most stores, products are grouped by categories. VVC products are generally found with other feminine hygiene products such as sanitary protection, tampons, douche products and vaginal contraceptives. We are not aware of any instance where the feminine hygiene section of a store is located adjacent to the dietary supplements or multivitamins. There is also a significant price difference between these two categories of products. VVC treatment products generally retail for $14.99 which is twice as much as the average retail price of $6.99 per unit for "ONE A DAY®" vitamins.

As we indicated in the letter dated November 22, 2000, we will include, as a flag or other material, the phrase "from the makers of MONISTAT®" somewhere on the product label. It will not intervene with the tradename, statement of identity or intended use. We feel that this will also help consumers make a clear connection to VVC treatment. Given these reasons, we believe that the possibility of consumers confusing our "1-DAY™" VVC treatment with any "ONE A DAY®" item and/or attempting to use them interchangeably is zero.

Please note that the final name change and labeling for the tioconazole product will be submitted via [redacted]

2. TIMING OF POSSIBLE PRODUCT OVERLAP IN THE MARKETPLACE

From FDA approval of NDA #21-308, it will take approximately 15 weeks to launch new MONISTAT® 1 Combination Pack. It will take 18 weeks to allow for current MONISTAT® 1 (Tioconazole) to move through the supply chain. And it will take 24 weeks to have 1-DAY™ on the shelf. Making the anticipated overlap for the two MONISTAT® 1 products approximately three weeks.

We do have concerns with being out of stock due to the 24 week timeframe for launching the 1-Day™ product. The reason it will take 24 weeks for the new "1-DAY™" is the long lead time (12 weeks) to produce the foil overwrap. In order to shorten this lead time we have asked [redacted] if we could print a "generic" overwrap as an interim measure. The "generic" overwrap would contain all of the current information with the exception of a Brand name. The product would only be identified as "Tioconazole 6.5% Vaginal Ointment Antifungal". We have provided a copy of the proposed label to [redacted] and they have agreed to discuss it with the OTC Division. If we are allowed to use the "generic" overwrap, we would be able to cut at least 10 weeks off the timetable. This shortened timetable would ensure the continued availability of a one day product and will help facilitate the described overlap of the MONISTAT® 1 (tioconazole) and MONISTAT® 1 Combination Pack to only three weeks.

If you have any questions or wish to discuss this issue further, please contact me at (908) 904-3708. We trust that this response will assist in resolving these issues.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

March 30, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to teleconferences dated Jan. 25, Feb.15 and Feb. 27, 2001 between FDA and Personal Products Company (PPC). During these teleconferences, FDA raised concerns regarding two issues identified from our submitted Actual Use Study that they viewed as non-compliance. The first observation was that 59.4% of subjects chose to use the product although they stated that they had not previously had a yeast infection diagnosed by a physician. The second observation was that 23.6% of the 242 consumers who did not experience symptom relief in eight days used an additional product instead of contacting their physician, however 16.5 % of this sub-group consulted a health care professional.

Background:
The protocol for the Actual Use Study entitled: "A Single Blind, observational Study to Evaluate the Safety Profile of a 1,200 mg Miconazole Nitrate Ovule Combination Pack of the Treatment of Vaginal Yeast Infection" was developed in conjunction with the FDA. The primary objective of the study was to evaluate the safety profile of a miconazole nitrate combination pack among medically unsupervised consumers who self-selected to use the study medication for the treatment of vaginal yeast infections. The secondary

objective was to document patterns of product use in this simulated consumer environment.

A total of 1355 consumers enrolled in the study. The results clearly demonstrate that the product is well tolerated, and a benign safety profile was demonstrated by an exceptionally low incidence of serious adverse events. Therefore, the first objective was accomplished.

The design of the Actual Use Study, a "large, simple" study done in a simulated consumer setting was somewhat unconventional and, to our knowledge, has not been conducted in this therapeutic area before. The non-compliance detected in this study may be provocative in that the data would suggest failure to heed a primary label instruction to see a physician if the consumer has not had a previously diagnosed yeast infection. 60% of consumers who used the product in this study reported not having been previously diagnosed with a yeast infection. However, a further investigation of the data shows that 85% of consumers who used the medication stated that they had a previous yeast infection.

While it is these results in the second objective that has caused concern for the agency, we can incorporate into the analysis, an Awareness and Usage Study that was sponsored by PPC in 1999 and a MONISTAT® Usage Survey for further insight into consumer behavior.

