

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-007

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**



DEY, L.P.
2751 Napa Valley Corporate Drive
Napa, CA 94558
TEL. (707) 224-3200 FAX (707) 224-1364

07 February 2007

Food and Drug Administration
Center for Drug Evaluation and Research
Badrul Chowdhury, MD, PhD, Division Director
Division of Pulmonary and Allergy Drug Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: New Drug Application No. 22-007 / A012
Formoterol Fumarate Inhalation Solution, 20 mcg/2 mL
Meeting Request / Discussion of Patent Certification

Dear Dr. Chowdhury:

Dey respectfully requests a meeting with appropriate FDA officials to fully explain the legal rationale for Dey's Statement of Non-Applicable Use addressing U.S. Patent No. 6,488,027 listed for the reference listed drug Foradil[®], in accordance with Section 505(b)(2)(B) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 314.50(l)(1)(iii) for NDA 22-007, Formoterol Fumarate Inhalation Solution, 20 mcg/2 mL.

Due to the imminent April 29, 2007 PDUFA date for this NDA, this matter is urgent.

Ms. Akilah Green (Regulatory Project Manager), recently telephoned us and stated CDER's belief that (a) Dey's current Paragraph 1 Patent Certification is not appropriate because the above-referenced patent is listed in the Orange Book, and (b) a Statement of Non-Applicable Use is not appropriate because the Orange Book does not show a use code for the patent.

Upon further consultation with our outside regulatory counsel, Dey maintains that the Statement of Non-Applicable Use is the proper certification for this patent, for the reasons stated in the patent certification amendment to our NDA in Module 1.3.5.2.

Ms. Green has recommended a prompt meeting to resolve this matter. We agree. Our regulatory counsel Charles Raubicheck will participate in the meeting. We understand that Elizabeth Dickinson, Esq. (FDA's Associate Chief Counsel for Drugs) has

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Badrul Chowdhury, MD, PhD, Division Director
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Dey respectfully requests that Ms. Dickinson be included in the discussion with Dey and outside counsel as soon as possible.

This amendment is being submitted entirely electronically on 1 CD-ROM with a total file size of approximately 1 MB. In addition, original signatures are provided in hard copy for the cover letter, Form FDA 356h and the Patent Certification. The submission is virus free. All files have been scanned using McAfee VirusScan Enterprise, version 7.1.0.

Due to the urgency of this matter, please contact me at 707-224-3200 x4750 to arrange the meeting. We will call the Agency by Friday, 09 February 2007 to follow-up on the status of this request. Please contact Marc Hefner at 707-224-3200 x2056 for electronic support.

Sincerely,



Michelle A. Carpenter, JD
Vice President, Regulatory and Clinical Affairs

cc: Charles J. Raubicheck, Esq.
Frommer Lawrence & Haug, LLP

Formoterol Fumarate Inhalation Solution 20 mcg/2 mL
Dey, LP

Original NDA 22-007 / 0012
1.3.5.2 Patent Certification - Page 1

AMENDED PATENT CERTIFICATION

Statement of Non-Applicable Use

In accordance with Section 505(b)(2)(B) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(b)(2)(B), applicant Dey, L.P. further amends its patent certification to the following Statement of Non-Applicable Use in NDA 22-207 for Formoterol Fumarate Inhalation Solution, 20 mcg/2 mL:

U.S. Patent No. 6,488,027 is a method of use patent which does not claim a use for which Dey is seeking approval.

Reasons:

- (1) FDA regulations define a method of use patent as a patent that claims "indications or other conditions of use" of a drug that are described in an approved application. 21 C.F.R. § 314.53(b).
- (2) Under this definition, the '027 patent is a method of use patent, because the patent claims *a condition of using* the reference listed drug Foradil®.
- (3) The condition of use covered by the '027 patent is the use of a dry powder inhaler device to deliver the drug (see the title and the claims of patent, copy attached). This inhaler device is described in the approved labeling for the RLD Foradil®.
- (4) Dey's formoterol fumarate drug product uses a nebulizer device to deliver the drug (see Dey's proposed labeling). Dey's product does not use the dry powder inhaler device covered by the '027 patent.
- (5) Therefore, the '027 patent does not apply to Dey's drug product.

