CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-261

ADMINISTRATIVE DOCUMENTS

NEW DRUG APPLICATION
NDA 21-261
MONISTAT® 3 Vaginal Cream Combination Pack
ITEM 13: PATENT INFORMATION

As per 21 CFR § 314.53, we hereby submit the following patent information.

(i) Patent Number: 5,514,698

Date of Patent Expiration: March 21, 2014

(ii) Type of Patent: Drug Product

(iii) Patent Owner: Ortho Pharmaceutical Corporation*, Raritan, NJ

(iv) Patent Owner does have a place of business in the United States.

The undersigned declares that Patent No. 5,514,698 covers the formulation and composition of the miconazole nitrate 4% vaginal cream and 2% external vulvar cream.

* Ortho Pharmaceutical Corporation is an affiliate of Johnson & Johnson. Advanced Care Products (ACP) was a division of Ortho Pharmaceutical Corporation and has since been merged with Personal Products Company.

EXCLUSIVITY SUMMARY for NDA # 21-261 SUPPL # _____
Trade Name Monistat-3® Combination Pack
Generic Names: Miconazole nitrate ceam 4% & Miconazole nitrate external cream 2%

Applicant Name Personal Products HFD- 560
Approval Date 2-2-01

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/_X_/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /X__/

      If yes, what type(SE1, SE2, etc.)? _____

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES /___/ NO /_X_/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      N/A

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

      N/A

d) Did the applicant request exclusivity?

YES /___/ NO /_X_/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

_____

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No - Please indicate as such).

YES /X/ NO /_ _/

If yes, NDA # NDA 17-450 Miconazole nitrate 2% cream & NDA 20-827 Miconazole nitrate 4% cream

Drug Names: Monistat-7® Cream, & Monistat-3® Cream

NOTE: This is a co-packaging of two existing NDA products

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # _____ YES /___/ NO /___/ Explain: _____

_____

_____

Investigation #2

IND # _____ YES /___/ NO /___/ Explain: _____

_____

_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____

Daniel Keravich 2-14-01
Signature of Preparer Date
Title: Project Manager

Charles Ganley /S/ 2/14/01 2-14-01
Signature of Office of Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Personal Products Company	01/04/01
TELEPHONE NO. *(Include Area Code)*	**FACSIMILE (FAX) Number** *(Include Area Code)*
908-904-3708	908-904-3748
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):* 199 Grandview Road, Room SF407 Skillman, New Jersey 08558	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)*
21-261

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
miconazole nitrate, USP	MONISTAT 3 Cream Combination Pack

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*
1-[2,4-dichloro-β-(dichlorobenzyloxy) phenethyl] imidazole

CODE NAME *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
vaginal cream & external cream	4% vaginal cream & external cream	intravaginal and external

(PROPOSED) INDICATION(S) FOR USE:
treatment of vulvovaginal candidiasis

APPLICATION INFORMATION

APPLICATION TYPE *(check one)*
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505 (B)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION *(check one)*
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION _____

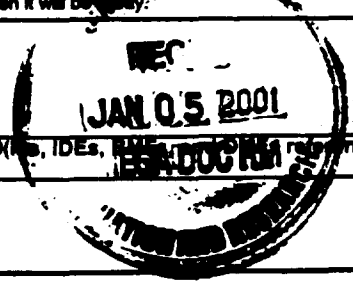
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ PRIOR APPROVAL (PA)

REASON FOR SUBMISSION
Revised Draft Labeling

PROPOSED MARKETING STATUS *(check one)* ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 — THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

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



Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, [illegible] referenced in the current application)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved : OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Personal Products Company	03/31/00
TELEPHONE NO. *(Include Area Code)* 732-524-1515	FACSIMILE (FAX) Number *(Include Area Code)* 732-524-1344

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*:
691 Route 1 South
P.O. Box 6024
North Brunswick, New Jersey 08902 USA

AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 21-261

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
miconazole nitrate, USP	MONISTAT 3 Cream Combination Pack

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)* 1-[2,4-dichloro-β-(dichlorobenzyloxy) phenethyl] imidazole nitrate

CODE NAME *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Vaginal Cream and External Cream	4% vaginal cream and 2% external cream	intravaginal and external

(PROPOSED) INDICATION(S) FOR USE:
Treatment of vulvovaginal candidiasis

APPLICATION INFORMATION

APPLICATION TYPE (check one)
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one)
☒ ORIGINAL APPLICATION ☐ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION
Secondary Packaging

PROPOSED MARKETING STATUS (check one) ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER-THE-COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

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

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

NDA 20-827 MONISTAT 3 Vaginal Cream

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

MEMORANDUM

Date: April 21, 2000

From: Supervisory Project Manager
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
and
Regulatory Project Manager
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaulation IV

Through: Charles Ganley, M.D. /S/ 4/25/00
Director
Division of Over-the-Counter Drug Products
and
Renata Albrecht, M.D. /S/ 4/25/00
Acting Director
Division of Special Pathogen and Immunologic Drug Products

Re: User Fee

To: Original NDA 21-261, Monistat 3 Cream Combination Pack

Original NDA 21-261 for Monistat 3 Cream Combination Pack, submitted by Personal Products (formerly Advanced Care Products) provides for the proposed over-the-counter use of three 200 mg miconazole nitrate vaginal cream pre-filled applicators (approved via NDA 20-827) co-packaged with a 9 g tube of miconzole nitrate 2% external cream (approved via NDA 17-450).