AWARENESS AND USAGE STUDY:
The purpose of this study was to examine women's awareness, attitudes, and experiences with vaginal yeast infections, including their treatment habits and practices. The study looked at a representative sample of 810 women, aged 16-65, with approximately 200 subjects in each Census region. After the representative sample was completed, supplemental interviews were conducted to boost sample sizes for analysis. The total number of interviews in each of three sample groups were:

1. Recent Sufferers (suffered VVC within past 2 years)	423
2. Past Sufferers (suffered VVC over 2 years ago)	390
3. Non-sufferers (never suffered VVC)	404

Among all women in this age group, 65% have had at least one yeast infection in their life. Within the past two years, 43% have suffered yeast infections, with 30% suffering one within the past year. Among women who have had a yeast infection within the past two years, 65% have suffered multiple infections within this time period.

Questions regarding the consumer's general knowledge about a yeast infection and what action would they take were open-ended (verbatim). The results of the study showed that the consumer's knowledge about yeast infections is directly related to her experience with them. Recent sufferers, particularly those who suffer infections frequently, are fairly knowledgeable with regard to causes, triggers, and treatment options, while women who have never had an infection or who only suffered once, are much less aware.

The study also showed that the doctor continues to be a major influence regarding yeast infection treatment, particularly among older women.

1) 70% of first time sufferers consulted a doctor.
2) 87% of past sufferers have consulted a doctor at some point regarding yeast infections.
3) 55% of all recent sufferers consulted a doctor for their last infection.
4) 37% of women who have had multiple yeast infections in the past two years say that they always or frequently consult a doctor when they get a yeast infection.

When recent sufferers were asked what they do when they first suspect a vaginal yeast infection, about 48% volunteered that they either call or visit a doctor, while 48% volunteered using a medication. Frequent sufferers are more inclined to just go get a medication, while those who have had only one yeast infection are more likely to visit their doctor.

Among women who have never had a yeast infection, 68% said that they would call the doctor's office, while 32% said they would just go to the store to buy a product. Of the women who would just go to the store, 15% said they would choose a product, 9% would consult the pharmacist regarding a product choice and 9% would consult a friend or relative.

Based on this study, it is clear to us that Doctors are the #1 source of information for yeast infection sufferers and almost all sufferers say the doctor is at least somewhat influential in their brand selection. Past and non-sufferers cite doctor recommendations as the most important feature to consider when choosing a brand to use.

MONISTAT® Usage Study:
This study was implemented on June 30, 1999 and completed on July 9, 1999. It was conducted by our internal Information Center and surveyed 200 consumers that called into our 800 number.

The results of this survey showed:

1) 63% said that they consulted a doctor to determine if they had a yeast infection.
2) 89% said that they consulted a doctor the first time they had a yeast infection.
3) 88% said that they were aware that the product packaging and advertising tell you to go see a doctor.

Looking at the totality of the available data, it would suggest that women are reading and understanding the label as proposed in our submission and are self-diagnosing and treating their vaginal yeast infections correctly.

In order to further assist consumers in understanding the need for physician intervention in the diagnosis of first-time yeast infections, PPC will suggest one or more of the following post-approval programs:

- A recently developed consumer education brochure-wide will be widely distributed to consumers and pharmacists.
- Launch a CME program on the treatment of vaginal yeast infections for pharmacists, who are a valuable source of information for consumers purchasing OTC products
- Make "First time sufferers, see your Dr." more prominent in new advertising and print executions (Our tracking programs indicate that Monistat advertising and awareness programs reach 90% of target consumers.)
- Add a banner to homepage of website that specifically says... "First time suffers, see your doctor before using"
- Address the issue more prominently in the Monistat Frequently Asked Questions (FAQ) (seen on website, monthly press releases, and various professional sales materials).
- Public Relations (PR) effort directed towards editors of leading women's magazines to write articles about appropriate physician consultation before using OTC products.
- Investigate a possible education program in conjunction with the CDC.

As this is most certainly a category issue and in order to achieve maximum consumer education, we would request that these types of programs be recommended to all companies that sell products in the VVC category.

If you have any questions or require any further information, I can be reached at (908) 904-3708 (phone) or (908) 904-3748 (fax).