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Formoterol Fumarate Inhalation Solution 20 mcg/2 mL
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Original NDA 22-007 / 0012
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(6) A Statement of Non-Applicable Use is an appropriate certification where a listed method of use patent does not apply to the applicant's drug product, irrespective of a use code. See *Purepac Pharmaceutical Co. v. Thompson*, 238 F.Supp.2d 191 (D.D.C. 2002), aff'd 357 F.3d 877 (D.C. Cir. 2004).

DEY, LP

By IA. Chaudry

Imtiaz A. Chaudry, PhD
Senior Vice President, Scientific Affairs

Dated Feb. 7, 2007

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u:\Submissions\Source Documents\Formoterol\NDA 22-007 0012\Statement of Non-Applicable Use
(00394944-4).DOC

02/07/2007



DEY, L.P.
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06 September 2006

Food and Drug Administration
Center for Drug Evaluation and Research
Badrul Chowdhury, MD, PhD, Division Director
Division of Pulmonary and Allergy Drug Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: New Drug Application No. 22-007 / A002
Formoterol Fumarate Inhalation Solution, 20 mcg/2 mL
Minor Amendment – Patent Certification Amendment

Dear Dr. Chowdhury,

Pursuant to 21 § CFR 314.50(i)(6), Dey, LP (Dey) is submitting this minor amendment to NDA 22-007 to amend the patent certification in Module 1.3.5.2. Upon further review of the Novartis patent 6,488,027 listed in the Orange Book, a Paragraph I certification is most appropriate for NDA 22-007. Patent 6,488,027 for formoterol fumarate, does not claim, or even mention or refer to, the drug formoterol fumarate, or indeed any drug, or an approved use formoterol fumarate or any other drug. Rather, the 6,488,027 patent claims solely an inhaler device. Therefore, in accordance with 21 § CFR 314.50(i)(1)(i)(A)(1) this submission amends the patent certification from a Paragraph IV to a Paragraph I certification stating that patent information has not been submitted to FDA for any patent that claims the drug on which investigations relied upon by Dey for approval were conducted, or that claims an approved use of such drug.

Alternatively, if patent 6,488,027 can be deemed a method of use patent, the labeling of the formoterol fumarate drug product for which Dey is seeking approval does not include any indication that is claimed or covered by the patent and therefore, in accordance with 21 § CFR 314.50(i)(1)(iii), a Statement of Non-Applicable Use is appropriate.

This application is being submitted entirely electronically on 1 CD with a total file size of approximately 1 MB. In addition, the contents of the index-md5.txt file is provided as an appendix as well as original signatures for the following documents:

- Cover letter
- Form FDA 356h
- Patent Certification

06 September 2006
Badrul Chowdhury, MD, PhD, Division Director
Page 2

The submission is virus free. All files have been scanned using McAfee VirusScan Enterprise, version 7.1.0. Please contact Marc Hefner at 707-224-3200 x2056 for electronic support.

For convenience, a copy of the Novartis patent 6,488,027, as listed in the United States Patent Office Database, is provided with this submission in Module 1.3.5.2 with the Patent Certification.

Dey would appreciate notification from the Agency on acceptance of either of these patent certifications. If you have any questions, please do not hesitate to contact me at 707-224-3200 x4750 or 707-396-0039 (cell).

Sincerely,



Michelle A. Carpenter, JD
Vice President, Regulatory and Clinical Affairs

1.3.5.2 Patent Certification

Paragraph I Certification

In accordance with Section 505(b)(2)(A)(i) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(b)(2)(A)(i), and 21 C.F.R. § 314.50(i)(1)(i)(A)(1), and upon further consideration, applicant Dey LP ("Dey") makes the following Patent Certification in its Section 505(b)(2) New Drug Application (NDA 22-207) for Formoterol Fumarate Inhalation Solution, 20 mcg/2 mL:

In Dey's opinion and to the best of its knowledge, patent information has not been submitted to FDA for any patent that claims the drug on which investigations relied upon by Dey for approval were conducted, or that claims an approved use of such drug.

This certification is appropriate, in that:

(1) Section 505(b) (2) (A) of the Act, and 21 C.F.R. § 314.50(i) (1) (i), only require a certification for a patent that claims "the drug for which investigations [relied upon by the applicant for approval] were conducted or that claims an approved use for such drug and for which [patent] information is required to be filed under section 505(b) and (c) of the act and [21 C.F.R.] § 314.53."