NDA 21-261 is an efficacy supplement administratively split out from NDA 17-450 for our own convenience. Because this is an administrative split for our own convenience the new NDA should be subject to a fee for an efficacy supplement. Because the clinical data required for approval is by reference to the already approved NDA (no new clinical data - see 3/27/2000 enclosed Memorandum of Telecon) no fee would be required if it were an efficacy supplement. Therefore, the new original NDA 21261, received on April 3, 2000, is not subject to a user fee. It may be accepted for team review.

/S/
Maria Rossana R. Cook, M.B.A. 4/24/00

/S/
Christina H. Chi, Ph.D.
Apr 21, 2000

INTEROFFICE MEMORANDUM-ANNOUNCEMENT OF NEW NDA

To:	E-mail Recipients
Subject:	New NDA (21-261)

The following new NDA has been received by HFD-560.

NDA #	21-261
Drug:	Monistat 3 Cream Combination Pack (Three 200 mg miconazole nitrate vaginal cream pre-filled applicators (approved via NDA 20-827) and a 9 gm tube of 2% miconazole nitrate external cream)
Applicant	Personal Products (New name For Advanced Care Products)
Pharmacological Class:	Vaginal Antifungal
Indication:	OTC Treatment of vulvo-vaginal candidiasis
Stamped Receipt Date:	April 3, 2000
Date of User Fee Payment:	[redacted]
Filing Date	June 2, 2000

Disciplines:	Medical (HFD-590/560)	Vol 1.
	Chemistry (HFD-550)	Vol 1
	Labeling (HFD-560)	Vol 1

A filability/ forward planning meeting to assess fileability of the NDA and projected review completion dates has been scheduled for April 24th at 4PM. Assigned members of the review team should be informed of the time/date of the forward planning meeting.

If the NDA is filed, a team meeting will be conducted at approximately at day 90 and every 30 days until the project is complete.

Please feel free to call me at 7-2248 if you have any questions.

Dan Keravich, M.S., M.B.A.
Regulatory Project Manager HFD-560

Meeting Minutes
NDA 21-261

Date: May 30th, 2000

Location: Corporate S200A

Subject: Fileability Meeting for Monistat 3 Cream Combination Pack NDA 21-261.

Applicant: Personal Products

Summary: Request to market a new 3day combination pack consisting of a 4% internal and 2% external cream combination. This new application was submitted as an administrative convenience of the FDA review divisions.

Stamped receipt Date: April 3, 2000

User Fee Date: February 3, 2001

Filing Date: June 2, 2000

Chairperson: Dan Keravich HFD-560
Christina Chi HFD-590

AGENDA

The review teams assigned by HFD-560 & HFD -590 were convened to determine whether by Personal Products Co NDA submission for NDA 21-261 were suitable for filing. The review team responses were as follows:

1. Project Management:	Dan Keravich- Fileable (checklist attached)
2. Clinical HFD 590:	Joe Winfield - Fileable
Clinical HFD 560:	Ling Chin
3. IDS	Cheryl Turner- Fileable
4. Chemistry	Dorota Matecka- Fileable
5. Filing Decision	Dr. L. Katz- Fileable

The following questions would be sent to the company for further information.

1. Labeling
   - Confirmation is needed to verify that the products contain the same inactive ingredients.
   - Current picture of product does not display a tube.
   - Feedback will be given to sponsor that the label needs to indicate that the product is a Combination product and identify the type of combination. The public needs to discern that this is a combination of two creams and not the cream suppository combination.
2. Safety data listed in submission will be forwarded to Medical Officer

It was determined that the timelines for reviewing this NDA would be no later than December 2000 if Project Completion allows.

Minutes Prepared by D. Keravich

Monistat copackaging
Telecon: 3/27/2000

APR 2 0 2000

MEMORANDUM OF TELECON

Date: March 27, 2000

Application: Copackaging of 2 approved products which has not received any NDA number.

Drugs: Monistat® 3, miconazole nitrate 4% cream and
Monistat® 7 Vaginal Cream, miconazole nitrate 2% cream.