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

April 12, 2001

Dr. Charles Ganley, M.D., Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Over-the-Counter Drug Products (HFD-560)
Attn: Division Document Room
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
Response to FDA Teleconference

Dear Dr. Ganley:

Reference is made to letters from Personal Products Company (PPC) to FDA, dated November 22, 2000 and March 23, 2001 and a teleconference dated April 3, 2001. In each of the letters, PPC agreed to change the name of the current MONISTAT® 1 (Tioconazole) product and indicated that we would maintain the use of the name MONISTAT® somewhere on the product label as a flag or other material (e.g. "from the makers of MONISTAT®") but it would not intervene with the tradename, statement of identity or intended use.

During the teleconference of April 3, 2001, PPC was informed that the FDA would approve the proposed name of "1-DAY™", but was objecting to the use of the MONISTAT® Brand name anywhere on the label, including it's use in our 800 telephone number or website.

As the result of the teleconference and FDA's objection to the use of MONISTAT® trademark in marketing copy, the telephone number which the consumer would use to report adverse events, and the website, PPC requests that the agency reconsider their decision. We will address each of the uses for the MONISTAT® name individually.

"FROM THE MAKERS OF MONISTAT®"

We strongly believe that this is an appropriate and truthful statement in connection with the 1-DAY™ product. Consumers are exposed to the terminology "from the makers of..." or variations of this term on a daily basis. When a company launches a new brand, it is almost always tied to another well known brand name within their portfolio of products. For example, "FLEXAGEN, From the makers of Advil" or "AQUAFINA, a product of The Pepsi Company".

Advertisements for newly released movies are generally positioned as "from the Director of". The same holds true for television programs. Special programs are positioned as "A Hallmark® Presentation", "Brought to you by National Geographic", or "Sponsored by Crest". Charitable Organizations, in promoting fund raising events, always advertise the event with the term "Sponsored by" followed by a list of corporate sponsors.

When a product, movie, television program, charitable organization, etc. use these terms, they are providing the consumer with an expectation depending on their respective reputation. When a new product launch is tied to a well-known national brand name, the expectation is a "quality" product. When a television program is from "Hallmark®", consumers usually expect a "family" program and when charitable organizations list corporate sponsors, it adds an air of legitimacy to the fundraiser.

In this case, the truthful statement "from the makers of Monistat" is intended to convey the message that this is a quality product that is being made available to consumers by Personal Products Company (PPC), the makers of Monistat. It is also intended to be an endorsement of the product by PPC. In other words, consumers can rely on this product for its quality and efficacy since it is endorsed by the makers of the most respected brand in the category.

The Agency has offered as a reason for disagreeing with the statement on the product package that the statement conveys that the product was manufactured by PPC. We respectfully believe that this position is contrary to the Agency's own regulations. As you know, FDA's regulations do not require that the name of the product manufacturer appear on the product label. Rather, the distributor's name may appear (21 CFR 201.1). In permitting this, the Agency does not appear to be concerned that consumers will be confused between the distributor and the manufacturer. In fact, the "1-DAY™" package will include the statement "Distributed by Personal Products Company, a division of McNeil-PPC, Inc" to clarify what PPC's role is with respect to the product.

With regard to sufferers of VVC, the large majority (84%)[1] say that they "always stick to the brand they know and trust". They also say that they are leery about trying a new brand without checking with their doctor (66%)[1], all products look and sound the same (62%)[1] and admit it is confusing what to buy (56%)[1]. Only one-third (33%)[1] of women agreed with the statement "All products available are similar so I buy the brand that is the cheapest."

"MONISTAT®" is by far the most recognized brand in the category of vaginal yeast infection products. Over two-thirds (68%) of women who have suffered yeast infections volunteer the brand name "MONISTAT®". Recent yeast infection sufferers are the most familiar with the brand, with almost three-fourths volunteering the MONISTAT brand name unaided. When aided to the brand name, MONISTAT enjoys almost universal awareness (97%) among yeast infection sufferers. In

[1] Monistat Awareness and Usage Study, 1999

contrast, only 14% of women volunteered the brand name "VAGISTAT®" unaided and 62% recognized the name when it was provided.

MONISTAT® is the most familiar brand to non-sufferers as well, with over half (52%) mentioning the brand unaided and 90% said that they had heard of the brand when aided to the name (8% for VAGISTAT® unaided, 55% aided). Awareness of "MONISTAT®" far surpasses all other brands in the category among non-sufferers on both and unaided and aided basis.

Consumer usage of "MONISTAT®" is driven primarily by Doctor recommendations and familiarity with the brand.

THE 800 TELEPHONE NUMBER:

The MONISTAT® toll free number is a nurse-staffed answer line provided to consumers not only to report adverse events or problems with any of the vaginal yeast infection products, it also serves as a source of information on yeast infections. MONISTAT® is the only OTC VVC brand that offers the consumer a fully trained nurse-staffed answer line. Our nurses are trained to direct "first time sufferers" to contact their physician. The nurses will also direct the consumer to contact their physician if it appears they are suffering from a "recurrent' infection or if they may have an infection other than one caused by yeast. We feel that this is a valuable service for the consumer. While we also provide the numeric telephone number on the carton and insert, which could be discarded, it is easier for the consumer to remember to dial MONISTAT if case of emergency.

THE MONISTAT WEBSITE:

One of the issues raised by FDA in the review of NDA 21-308 was the need for more detailed consumer education. We have designed our website to be a valuable tool for the consumer. It is divided into six sections: Home, The Basics, Choose Your Cure, Health Tips, FAQ's and a Site Map, all of which is accessible in both English and Spanish. At the end of each section is a reminder to call our toll free number if the consumer has any other questions or if they need further information. For example, the section entitled "The Basics" provides the consumer with basic information about a yeast infection and how to recognize it's symptoms. It instructs someone who thinks they have a yeast infection for the first time to "see your doctor". In "Choose Your Cure" it provides information on possible cures and explains the difference in each of our products, including the tioconazole product, in order to help a consumer choose a product that fits their needs.

As noted above, it is extremely important to the consumer that they have a brand that they "know and trust". By placing the statement "from the makers of MONISTAT"on the fifth panel, the toll free number and the website address on the package and insert, we are providing them with the reassurance that the product is of the same "quality" that they have come to know and trust, that they can rely on having the same level of medical competence that they have come to expect if there is an emergency or just to provide them with sound medical advice to see their physician.
By not providing this information to the consumer, we feel that we would be doing them a disservice. We also believe that removing this information from the package would be contrary to

the direction that is being provided from FDA in providing essential consumer education materials in support of the approval of NDA 21-308.

We would also request that the review of NDA 21-308 continue as scheduled. We will be providing copies of our final labeling for the Tioconazole to Bristol Myers Squibb. Once they have reviewed the labeling for accuracy in duplication of FDA requirements, they will provide it to the agency.

If you have any questions, or wish to discuss the issue further, please call me at (908)-904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Daniel Keravich, Project Manager, DOTCDP (HFD-560)
Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

May 4, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to a teleconference between the Food and Drug Administration (FDA) and Personal Products Company (PPC) on April 23, 2001. During that teleconference, FDA requested that PPC submit additional data in support of NDA 21-308, MONISTAT® 1 Combination Pack.

FDA has requested that PPC propose changes to the Drug Fact Label for the above captioned product. This is to address the agency's concern from the Actual Use Study, entitled: "A Single Blind, Observational Study to Evaluate the Safety Profile of a 1,200 mg Miconazole Nitrate Ovule Combination Pack for the Treatment of Vaginal Yeast Infection", that showed some evidence that consumers were reading and understanding the label but not heeding the warnings regarding the correct use of the product. In response to that request, PPC is providing the agency with four possible back label scenarios. We have based these proposals on our knowledge and understanding of what draws consumers attention to product communication on package, as well as in print advertising. While this expertise is generally applied to communicating product benefit information, it is helpful in this case as well.

1. Using normal bolding (black in color) for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").
2. Using bolded headings and bullets in color for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").
3. Using bolded heading, bullets and all text in color for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").
4. Using a colored shaded background for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").

We are providing these proposals in Drug Fact format as hard copy and on two disks in Word format.

The agency requested updated data on the number of units that have been prescribed in the US and the number of OTC units sold in Canada and in Europe. That information can be found in the attached tables.

We are also providing the agency with a retain sample of the actual carton and package insert that was used for the Actual Use Study.

As discussed during the teleconference, PPC will commit to a Post Approval, Phase IV study to track the impact of these proposed label changes.

If you have any questions or require any further information, I can be reached at (908) 904-3708 (phone) or (908) 904-3748 (fax).

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

May 25, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr, Goldberger:

Reference is made to a letter from Personal Products Company (PPC) to the Food and Drug Administration (FDA) dated May 4, 2001 in which PPC committed to a Post Approval, Phase IV study to track the effect of making FDA proposed changes to the MONISTAT® 1 Combination Pack carton on consumer compliance. Reference is also made to conference calls on May 16, 2001 and May 22, 2001. During these conference calls, FDA requested that PPC submit color copies of the proposed front panel carton copy for this NDA. FDA also confirmed that the target approval date for this NDA is June 28, 2001.

