CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-758

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

NDA NUMBER
21-758

NAME OF APPLICANT / NDA HOLDER
Medicis Pharmaceutical Corporation

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
[redacted] fluocinonide) Cream 0.1%

ACTIVE INGREDIENT(S)	STRENGTH(S)
fluocinonide	0.1%

DOSAGE FORM
0.1%

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).
Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent

d. Name of Patent Owner	Address *(of Patent Owner)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☐ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

PSC Media Arts (301) 443-1090 EF

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1	Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.2	Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.3	If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No
2.4	Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**.		
2.5	Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☐ No
2.6	Does the patent claim only an intermediate?	☐ Yes	☐ No
2.7	If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1	Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
3.2	Does the patent claim only an intermediate?	☐ Yes	☐ No
3.3	If the patent referenced in **3.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1	Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
4.2	Patent Claim Number *(as listed in the patent)*	Does the patent claim referenced in **4.2** claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☐ Yes ☐ No	
4.2a	If the answer to **4.2** is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the approved labeling.)*	

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.	☒ Yes	

6. Declaration Certification

6.1 ***The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide Information below)*	Date Signed
	3/25/04

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

☒ NDA Applicant/Holder	☐ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name
R. Todd Plott, MD, Vice President Clinical Research and Regulatory Affairs

Address	City/State
Medicis Pharmaceutical Corporation 8125 North Hayden Road	Scottsdale AZ
ZIP Code 85258	Telephone Number 602 808 8800
FAX Number *(if available)* 602 778 6051	E-Mail Address *(if available)* tplott@medicis.com

The public reporting burden for this collection of information has been estimated to average 9 hours 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:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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.

PSC Media Arts (301) 443-1090 EF

EXCLUSIVITY SUMMARY FOR NDA # __21-758__ SUPPL #_N/A_____

Vanos Generic Name fluocinonide Cream 0.1%

Applicant Name _Medicis Pharmaceuticals HFD # 540

Approval Date If Known _February 11, 2005_____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES /_X__/ NO /___/

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

__505(b)(1)_____

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.

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?

N/A

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

YES /___/ NO /__X_/

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Writen Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

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

YES /___/ NO /_X__/

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (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 /__X_/ NO / __/

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

NDA# _16-908_____ _Lidex Cream_____

NDA# __16-909_____ _Lidex_Ointment_____

NDA# __17-373_____ _Lidex Gel_____

NDA# __18-849_____ Lidex_Solution_____

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.)

N/A /_X__/ 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 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.) IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

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 /_X__/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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.

(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 /_X__/ 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 8:

_____N/A_____

(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 /_X__/ 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 /_X__/

If yes, explain:

N/A

(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 /_X__/

If yes, explain:

N/A

(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:

MP-0201-05, MP-0201-06, MED-00-018, MED-01-022, MED-02-004, and MED-02-005

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

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 /_X__/

Investigation #2 YES /___/ NO /_X__/

Investigation #3	YES /___/	NO /__X_/
Investigation #4	YES /___/	NO /__X_/
Investigation #5	YES /___/	NO /_X__/
Investigation #6	YES /___/	NO /__X_/

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

_____N/A_____ _____

_____ _____

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 /_X__/
Investigation #2	YES /___/	NO /_X__/
Investigation #3	YES /___/	NO /_X__/
Investigation #4	YES /___/	NO /_X__/
Investigation #5	YES /___/	NO /_X__/
Investigation #6	YES /___/	NO /___/

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

____N/A_____ _____

_____ _____

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"):

MP-0201-05, MP-0201-06, MED-00-018, MED-01-022, MED-02-004, and MED-02-005

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 # 61,701__ YES /_X__/ ! NO /___/ Explain: _____

Investigation #2

IND # 61,701__ YES /_X__/ ! NO /___/ Explain: _____

Investigation #3

IND # 61,701__ YES /_X__/ ! NO /___/ Explain: _____

Investigation #4

IND # 61,701__ YES /_X__/ ! NO /___/ Explain: _____

Investigation #5

IND # 61,701__ YES /_X__/ ! NO /___/ Explain: _____

Investigation #6

IND # 61,701__ YES /_X__/ ! 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 _____

_____N/A_____ ! _____

Investigation #2 !

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

_____N/A_____ ! _____

Investigation #3 !

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

_____N/A_____ ! _____

Investigation #4 !

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

_____N/A_____ ! _____

Investigation #5 !

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

_____N/A_____ ! _____

Investigation # !

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

_____N/A_____ ! _____

(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 /_X__/

If yes, explain: _____

_____N/A_____

February 11, 2005
Melinda Harris-Bauerlien, M.S. Date
Regulatory Project Manager

February 11, 2005
Jonathan Wilkin, M.D. Date
Division Director

Form OGD-011347 Revised 05/10/2004

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

/s/

Melinda Harris-Bauerlien
2/11/05 02:13:19 PM

Jonathan Wilkin
2/11/05 02:58:22 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-758 Supplement Type (e.g. SE5): N/A Supplement Number: N/A

Stamp Date: April 12, 2004 Action Date: February 12, 2005

HFD-540 Trade and generic names/dosage form: [redacted] (fluocinonide) Cream, 0.1%

Applicant: Medicis Pharmaceutical Corporation Therapeutic Class: 3S

Indication(s) previously approved:

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

Number of indications for this application(s): 1

Indication #1: Relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses

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

- ☐ Yes: Please proceed to Section A.

xNo: 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:

Min _____ **kg**_____ **mo.** 3 **yr.** 0 **Tanner Stage**_____
Max_____ **kg**_____ **mo.**_____ **yr.** <18 **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**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other: HPA axis suppression studies are currently being conducted.

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}

Melinda Harris, M.S.
Regulatory Project Manager

cc: **NDA 21-758**
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

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

/s/

Melinda Harris
10/14/04 10:36:10 AM

Brenda Vaughan
10/18/04 06:05:24 PM

Markham Luke
10/20/04 04:40:19 PM
Pediatric studies in 0 to 3 months are waived due to safety concerns and practicality of study.

Stanka Kukich
10/20/04 05:23:17 PM

MEDICIS

The Dermatology Company®

DEBARMENT AND FELONY CONVICTION CERTIFICATION

Pursuant to Sections 306(a) and (b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 335(a) and (b))

NDA 21-758

[redacted] fluocinonide) Cream 0.1%

This is to certify:

1. that we did not use in any capacity the services of any person debarred under subsection (a) or (b) of this section in connection with the development or submission of this application;

2. that we will not use in any capacity the services of any person debarred under subsection (a) or (b) of this section in connection with this application; and

3. that neither the applicant nor affiliated persons responsible for the development or submission of this application have been convicted within the past (5) years of offenses described in subsections (a) and (b) of this section.

List of Convictions: none.

R. Todd Plott MD 3/25/04

R. Todd Plott, M.D. Date
Vice President
Clinical Research and Regulatory Affairs

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: January 5, 2005 **DOCUMENT DATE:** Nov. 22, 2004	**DESIRED COMPLETION DATE:** February 12, 2005 **PDUFA DATE:** Feb. 12, 2005	**ODS CONSULT #:** 05-0001

TO: Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH: Melinda Harris-Bauerlien
Project Manager
HFD-540

PRODUCT NAME: **Vanos** (Fluocinonide Cream) 0.1% **NDA #:** 21-758	**SPONSOR:** Medicis Pharmaceuticals

SAFETY EVALUATOR: Tia M. Harper-Velazquez, Pharm.D.

RECOMMENDATIONS:

1. DMETS has no objection to the use of the proprietary name, Vanos. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

2. DMETS recommends implementation of the labeling revisions as outlined in Section III of this review in order to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name Vanos acceptable from a promotional perspective.

Carol Holquist, R.Ph.
Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: January 31, 2005

NDA NUMBER: 21-758

NAME OF DRUG: **Vanos**
(Fluocinonide Cream)
0.1%

NDA SPONSOR: Medicis Pharmaceuticals

I. INTRODUCTION

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540), for an assessment of the proprietary name "Vanos" regarding potential name confusion with other proprietary and/or established drug names. This is the third proprietary name reviewed for this application. The first proprietary name, [redacted] was previously reviewed by DMETS on August 18, 2004, and was found unacceptable (See ODS Consult # 04-0188). Comments pertaining to the proposed container labels, carton and insert labeling were forwarded to the Division at that time. Since the initial review, DMETS has learned through discussions with the review division that this product is not the same as the currently marketed Lidex. Upon preliminary review, the second proprietary name, [redacted], was also found unacceptable, and comments were forwarded to the Division on January 28, 2005 via email. In light of this preliminary information, the sponsor requested to have Vanos reviewed as the primary name. Updated package insert labeling was provided for review and comment.

PRODUCT INFORMATION

Vanos is the proposed name for fluocinonide cream, a corticosteroid indicated for the treatment of plaque-type psoriasis. A thin layer of Vanos will be applied to the affected skin areas twice a day as directed by a physician. The use of Vanos in patients under 18 years of age is not recommended. Vanos will be available in a strength of 0.1%, and dispensed in 30 gram and 60 gram tubes.

II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[i,ii] as well as several FDA databases[iii] for existing drug names which sound-alike or look-alike to "Vanos™" to a degree where potential confusion between drug names could occur

[i] MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[ii] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[iii] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support proprietary name consultation requests, New Drug Approvals 1998-2004, and the electronic online version of the FDA Orange Book.

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[iv] and the data provided by Thomson & Thomson's SAEGIS™ Online Service[v] were also conducted. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS 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 DMETS to gather professional opinions on the safety of the proprietary name, Vanos. Potential concerns regarding drug marketing and promotion related to the proposed name was also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and 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.

1. DDMAC did not have any concerns from a promotional perspective regarding the proposed name Vanos.

2. The Expert Panel identified nine currently marketed proprietary names as having the potential for confusion with Vanos. These products are listed in Table 1 (see below and page 4), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	**Dosage form(s), Established Name**	**Usual Adult Dose***	**Other****
Vanos (Rx)	**Fluocinonide Cream 0.1%**	**Apply a thin layer to affected area twice daily, as directed by a physician.**	
Vantas (Rx)	Histrelin Acetatem Implant 50 mg	One implant per year.	**L/A, S/A
Vumon (Rx)	Teniposide Injection 10 mg/mL	0.1 mg/mL to 0.2 mg/mL administered over 30 to 60 minutes.	**L/A
Vanex-HD (Rx)	Hydrocodone, Phenylephrine, and Chlorpheniramine Liquid 1.7 mg/5 mg/2 mg	2 teaspoonfuls (10 mL) 3 to 4 times a day, not to exceed 8 teaspoonfuls in 24 hours.	**L/A, S/A
Vanco (Rx)	Vancomycin Powder Injection: 500 mg, 1 gram, 5 grams, and 10 grams Powder for Oral Solution: 1 gram	500 mg every 6 hours or 1 gram every 12 hours.	**L/A, S/A
Lonox (Rx)	Diphenoxylate and Atropine Tablets 2.5 mg/0.025 mg	Initially take 2 tablets 4 times daily, then individualize according to response.	**L/A
Lantus (Rx)	Insulin Glargine 100 IU/mL	Dose is individualized, usually 2 IU to 100 IU subcutaneously once	**L/A

[iv] WWW location http://www.uspto.gov.

[v] Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

Product Name	Dosage form(s), Established Name	Usual Adult Dose*	Other**
Vanos (Rx)	**Fluocinonide Cream 0.1%**	**Apply a thin layer to affected area twice daily, as directed by a physician.**	
		daily.	
Xanax (Rx)	Alprazolam Tablets 0.25 mg, 0.5 mg, 1mg, and 2 mg	0.25 mg to 0.5 mg 3 times daily; max 4 mg daily in divided doses.	**L/A
Xanax XR (Rx)	Alprazolam Extended-release Tablets 0.5 mg, 1 mg, 2 mg, and 3 mg	0.5 mg to 1 mg once daily, preferably in the morning.	**L/A
Vantin (Rx)	Cefpodoxime Tablets 100 mg and 200 mg	Pneumonia 200 mg every 12 hours for 14 days. Bronchitis and sinusitis 200 mg every 12 hours for 10 days. Pharyngitis and Tonsillitis 100 mg every 12 hours for 5-10days. Skin and Skin Structures 400 mg every 12 hours for 7-14 days. Urinary Tract Infection 100 mg every 12 hours for 7 days Uncomplicated Gonorrhea 200 mg once as a single dose.	**L/A, S/A
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

B. PHONETIC ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs though the phonetic algorithm. The phonetic search modules return a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Vanos were discussed by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Vanos with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 123 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Vanos (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the

participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Vanos as dir #1	Vanos, use as directed, dispense #1.
Inpatient RX: Vanos as dir #1	

2. Results:

   None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See appendix A for the complete listing of interpretations from the verbal and written studies.

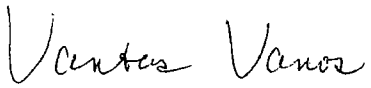
D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name "Vanos", the primary concerns raised were related to nine look-alike and/or sound-alike names currently marketed in the United States. The products considered to have potential for name confusion with Vanos were: Vantas, Vumon, Vanex-HD, Vanco, Lantus, Xanax, and Xanax XR. Upon further review of the names gathered from EPD, the names Lantus, Xanax, and Xanax XR, were not reviewed further due to a lack of convincing look-alike/sound-alike similarities with Vanos, in addition to numerous differentiating product characteristics such as dosage form, route of administration, product strength, and dosing regimen.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of the misinterpretations were misspelled/phonetic variations of the proposed name, Vanos.

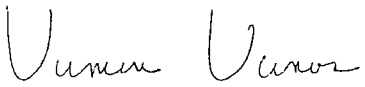
1. Vantas was identified to have look-alike and sound-alike similarity to the proposed name, Vanos. Vantas is a long-acting implant indicated for the palliative treatment of advanced prostate cancer. Once inserted, Vantas must be removed after 12 months of therapy. The look-alike and sound-alike similarities between the names can be attributed to the letters "V", "a", "n", and "s", which appear in both names. Additionally, the next to the last letters in each name ("a" vs. "o') can look similar when scripted, although they differ phonetically. The "t" (in Vantas) further distinguishes the names phonetically, as well as visually, if the "t" is written with a prominent upstroke. Both products are also available as a single strength. However, they differ in dosage form (implant vs. cream), route of administration (subcutaneous vs. topical), and dosing regimen (yearly vs. twice daily). In addition, because Vantas is indicated for the palliative treatment of prostate cancer, it will likely be prescribed by physician specialists, such as oncologists, unlike Vanos which will likely be prescribed by dermatologists or general practitioners. DMETS believes that the aforementioned product differences, in addition to the differences in prescriber population, will minimize the risk of confusion and error due to look-alike and sound-alike similarities between Vantas and Vanos.

Vantas **Vanos**



2. Vumon looks similar to the proposed name, Vanos. Vumon contains teniposide, and is indicated for the treatment of patients with refractory childhood acute lymphoblastic leukemia. Vumon is administered at a concentration of 0.1 mg/mL to 0.2 mg/mL over 30 to 60 minutes. Both names contain five letters. The first three letters of each name ("Vum" vs. "Van) can look similar, particularly if the "a" (in Vanos) is written with an open loop. Likewise, if the last letter "s" (in Vanos) is not closed, the last two letters of each name can look similar when scripted ("on" vs. "os"). Vumon and Vanos also have overlapping numerals in their strengths (10 mg/mL vs. 0.1%). Despite theses similarities, there are product differences between Vumon and Vanos, which help to distinguish them from one another. These include route of administration (intravenous vs. topical), dosage form (injection vs. cream), and dosing regimen (infused over 30 to 60 minutes vs. twice daily). Vumon is also supplied in 5 mL ampules, whereas Vanos will be supplied in 30 and 60 gram tubes. Also, because Vumon is an antineoplastic agent, it will not likely be stored near Vanos on pharmacy shelves. DMETS believes that the aforementioned differences minimize the potential for confusion between Vumon and Vanos.

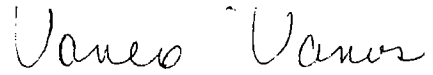
Vumon **Vanos**



3. Vanex-HD was identified to look and sound similar to Vanos when the modifier "HD" is omitted from the proprietary name. Vanex-HD is a Schedule III narcotic drug product containing the active ingredients hydrocodone, phenylephrine, and chlorpheniramine. It is indicated for the symptomatic relief of cough, nasal and eustachain tube congestion, and discomfort associated with the common cold, sinusitis, and acute upper respiratory tract infections. The recommended dose is two teaspoonfuls (10 mL) three to four times a day, not to exceed eight teaspoonfuls in 24 hours. The look-alike and sound-alike similarities can be attributed to the identical letter combination at the beginning of each name ("Van"). If the "o" (in Vanos) is written with an open loop, the remaining letters of the names can look somewhat similar, although they are

phonetically distinguishable from each other when pronounced ("ex" vs. "os"). Both products are available in a single strength. However, they differ in route of administration (oral vs. topical), dosage form (oral liquid vs. cream), and dosing regimen (twice daily vs. 3 to 4 times daily). Also, because Vanos is a topical product, it is likely that prescriptions for Vanos may be written with directions that state "use as directed", unlike Vanex-HD, which will likely be written with specific directions such as "Take 2 teaspoonfuls 3 times daily as needed". DMETS believes that the aforementioned product differences will minimize the risk of confusion between Vanex-HD and Vanos.

Vanex **Vanos**



4. Vanco looks and sounds similar to the proposed name, Vanos. Vanco is the commonly used abbreviated form of the established name, Vancomycin, an antibiotic indicated for the treatment of severe infections not treatable with other antimicrobials, particularly *staphylococcal* and *streptococcal* infections. The look-alike and sound-alike similarities can be attributed to the identical letter combination at the beginning of each name ("Van"). In addition, both names end with an "o" sound, even though the letter "o" appears at a different position in each name when the names are written. If it is not muffled when pronounced, the "s" at the end of the proposed name, Vanos, helps to distinguish the names from each other when spoken. In addition, both products are administered twice daily, and have overlapping numerals in their strengths (1 gram vs. 0.1%). Despite these similarities, the products differ in route of administration (intravenous vs. topical), and dosage form (powder for injection vs. cream). In addition, because Vanco is available in multiple strengths, a strength would likely be indicated on a prescription order prior to dispensing and administering the medication to a patient, unlike Vanos, which can be prescribed and dispensed without a strength being indicated. Because Vanco is an antibiotic, it is also likely that the dose will be indicated on prescriptions orders. Lastly, Vanco is also administered mostly in in-patient clinical settings, under a supervision of healthcare personnel, unlike Vanos which can be used in both in-patient and out-patient settings. Although there are look-alike and sound-alike similarities between the names, the differences in route of administration, dosage form, and context of use, minimize DMETS' concerns regarding the potential for confusion and error between Vanco and Vanos.

Vanco **Vanos**

5. Lonox looks similar to the proposed name, Vanos. Lonox is a combination drug product, containing diphenoxylate and atropine, in strengths of 1.5 mg and 0.025 mg, respectively. It is indicated for the treatment of diarrhea. The initial recommended dose is two tablets four times daily, after which the dose is individualized according to patient response. Both names contain five letters, and the first four letters of the names ("Lono" vs. "Vano") can look similar, depending on how the "V" in Vanos is written. Additionally, if the letter "x" in Lonox is written without lifting the pen, it can resemble a lower case "s". Although the recommended dosing regimen for Lonox is four times daily, because the dose is individualized according to patient response, there is a potential for patients to take the medication twice daily, which would overlap with the recommended twice daily dosing regimen for Vanos. Also, because both prescriptions are available in only one strength, prescriptions for Lonox and Vanos could be filled and dispensed without a strength being indicated. However, Lonox and Vanos differ in route of

administration (oral vs. topical), dosage form (tablet vs. cream), and indication (diarrhea vs. psoriasis). DMETS believes that these differences, in addition to a lack of convincing look-alike similarities, minimize the potential for confusion and error between Lonox and Vanos.

Lonox	Vanos
Lonox	Vanos

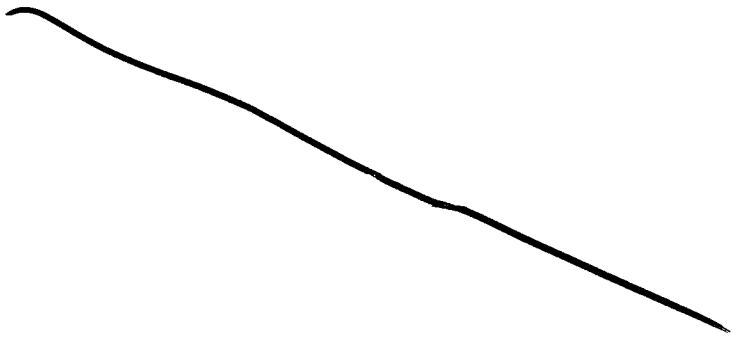
6. Vantin was identified to look and sound similar to the proposed name, Vanos. Vantin is a cephalosporin antibiotic, indicated for the treatment of infection, including pneumonia, bronchitis, sinusitis, pharyngitis, urinary tract infections, and uncomplicated gonorrhea. Vantin is available as a 100 mg and 200 mg tablet. The recommended dose varies, depending on the condition being treated. Both begin with the letter combination "Van" which contributes to both the look-alike and sound-alike similarities between the names. Both products are dosed twice daily and have overlapping numerals in their strengths (100 mg vs. 0.1%). The presence of the upstroke letter "t" in Vantin helps to distinguish the names from one anther when written. In addition, the ending letters of the names ("tin" vs. "os") are also phonetically different, thus minimizing the sound-alike similarities between the names. Vantin and Vanos also differ in route of administration (oral vs. topical), and dosage form (tablet vs. cream). DMETS believes that the lack of convincing look-alike and sound-alike similarities between the names, in addition to the differences in product characteristics, such as route of administration and dosage form, minimize the potential for confusion between Vantin and Vanos.

Vantin	Vanos
Vantin	Vanos

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

In review of the updated insert labeling for Vanos, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

PACKAGE INSERT LABELING



IV. RECOMMENDATIONS

A. DMETS has no objection to the use of the proprietary name, Vanos. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

B. DMETS recommends implementation of the labeling revisions as outlined in Section III of this review in order to minimize potential errors with the use of this product.

C. DDMAC finds the proprietary name Vanos acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

Tia M. Harper-Velazquez, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

Alina Mahmud, R.Ph., M.S.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A. DMETS prescription study results.

Voicemail	Outpatient	Inpatient
Banex	Vanos	Vanos
Banis	Vanos	Vanos
Sannas	Vanos	Vanos
Stanis	Vanos	Vanos
Vanas	Vanos	Vanos
Vanas	Vanos	Vanos
Vanice	Vanos	Vanos
Vanice	Vanos	Vanos
Vanis	Vanos	Vanos
Vanis	Vanos	Vanos
Vanise	Vanos	Vanos
Zanis	Vanos	Vanos
Zanus	Vanos	Vanos
	Vanos	Vanos
		Vanos
		Vionos
		Vonos

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/s/

Tia Harper-Velazquez
2/8/05 10:45:19 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
2/8/05 12:27:55 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
2/8/05 12:37:22 PM
DRUG SAFETY OFFICE REVIEWER

MEDICIS

The Dermatology Company®

February 8, 2005

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

Phase 4 Commitment Request

Re: NDA 21-758: Fluocinonide Cream 0.1%

Dear Dr. Wilkin:

Reference is made to the New Drug Application (NDA) for Fluocinonide Cream 0.1% submitted in accordance with 21 CFR 314.50 on April 7, 2004. Further reference is made to the February 7, 2005, fax from FDA stipulating the Phase 4 Commitments for this NDA.

Medicis commits to conducting a dermal carcinogenicity study with Fluocinonide Cream 0.1%.

Development of dosing formulations:	By August 15, 2005
Development and validation of analytical methodology:	By February 15, 2006
90-day dose range-finding study:	By December 15, 2006
Study protocol submission:	By June 15, 2007
Study start date:	By February 15, 2008
Final report submission:	By August 15, 2011

Medicis commits to conducting a study to determine the photocarcinogenic potential of Fluocinonide Cream 0.1%

90-day dose range-finding study:	By December 15, 2006
Study protocol submission:	By June 15, 2007
Study start date:	By February 15, 2008
Final report submission:	By August 15, 2010

Should you have any questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051.

Sincerely,

R. Todd Plott

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation V

FACSIMILE TRANSMITTAL SHEET

DATE: February 8, 2005

To: Michelle Wells	**From:** Melinda Harris-Bauerlien, M.S. Project Manager
Company: Medicis Pharmaceuticals	Division of Dermatologic & Dental Drug Products
Fax number: (602) 778-6051	**Fax number:** (301) 827-2091 or 2075
Phone number: (602) 808-3851	**Phone number:** (301) 827-2020

Subject: NDA 21-758

Total no. of pages including cover: 7

Comments

Minutes from the 1/13 and 2/3 CMC tcons are provided

Document to be mailed: ☐ YES ☑ NO

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MEMORANDUM OF TELECON

DATE: 2/3/05, 10:30 A.M.

APPLICATION NUMBER: NDA 21-758
DRUG PRODUCT: TRADENAME (fluocinonide) Cream, 0.1%

BETWEEN:

Name: Todd Plott, M.D., Vice President, Clinical Research & Regulatory Affairs
Bhiku Patel, Ph.D., Executive Director, Product Development
Michelle Wells, Associate Director, Regulatory Affairs
Willy Brondum, RA Manager CMC
Steve Newhard, VP Quality and Technical Services
Xiaoming Lin, Associate Director, Clinical Research

Phone: (877) 847-8112

Representing: Medicis Pharmaceuticals

AND

Name: Division of Dermatologic and Dental Drug Products, HFD-540
Ramesh Sood, Ph.D./Chemistry Team Leader
Ernest Pappas, M.S., Chemistry Reviewer
Melinda Harris-Bauerlien, M.S., Regulatory Project Manager

SUBJECT: NDA 21-758

The teleconference was requested by the Agency to request specific information from the Sponsor concerning the submitted NDA.

The Agency stated that on page 1, point 3 of the December 29, 2004 submission, the sponsor has stated that the viscosity specification is to be determined. They Agency stated that the proposed specifications of " TBD" is not acceptable and should have a numerical range.

1. *The Sponsor responded that they have manufactured several batches and all were within specification. They were concerned that most were near the upper limit rather than the lower limit.* . The sponsor proposed an in-process bulk specification of [redacted]

2. The Agency requested that the sponsor submit the revised specification and they will review it.

The sponsor responded that they will send it by the end of the day.

3. The Agency stated that the original submission did not contain a stability commitment. They should follow the ICH guidelines. They should indicate that they will provide stability on the first 3 commercial batches.

   The sponsor responded that they have stated it on page 1 of 5 in the December 29, 2004 submission. They will provide a revised statement that clearly describes the postapproval stability commitment by the end of the day.

4. The Agency asked if there was any difference in the batch [redacted]

   The Sponsor responded that there is no difference in feel, before or after stability from the others. All batches behaved the same way.

The Sponsor stated that they would respond via fax and formal submission to the NDA. The conversation ended amicably.

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/s/

Melinda Harris-Bauerlien
2/8/05 10:28:39 AM
CSO

Ramesh Sood
2/8/05 11:47:37 AM
CHEMIST

MEMORANDUM OF TELECON

DATE: 1/13/05, 11:00 A.M.

APPLICATION NUMBER: NDA 21-758
DRUG PRODUCT: TRADENAME (fluocinonide) Cream, 0.1%

BETWEEN:

Name: Todd Plott, M.D., Vice President, Clinical Research & Regulatory Affairs
Bhiku Patel, Ph.D., Executive Director, Product Development
Michelle Wells, Associate Director, Regulatory Affairs
Willy Brondum, RA Manager CMC
Kuljit Bhatia, Director, Product Development
Thomas Siebenaler, Manager QC
Terri Magee, Director QC

Phone: (877) 847-8112

Representing: Medicis Pharmaceuticals

AND

Name: Division of Dermatologic and Dental Drug Products, HFD-540
Ramesh Sood, Ph.D./Chemistry Team Leader
Ernest Pappas, M.S., Chemistry Reviewer
Melinda Harris-Bauerlien, M.S., Regulatory Project Manager

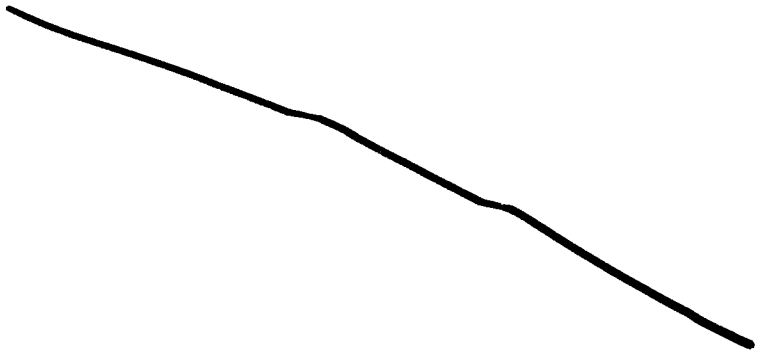
SUBJECT: NDA 21-758

The teleconference was requested by the Agency to request specific information from the Sponsor concerning the submitted NDA.

1. The Agency stated that they have a concern that there is no microscopic exam[redacted] the manufacturing process. The Agency indicated that a microscopic examination be included since the visual examination is too subjective. Information was given that the [redacted] substance was added [redacted]. The FDA asked how they know the [redacted]

   They will add a visual examination of the manufacturing process.

2.



3.

The Sponsor stated that they would respond via fax and formal submission to the NDA. The conversation ended amicably.

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/s/

Melinda Harris-Bauerlien
2/8/05 11:34:32 AM
CSO

Ramesh Sood
2/8/05 11:43:21 AM
CHEMIST

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation V

FACSIMILE TRANSMITTAL SHEET

DATE: February 7, 2005

To: Michelle Wells	**From:** Melinda Harris-Bauerlien, M.S. Project Manager
Company: Medicis Pharmaceuticals	Division of Dermatologic & Dental Drug Products
Fax number: (602) 778-6051	**Fax number:** (301) 827-2091 or 2075
Phone number: (602) 808-3851	**Phone number:** (301) 827-2020

Subject: NDA 21-758

Total no. of pages including cover: 3

Comments;

**Following are the Phase 4 commitments for NDA 21-758. If these are acceptable please fax a response restating the commitments and that they are acceptable.

Please also send in a formal submission to your NDA.

Document to be mailed: ☐ YES ☑ NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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NDA 21-758 TRADENAME Cream Phase 4 commitments

1. The applicant commits to conducting a dermal carcinogenicity study with TRADENAME (fluocinonide) cream.

Development of dosing formulations:	By August 15, 2005
Development and validation of analytical methodology:	By February 15, 2006
90-day dose range-finding study:	By December 15, 2006
Study protocol submission:	By June 15, 2007
Study start date:	By February 15, 2008
Final report submission:	By August 15, 2011

2. The applicant commits to conducting a study to determine the photocarcinogenic potential of TRADENAME (fluocinonide) cream.