(2) U.S. Patent No. 6,488,027 ("the '027 patent"), the patent listed in the Orange Book for formoterol fumarate, does not claim, or even mention or refer to, the drug formoterol fumarate, or indeed any drug, or an approved use formoterol fumarate or any other drug. Rather, the '027 patent claims solely an inhaler device (the first three words of each claim in the patent). A "device" is an instrument which does not achieve its primary intended purposes through chemical action within or on the body, and which is not dependent upon being metabolized for the achievement of such purposes, 21 U.S.C. § 321(h), clearly a definition covering an inhaler device. (In contrast, a "drug" is an article which does achieve its principal purposes through chemical action and metabolism, 21 U.S.C. § 321(g), clearly covering formoterol fumarate).

(3) Consequently, patent information has not been submitted to FDA for any "drug" at all, or for "an approved use" of a drug, and this Paragraph I certification properly addresses the '027 patent.

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Formoterol Fumarate Inhalation Solution 20 mcg/2 mL
Dey, LP

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1.3.5.2 Patent Certification - Page 2

Alternative Certification: Statement of Non-Applicable Use

In accordance with Section 505(b) (2) (B) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(b) (2) (B), and 21 C.F.R. § 314.50(i) (1) (iii), and upon further consideration, applicant Dey makes the following Statement of Non-Applicable Use in its Section 505(b) (2) New Drug Application (NDA 22-207) for Formoterol Fumarate Inhalation Solution, 20 mcg/2 mL:

If the '027 patent can be deemed a method of use patent, the labeling of the formoterol fumarate drug product for which Dey is seeking approval does not include any indication that is claimed or covered by the patent.

This certification is appropriate, in that:

(1) The '027 patent does not claim a "drug" as defined in Title 21. Thus the only way it could properly be listed is if the claimed invention were considered to be a method of use. In FDA's patent listing regulation (which is cross-referenced in the agency's patent certification regulation), a "method of use" patent is defined as a patent that claims "indications or other conditions of use" described in an approved application. 21 C.F.R. § 314.53(b). An "indication" is the use of a drug in the treatment, prevention or diagnosis of a recognized disease or condition or an important manifestation of a disease or condition or for relief of symptoms associated with a disease or syndrome. 21 C.F.R. § 201.57(c). Under these definitions, as the '027 patent's claims are silent as to any indication, the '027 patent may only be construed as a method of use patent to the extent it claims a "condition of using the reference listed drug" Foradil[®], namely, an inhaler device for delivering that drug, a dry powder form of formoterol fumarate.

(2) Dey's formoterol fumarate drug product, as set forth in its proposed labeling, is a solution indicated for maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema.

(3) The '027 patent does not claim or cover the indication for Dey's formoterol fumarate drug product, namely, maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema. In fact, the '027 patent does not claim or cover any indication at all.

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Formoterol Fumarate Inhalation Solution 20 mcg/2 mL
Dey, LP

Original NDA 22-007 / 0002
1.3.5.2 Patent Certification - Page 3

And, to the extent that the claimed device is considered a condition of using the reference listed drug (a dry powder inhaled form of formoterol fumarate), Dey is not seeking approval for that condition of use.

(4) Precedent for certifying to a listed patent by a Statement of Non-Applicable Use is the decision entitled *Purepac Pharmaceutical Co. v. Thompson*, 238 F.Supp.2d 191 (D.D.C. 2002), aff'd 357 F.3d 877 (D.C. Cir. 2004).

(5) Consequently, the '027 patent is properly addressed by this Statement of Non-Applicable Use.

By IA. Chaudry

Dated 9/6/06

Imtiaz A. Chaudry, PhD
Senior Vice President, Scientific Affairs
Dey, LP

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10/31/06

Patent and Exclusivity Search Results from query on Appl No 020831 Product 001 in the OB_Rx list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code
020831	001	6488027	MAR 08,2019			
020831	001	6887459	NOV 28,2020			U-762

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
020831	001	NCE	FEB 16,2006
020831	001	NPP	JUN 27,2006

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents submitted on FDA Form 3542 and listed after August 18, 2003 will have one to three patent codes indicating specific patent claims as submitted by the sponsor and are detailed in the above table.
3. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.
4. *PED and PED represent pediatric exclusivity. Patents with pediatric exclusivity granted after August 18, 2003 will be indicated with *PED as was done prior to August 18, 2003. Patents with *PED added after August 18, 2003 will not contain any information relative to the patent itself other than the *PED extension. Information related specifically to the patent will be conveyed on the original patent only.
5. U.S. