CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-266

21-267

ADMINISTRATIVE DOCUMENTS

13. PATENT AND EXCLUSIVITY INFORMATION FOR VFEND™ IV AND ORAL (VORICONAZOLE)

1.	Active Ingredient:	(2R,3S)-2-(2,4-difluorophenyl)-3-(5-fluoro-4-pyrimidinyl)-1-(1*H*-1,2,4-triazol-1-yl)-2-butanol with an empirical formula of $C_{16}H_{14}F_3N_5O$ and a molecular weight of 349.3.
2.	Strengths:	Oral – 50 or 200 mg IV – 200 mg per vial
3.	Trade Name:	VFEND™
4.	Dosage Form/Route of Administration:	Oral and IV
5.	Application Firm Name:	Pfizer Inc
6.	NDA Number:	Oral – 21,266 IV – 21,267
7.	Exclusivity Period:	Five years from date of approval
8.	Applicable Patent Numbers and Expiration Dates:	5,116,844 exp. August 11, 2009 5,364,938 exp. November 15, 2011 5,567,817 exp. October 22, 2013 5,773,443 exp. January 25, 2011

14. PATENT CERTIFICATION

With respect to the drug, VFEND™, which is the subject of this Application (NDA 21-266 and NDA-21-267) and the U.S. patents that are listed in Item 13 of this Application, Pfizer certifies that the drug, VFEND™, pharmaceutical compositions thereof, and methods of treating fungal infections are claimed in U.S. Patents Nos. 5,116,844; 5,364,938; 5,567,817 and 5,773,443.

EXCLUSIVITY SUMMARY for NDAs # 21-266 & 21-267 SUPPL #

Trade Name VFEND™ Generic Name voriconazole

Applicant Name Pfizer Inc. HFD- 590

Approval Date May 24, 2002

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 /_x__/ NO /___/

      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.

      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:

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 /___/ NO /__x_/

If yes, NDA # _____ Drug Name

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 /_x__/

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 /__X_/

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 /___/ N/A __X__

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: _____

_____

_____

Jouhayna Saliba, Pharm.D.
Regulatory Project Manager

Renata Albrecht, M.D.
Acting Division Director

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Renata Albrecht
6/12/02 01:25:28 PM

Item 16
NDA 21-266
Oral Tablets

DEBARMENT CERTIFICATION
[FD&C Act 306(k)(1)]

Pfizer hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

William H. Harvey — November 2, 2000

Signature of Company Representative — Date

Item 16
NDA 21-267
IV for Infusion

DEBARMENT CERTIFICATION
[FD&C Act 306(k)(1)]

Pfizer hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

Signature of Company Representative

November 2, 2010
Date

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDAs #: 21-266 & 21-267 **Supplement Type (e.g. SE5):** _____ **Supplement Number:**

Stamp Date: November 17, 2000 **Action Date:** December 17, 2001 (AE)
Class I Resubmission/ Stamp Date: March 26, 2002 **Action Date:** May 24, 2002 (AP)

HFD 590 **Trade and generic names/dosage form:** VFEND™ (voriconazole) Tablets and VFEND™ (voriconazole for infusion)

Applicant: Pfizer Inc. **Therapeutic Class:** Antifungal

Indication(s) previously approved: N/A – application not previously approved

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 2

Indication #1: Invasive aspergillosis

Is there a full waiver for this indication (check one)?

- ☐ **Yes: Please proceed to Section A.**

- X **No: Please check all that apply:** ____**Partial Waiver** __X__**Deferred** ____**Completed**
  NOTE: More than one may apply
  Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:**_____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred: 2-18 years of age deferred
0-2 years of age deferred (company plans to request a waiver December 1, 2002)

Min_____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- X **Adult studies ready for approval**
- X **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): 12/31/2003

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min_____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960, 301-594-7337

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: Serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium* spp., including *Fusarium solani*, in patients intolerat of or refractory to other therapy

Is there a full waiver for this indication (check one)?

- ☐ **Yes: Please proceed to Section A.**

X **No: Please check all that apply: ____Partial Waiver ___X_Deferred ____Completed**
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:_____**

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min____	**kg____**	**mo.____**	**yr.____**	**Tanner Stage____**
Max____	**kg____**	**mo.____**	**yr.____**	**Tanner Stage____**

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:_____**

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960, 301-594-7337

Section C: Deferred Studies

Age/weight range being deferred: 2-18 years of age deferred
0-2 years of age deferred (company plans to request a waiver December 1, 2002)

Min ____ kg____ mo.____ yr.____ Tanner Stage____
Max____ kg____ mo.____ yr.____ Tanner Stage____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- X **Adult studies ready for approval**
- X **Formulation needed**
- ☐ **Other:_____**

Date studies are due (mm/dd/yy): 12/31/2003

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min ____ kg____ mo.____ yr.____ Tanner Stage____
Max____ kg____ mo.____ yr.____ Tanner Stage____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960, 301-594-7337

Revised 1-18-02

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jouhayna Saliba
6/14/02 01:46:59 PM

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDAs 21-266 _____ _____ _____
21-267

Drug Vfend™ (Voriconazole) Tablets and IV Applicant Pfizer

RPM Jouhayna S. Saliba Phone 301-827-2127

505(b)(1) _X_
505(b)(2) Reference listed drug _____

☐Fast Track ☐Rolling Review Review priority: Class I resubmission

Pivotal IND(s) _____

Application classifications:
Chem Class 1S
Other (e.g., orphan, OTC) _____

PDUFA Goal Dates:
Primary 05/24/02
Secondary 05/24/02

Arrange package in the following order:

Indicate N/A (not applicable), X (completed), or add a comment.

GENERAL INFORMATION:

- User Fee Information: User Fee Paid **N/A(resubmission)**
  User Fee Waiver (attach waiver notification letter) ____
  User Fee Exemption ____

Action Letters	X	AP	AE	NA
♦ Labeling & Labels				
FDA revised labeling and reviews				X
Original proposed labeling (package insert, patient package insert)				X
Other labeling in class (most recent 3) or class labeling				X
Has DDMAC reviewed the labeling?	X Yes (include review) ☐ No			
Immediate container and carton labels				X
Nomenclature review				X

- Application Integrity Policy (AIP) ☐ Applicant is on the AIP. This application ☐ is _X_ is not on the AIP.

Exception for review (Center Director's memo)	N/A
OC Clearance for approval	N/A

♦ Status of advertising (if AP action) ☐ Reviewed (for Subpart H – attach review)	X Materials requested in AP letter
♦ Post-marketing Commitments	
Agency request for Phase 4 Commitments	
Copy of Applicant's commitments	X
♦ Was Press Office notified of action (for approval action only)?	☐X Yes ☐ No
Copy of Press Release or Talk Paper	
♦ Patent	
Information [505(b)(1)]	X
Patent Certification [505(b)(2)]	N/A
Copy of notification to patent holder [21 CFR 314.50 (i)(4)]	N/A
♦ Exclusivity Summary	X
♦ Debarment Statement	X
♦ Financial Disclosure	
No disclosable information	
Disclosable information – indicate where review is located (page 26 of the Medical Officer's review on invasive aspergillosis)	X
♦ Correspondence/Memoranda/Faxes	X
♦ Minutes of Meetings	X
Date of EOP2 Meeting 6/24/96 and 2/25/98	
Date of pre NDA Meeting 7/26/00	
Date of pre-AP Safety Conference 11/9/01	
♦ Advisory Committee Meeting	X
Date of Meeting	10/04/01
Questions considered by the committee	X
Minutes or 48-hour alert or pertinent section of transcript	X
♦ Federal Register Notices, DESI documents	X

CLINICAL INFORMATION:	**Indicate N/A (not applicable), X (completed), or add a comment.**
♦ Summary memoranda (e.g., Office Director's memo, Division Director's memo, Group Leader's memo)	X

- Clinical review(s) and memoranda X
- Safety Update review(s) X
- Pediatric Information
  ☐ Waiver/partial waiver (Indicate location of rationale for waiver) ☐ XDeferred
  Pediatric Page..... X
  ☐ Pediatric Exclusivity requested? ☐ Denied ☐ Granted ☐X Not Applicable
- Statistical review(s) and memoranda X
- Biopharmaceutical review(s) and memoranda..... X
- Abuse Liability review(s) ..... N/A
  Recommendation for scheduling ..... N/A
- Microbiology (efficacy) review(s) and memoranda X
- DSI Audits (See MO review on aspergillosis, page 20)
  ☐Clinical studies ☐ bioequivalence studies .....

CMC INFORMATION: **Indicate N/A (not applicable), X (completed), or add a comment.**

- CMC review(s) and memoranda X
- Statistics review(s) and memoranda regarding dissolution and/or stability ..... N/A
- DMF review(s) X
- Environmental Assessment review/FONSI/Categorical exemption ...(They qualify for categorical exclusion, see Chemistry review)..... X
- Micro (validation of sterilization) review(s) and memoranda X
- Facilities Inspection (include EES report)
  Date completed 21-266 May 29,2001 ..... ☐X Acceptable ☐ Not Acceptable
  21-267 February12, 2002
- Methods Validation .....Requested (see Chemistry review)..... ☐ Completed ☐ Not Completed

PRECLINICAL PHARM/TOX INFORMATION:

Indicate N/A (not applicable), X (completed), or add a comment.

- Pharm/Tox review(s) and memoranda X
- Memo from DSI regarding GLP inspection (if any) ..... N/A
- Statistical review(s) of carcinogenicity studies ..... N/A
- CAC/ECAC report ..... N/A

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDAs_____ _____ **21-266 & 21-267 for the indications of invasive aspergillosis and fungal pathogens to include *Scedosporium apiospermum* and *Fusarium* species**

Drug **Vfend™ (Voriconazole) Tablets and IV** Applicant **Pfizer**

RPM **Jouhayna S. Saliba** Phone **301-827-2127**

505(b)(1) __X___
505(b)(2) Reference listed drug **Voriconazole**

☐Fast Track ☐Rolling Review Review priority: X S __ P

Pivotal IND(s) _____

Application classifications:
Chem Class **1S**
Other (e.g., orphan, OTC) _____

PDUFA Goal Dates:
Primary **12/17/01**
Secondary **02/17/02**

Arrange package in the following order:

Indicate N/A (not applicable), X (completed), or add a comment.

GENERAL INFORMATION:

- User Fee Information: User Fee Paid _X_
  User Fee Waiver (attach waiver notification letter) ____
  User Fee Exemption ____

Action Letters **1) AE for the indication of invasive aspergillosis and fungal pathogens to include *Scedosporium apiospermum* and *Fusarium* species. 2) AE for the indication of esophageal candidiasis 3) NA for the empiric antifungal therapy in febrile neutropenic patients .** AP _X_ AE _X_NA

- Labeling & Labels
  - FDA revised labeling and reviews..... X
  - Original proposed labeling (package insert, patient package insert) X
  - Other labeling in class (most recent 3) or class labeling..... X
  - Has DDMAC reviewed the labeling? ..... X Yes (include review) ☐ No
  - Immediate container and carton labels X
  - Nomenclature review X

- Application Integrity Policy (AIP) ☐ Applicant is on the AIP. This application ☐ is _X_ is not on the AIP.
  - Exception for review (Center Director's memo)..... N/A
  - OC Clearance for approval..... N/A

- Status of advertising (if AP action) ☐ Reviewed (for Subpart H – attach review) ☐ Materials requested in AP letter

- Post-marketing Commitments
  - Agency request for Phase 4 Commitments..... N/A
  - Copy of Applicant's commitments ..... N/A

- Was Press Office notified of action (for approval action only)?..... ☐ Yes ☐ No
  - Copy of Press Release or Talk Paper..... N/A

- Patent
  - Information [505(b)(1)] X
  - Patent Certification [505(b)(2)]..... N/A
  - Copy of notification to patent holder [21 CFR 314.50 (i)(4)]..... N/A

- Exclusivity Summary ..... N/A

- Debarment Statement X

- Financial Disclosure
  - No disclosable information .....
  - Disclosable information – indicate where review is located (page 22 of the Medical Officer's review on invasive aspergillosis) X
- Correspondence/Memoranda/Faxes X

- Minutes of Meetings X
  - Date of EOP2 Meeting 6/24/96 and 2/25/98
  - Date of pre NDA Meeting 7/26/00
  - Date of pre-AP Safety Conference 11/9/01

- Advisory Committee Meeting X
  - Date of Meeting 10/04/01
  - Questions considered by the committee X
  - Minutes or 48-hour alert or pertinent section of transcript .....

- Federal Register Notices, DESI documents X

CLINICAL INFORMATION:

Indicate N/A (not applicable), X (completed), or add a comment.

- Summary memoranda (e.g., Office Director's memo, Division Director's memo, Group Leader's memo) ..... _____
- Clinical review(s) and memoranda X
- Safety Update review(s) ..... _____
- Pediatric Information
  ☐ Waiver/partial waiver (Indicate location of rationale for waiver) ☐ Deferred
  Pediatric Page..... N/A
  ☐ Pediatric Exclusivity requested? ☐ Denied ☐ Granted ☐ Not Applicable
- Statistical review(s) and memoranda X
- Biopharmaceutical review(s) and memoranda..... X
- Abuse Liability review(s) ..... N/A
  Recommendation for scheduling ..... N/A
- Microbiology (efficacy) review(s) and memoranda X
- DSI Audits ..... N/A
  ☐Clinical studies ☐ bioequivalence studies ..... _____

CMC INFORMATION:

Indicate N/A (not applicable), X (completed), or add a comment.

- CMC review(s) and memoranda X
- Statistics review(s) and memoranda regarding dissolution and/or stability ..... N/A
- DMF review(s) X
- Environmental Assessment review/FONSI/Categorical exemption ...(They qualify for categorical exclusion, see Chemistry review)..... X
- Micro (validation of sterilization) review(s) and memoranda X
- Facilities Inspection (include EES report)
  Date completed 21-266 May 29,2001 21-267 November 14, 2001 ..... ☐X Acceptable for tablets ☐X Not Acceptable for IV

- Methods Validation .....Requested (see Chemistry review)..... ☐ Completed ☐ Not Completed

PRECLINICAL PHARM/TOX INFORMATION:

Indicate N/A (not applicable), X (completed), or add a comment.

- Pharm/Tox review(s) and memoranda X
- Memo from DSI regarding GLP inspection (if any) ..... N/A
- Statistical review(s) of carcinogenicity studies ..... N/A
- CAC/ECAC report ..... N/A

USER FEE VALIDATION SHEET

NDA # 21-267 Supp. Type & # N 000 UFID # 3944
(e.g., N000, SLR001, SE1001, etc.)

1. (YES) NO **User Fee Cover Sheet Validated?** **MIS_Elements Screen Change(s):**

2. (YES) NO **APPLICATION CONTAINS CLINICAL DATA?**
(Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

REF **IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.**

3. YES (NO) **SMALL BUSINESS EXEMPTION**

4. YES (NO) **WAIVER GRANTED**

5. YES (NO) **NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other then bundling).**
If YES, list all NDA #s, review division(s) and those for which an application fee applies.

NDA #	Division		
N_____	HFD-_____	Fee	No Fee
N_____	HFD-_____	Fee	No Fee

6. (YES) NO **BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required**
(Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N_____	HFD-_____	N_____	HFD-_____

7. P (S) **PRIORITY or STANDARD APPLICATION?**

/S/ 1/24/01 /S/ 1-Feb-01
PM Signature / Date CPMS Concurrence Signature / Date

2/14/00

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Pfizer Global Research and Development
Eastern Point Road
Groton, CT 06340

2. TELEPHONE NUMBER *(Include Area Code)*

(212) 733-5688

3. PRODUCT NAME

VFEND (voriconazole) IV

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

(Data also contained in NDA N021266)

5. USER FEE I.D. NUMBER

3944

6. LICENSE NUMBER / NDA NUMBER

N021267

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☒ NO *(See reverse side if answered YES)*

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
	John E. Wolleben Sr. Vice President, Regulatory Affairs	9/19/00

FORM FDA 3397 (5/98)

USER FEE VALIDATION SHEET

NDA # 21266 Supp. Type & # N000 UFID # 3943
(e.g., N000, SLR001, SE1001, etc.)

1. (YES) NO **User Fee Cover Sheet Validated?** **MIS_Elements Screen Change(s):**

2. (YES) NO **APPLICATION CONTAINS CLINICAL DATA?**
(Circle YES if NDA contains study or literature reports of what are explicitly or implicitly represented by the application to be adequate and well-controlled trials. Clinical data do not include data used to modify the labeling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).

REF **IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION.**

3. YES (NO) **SMALL BUSINESS EXEMPTION**

4. YES (NO) **WAIVER GRANTED**

5. YES (NO) **NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (other then bundling).**
If YES, list all NDA #s, review division(s) and those for which an application fee applies.

NDA #	Division		
N_____	HFD-_____	Fee	No Fee
N_____	HFD-_____	Fee	No Fee

6. (YES) NO **BUNDLING POLICY APPLIED CORRECTLY? No Data Entry Required**
(Circle YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Circle NO if application should be split into more than one application or be submitted as an original instead of a supplement. If NO, list resulting NDA #s and review division(s).

NDA #	Division	NDA #	Division
N_____	HFD-_____	N_____	HFD-_____

7. P (S) **PRIORITY or STANDARD APPLICATION?**

/S/ 1/24/01
PM Signature / Date

/S/ 1 Feb 01
CPMS Concurrence Signature / Date

2/14/00

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

1. APPLICANT'S NAME AND ADDRESS

Pfizer Global Research and Development
Eastern Point Road
Groton, CT 06340

2. TELEPHONE NUMBER *(Include Area Code)*

(212) 733-5688

3. PRODUCT NAME

VFEND (voriconazole) Oral

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO _____ (APPLICATION NO. CONTAINING THE DATA).

(Data also contained in NDA N021267)

5. USER FEE I.D. NUMBER

3943

6. LICENSE NUMBER / NDA NUMBER

N021266

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☒ NO *(See reverse side if answered YES)*

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Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

DHHS, Reports Clearance Officer
Paperwork Reduction Project (0910-0297)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
	John E. Wolleben Sr. Vice President, Regulatory Affairs	9/19/00

FORM FDA 3397 (5/98)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

sion/Office): HFD-805 (Peter Cooney)			FROM: HFD-540	
ATE: 12/11/00	IND NO.	NDA NO.: 21-267	TYPE OF DOCUMENT: NDA	DATE OF DOCUMENT: Nov. 17, 00
AME OF DRUG: Voriconazole		PRIORITY CONSIDERATION: Standard	CLASSIFICATION OF DRUG: anti-fungal	DESIRED COMPLETION DATE: 6/1/01
AME OF FIRM: Pfizer				

REASON FOR REQUEST

I. GENERAL

] NEW PROTOCOL	☐ PRE-NDA MEETING	☐ RESPONSE TO DEFICIENCY LETTER
] PROGRESS REPORT	☐ END OF PHASE II MEETING	☐ FINAL PRINTED LABELING
] NEW CORRESPONDENCE	☐ RESUBMISSION	☐ LABELING REVISION
] DRUG ADVERTISING	☐ SAFETY/EFFICACY	☐ ORIGINAL NEW CORRESPONDENCE
] ADVERSE REACTION REPORT	☒ ~~PAPER~~ NDA - electronic	☐ FORMULATIVE REVIEW
] MANUFACTURING CHANGE/ADDITION	☐ CONTROL SUPPLEMENT	☐ OTHER *(Specify below)*
] MEETING PLANNED BY _____		

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
] TYPE A OR B NDA REVIEW	☐ CHEMISTRY
] END OF PHASE II MEETING	☐ PHARMACOLOGY
] CONTROLLED STUDIES	☐ BIOPHARMACEUTICS
] PROTOCOL REVIEW	☐ OTHER
] OTHER	

III. BIOPHARMACEUTICS

. SOLUTION	☐ DEFICIENCY LETTER RESPONSE
] BIOAVAILABILITY STUDIES	☐ PROTOCOL– BIOPHARMACEUTICS
] PHASE IV STUDIES	☐ IN–VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

] PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL	☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
] DRUG USE *e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES*	☐ SUMMARY OF ADVERSE EXPERIENCE
] CASE REPORTS OF SPECIFIC REACTIONS *(List below)*	☐ POISON RISK ANALYSIS
] COMPARATIVE RISK ASSESSEMENT ON GENERIC DRUG GROUP	

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

OMMENTS/SPECIAL INSTRUCTIONS *(Attach additional sheets if necessary)*

Micro sterility consult on NDA 21-267

To get to EDR.
type EDR
then put in NDA # 21-267
then you can access the CMC section from there.
If you have any questions - please call me at (72423)

IGN/ /S/	12-11-00	METHOD OF DELIVERY *(Check one)* ☐ MAIL ☐ HAND
IGNATURE OF RECEIVER		SIGNATURE OF DELIVERER

FORM FDA 3331 (7/93)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Division/Office): **HFD-550 (Dr. Chambers)**			FROM: **HFD-590 (Dr. Tiernan)**	
DATE **February 16, 2001**	IND NO.	NDA Nos. **21-266** **21-267**	TYPE OF DOCUMENTS **N**	DATE OF DOCUMENTS **November 17, 2000**
NAME OF DRUG **Vfend (voriconazole) Tablets** **Vfend (voriconazole) IV**	PRIORITY CONSIDERATION		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE **June 17, 2001**

NAME OF FIRM: **Pfizer Global Research & Development**

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- √ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Please see attached memo from Dr. Tiernan.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one) ☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
OPDRA

FROM: **Cheryl Dixon/Diana Willard**
HFD-590 (Division of Special Pathogen and Immunologic Drug Products)

DATE:	IND NO.:	NDA NOs.:	TYPE OF DOCUMENTS:	DATE OF DOCUMENTS:
Feb. 26, 2001		**21-266** **21-267**	**NDAs**	**Nov. 17, 2000**

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
Vfend (voriconazole)		**Anti-Fungal**	

NAME OF FIRM: **Pfizer**

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE—NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:
  Electronic NDA

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER:	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

This NDA, recently submitted to the Division, contains a historically controlled study for the indication of invasive aspergillosis. Our statistician would like the following 2 questions answered:

1. Have the usual biases associated with historical controls been adequately addressed in the design and conduct of Protocol A1501003?
2. Are the two study populations, Protocol 150-304 and Protocol A1501003, comparable? If so, what conclusions can be drawn?

The Division appreciates OPDRA's willingness to assist us in analyzing another historically controlled study. An epidemiologist's perspective would greatly enhance our ability to interpret the data. Should OPDRA's

epidemiologist have any specific questions, please don't hesitate to contact:

Cheryl Dixon (Statistician Reviewer) 301-827-2213
Karen Higgins (Stats Team Leader) 301-827-2171
Rose Tiernan (Medical Officer reviewer) 301-827-2375
Marc Cavaille-Coll (Medical Officer Team Leader) 301-827-2414

SIGNATURE OF REQUESTER: Diana Willard March 1, 2001	METHOD OF DELIVERY (Check one):
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

/s/

Diana Willard
3/1/01 01:47:05 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

Division/Office): OPDRA

FROM: Division of Special Pathogen and Immunologic Drug Products HFD-590

DATE:	IND NO.:	NDA NO:	TYPE OF DOCUMENT :	DATE OF DOCUMENT:
November 9, 2000	[redacted]	21-266/21-267	Trade name consult request	November 9, 2000

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
Voriconazole		Anti-fungal	February 2001

NAME OF FIRM: Pfizer

REASON FOR REQUEST

I. GENERAL

NEW PROTOCOL
☐ PROGRESS REPORT
☐ NEW CORRESPONDENCE
☐ DRUG ADVERTISING
☐ ADVERSE REACTION REPORT
☐ MANUFACTURING CHANGE/ADDITION
☐ MEETING PLANNED BY
☐ PRE–NDA MEETING
☐ END OF PHASE II MEETING
☐ RESUBMISSION
☐ SAFETY/EFFICACY
☐ PAPER NDA
☐ CONTROL SUPPLEMENT
☐ RESPONSE TO DEFICIENCY LETTER
☐ FINAL PRINTED LABELING
☐ LABELING REVISION
☐ ORIGINAL NEW CORRESPONDENCE
☐ FORMULATIVE REVIEW
X OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER:	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

III. BIOPHARMACEUTICS

☐ DISSOLUTION
☐ BIOAVAILABILTY STUDIES
☐ PHASE IV STUDIES
☐ DEFICIENCY LETTER RESPONSE
☐ PROTOCOL-BIOPHARMACEUTICS
☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
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☐ SUMMARY OF ADVERSE EXPERIENCE
☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: Trade name review: LNC committee approved VFEND July 1999. (Pfizer's preference is V-FEND.
NDA is expected to come in end of November.

SIGNATURE OF REQUESTER: Jouhayna Saliba	METHOD OF DELIVERY (Check one): X E- MAIL ☐ HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

HFD-590
Matthew Bacho

REQUEST FOR TRADEMARK REVIEW

To: Labeling and Nomenclature Committee
Attention: Dan Boring, Chair (HFD-530), 9201 Corporate Blvd, Room S447

From: Division of Special Pathogen and Immunologic Drug Products	**HFD-590**
Attention: Matthew Bacho	**Phone:** (301) 827-2127
Date: July 2, 1999	
Subject: Request for Assessment of a Trademark for a Proposed New Drug Product	
Proposed Trademark: VFEND (V-FEND)	**NDA/ANDA#** IND
Established name, including dosage form: Voriconazole (Oral and I.V., respectively)	
Other trademarks by the same firm for companion products: N/A	
Indications for Use (may be a summary if proposed statement is lengthy): Triazole Antifungal Agent	
Initial Comments from the submitter (concerns, observations, etc.): Their strong preference is for "VFEND" but they would appreciate consideration of "V-FEND".	

Note: Meetings of the Committee are scheduled for the 4th Tuesday of the month. Please submit this form at least one week ahead of the meeting. Responses will be as timely as possible.

cc: Original IND ; HFD-590/division file; HFD-590/Matthew Bacho/Gene Holbert

IND —
IND —

CDER LABELING AND NOMENCLATURE COMMITTEE

CONSULT #	1233	HFD#	590	PROPOSED PROPRIETARY NAME:	PROPOSED ESTABLISHED NAME:
ATTENTION:	Matthew Bacho			VFEND	voriconazole
RE:	~~NDA~~/IND #				

A. Look-alike/Sound-alike

DeFEN LA

Potential for confusion:

XXX Low ____ Medium ____ High

____ Low ____ Medium ____ High

____ Low ____ Medium ____ High

____ Low ____ Medium ____ High

____ Low ____ Medium ____ High

B. Misleading Aspects:

C. Other Concerns:

D. Established Name

____ Satisfactory

____ Unsatisfactory/Reason

Recommended Established Name

E. Proprietary Name Recommendations:

XXX ACCEPTABLE ____ UNACCEPTABLE

F. Signature of Chair/Date /S/ 9/14/99

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21266/000
Priority: 1S
Org Code: 590
Stamp: 17-NOV-2000 Regulatory Due: 17-DEC-2001
Action Goal:
District Goal: 19-JUL-2001
Applicant: PFIZER GLOBAL
EASTERN POINT RD
GROTON, CT 06340
Brand Name: VFEND (VORICONAZOLE) 50/200MG TABLETS
Established Name:
Generic Name: VORICONAZOLE
Dosage Form: TAB (TABLET)
Strength: 50, 200 MG

FDA Contacts:
J. SALIBA (HFD-590) 301-827-2423 , Project Manager
G. HOLBERT (HFD-590) 301-827-2399 , Review Chemist
N. SCHMUFF (HFD-590) 301-827-2425 , Team Leader

Overall Recommendation:

ACCEPTABLE on 29-MAY-2001 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: 1211022
PFIZER INC
EASTERN POINT RD
GROTON, CT 06340
DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 18-JAN-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION
Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 29-NOV-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: DRUG SUBSTANCE MANUFACTURER
DRUG SUBSTANCE RELEASE TESTER

Establishment: 2211583
PFIZER INC
100 JEFFERSON RD
PARSIPPANY, NJ 07054
DMF No:
AADA No:

Profile: TCM OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 29-NOV-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Responsibilities: FINISHED DOSAGE PACKAGER

Establishment: 2410924
PFIZER INC
630 FLUSHING AVE
DMF No:
AADA No:

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

BROOKLYN, NY 11206

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 08-MAR-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Profile: TCM OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 08-MAR-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: FINISHED DOSAGE MANUFACTURER
FINISHED DOSAGE PACKAGER
FINISHED DOSAGE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER

Establishment: 9610425
PFIZER LTD
CT139NJ
SANDWICH, KENT, UK

DMF No:
AADA No:

Profile: CRU OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 30-NOV-2000
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: INTERMEDIATE MANUFACTURER

Establishment: 9611016
PFIZER PHARMACEUTICALS INC

RINGASKIDDY, COUNTY CORK, EI

DMF No: ~~~
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 24-MAY-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Responsibilities: DRUG SUBSTANCE MANUFACTURER
DRUG SUBSTANCE RELEASE TESTER

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 21267/000
Priority: 1S
Org Code: 590
Stamp: 17-NOV-2000 Regulatory Due: 17-DEC-2001
Action Goal:
District Goal: 19-JUL-2001
Applicant: PFIZER GLOBAL
EASTERN POINT RD
GROTON, CT 06340
Brand Name: VFEND (VORICONAZOLE) 20 MG IV
Established Name:
Generic Name: VORICONAZOLE
Dosage Form: INJ (INJECTION)
Strength: 200 MG/VIAL

FDA Contacts: J. SALIBA (HFD-590) 301-827-2423 , Project Manager
G. HOLBERT (HFD-590) 301-827-2399 , Review Chemist
N. SCHMUFF (HFD-590) 301-827-2425 , Team Leader

Overall Recommendation:

WITHHOLD on 14-NOV-2001 by P. LEFLER (HFD-324) 301-827-0062
WITHHOLD on 29-MAY-2001 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: [redacted]
DMF No:
AADA No:

Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 29-NOV-2000
Decision: ACCEPTABLE
Reason: BASED ON PROFILE
Profile: SVL OAI Status: OAI ALERT
Last Milestone: OC RECOMMENDATION
Milestone Date: 14-NOV-2001
Decision: WITHHOLD
Reason: EIR REVIEW-CONCUR W/DISTRICT

Responsibilities: [redacted]

Establishment: 1211022
PFIZER INC
EASTERN POINT RD
GROTON, CT 06340
DMF No:
AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 18-JAN-2001
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION
Profile: CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 29-NOV-2000

Responsibilities: DRUG SUBSTANCE MANUFACTURER
DRUG SUBSTANCE RELEASE TESTER
FINISHED DOSAGE STABILITY TESTER

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Establishment: **1819598**
PFIZER INC
100 PFIZER DRIVE
TERRE HAUTE, IN 47802

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **12-FEB-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE RELEASE TESTER**
FINISHED DOSAGE STABILITY TESTER

Establishment: **9610425**
PFIZER LTD
CT139NJ
SANDWICH, KENT, UK

DMF No:
AADA No:

Profile: **CRU** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **30-NOV-2000**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **INTERMEDIATE MANUFACTURER**

Establishment: **9611016**
PFIZER PHARMACEUTICALS INC

RINGASKIDDY, COUNTY CORK, EI

DMF No: ——
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **24-MAY-2001**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**
DRUG SUBSTANCE RELEASE TESTER

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: 6/28/01	DUE DATE: 8/17/01	OPDRA CONSULT: 01-0139

TO:

Mark Goldberger, M.D.
Director, Division of Special Pathogen and Immunologic Drug Products
HFD-590

THROUGH:

Jouhayna Saliba
Project Manager, Division of Special Pathogen and Immunologic Drug Products
HFD-590

PRODUCT NAME:	MANUFACTURER: Pfizer, Inc.
——— (Voriconazole) 50 mg and 200 mg Film-coated Tablets; Lyophilized Powder for Injection NDA #: 21-266/21-267	

SAFETY EVALUATOR: Jennifer Fan, Pharm.D.

SUMMARY: In response to a consult from the Division of Special Pathogen and Immunologic Drug Products (HFD-590), OPDRA conducted a review of the proposed proprietary name " to determine the potential for confusion with approved proprietary and established names as well as pending names.

OPDRA RECOMMENDATION:
OPDRA does not recommend the use of the proprietary name, '———

Carol Holquist, R.Ph. for
Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment
Phone: 301-827-3246
Fax: 301-443-5161

Martin Himmel, M.D.
Deputy Director
Office of Post-Marketing Drug Risk Assessment
Center for Drug Evaluation and Research
Food and Drug Administration

HFD-400; Rm. 15B32
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: July 27, 2001

NDA NUMBERS: 21-266/21-267

NAME OF DRUG: ——— (Voriconazole), 50 mg and 200 mg Film-coated Tablets; Lyophilized Powder for Solution for Infusion

NDA HOLDER: Pfizer, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Special Pathogen and Immunologic Drug Products (HFD-590) for assessment of the tradename " ———", regarding potential name confusion with other proprietary/generic drug names. The sponsor's prior tradename submissions for this product ("VFEND" and "V-FEND") were found unacceptable by OPDRA on February 20, 2001 (see OPDRA Consult 00-0318).

PRODUCT INFORMATION

——— (voriconazole) is a broad-spectrum, triazole antifungal agent that is indicated for the treatment of invasive aspergillosis, serious *Candida* infections, serious fungal infections, and empirical treatment of presumed fungal infections in febrile immunocompromised patients. ——— ' is available as a 50 mg and 200 mg film-coated tablet as well as a sterile lyophilized powder equivalent to 200 mg voriconazole in a single use vial for intravenous infusion. The film-coated tablets should be taken at least one hour before, or one hour following, a meal. VFEND/V-FEND I.V. for infusion requires reconstitution and dilution prior to administration as an infusion, at a maximum rate of 3 mg/kg per hour over 1-2 hours. See chart below for dosing information.

	INTRAVENOUS	ORAL	
		Patients 40 kg and above	Patients less than 40 kg
Loading Dose Regimen (1st 24 hrs)	Two doses of 6 mg/kg 12 hrs apart	Two doses of 400mg 12 hrs apart	Two doses of 200 mg 12 hrs apart
Maintenance Dose (after 1st 24 hrs)	3 mg/kg every 12 hrs	200 mg every 12 hrs	100 mg every 12 hrs

II. RISK ASSESSMENT:

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts[1,2,3] as well as several FDA databases[4] for existing drug names which sound alike or

[1] MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K

look alike to ——— ' to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database[5] and data provided by Thomson & Thomson's SAEGIS™ Online Service[6] were also conducted. An expert panel discussion was conducted to review all findings from the searches. In addition, OPDRA conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by OPDRA to gather professional opinions on the safety of the proprietary name " ——— Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of OPDRA Medication Errors Prevention Staff and representation from the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

The Expert Panel had concerns with the "vor" ending of ——— , which may sound-alike and look-alike to names ending in "cor" and "clor". Several product names were identified in the Expert Panel Discussion that were thought to have potential for confusion with ' ——— These products are listed in Table 1, along with the dosage forms available and usual FDA-approved dosage.

Table 1

———			
Zocor	Simvastatin (HMG-CoA Reductase Inhibitor – Rx) Tablet: 5 mg, 10 mg, 20 mg, 40 mg, and 80 mg	Initial: 20 mg once a day in the evening. Dose range: 5 to 80 mg/day.	S/A, L/A per OPDRA
Asacol	Mesalamine (Gastrointestinal – Rx) Tablet: 400 mg (delayed-release)	800 mg three times a day for 6 weeks.	S/A, L/A per OPDRA

(Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2000).

[2] American Drug Index, 42nd Edition, online version, Facts and Comparisons, St. Louis, MO.

[3] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

[4] The Established Evaluation System [EES], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-00, and the electronic online version of the FDA Orange Book.