90-day dose range-finding study:	By December 15, 2006
Study protocol submission:	By June 15, 2007
Study start date:	By February 15, 2008
Final report submission:	By August 15, 2010

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/s/

Melinda Harris-Bauerlien
2/7/05 02:16:46 PM
CSO

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The Dermatology Company®

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February 7, 2005

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

N-021758
NEW CORRESP

Phase 4 Commitment Request

Re: NDA 21-758: Fluocinonide Cream 0.1%

Dear Dr. Wilkin:

Reference is made to the New Drug Application (NDA) for Fluocinonide Cream 0.1% submitted in accordance with 21 CFR 314.50 on April 7, 2004. Further reference is made to the February 7, 2005, fax from FDA stipulating the Phase 4 Commitments for this NDA.

Medicis Pharmaceutical Corporation hereby commits to the conducting the dermal carcinogenicity study and photocarcinogenicity study as outlined in FDA's request.

Should you have any questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051.

Sincerely,

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

2 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Administrative- 1

MEDICIS

The Dermatology Company

DUPLICATE

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FEB 04 2005
CDR / CDER

February 3, 2005

ORIG AMENDMENT
N-000(BC)

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: NDA 21-758 Fluocinonide Cream 0.1% **Response to FDA Information Request**

Dear Dr. Wilkin:

Pursuant to 21 CFR 314.60, Medicis hereby submits this Response to the February 3, 2005 Verbal FDA Information Request with regard to the pending New Drug Application (NDA) 21-758 for Fluocinonide Cream 0.1%.

Reference is made to our original NDA 21-758 for Fluocinonide Cream 0.1% submitted on April 7, 2004; the October 29, 2004 response to the September 21, 2004 FDA CMC and Clinical Request for Information Fax; the December 20, 2004 [redacted] Amendment; the December 28, 2004 Response to the December 21, 2004 FDA Information Request; and the January 14, 2005 Response to the January 13, 2005 FDA Information Request.

To facilitate review, this submission contains a table of contents reflecting the organization of our response as submitted on compact disk and in hard copy.

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051.

Sincerely,

R. Todd Plott

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

wb

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

ORIGINAL

MEDICIS

The Dermatology Company®

RECEIVED

JAN 2 5 2005

MEGA / CDER

January 23, 2005

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

ORIG AMENDMENT
N-000-BL

RESPONSE TO FDA REQUEST FOR LABELING REVISIONS

RE: NDA 21-758 Fluocinonide Cream 0.1%

Dear Dr. Wilkin:

Reference is made to the New Drug Application (NDA) for Fluocinonide Cream 0.1% submitted in accordance with 21 CFR 314.50 on April 7, 2004. Further reference is made to the January 21, 2005, e-mail from Melinda Harris-Bauerlien communicating FDA's proposed changes to the labeling.

Pursuant to 21 CFR 314.60, Medicis hereby submits this response to the January 21, 2005, contact.

To facilitate review, this submission contains a table of contents reflecting the organization of our response as submitted on compact disk and in hard copy.

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051.

Sincerely,

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

1 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Administrative- 2

1 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Administrative- 3

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and Technical Support (DMETS), HFD-420
PKLN Rm. 6-34

FROM:
Melinda Harris-Bauerlien, M.S.
Project Manager, DDDDP, HFD-540

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
January 4, 2005		[redacted]	New tradenames for review	November 22, 2004

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Fluocinonide Cream 0.1%		3S	PDUFA deadline February 12, 2005

NAME OF FIRM: Medicis Pharmaceuticals

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)*: Trade name review

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
- ☐ 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, CONCERNS, and/or SPECIAL INSTRUCTIONS:

DMETS reviewed the tradename [redacted] and found it unacceptable on 11/19/04. The Sponsor has submitted 2 alternate tradenames. Their first choice is [redacted] and the alternate is Vanos.

The PDUFA deadline is February 12, 2005. Please let me know if you think you may be able to meet this deadline.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Melinda Harris-Bauerlien, M.S.	☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

Melinda Harris-Bauerlien
1/5/05 09:05:41 AM

3 Page(s) Withheld

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_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Administrative 4

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RECEIVED
DEC 1 5 2004
MEGA/CDER

December 14, 2004

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

N1-000/BM
ORIG AMENDMENT

Re: NDA 21-758 Fluocinonide Cream 0.1%

Dear Dr. Wilkin:

Reference is made to the New Drug Application (NDA) for Fluocinonide Cream 0.1%, submitted in accordance with 21 CFR 314.50 on April 27, 2004.

Further reference is made to today's discussion with Felicia Curtis regarding Ms. Bauerlien's request on December 13, 2004 for electronic copies of the clinical study plots for MP-0201-05 and MP-0201-06, and to Medicis' response on December 13, in which we submitted paper and electronic copies in PDF format for the specifically requested plots.

In order to avoid further difficulty with reviewing the data plots, we are hereby providing the agency with electronic copies of *all* figures for the above-mentioned studies in Word format.

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051.

Sincerely,

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

DUPLICATE

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODE V

FACSIMILE TRANSMITTAL SHEET

DATE: December 13, 2004

To: Michelle Wells, RAC R.Todd Plott, M.D.	**From:** Melinda Harris-Bauerlien, Regulatory Management Officer
Company: Medicis	Division of Division of Dermatologic & Dental Drug Products
Fax number: 602-778-6051	**Fax number:** (301) 827-2075/2091
Phone number: 602-808-3851	**Phone number:** (301) 827-2020

Subject: Facsimile Transmission for NDA 21-758

Total no. of pages including cover: 3

Document to be mailed: ☐ YES ☑ NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-2020. Thank you.

Document to be mailed: ☐ YES ☑ NO

Please call me when you receive this facsimile transmission.

Thank you.

Sincerely,
Melinda Harris-Bauerlien

NDA 21-758

The [redacted] plots for NDA 21-758 in the EDR are much harder to read than the hard copies the sponsor sent us in Volume 7 entitled Controlled Clinical Studies. Therefore my team leader and I would like to request that the sponsor send us more legible electronic copies of the plots in Word or Excel formats so we can copy them into the statistical review.

The plots I need are from 2 studies:

Study MP-0201-05
Figure 2 (Clinical Study Report, Volume 7, Item 8, page 57)
Figure 6 (Clinical Study Report, Volume 7, Item 8, page 60)
Figure 7 (Clinical Study Report, Volume 7, Item 8, page 61)
Figure 8 (Clinical Study Report, Volume 7, Item 8, page 62)

Study MP-0201-06
Figure 2 (Clinical Study Report, Volume 7, Item 8, page 1948)
Figure 7 (Clinical Study Report, Volume 7, Item 8, page 1953)
Figure 8 (Clinical Study Report, Volume 7, Item 8, page 1954)
Figure 9 (Clinical Study Report, Volume 7, Item 8, page 1954)

The page numbers I have given correspond to the document in the electronic submission (not the hard copy).

Please send all 16 figures from these 2 studies.

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

/s/

Felicia Curtis
12/13/04 01:29:18 PM
CSO

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BS
N-000(BM)
ORIG AMENDMENT

December 13, 2004

RECEIVED
DEC 14 2004
MEGA/CDER

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

Re: NDA 21-758 Fluocinonide Cream 0.1%

Dear Dr. Wilkin:

Reference is made to New Drug Application (NDA) for Fluocinonide Cream 0.1%, submitted in accordance with 21 CFR 314.50 on April 27, 2004.