Between Sponsor: **Advanced Care Products:**
Charles Cush, Marketing Product Director, Monistat
Lynn Pawelski, Associate Director, Regulatory Affairs
David Upmalis, M.D., Executive Director, Clinical Affairs

and FDA: **Division of Over the Counter Drug Products, HFD-560:**
Linda Katz, M.D., Deputy Division Director
Helen Cothran, Team Leader
Ling Chin, M.D., Medical Officer
Cheryl Turner, R.N., Interdisciplinary Scientist
Rosemary Cook, Supervisory Project Manager
Daniel Keravich, Project Manager

Division of Anti-Inflamatory, Analgesics, and Opthalmology Drug Products, HFD-550:
Wiley Chambers, M.D., Deputy Division Director

Division of Special Pathogen and Immunologic Drug Products, HFD-590:
Renata Albrecht, M.D., Acting Division Director
Brad Leissa, M.D., Medical Team Leader
Joseph Winfield, M.D., Medical Officer
Dorota Matecka, Ph.D., Chemistry Reviewer
Funmi Ajayi, Ph.D., Biopharmaceutics Team Leader
Christina Chi, Ph.D., Project Manager

Subject: To discus administrative strategy alternatives in submitting an application for copackaging two approved drug products for over-the-counter (OTC) marketing: Monistat® 3 Vaginal Cream, miconazole nitrate 4% as the intravaginal cream and Monistat® 7 Vaginal Cream, miconazole nitrate 2% to be used as the external vulvar cream to provide external symptom relief only.

Monistat copackaging
Telecon: 3/27/2000

Indication: Treatment of vulvovaginal candidiasis and the symptomatic relief of the external vulva.

Background:

12/3/1999: ACP submitted a supplement application to copackage Monistat® 3 Vaginal Cream and Monistat® 1 Vaginal Cream for OTC marketing to NDA 20-670 for Monistat® 3 Combination Pack (Monistat® 3 Vaginal Suppository and Monistat® 1 Vaginal Cream).

1/5/1999: The Agency called ACP and explained that this application could not be submitted as a supplement to NDA 20-670 because the primary drug product is of different formulation, therefore, this application is not fileable.

1/27/2000: Following the Agency's request, ACP withdrew the application.

1/27/2000: ACP submitted a request for a meeting to discuss copackaging issues.

2/2/2000: The Agency called ACP and explained that there will be no need of a re-review of clinical data as each creams have the approved indication for its intended use.

2/11/2000: The Agency called ACP and provided information that the submission could be submitted as a new NDA with half of the cost of a user's fee and is subject to one year review clock or as an efficacy supplement without any user's fee and is also subject to one year review clock.

Discussion Points:

The Agency provided the following information:

- The application can not be submitted as a chemistry supplement to either NDA 20-827 or NDA 17-450 since the new product will require a labeling consolidation from two different products' labelings. Chemistry is only one of the many disciplines to review the labeling of this new product. Other disciplines, [redacted] will also be involved in the labeling review.

- The application can be submitted as a new NDA which does not contain any new clinical data, instead all pertinent clinical data are to be referenced to

other existing NDAs. The Chemistry section can also be crossed referenced with other existing NDA. Therefore, this new NDA will be subject to half of the cost of a user's fee. Under PDUFA, the review clock is subject to 10 - 12 months, but the Agency's target completion date is 10 months.

- The application can also be submitted as an efficacy supplement to NDA 17-450 (cf. CDER bundling policy). Because this efficacy supplement will not contain any new clinical data, instead all pertinent clinical data are to be referenced to other existing NDAs, therefore, this supplement will not be subject to any user's fee. For administrative purposes, this supplement will be given a new NDA number, but it will still not be subject to any user's fee. The Agency will write a memorandum to the NDA file at the Office of CDER's Director to document this conversion. Under PDUFA, the review clock is subject to 10 - 12 months, but the Agency's target completion date is 10 months.

- The Agency can neither commit to a shorter review time nor to expedite the review process due to the quantity and the various applications it is currently reviewing.

- The Agency suggested that prefilled applicators, rather than a reusable applicator, be used to avoid filling the applicator with the wrong cream.

- The Agency reminded that carton labeling should be submitted in compliance with Drug Facts Format" 21 CFR 201.66.

The sponsor provided the following response:

- They will submit the application as an efficacy supplement at the end of the month to DOTCDP and provide DSPIDP with a copy.

- Only prefilled applicators will be used in the copackaged product.

Action/Follow-up Items:	**Responsible party:**
• Submission of the application as an efficacy supplement to NDA 17-450.	ACP
• Conversion of the efficacy supplement to a new NDA.	DOTCDP

Monistat copackaging
Telecon: 3/27/2000

- Draft a memorandum to the File of NDA 21-261 at the Office of CDER's Director to document the administrative split/conversion. — DOTCDP

The telecon was adjourned amicably.