[5] WWW location http://www.uspto.gov/tmdb/index.html.

[6] WWW location http://www.thomson-thomson.com.

Cozaar	Losartan Potassium (Angiotensin II Receptor Antagonists – Rx) Tablet: 25 mg, 50 mg, 100 mg	Initial: 50 mg once daily. Can be given once or twice daily with total dose range from 25 mg to 100 mg.	L/A per OPDRA
Azmacort	Triamcinolone Acetonide (Corticosteroid – Rx) Aerosol: 100 mcg per actuation from mouthpiece	2 inhalations (200 mcg) 3 to 4 times a day or 4 inhalations (400 mcg) twice daily.	S/A per OPDRA
		*Frequently used, not all-inclusive	**S/A(Sound-alike), L/A (Look-alike

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

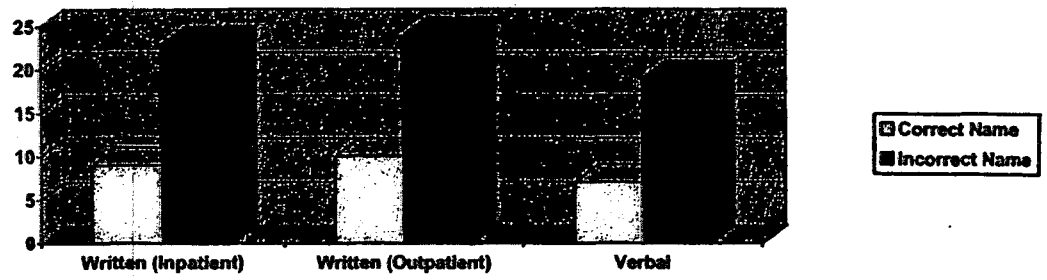
Studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of "—" and with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 117 health care professionals (nurses, pharmacists, and physicians). This exercise was conducted in an attempt to simulate the prescription ordering process. An OPDRA staff member wrote one inpatient prescription and one outpatient prescription, each consisting of a combination of marketed and unapproved drug products and prescriptions for — (see below). These written prescriptions were optically scanned and one prescription was delivered via e-mail to each study participant. In addition, one OPDRA staff member recorded a verbal outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via e-mail.

Inpatient: — 200 mg over 1-2 hr q 12h *Outpatient:* — 50 mg Sig: ii po q 12^{o} #60	*Outpatient:* — 50 mg Take 2 by mouth every 12 hours. #60

2. Results:

Results of these exercises are summarized below:

	39	32 (82%)	9 (28%)	23 (72%)
	39	34 (87%)	10 (29%)	24 (71%)
	39	26 (67%)	7 (27%)	19 (73%)
	117	92 (79%)	26 (28%)	66 (72%)



Among the written inpatient prescriptions, 23 (72%) out of 32 respondents interpreted ——— incorrectly. Interpretations included *Azanor, Azavron, Aganor, Aravon, Avavor, Azarron, Aprovor, Ajovron, Avarron, Azonor, Avanor, Afaron, Afavor, Azaror, Azaron, Aravvor, Azavro, Azanor,* and *Ajavor.*

Among the written outpatient prescriptions, 24 (71%) out of 34 respondents interpreted ——— incorrectly. Twenty (59%) respondents interpreted ——— as *Azacor.* Two (6%) respondents interpreted ——— " as *Cozaar.* Other interpretations included *Azacol* (3%) and *Azavoi* (3%).

Among the verbal outpatient prescriptions, 19 (73%) out of 26 respondents interpreted ——— incorrectly. Interpretations included *Effavor, Efavor, Esavor, Azavar, Affayfor, Evasor, Evaphor, Avavor, Azevor, Azabor, Azavon, Azafor, Evavior, Ezaphor, SS4, Afavore,* and *Eefavor.*

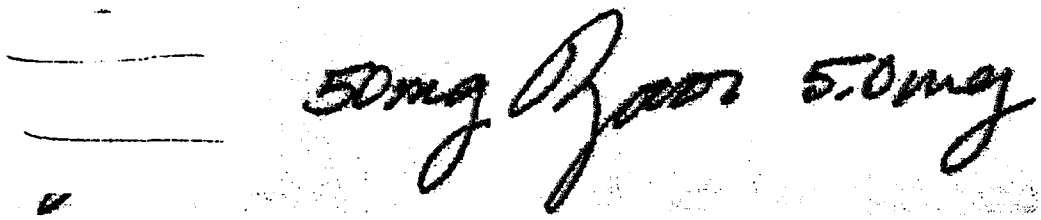
C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name ——— , the primary concerns raised were related to sound-alike, look-alike names that already exist in the U.S. marketplace. Such drug proprietary names include *Azmacort, Zocor, Asacol,* and *Cozaar.*

Azmacort is the proprietary name for triamcinolone acetate inhaler and is indicated for the maintenance of asthma as prophylactic therapy. *Azmacort* sounds similar to ——— since the "azma" and "aza" and also the "cor" and "vor" sound alike, respectively. However, *Azmacort* is supplied as an inhaler where it administers 100 mcg per actuation while ——— " is available as a 50 mg and 200 mg tablet and 10 mg/mL (20 mL) vial. The dosage forms of these two drug products are different (aerosol vs. tablet vs. injection), different administration directions ("Take 2 puffs 3 to 4 times a day" vs. "Take 1 tablet (200 mg) every 12 hours" vs. "3 mg/kg every 12 hours"), and the strengths are different. These differences may decrease the potential risk of a medication error occurring between these two drug products.