Further reference is made to today's FDA fax and discussion with Melinda Harris-Bauerlien regarding requested copies of the following enclosed controlled clinical study plots:

Study MP-0201-05
Figure 2, page 57
Figure 6, page 60
Figure 7, page 61
Figure 8, page 62

Study MP-0201-06
Figure 2, page 1948
Figure 7, page 1953
Figure 8, page 1954
Figure 9, page 1954

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051.

Sincerely,

R. Todd Plott MD

ORIGINAL

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

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Withheld Track Number: Administrative- 6

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✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Administrative- 7

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_____ Deliberative Process

Withheld Track Number: Administrative- 8

MEDICIS

The Dermatology Company®

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MEGA / CDER

October 29, 2004

N-000(BZ)

ORIG AMENDMENT

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

Response to
FDA Request For Information Fax

Re: NDA 21-758 [redacted]™ (fluocinonide) Cream 0.1%

Dear Dr. Wilkin:

Pursuant to 21 CFR 314.60, Medicis hereby submits this Response to the September 21, 2004 FDA CMC and Clinical Request for Information Fax pertaining to the New Drug Application (NDA) 21-758 for [redacted]™ (fluocinonide) Cream 0.1%. Furthermore, this response also includes unsolicited updates to the product labeling and patent information sections.

Reference is made to our original NDA 21-758 for [redacted]™ (fluocinonide) Cream 0.1% submitted in accordance with 21 CFR 314.50 on April 7, 2004.

[redacted]

Enclosed please find our complete response to the FDA Request for Information Fax.

To facilitate review, this submission contains a table of contents reflecting the organization of our response as submitted on compact disk and in hard copy.

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051

Sincerely,

ORIGINAL

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

wb

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

2 Page(s) Withheld

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_____ Draft Labeling

✓ Deliberative Process

Withheld Track Number: Administrative- 9

MEDICIS
The Dermatology Company®

ORIGINAL

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JUL 2 2 2004
MEGA/CDER

July 21, 2004

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

N-000 (82)
ORIG AMENDMENT

RESPONSE TO FDA PRELIMINARY NOTICE

Re: NDA 21-758 [redacted]™ Fluocinonide Cream 0.1%

Dear Dr. Wilkin:

Reference is made to New Drug Application (NDA) for [redacted] (fluocinonide) Cream 0.1%, submitted in accordance with 21 CFR 314.50 on April 27, 2004.

Further reference is made to the June 24, 2004, letter from the FDA providing preliminary notice of potential review issues.

Enclosed please find a complete response to the preliminary issues identified by the FDA. This information is being provided on compact disk and in hard copy to facilitate review.

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051

Sincerely,

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:	FROM:
Division of Drug Marketing, Advertising and Communications, HFD-42 PKLN Room 17B04	Melinda Harris, MS Project Manager, Division of Dermatologic and Dental Drug Products, HFD-540

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 13, 2004		21-758	New NDA	April 7, 2004

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
[redacted] fluocinonide) Cream, 0.1%		3S	September 1, 2004 (labeling is September 7, 2004)

NAME OF FIRM: Medicis Pharmaceuticals

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)*:
- ☐ DDMAC review of labels

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
- ☐ 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:

Labels for the carton/container and Package insert are provided. A hard copy will be sent via courier.

A labeling day has been scheduled for September 7, 2004. Please provide comments in a sufficient amount of time prior to the meeting.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Melinda Harris, MS (827-2049)	☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

Melinda Harris
7/13/04 03:10:06 PM

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and Technical Support (DMETS), HFD-420
PKLN Rm. 6-34

FROM:
Melinda Harris, M.S.
Project Manager, Division of Dermatologic and Dental Drug Products, HFD-540

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
July 13, 2004		21-758	New NDA	

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Ulidex (fluocinonide) Cream, 0.1%		3S	October 30, 2004

NAME OF FIRM: Medicis Pharmaceutical Corporation

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)*: Trade name review

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
- ☐ 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, CONCERNS, and/or SPECIAL INSTRUCTIONS:

Please review the Tradename [redacted]'. The Package Insert and carton and container labels are attached. I will also send a hard copy.

Please let me know if you need anything further.

PDUFA DATE: **February 12, 2005**

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Melinda Harris, MS (827-2049)	X☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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

/s/

Melinda Harris
7/13/04 02:38:43 PM

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation V

FACSIMILE TRANSMITTAL SHEET

DATE: June 24, 2004

To: R. Todd Plott, M.D.	**From:** Melinda Harris, M.S. Project Manager
Company: Medicis Pharmaceutical Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (602) 778-6051	**Fax number:** (301) 827-2091 or 2075
Phone number: (602) 808-3851	**Phone number:** (301) 827-2020

Subject: NDA 21-758 [redacted]

Total no. of pages including cover: 6

Comments: Filing letter is provided

Document to be mailed: ☐ YES ☑ NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-2020. Thank you.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-758

Medicis Pharmaceutical Corporation
Attention: R. Todd Plott, M.D.
Vice President
8125 North Hayden Road
Scottsdale, AZ 85258

Dear Dr. Plott:

Please refer to your April 7, 2004, new drug application (NDA), received April 12, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [redacted] (fluocinonide) Cream, 0.1%.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on June 13, 2004, in accordance with 21 CFR 314.101(a).

We are providing the following comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

Chemistry, Manufacturing and Controls

In the table which lists the Manufacturing Information, it appears that at Pantheon's Burlington site, no manufacturing and packaging is performed, only release and stability testing.

Pharmacology/Toxicology

1. The proposed package insert does not use the current labeling format for the Carcinogenesis, Mutagenesis, Impairment of Fertility, and Pregnancy sections under the PRECAUTIONS heading of the label.

2. A formal commitment to conduct the following Phase 4 nonclinical studies, with corresponding timelines, was not contained in the [redacted] cream NDA submission: a) dermal carcinogenicity study, and b) a study to determine the photoco-carcinogenic potential o [redacted] cream.

Clinical Pharmacology

The information for Study MP-0201-06 appears to be incomplete.

Clinical and Biostatistics

1. As previously agreed, HPA-axis suppression study results in pediatric patients could be submitted during the NDA review cycle; however, it is uncertain whether definitive HPA axis suppression data in pediatric patients will be submitted prior to close of the clinical review or within PDUFA goal dates. At this juncture, the number of pediatric cohorts to be studied is not known and the HPA axis study had not begun as of June 3, 2004. These data are needed well before the time of review closure in order to provide necessary support for the indication for the relief of the inflammatory and pruritic manifestation of corticosteroid responsive dermatoses indication.

2. Pediatric subjects have not been enrolled in pivotal Phase 3 studies conducted by the Applicant with use of fluocinonide cream, 0.1% in the treatment of corticosteroid-responsive dermatoses. Pediatric subjects have not been studied in the Phase 2 HPA-axis suppression safety studies conducted by the Applicant.

3. The proposed once daily application for treatment of corticosteroid responsive dermatoses is problematic in that efficacy results indicate that optimal dosing differs between the two representative disease entities studied for corticosteroid responsive dermatoses indication (atopic dermatitis and plaque psoriasis). You have indicated at the June 3, 2004 t-con that adult subjects with atopic dermatitis did not derive additional benefit from twice daily applications of fluocinonide 0.1% cream, but adult subjects with plaque psoriasis showed greater efficacy with bid application.

4. The study reports and protocols for Studies MP-0201-05 and MP-0201-06 do not provide adequate information about how the efficacy evaluator was kept blinded to treatment regimen (QD or BID), or how patients were informed which regimen to use.

We request that you submit the following information:

Chemistry, Manufacturing and Controls

Please revise the table which lists the Manufacturing Information (Appendix 4.10; Item 4, page 744 of 1952) to include the correct responsibility of Pantheon's Burlington site.