/S/
Christina H. Chi, Ph.D.
4/13/2000

/S/
Concurrence: HFD-590/TL/BLeissa

cc: Original NDA 21-261
Original NDA 17-450
Original NDA 20-827

HFD-560/Div.File
HFD-560/DepDivDir/LKatz
HFD-560/TL/HCothran
HFD-560/ClinRev/LChin(3/29/2000)
HFD-560/LabelingRev/CTurner
HFD-560/CPM/RCook
HFD-560/PM/DKeravich

HFD-550/DepDivDir/WChambers
HFD-104/SRPM/THassall(3/30/2000)

HFD-590/Div.File
HFD-590/ActDivDir/RAlbrecht
HFD-590/TL/BLeissa 3/28/2000
HFD-590/ClinRev/JWinfield
HFD-590/ChemRev/DMatecka
HFD-590/BioPharmRev/FAjayi
HFD-590/PM/CChi

Recorded and prepared by: CChi 3/27/2000
Circulated: 3/28/2000 No response received after 4/1/00: minutes is considered as acceptable.

TELECON, ACP.

Monistat copackaging
2/11/2000 Telecon

APR 2 0 2000

MEMORANDUM OF TELECON

Date: February 11, 2000

Application: No NDA number yet.

Drugs: Monistat® 3, miconazole nitrate 4% cream
Monistat® 7 Vaginal Cream, miconazole nitrate 2% cream.

Between Sponsor: **Advanced Care Products:**
Lynn Pawelski, Associate Director, Regulatory Affairs

and FDA: **Division of Over the Counter Drug Products, HFD-560:**
Rosemary Cook, Supervisory Project Manager

Division of Special Pathogens and Immunologic Drug Products, HFD-590:
Christina Chi, Ph.D., Project Manager

Subject: To discus administrative strategy alternatives in submitting an application for copackaging two approved drug products for over-the-counter (OTC) marketing: Monistat® 3 Vaginal Cream, miconazole nitrate 4% intravaginal cream, and Monistat® 7 Vaginal Cream, miconazole nitrate 2% external vulvar cream.

Indication: Treatment of vulvovaginal candidiasis and the symptomatic relief of the external vulva.

Background:

12/3/1999: ACP submitted a labeling supplemental application (SLR-008) to copackage Monistat® 3 Vaginal Cream and Monistat® 1 Vaginal Cream for OTC marketing to NDA 20-670 for Monistat® 3 Combination Pack (Monistat® 3 Vaginal Suppository and Monistat® 1 Vaginal Cream).

1/5/1999: The Agency called ACP and explained that this application coumld not be submitted as a supplement to NDA 20-670 because the primary drug product is of different formulation, therefore, this application is not fileable.

Monistat copackaging
2/11/2000 Telecon

1//1999:	Following the Agency's request, ACP withdrew the application.
1/27/2000:	ACP submitted a request for a meeting to discuss copackaging issues.
2/2/2000:	The Agency called ACP and explained that there will be no need of an re-review of clinical data as each creams have the approved indication for it's intended use.

Discussion Points:

The Agency provided the following information:

- The application can be submitted as a new NDA which does not contain any new clinical data, instead all pertinent clinical data are to be referenced to other existing NDAs. Under PDUFA, the review clock is subject to one year, but the Agency's target completion date is 10 months.

- The application can also be submitted as an efficacy supplement. Since this efficacy supplement will not contain any new clinical data, instead all pertinent clinical data are to be referenced to other existing NDAs. Under PDUFA, the review clock is subject to one year, but the Agency's target completion date is 10 months.

Action/Follow-up Items:	**Responsible party:**
Submission of the application either as a new NDA or as an efficacy supplement.	ACP

The telecon was adjourned amicably.

Christina H. Chi, Ph.D. 4/20/2000

cc: Original NDA 17-450
Original NDA 20-827
Original NDA 21-261

MEMORANDUM OF TELECON

Meeting Date: March 31,2000

Time : 4:15PM
Location: S200A, 9210 Corporate Blvd
Rockville MD

Application: NDA 21-261

Type of Meeting: Sponsor feedback, New NDA & Copackaging

Meeting Recorder: Daniel P. Keravich, MS., Pharm., MBA.

FDA Attendees titles & Office Division:
Daniel Keravich, MS., Pharm., MBA., Project Manager, DOTCDP, HFD-560

External Constituents Attendees and titles:
Lynn Pawelski
Associate Director, Advanced Care Products (Personal Products)

Meeting Objective:
To provide sponsor with guidance and feedback concerning the method of submission for the combination (copackaged) product.

Background
Please reference the Telcon meeting with ACP on 3/27/00. The agency provides some guidance to ACP on the options available for the submission of a combination product consisting of Miconazole cream 4 % and Miconazole cream 2% for external use. Based on the options provided, ACP has indicated that it will submit an efficacy supplement to the external cream NDA and HFD- 560 (DOTCDP) would convert the application to a new NDA.