At this time, PPC is submitting a draft protocol entitled: "A Postmarketing Study to Evaluate Conditions of Use of OTC 1,200 mg. Miconazole Nitrate Soft Gel Vaginal Ovule Combination Pack in the Treatment of Vaginal Yeast Infection" for your review. We are also providing color copies of the proposed Principal Display Panel for the MONISTAT® 1 Combination Pack carton.

If you have any questions, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Daniel Keravich, Project Manager, DOTCDP (HFD-560)
Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590) (enclosure: copies of proposed PDP, current Rx package and protocol)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

June 8, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to a fax received by Personal Products Company (PPC) on May 23, 2001 from the Food and Drug Administration (FDA) and a teleconference dated June 5, 2001. The fax is a draft of FDA's proposed changes to the Drug Facts panel and Consumer Information Leaflet, while the teleconference provided PPC with some changes to the proposed Principal Display Panel (PDP) for NDA 21-308, MONISTAT® 1 Combination Pack.

PPC has reviewed the proposed changes and has the following comments:

DRUG FACTS PANEL:

1. PPC accepts the following FDA additions:
   a). Under the heading **Ask a doctor before use if you have** the addition of "You may have a more serious condition." after "lower abdominal, back or shoulder pain,.....discharge."
   b). Under the heading **Stop use and ask a doctor if,** the addition of "or hives".
   c). Under the heading **Directions** the change from "complete instructions" to "complete directions and information" at the end of the sentence beginning "before using this product....". Also the addition of "Throw applicator away after use."in the third bullet.
2. Under **Other Information** we would suggest placing the statement "do not purchase if carton is open" as the first bullet. PPC does not feel that it is necessary to elaborate on this statement since the outer carton flaps are glued and any attempt to tamper with the package would be evident to the consumer, as per 21 CFR 211.132(c).

1. Using normal bolding (black in color) for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").
2. Using bolded headings and bullets in color for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").
3. Using bolded heading, bullets and all text in color for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").
4. Using a colored shaded background for those areas that contain the information regarding a first time yeast infection ("Ask a doctor before use if you have"), and the section on symptom improvement ("Stop use and ask a doctor if").

We are providing these proposals in Drug Fact format as hard copy and on two disks in Word format.

The agency requested updated data on the number of units that have been prescribed in the US and the number of OTC units sold in Canada and in Europe. That information can be found in the attached tables.

We are also providing the agency with a retain sample of the actual carton and package insert that was used for the Actual Use Study.

As discussed during the teleconference, PPC will commit to a Post Approval, Phase IV study to track the impact of these proposed label changes.

If you have any questions or require any further information, I can be reached at (908) 904-3708 (phone) or (908) 904-3748 (fax).

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

June 22, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT -POST APPROVAL, POST MARKETING STUDY COMMITMENT

Dear Dr. Goldberger

Reference is made to the submission of a draft proposal and a second draft entitled "A Postmarketing Study to Evaluate Conditions of Use of OTC 1200 mg Miconazole Nitrate Soft Gel Vaginal Ovule Combination Pack in the treatment of Vaginal Yeast Infection", by Personal Products Company (PPC) to the Food and Drug Administration on May 25, 2001 and June ~~16~~ 15, 2001 respectively. Reference is also made to a fax received from FDA on June 13, 2001, and two conference calls between FDA and PPC on June 15, 2001 and June 19, 2001.

In response to both the fax and the conference calls, PPC is submitting a revised draft proposal for the postmarketing study entitled "A Postmarketing Study to Evaluate Conditions of Use of MONISTAT® 1Combination Pack in the Treatment of VVC" for your review. (The title has been change to reflect the product name.)

Since PPC is fully committed to completing this study in a timely fashion, we would like to be able to finalize a protocol as soon as possible. If this draft proposal is acceptable to the FDA, we will provide the agency with a draft protocol by Wednesday, June 27, 2001. It is our expectation that this study may take a minimum of 1-2 years to complete.

If you have any question, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Product Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Brad Leissa,M.D., Team Leader, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)
Linda Hu, M.D., Medical Officer, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

June 27, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – Postmarketing Commitment

Dear Dr. Goldberger:
Reference is made to the fax dated June 25, 2001 from the Food and Drug Administration (FDA) to Personal Products Company (PPC), regarding the labeling and Postmarketing Study for the above captioned product. Reference is also made to letters dated May 4, 2001, June 22, 2001 and June 26, 2001 from PPC to FDA.