Pharmacology/Toxicology

1. It is recommended that the Sponsor update the nonclinical portions of the [redacted] cream label (i.e., Carcinogenesis, Mutagenesis, Impairment of Fertility and Pregnancy sections under the PRECAUTIONS heading of the label) to current labeling standards. It is requested that the Sponsor provide an estimate of the maximum daily human topical dose of [redacted] cream in mg/kg and mg/m^2 to the NDA. It is recommended that the Sponsor

include multiples of human exposure levels (based on mg/m^2 comparisons) in the nonclinical portions of the [redacted] cream label based on the submitted estimate of the maximum daily human topical dose of the [redacted] cream. [redacted]

2. The Sponsor does acknowledge the Division's recommendation for two additional nonclinical Phase 4 studies to support [redacted] cream, 1) a non-clinical dermal carcinogenicity study and 2) a study to determine photoco-carcinogenic potential of the product. However, a formal commitment to conduct the recommended Phase 4 studies with a corresponding timeline was not included in the NDA submission.

   It is recommended that the Sponsor submit information to the NDA to clarify the Sponsor's commitment to conduct the two recommended nonclinical Phase 4 studies and provide the corresponding timeline for conduct of each study.

Clinical Pharmacology/Biopharmaceutics

Please provide information (including a table in SAS format) regarding doses applied at each application in QD group vs. BID group and % body surface area applied for those patients involved in the HPA axis assessment in Study MP-0201-06.

Clinical and Biostatistics

1. According to a t-con held on June 3, 2004, you have agreed to conduct HPA-axis suppression safety studies with use of fluocinonide cream, 0.1% applied topically qd (once daily) or bid (twice daily) for 2 weeks with a total of 30 pediatric patients, ≥12 to 17 years of age with atopic dermatitis. Testing will be conducted sequentially (12 years - <17, 6 years - <12 years, 2 years - <6 years, and 3 months – <2 years) with a stopping rule of 5 subjects with suppression at a specific dose level, and or regimen (qd or bid); however, the specific cohort is to be completed. Please identify your most current target date for submission of the HPA axis data.

2. Adrenal suppression study results for QD and BID application of this product in pediatric and adult populations should be proposed for inclusion in an updated label.

3. Please provide information about how patients were informed to use the study medication QD or BID and procedures that were used to ensure that the efficacy evaluator did not have access to information about the patients' treatment regimens in Studies MP-0201-05 and MP-0201-06.

If you have any questions, call Melinda Harris, M.S., Project Manager, at (301) 827-2020.

Sincerely,

{See appended electronic signature page}

Jonathan Wilkin, M.D.
Director
Division of Dermatologic & Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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

/s/

Jonathan Wilkin
6/24/04 11:17:38 AM

MEDICIS

The Dermatology Company®

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JUN 0 9 2004
MEGA/CDER

June 8, 2004

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

RESPONSE TO FDA FAX REQUEST

N.000(C)

NEW CORRESP

Re: NDA 21-758 [redacted] ™ Fluocinonide Cream 0.1%

Dear Dr. Wilkin:

Reference is made to New Drug Application (NDA) for [redacted] (fluocinonide) Cream 0.1%, submitted in accordance with 21 CFR 314.50 on April 27, 2004.

Further reference is made to today's FDA fax and discussion with Melinda Harris regarding why Form FDA 3455s, *Disclosure: Financial Interests and Arrangements of Clinical Investigators*, were not included in the submission.

Form FDA 3455s were not included in the NDA because there were no financial arrangements, payments, proprietary interest, or equity interest with any of the clinical investigators used in the study. Medicis submitted Form FDA 3454: *Certification: Financial Interests and Arrangements of Clinical Investigators*, certifying that Medicis has not entered into any financial arrangements with the clinical investigators.

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-3851 or by fax at 602-778-6051

Sincerely,

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

ORIGINAL

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

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APR 12 2004
CDR / CDER

N-000
ORIG AMENDMENT

ORIGINAL NDA
FILING

April 7, 2004

Jonathan K. Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products (HFD-540)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Corporate 2, Room N214
Rockville, MD 20850

Re: NDA 21-758
[redacted]™ (fluocinonide) Cream 0.1%

Dear Dr. Wilkin:

In accordance with the regulations set forth in 21 CFR 314, Medicis Pharmaceutical Corporation is submitting herewith a New Drug Application (NDA) for [redacted]™ (fluocinonide) Cream 0.1%.

Lidex® (fluocinonide) Cream 0.05% has been approved under NDA 16-908 since June 30, 1971, and Lidex® 0.05% (fluocinonide) Ointment has been approved under NDA 16-909 since September 22, 1971. The enclosed NDA presents a new cream formulation containing 0.1% fluocinonide as a Class I super-high potency topical corticosteroid to be indicated for the relief of the inflammatory and pruritic manifestation of corticosteroid-responsive dermatoses. Previous information concerning this formulation has been submitted to the Agency under Investigational New Drug Application (IND) 61,701.

This submission is being submitted entirely electronically on a single CD-ROM, with a total file size of approximately 650 megabytes. Except for required forms with original signatures, by agreement with the Agency, no paper copy is being submitted pending the Agency's further request. The format of the electronic application is in conformance with FDA guidance. The folder structure corresponds to the items listed on page 2 of Form FDA 356h as follows:

ORIGINAL

8125 North Hayden Road, Scottsdale, AZ 85258
Telephone: (602) 808-8800 Facsimile: (602) 808-0822
Web Site: http://www.medicis.com

Item Number	Description	Folder Name
1	Index	main folder
2	Labeling	labeling
3	Summary	summary
4	Chemistry, manufacturing and controls section	cmc
5	Nonclinical pharmacology and toxicology section	pharmtox
6	Human pharmacokinetics and bioavailability section	NA
7	Clinical microbiology section	NA
8	Clinical data section	clinstat
9	Safety update report	NA
10	Statistical section	clinstat
11	Case report tabulations	crt
12	Case report forms	crf
13	Patent information	other
14	Patent certification	NA
15	Establishment description	other
16	Debarment certification	other
17	Field copy certification	other
18	User fee cover sheet	other
19	Financial information	other
20	Other: Regulatory Meeting Records	other

NA=not applicable

Please note that all pages in the submission (with exceptions noted herebelow) have unique pagination within the Item: pages are consecutively paginated by Item Number. The following sections are not paginated: Item 11, Case Report Tabulations; Item 12, Case Report Forms; Items 13 through 19, forms and certifications.

Medicis hereby certifies that all files and directories on the CDs have been scanned and checked for viruses using Trend OfficeScan Corporate Edition, Version 3.54 (Engine 6.810).

An archival copy of the following forms with original signatures accompanies this electronic submission:

- This cover letter
- Form FDA 356h, Application to Market a New Drug, Biologic, or Antibiotic Drug for Human Use
- Form FDA 3542a, Patent Information Submitted with the Filing of an NDA, Amendment, or Supplement
- Debarment and Felony Conviction Certification
- Field Copy Certification
- Form FDA 3397, User Fee Cover Sheet
- Form FDA 3454, Certification: Financial Interests and Arrangements of Clinical Investigators

Medicis hereby certifies that the Los Angeles District Office has been notified that an electronic submission of this NDA has been made to the CDER Electronic Document Room.

The User Fee in the amount of $573,500.00, was provided in the form of Cashier's Check No. 173404, on 4/5/2004, however, on March 3, 2004, Medicis submitted a small business exception user fee waiver request for consideration by the Agency.

During the February 25, 2004 teleconference, following the pre-NDA meeting, Medicis agreed to conduct pediatric HPA axis suppression studies to collect data that would be submitted when the studies are completed, as an amendment to the NDA, pursuant to 21 CFR 314.60. The pediatric protocol, MP-0201-07 *An Open-Label Adrenal Suppression Study of Fluocinonide 0.1% Cream in Pediatric Subjects with Atopic Dermatitis*, was submitted to IND 61,701, with a request for a Special Protocol Assessment on March 2, 2004. Medicis expects to initiate the studies immediately after the incorporation of any additional Agency recommendations.