Zocor is the proprietary drug name for simvastatin and is indicated in patients with coronary heart disease, hypercholesterolemia, and hyperlipidemia. *Zocor* and " —— do sound alike due to the similarities in pronunciation with "zocor" and "zavor", respectively. A practitioner may prescribe "an ·——prescription" where the practitioner dispensing the prescription may misinterpret it as "a *Zocor* prescription". Even when scripted, the "A" and the "z" in —— can resemble an uppercase, scripted "Z" and the "v" can look like a "c" so that —— ' would look similar to *Zocor*. (See below) *Zocor* is available as a 5 mg, 10 mg, 20 mg, 40 mg, and 80 mg tablet where ——." is available in a 50 mg and 200 mg tablet as well as a 200 mg lyophilized powder. Even though there are no exactly overlapping strengths, the 5 mg and 20 mg may be written as 5.0 mg and 20.0 mg with a trailing zero where the decimal point can be missed when reading the prescription. Both drug products have the same dosage form (tablet), the same route of administration (oral), and the same numbers in their strengths (50 mg and 200 mg vs. 5.0 mg and 20.0 mg). If a patient was given —— instead of *Zocor*, the patient's coronary heart disease, hypercholesterolemia, and hyperlipidemia would not be adequately treated. Also, the patient would be exposed to unnecessary adverse effects such as hepatic toxicity, photophobia and/or blurring, color vision change, and rash. If the mistake was later discovered after administering the —— " and the problem was corrected by administering the *Zocor* to the patient before the " —— ' was out of the patient's system, a drug-drug interaction can occur between *Zocor* and the —— *Zocor* belongs to a particular drug category, the *Statins*, where ——is likely to increase the plasma concentration of statins that are metabolized by CYP3A4. An increased level of statins have been associated with myopathy. If *Zocor* was dispensed instead of —— . then the patient's serious fungal infection would not be treated. Also, the patient would experience unnecessary side effects such as abdominal pain, constipation, headaches, and asthenia. The patient would also be at risk for myopathy. *Zocor* is also rated as Pregnancy Category X. The fetus of a pregnant woman would be harmed if *Zocor* was inadvertently administered to a pregnant woman.

Writing Sample:



—— ·50 mg *Zocor 5.0 mg*

Asacol is the proprietary drug name for mesalamine and is indicated for the remission and treatment of mildly to moderately active ulcerative colitis. *Asacol* sounds quite similar to —— ", but slightly resembles ——." when scripted. The "Asa" and "Aza" sound alike as well as the "ol" and "or", respectively. Both drug products are also available in tablet form. *Asacol* is only available in 400 mg while —— ' is available in 50 mg and 200 mg. Even though the strengths are different, a practitioner may disregard the strengths and dispense the wrong medication, especially when the names are similar and the practice setting is chaotic. For example, Cerebyx and Celebrex do not share the same strengths or dosage form; however, there have been reported cases of the name confusion. A practitioner may also adjust the amount of tablets given to satisfy the prescribed dosage. For example, a physician may prescribe "Asacol 400 mg; 2 tablets 3 times a day" where a practitioner may dispense ' —— · 200 mg; 4 tablets 3 times a day" giving the patient an overdose of ' —— ' as well as the wrong medication. According to the written oupatient portion of the OPDRA study, 20 (59%) out of 34 respondents

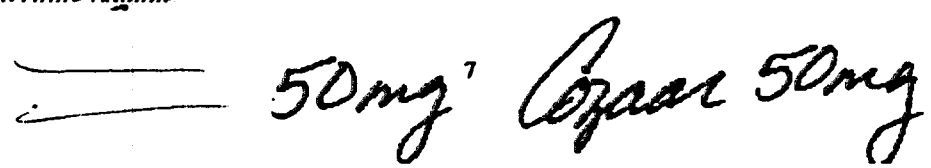
interpreted ——— as *Azacor*. One respondent (3%) interpreted ——— as *Azacol*, which when phonetically said is *Asacol*. Another respondent who interpreted ——— correctly commented that '——— can be confused with *Asacol*. If a nurse gave a prescription over the phone to a pharmacist, the pharmacist can easily mistaken it for *Asacol*. If *Asacol* was given instead of ———', then the patient's fungal infection would not be treated. Also, the patient would experience unnecessary side effects such as headaches, bloody diarrhea, abdominal pains, and conjunctivitis. If ——— " was given instead of *Asacol*, then the patient's ulcerative colitis would not be treated. Also, the patient would be exposed to unnecessary adverse effects such as hepatic toxicity, photophobia and/or blurring, color vision change, and rash.

Writing Sample:

Asacol

Cozaar is proprietary drug name for losartan potassium and is indicated for the treatment of hypertension alone or in combination with other antihypertensive agents. Even though there are no sound-alike properties between *Cozaar* and '———except for the "ar" and "or", respectively, they do look similar when scripted. (See below.) Like ' ——— ', *Cozaar* is available as a 50 mg tablet (also available in 25 mg and 100 mg) and can be dosed twice a day. These two drug products share the same route of administration (oral), the same dosage form (tablet), the same strength (50 mg), and the same dosing schedule (twice a day). Also, from the written outpatient portion of the OPDRA study, 2 (6%) out of 34 respondents interpreted ——— ' as *Cozaar*. Although there are limitations to the predictive value of the OPDRA studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretations with these drug products. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population. If *Cozaar* was dispensed instead of ' ——— , then the patient's fungal infection would not be treated. Also, the patient would be exposed to unnecessary side effects such as a persistent dry cough, hypotension, dizziness, fatigue, abdominal pain, chest pain, nausea, and headache. Also, *Cozaar* is rated in Pregnancy Category C (first trimester) and D (second and third trimesters). The fetus would be harmed if *Cozaar* was mistakenly given to a pregnant female. If ——— was given instead of *Cozaar*, then the patient's hypertension would not be controlled. Also, the patient would be exposed to unnecessary adverse effects such as hepatic toxicity, photophobia and/or blurring, color vision change, and rash.

Writing Sample:



——— *50 mg* *Cozaar 50 mg*

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

Please refer to OPDRA Consult 00-0318 for labeling and packaging recommendations.

IV. RECOMMENDATIONS:

OPDRA does not recommend the use of the proprietary name ———

OPDRA would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, R.Ph. at 301-827-3231.

Jennifer Fan, Pharm.D.
Safety Evaluator
Office of Post-Marketing Drug Risk Assessment

Concur:

Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Post-Marketing Drug Risk Assessment

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jennifer Fan
8/20/01 10:29:28 AM
PHARMACIST

Carol Holquist
8/20/01 11:15:54 AM
PHARMACIST

Martin Himmel
8/27/01 04:29:29 PM
MEDICAL OFFICER