PPC commits to the completion of the Postmarketing Study entitled "A Postmarketing Study to Evaluate Conditions of Use of MONISTAT® 1 Combination Pack in the Treatment of Vulvovaginal Candidiasis". We will be submitting a draft protocol/questionnaire for your approval by July 16, 2001.

If there are any questions or if you require any additional information, I can be reached at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Brad Leissa, M.D., Team Leader, DSPIDP (HFD-590)
Lorene Kimzey, R.N, DSPIDP (HFD-590)
Leo Chan, RPh., CSO, DSPIDP (HFD-590)
Diana Willard, Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)
Babette Merritt, CSO, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

June 26, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to the fax dated June 25, 2001 from the Food and Drug Administration (FDA) to Personal Products Company (PPC) regarding the labeling and Postmarketing Study for the above captioned product.

Section 1 Reviewer's Comments:

A. Comments on item # 9: PPC commits to making the agreed upon changes to the statement of identity to be consistent with the USP designations, "Miconazole Nitrate Vaginal Insert, 1200 mg and Miconazole Nitrate Cream, 2%." This statement of identity will be consistent across the PDP, Consumer Information Leaflet, 9 gram tube and blister pack.

B. Drug Facts Panel: PPC commits to making the changes outlined in items 1, 2, 4 5, and 6. For number 3, as agreed, we will maintain the warfarin warning to be consistent with the MONISTAT® 3 Cream Combination Pack Label. The warning will read: **"Ask a doctor or pharmacist before use if you are** taking the prescription blood thinning medicine warfarin, because bleeding or bruising may occur"

C. Consumer Information Leaflet: PPC commits to making all changes outlined in this section.

D. Attachment 2: 9 gram tube: PPC commits to making the changes outlined in this section. FDA has agreed that we may use our current inventory of 9 gram tubes for a period not to exceed six

months from approval. All requested changes, with the exception of the new statement of identity, have been made to our current inventory.

E. Attachment 3: Blister Pack: PPC commits to changing the statement of identity on the Blister Pack to be consistent, Miconazole Nitrate Vaginal Insert 1200 mg. We also commit to use the approved labeling after exhausting current inventory.

F. Attachment 5: Carton (excluding PDP): PPC commits to making the top, bottom and side panels consistent with the final decision on the statement of identity.

We are also including our response to FDA comments on our draft proposal for a study entitled "A Postmarketing Study to Evaluate Conditions of Use of MONISTAT® 1 Combination Pack in the Treatment of Vulvovaginal Candidiasis".

If you have any questions, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Brad Leissa, M.D., Team Leader, DSPIDP (HFD-590)
Lorene Kimzey, R.N, DSPIDP (HFD-590)
Leo Chan, RPh., CSO, DSPIDP (HFD-590)
Diana Willard, Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)
Babette Merritt, CSO, DOTCDP (HFD-560)

Personal Products
COMPANY

DIVISION OF McNEIL-PPC, INC.
199 GRANDVIEW ROAD
SKILLMAN, NJ 08558

June 29, 2001

Dr. Mark Goldberger
Director, Division of Special Pathogens and
Immunologic Drug Products (HFD-590)
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Boulevard
Rockville, MD 20850

NDA 21-308
MONISTAT® 1 Combination Pack
NDA AMENDMENT – REQUEST FOR ADDITIONAL INFORMATION

Dear Dr. Goldberger:

Reference is made to the fax dated June 29, 2001 from the Food and Drug Administration (FDA) to Personal Products Company (PPC) regarding the approval of MONISTAT® 1 Combination Pack.

The carton label that is attached to the approval contains one mistake in the Drug Facts portion of the back label, the entire warfarin warning is bolded. We will correct that in the final printed label, prior to launch, so that it reads "**Ask a doctor or pharmacist before use if you are** taking the prescription blood thinning medicine warfarin, because bleeding or bruising may occur"

If you have any questions, please call me at (908) 904-3708.

Sincerely,

Barbara Popek

Barbara Popek
Manager, Regulatory Affairs
Personal Products Company

Cc: Christina Chi, Ph.D., Project Manager, DSPIDP (HFD-590)
Daniel Keravich, Project Manager, DOTCDP (HFD-560)
Babette Merritt, CSO, DOTCDP (HFD-560)