Medicis acknowledges the request made by the Agency at the February 25, 2004 teleconference for 2 additional Phase 4 studies, 1) a non-clinical dermal carcinogenicity study and 2) a study to determine photoco-carcinogenic potential of the product.

Should you have questions or need additional information, please contact Michelle Wells, RAC, Associate Director, Regulatory Affairs, at 602-808-8800 or direct at 602-808-3851.

Sincerely,

for

R. Todd Plott, M.D.
Vice President
Clinical Research and Regulatory Affairs

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-758	Efficacy Supplement Type SE- N/A	Supplement Number N/A	
Drug: Vanos (fluocinonide) Cream, 0.1%		Applicant: Medicis Pharmaceuticals	
RPM: Melinda Harris-Bauerlien, M.S.		HFD-540	Phone # 301-827-2020

Application Type: **(X)** 505(b)(1) **( )** 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.) **If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.** **( )** Confirmed and/or corrected N/A	Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): N/A

❖ Application Classifications:	
• Review priority	**(X)** Standard **( )** Priority
• Chem class (NDAs only)	3
• Other (e.g., orphan, OTC)	N/A
❖ User Fee Goal Dates	February 12, 2005
❖ Special programs (indicate all that apply)	**(X)** None Subpart H **( )** 21 CFR 314.510 (accelerated approval) **( )** 21 CFR 314.520 (restricted distribution) **( )** Fast Track **( )** Rolling Review **( )** CMA Pilot 1 **( )** CMA Pilot 2
❖ User Fee Information	
• User Fee	**(X)** Paid UF ID number _4739
• User Fee waiver	**( )** Small business **( )** Public health **( )** Barrier-to-Innovation **( )** Other (specify) ___ N/A
• User Fee exception	**( )** Orphan designation **( )** No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) **( )** Other (specify) N/A
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	**( )** Yes **(X)** No
• This application is on the AIP	**( )** Yes **(X)** No

• Exception for review (Center Director's memo)	N/A
• OC clearance for approval	N/A
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.	**(X)** Verified
❖ Patent	
• Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	**(X)** Verified
• Patent certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ( ) Verified N/A 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii) N/A
• [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	**N/A**
• [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).*	**(X)** N/A (no paragraph IV certification) ( ) Verified
• [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. Answer the following questions for each paragraph IV certification: (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))). *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).* (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "**No**," continue with question (3).* (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant? (Note: This can be determined by confirming whether the Division has	( ) Yes ( ) No N/A ( ) Yes ( ) No N/A ( ) Yes ( ) No N/A

received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))). *If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*	
(4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)? *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "**No**," continue with question (5).*	( ) Yes ( ) No N/A
(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification? (Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period). *If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.*	( ) Yes ( ) No N/A
❖ Exclusivity (approvals only)	
• Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)	No
• Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	( ) Yes, Application #_____ **(X)** No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	N/A

General Information	
✓ Actions	
• Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	N/A
• Status of advertising (approvals only)	(X) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	(X) Yes ( ) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	February 10, 2005
• Most recent applicant-proposed labeling	N/A
• Original applicant-proposed labeling	April 7, 2004
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	DMETS – 11/19/04 and 2/8/05 DDMAC – 8/26/04
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	February 9, 2005
• Reviews	DMETS – 11/19/04 and DDMAC – 8/26/04
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	February 7, 2005
• Documentation of discussions and/or agreements relating to post-marketing commitments	February 8, 2005
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	Yes
❖ Memoranda and Telecons	Yes
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	January 23, 2003
• Pre-NDA meeting (indicate date)	January 16, 2004
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	Post Pre-NDA February 25, 2004
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A

Summary Application Review	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	February 11, 2005
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	February 11, 2005
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	N/A
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	February 11, 2005
❖ Risk Management Plan review(s) *(indicate date/location if incorporated in another rev)*	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	October 20, 2004
❖ Demographic Worksheet *(NME approvals only)*	N/A
❖ Statistical review(s) *(indicate date for each review)*	January 6, 2005
❖ Biopharmaceutical review(s) *(indicate date for each review)*	January 11, 2005 and January 27, 2005
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	February 4, 2005
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	February 4, 2005
• Review & FONSI *(indicate date of review)*	February 4, 2005
• Review & Environmental Impact Statement *(indicate date of each review)*	February 4, 2005
❖ Microbiology (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	N/A
❖ Facilities inspection (provide EER report)	Date completed: June 24, 2004 **(X)** Acceptable **( )** Withhold recommendation
❖ Methods validation	**(X)** Completed **( )** Requested **( )** Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	December 14, 2004
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2006.

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS
R. Todd Plott, MD
Vice President, Clinical Research & Regulatory Affairs
Medicis Pharmaceutical Corporation
8125 North Hayden Road
Scottsdale AZ 85258

2. TELEPHONE NUMBER *(Include Area Code)*
(602) 808-8800

3. PRODUCT NAME
[redacted] (Fluocinonide) Cream 0.1%

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER
NDA 21-758

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
☒ YES ☐ NO

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).

6. USER FEE I.D. NUMBER
4739

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

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FORTHIS APPLICATION?
☐ YES ☒ NO
(See Item 8, reverse side if answered YES)

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:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
[signature]	Vice President, Clinical Research & Regulatory Affairs	3/25/04

FORM FDA 3397 (12/03)

PSC Media Arts (301) 443-1090 EF

USER FEE PAYMENT & PDUFA/FDAMA VALIDATION SHEET

Must be completed for ALL original NDAs, efficacy supplements and initial rolling review submissions

DA # 21-758 SUPP TYPE & # NEW Division 540 UFID # 4739

Applicant Name: Medicis Pharmaceuticals Drug Name: TRADENAME(fluocinonide)Cream 0.1%

For assistance in filling out this form see the Document Processing Manual for complete instructions and examples.

1. Was a Cover Sheet submitted?
   ☒ Yes ☐ No

2. Firm in Arrears?
   ☐ Yes ☒ No

3. Bundling Policy Applied Appropriately? Refer to Draft "Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees" http://www.fda.gov/cder/guidance
   ☐ Yes ☒ No (explain in comments)

4. Administrative Split? (list all NDA#s and Divisions)

NDA #/Doc Type	Div.	Fee? (Y/N)
n/a		

5. Type 6?
   ☐ Yes ☒ No

   Type 6 to which other application?

   NDA #_____ Supp Type &#_____

6. Clinical Data Required for Approval? (Check one)
   ☒ Yes*

   ☐ Yes, by reference to another application

   NDA #_____ Supp Type & #_____

   ☐ No

   * 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., adding an adverse reaction, contraindication or warning to the labeling).

7. 505(b)(2) application? (NDA original applications only) Refer to Draft "Guidance for Industry Applications Covered by Section 505(b)(2)" http://www.fda.gov/cder/guidance
   ☐ Yes ☒ No ☐ To be determined

8. Subpart H (Accelerated Approval/Restricted Distribution)?
   ☐ Yes ☒ No ☐ To be determined

9. Exclusion from fees? (Circle the appropriate exclusion. For questions, contact User Fee staff)

   List of exclusions:

   2 – No fee - administrative split
   4 – No fee - 505b2
   7 – Supplement fee - administrative split
   9 – No fee Subpart H supplement– confirmatory study
   11 – No fee Orphan Exception
   13 – No fee State/Federal exemption from fees

10. Waiver Granted?
    ☐ Yes (letter enclosed) ☒ No

    Select Waiver Type below: Letter Date: _____

    ☐ Small Business ☐ Barrier-to-Innovation
    ☐ Public Health ☐ Other (explain)

11. If required, was the appropriate fee paid?
    ☒ Yes ☐ No

12. Application Review Priority
    ☐ Priority ☒ Standard ☐ To be determined

13. Fast Track/Rolling Review Presubmission?
    ☐ Yes ☒ No

Comments

Melinda Harris Bauerlein 1/11/05
PM Signature/Date

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