Discussion:
I called Ms Pawelski to re-clarify the methods by which ACP could submit the application. Based on Thomas Hassel's email (attached) I instructed Ms. Pawelski that it would be easier f or the agency to address this new combination product if ACP was to reference this meeting on 3/27 in the cover letter of the submission. ACP should state language in the cover letter that the application is eligible as an efficacy supplement, is being submitted as an NDA for the administrative convenience.

Ms. Pawelski agreed and would call FDA Drug registration to obtain a new NDA number for this submission.

The meeting ended cordially.

Daniel Keravich

Division of Over-the-Counter Drug Products
Labeling Review

NDA #: 21-261 BL
SUBMISSION DATES: January 4, 2001 and January 12, 2001
SUBMISSION TYPE: Minor amendment- Revised draft labeling in response to Agency's comments on a pending application
SPONSOR: Personal Products Company, Division of McNeil-PPC, Inc.
DRUG PRODUCT: Monistat 3 Combination Pack (3 day vaginal antifungal cream and external cream)
INDICATION: treats vaginal yeast infections
relieves external itching and irritation due to a vaginal yeast infection
ACTIVE INGREDIENT: miconazole nitrate 4% (200 mg in each applicator)
miconazole nitrate 2% (external cream)
REVIEWER: Helen Cothran
REVIEW DATE: 1/16/2001
PROJECT MANAGER: Dan Keravich

Background
Reference is made to the sponsor's NDA submission of 4/3/00 and 9/20/00 (NDA 21-261) for Monistat 3 Combination Pack containing 2 approved products: miconazole nitrate 4% for use as a 3-day OTC vaginal antifungal cream plus miconazole nitrate 2% OTC vaginal antifungal external cream for use up to 7 days. The agency's comments on labeling were faxed to the firm on 12/1/00 and 12/27/00. This is a review of revised draft labeling submitted 1/4/01 and 1/12/01. The labeling consists of color mock-up labeling for the carton, consumer information leaflet, 9 gram tube (external vulvar cream), and prefilled applicator overwrap. In the 1/4/01 submission, the sponsor requested permission to use the currently available tube and overwrap components for the launch of the product . They stated their intent to commit to incorporate the new tube and overwrap labeling for this NDA within 180 days of approval or at the next printing. In the 1/12/01 submission, the firm requested revised labeling for the "warfarin warning."

Reviewer's Comments

Carton Label
1. On the hanging flap, the sponsor needs to commit to removing the word "New" in the phrase "New Combo Pack!" after the first 6 months of OTC marketing.
2. On the PDP, the declaration of net quantity of contents statement still does not clearly indicate that the statement refers to 2 products. The placement of the phrase "(9g) Tube" after the phrase "(5g) each applicator" is confusing. The sponsor could place "(9g) Tube" on a separate line or separate the two phrases with the word "and."
3. In the Drug Facts box, the sponsor requested that the warning agreed to in the 12/27/00 fax "**Ask a doctor or pharmacist before use if you** are taking a prescription blood thinning medicine, such as warfarin" be revised to read: "**Ask a doctor or pharmacist before use if you** are taking the prescription blood thinning medicine warfarin (coumadin)". The sponsor stated that "a consumer may not recognize the trade name "warfarin" but may be more familiar with the generic name "coumadin"." The agency does not agree with the firm's request because brand names (e.g., coumadin) shall not appear in any part of the "Drug Facts" portion of the labeling, but may appear elsewhere in the labeling outside of the boxed area (see

OTC Labeling Requirements Final Rule (64 FR 13268)). Therefore, the warning on the carton label must read "**Ask a doctor or pharmacist before use if you** are taking a prescription blood thinning medicine, such as warfarin." However, in the Consumer Information Leaflet, the warning may be revised as follows: "**Ask a doctor or pharmacist before use if you** are taking the prescription blood thinning medicine warfarin (coumadin), because bleeding and bruising may occur."

9 Gram tube

4. The labeling revisions are acceptable.

Applicator overwrap

5. The labeling revisions are acceptable.

Consumer Information Leaflet

6. Revise the heading "**Use**" to "**Uses**".
7. In the **Warnings** section, revise the 5th bulleted warning to read: "Ask a doctor or pharmacist before use if you are taking the prescription blood thinning medicine warfarin (coumadin), because bleeding and bruising may occur." See comment 3 above.
8. Under the heading "**Side effects**," revise the third sentence to read "Stop using MONISTAT® 3 Vaginal Cream Combination Pack and consult your doctor if you have abdominal pain, hives, or skin rash, or if you have severe vaginal burning, itching, or irritation."
9. In the 4th direction, first sentence, under the heading " **Directions for Use MONISTAT® 3 Vaginal Cream,**" the word "back" needs to be added as follows: "Gently insert the applicator into the vagina as far back as it will go comfortably."
10. The sponsor's use of a picture of a hand (instead of an arrow) to show where the applicator is inserted is acceptable.

Recommendations:

1. The above revisions must be made before this application can be approved.
2. Additionally, the agency denies the sponsor's request to use the current tube and current overwrap labeling for the product launch and incorporate new labeling within 180 days or at the next printing. As stated in the agency's 12/27/00 fax to the sponsor, the labeling approved for this NDA must be used.
3. The above comments and recommendations may be conveyed to the sponsor.

/S/ 1/19/01

Hĕlen Cothran, B.S.
Team Leader, HFD-560

Division of OTC Drug Products Labeling Review for NDA 21-261

NDA # 21-261 and 21-261 BL	**Sponsor : Personal Products, Division of McNeil-PPC, Inc.**
Drug Product: Miconazole nitrate 4% for use as a 3-day OTC vaginal antifungal cream, with miconazole nitrate 2% external OTC vaginal antifungal cream for use up to 7 days.	**# of Stock Keeping Units in Submission:** 1 carton containing 3 prefilled applicators and 1 tube of cream for external use
Submission Dates: 4/3/00 and 9/20/00	**Review Dates**: 5/20/00 and 9/29/00
Type of Submissions: Labeling for a new NDA (labeling includes carton, tube, overwrap, and educational brochure). Revised carton labeling submitted 9/20/00.	**Reviewers:** Cheryl Turner, HFD-560 Helen Cothran, HFD-560 Division of OTC Drug Products

Background:
This is a review of Monistat 3 Combination Pack containing 2 approved products: miconazole nitrate 4% for use as a 3-day OTC vaginal antifungal cream plus miconazole nitrate 2% OTC vaginal antifungal external cream for use up to 7 days. In a telecon with the firm on 9/12/00, the agency discussed its concern that consumers may not be able to distinguish between the various Monistat 3 products. The firm submitted revised carton labeling on 9/20/00 to address the agency's concerns. This labeling review consists of the tube, applicator overwrap, and consumer information leaflet submitted 4/3/00 and the revised carton labeling (NDA 21-261 BL) submitted 9/20/00. The example drug facts label is attachment 1, the labeling review of the carton is in the checklist below, the labeling review of the tube is attachment 2, the labeling review of the applicator overwrap is attachment 3, and the labeling review of the consumer information leaflet is attachment 4.

Stock Keeping Unit: (describe unit):
A carton labeled as a "Combination Pack" containing 2 miconazole nitrate cream products of different concentration:
1. (3 prefilled applicators) of miconazole nitratrate 4% (200 mg in each applicator).
2. (1 tube - net weight 0.32 oz (9 grams)) of miconazole nitrate 2% external cream.

Content of Submission	Yes	No
1. A cover letter stating that the submission includes new labeling in the Drug Facts format for the drug product and shelf keeping unit(s);	✓	
2. A table of contents or index	✓	
3. The most recent approved labeling * **This is a new submission containing 2 products that were previously approved as individual products. The external cream (miconazole nitrate 2%) is referenced to NDA 17-450 for Monistat 7, and the cream contained in the applicator (miconazole nitrate 4%) is referenced to NDA 20-827 for Monistat 3.**	✓	
4. A representation of the proposed labeling, including any outserts, panel extensions, or other graphical or package techniques intended to be used with the product.	✓	
5. Information on formatting, text style, and text size as illustrated in 64 FR 13254 at 13293.	✓	

**Additional labeling submitted under 21 CFR 314.70(c) or (d) since the last approved labeling should be include in the submission with the date of submission referenced and how they were submitted (e.g. annual report, pending supplement).*
The information provided is adequate for review: ✓ *Yes* _____ *No*

Principal Display Panel

Paragraph 21 CFR	Description of Paragraph	Adequate (yes/no)	Comments
201.60	Principle Display Panel	**Yes**	**Note:** On the hanging flap, the word "New" in the phrase "New Combo Pack!" must be deleted after 6 months of OTC marketing.

Paragraph 21 CFR	Description of Paragraph	Adequate (yes/no)	Comments
201.61	Statement of Identity (SOI) • Established name of drug • Statement of general pharmacological category(ies) or the principal intended actions • Bold type • Size related to the most prominent printed matter	**Yes** **Yes** **Yes** **Yes**	
201.62	Declaration of net quantity of contents	**No**	Sponsor needs to clarify that the net quantity of contents statement refers to 2 products. We suggest that the word "applicator" be added after "each."
201.63	Pregnancy/breast feeding warnings	**Yes**	
201.1	Name and place of business of manufacturer, packer, or distributor	**Yes**	
201.17	Location of expiration dates	**No**	Identify location of expiration date on carton
201.18	Control numbers	**No**	Identify location of lot number on carton

Labeling Content [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments
(c)(1)	Drug Facts, Drug Facts (continued)	**Yes**	
(c)(2)	Active ingredient, established name, quantity Miconazole nitrate 4% (200 mg in each applicator) Miconazole nitrate 2% (as external cream)	**No**	**Revise to:** ***Active ingredients*** Miconazole nitrate 4% (200 mg in each applicator) Miconazole nitrate 2% (external cream)
(c)(3)	Purpose	**No**	Revise "Vaginal Antifungal" to "Vaginal antifungal"
(c)(4)	***Uses*** • treats repeat vaginal yeast infections • relieves external itching and irritation due to a repeat vaginal yeast infection	**No**	**Revise to:** ***Uses*** • treats vaginal yeast infections • relieves external itching and irritation due to a vaginal yeast infection
(c)(5)	**(I) For vaginal use only.**	**No**	**Remove period at end of sentence**
(c)(5)	(ii) All applicable warnings	**Yes**	
	(A) Allergic reaction warnings	**NA**	
	(B) Reye's syndrome warning	**NA**	
	(C) Flammability warning, with appropriate signal word	**NA**	

Labeling Content [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments
	(D) Water soluble gum warning, "Choking"	**NA**	
	(E) "Alcohol warning"	**NA**	
	(F) "Sore throat warning"	**NA**	
	(G) "Dosage warning"	**NA**	
(c)(5)	(iii) **"Do not use"** followed by all contraindications Manufacturer did not provide a "Do not use" section	**No**	**Revise to:** **Do not use** if you have never had a vaginal yeast infection diagnosed by a doctor
(c)(5)	(iv) **Ask a doctor before use if you have** • never had a vaginal yeast infection diagnosed by a doctor • 1 or more of the following: abdominal pain, fever, chills, nausea, vomiting, foul-smelling vaginal discharge • vaginal yeast infections often (such as once a month or 3 in 6 months) • been exposed to the human immunodeficiency virus (HIV) that causes AIDS	**No** ()	**Revise to:** **Ask a doctor before use if you have** • vaginal itching and discomfort for the first time • lower abdominal, back or shoulder pain, fever, chills, nausea, vomiting, or foul-smelling vaginal discharge • vaginal yeast infections often (such as once a month or 3 in 6 months). You could be pregnant or have a serious underlying medical cause for your symptoms, including diabetes or a weakened immune system. • been exposed to the human immunodeficiency virus (HIV) that causes AIDS
	(v) "Ask a doctor or pharmacist before use if you are"	**No, add new subheading and warning.** **Reviewer's comment: warfarin warning added because adverse effects (bruising, bleeding, increased INRs and prothrombin time) have been reported with use of warfarin and vaginal antifungal products containing miconazole**	**Ask a doctor or pharmacist before use if you** • are taking a blood thinning medicine, such as warfarin
(c)(5)	(vi) **When using this product** • do not use tampons, douches, spermicides or other vaginal products • do not have vaginal intercourse • condoms and diaphragms may be damaged and fail to prevent pregnancy or sexually transmitted diseases (STDs)	**No**	**Revise to:** **When using this product** • do not use tampons, douches, spermicides or other vaginal products. Condoms and diaphragms may be damaged and fail to prevent pregnancy or sexually transmitted diseases (STDs). • do not have vaginal intercourse

Labeling Content [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments
(c)(5)	(vii) **Stop use and ask a doctor if** • symptoms do not get better in 3 days • symptoms last more than 7 days • you get abdominal pain, fever, chills, nausea, vomiting, foul-smelling vaginal discharge, or rash	**No**	**Stop use and ask a doctor if** • symptoms do not get better in 3 days • symptoms last more than 7 days • you get a rash, abdominal pain, fever, chills, nausea, vomiting, or foul-smelling vaginal discharge
(c)(5)	(viii) Any required warnings	**NA**	
(c)(5)	(ix) The pregnancy/breast feeding warning	**Yes**	
(c)(5)	(x) Keep out of reach of children	**Yes**	
(c)(6)	***Directions*** • before using this product read the enclosed consumer information leaflet for complete instructions • adults and children 12 years of age and over: • **applicators:** insert one applicatorful into the vagina at bedtime for 3 nights in a row • **external cream:** squeeze a small amount of cream onto your fingertip. Gently apply the cream onto the itchy, irritated skin outside the vagina. Use daily for up to 7 days as needed. • children under 12 years of age: ask a doctor	**No**	***Revise to:*** ***Directions*** • before using this product read the enclosed consumer information leaflet for complete instructions • adults and children 12 years of age and over: • **applicators:** insert 1 applicatorful into the vagina at bedtime for 3 nights in a row. Throw applicator away after use. • **external cream:** squeeze a small amount of cream onto your fingertip. Apply the cream onto the itchy, irritated skin outside the vagina. Use 2 times daily for up to 7 days, as needed. • children under 12 years of age: ask a doctor
(c)(7)	Other information and additional information not included in (c)(2) – (c)(6), (c)(8), (c)(9) of this section. Storage Statement	**No**	See revised storage information in (c)(7)(iii) below
(c)(7)	(i) Certain ingredients (e.g. Na)	**NA**	
(c)(7)	(ii) phenylalanine	**NA**	
(c)(7)	(iii) additional information ***Other information*** • do not use if seal over tube opening has been punctured or embossed design (embossed design) is not visible • do not purchase if carton is opened • do not use if applicator wrapper is missing or damaged (each applicator is individually wrapped)	**No**	Revise temperature to be consistent with the Office of New Drug Chemistry (ONDC) recommendations as follows: ***Other information*** • store at 20-25°C (68-77°F) • do not purchase if carton is opened • do not use if seal over tube opening has been punctured or embossed design is not visible • do not use if applicator wrapper is missing or damaged (each applicator is individually wrapped)

Labeling Content [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments
	• store at room temperature 20°-25°C (68°-77°F), avoid heat over 25°C or 77°F.		
(c)(8)	***Inactive ingredients.***	**Yes**	
(c)(9)	***Questions***	**Yes**	

Labeling Format [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments
(d)(1)	Drug Facts: first letter of words uppercase	**Yes**	
(d)(1)	Headings, subheadings: first letter of first word uppercase	**Yes**	
(d)(1)	Left justification	**Yes**	
(d)(2)	Drug Facts type size greater than largest type size used in Drug Facts labeling	**Yes**	
(d)(2)	Heading 8 pt or 2 point sizes greater than text point size	**Yes**	
(d)(2)	Type size 6 pt size for information in Drug Facts	**Yes**	
(d)(2)	Subheadings ≥ 6 point type size	**Yes**	
(d)(2)	Drug Facts (continued) type size no smaller than 8-point type	**Yes**	
(d)(3)	No reverse type	**Yes**	
(d)(3)	Letters do not touch	**Yes**	
(d)(3)	≥.5 pt leading (space between lines)	**Yes**	
(d)(3)	No more than 39 characters per inch	**Yes**	
(d)(3)	Bold Italic headings and title	**Yes**	
(d)(3)	Bold subheading except (continued)	**Yes**	
(d)(3)	Black or dark type	**Yes**	
(d)(3)	White or neutral background	**Yes**	
(d)(3)	Contrasting dark color for title and heading	**Yes**	
(d)(4)	Bullet: solid circle or square 5 pt type, same shape and color, left justified or separated from heading or subheading by at least two square "EMS"	**Yes**	
(d)(4)	Bullet on same lines: end of statement separated from bulleted statement by two "EMS"	**Yes**	
(d)(4)	Bullet on same lines: additional bulleted statement does not continue on next line	**Yes**	
(d)(4)	Vertical alignment of bulleted statements	**Yes**	
(d)(5)	Appear on more than one panel	**Yes**	

Labeling Format [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments
(d)(5)	Visual graphic signals continuation	**Yes**	
(d)(6)	Left justification of information required by (c)(2)	**Yes**	
(d)(6)	Right justification of information required by (c)(3)	**Yes**	
(d)(6)	Alphabetical order of active ingredients	**Yes**	
(d)(6)	Information required by (c)(4), (c)(6) - (c)(9) may start on same line as required headings	**Yes**	
(d)(6)	None of information required in (c)(5) shall appear on same line as Warnings	**Yes**	
(d)(7)	Graphical images should not interrupt the heading, subheading and information. Hyphens should not be used except to punctuate compound words.	**Yes**	
(d)(8)	Enclosed box using barline	**Yes**	
(d)(8)	Horizontal barline separates headings listed in (c)(2) - (c)(9)	**Yes**	
(d)(8)	Horizontal hairline precedes heading immediately after Drug Facts	**Yes**	
(d)(8)	Horizontal hairline follows the title	**Yes**	
(d)(8)	Horizontal hairline extending within 2 spaces on either side of the Drug Facts box shall immediately follow the title and precede the subheadings set forth in (c)(5) [except (c)(5) (ii) A – G]	**Yes**	
(d)(9)	Directions in table format when dosage instructions are provided for three or more age groups or populations	**NA**	
(d)(9)	Horizontal barline preceding the next heading may end the table	**NA**	

APPEARS THIS WAY
ON ORIGINAL

Reviewer's Recommendations:

1. As you are aware, the Agency is developing class labeling for all OTC vaginal antifungal products. When the guidance for OTC vaginal antifungal drug products is finalized, we recommend that the sponsor draft the labeling for this product according to the format used in the Agency's final guidance document.
2. With regard to the revisions to the PDP noted in the 9/20/00 submission, the firm has committed to making the same changes to the other Monistat 3 Combination Packs.
3. The reviewer's comments and recommendations, see above and Attachments 1 through 4, may be conveyed to the sponsor.

/S/ 11/7/00
Cheryl Turner, R.N., IDS

/S/ 11/7/00
Helen Cothran, B.S., Team Leader

Attachment 1: example drug facts label
Labeling review of the carton panels- see checklist
Attachment 2: labeling review- tube
Attachment 3: labeling review - applicator overwrap
Attachment 4: labeling review - consumer information leaflet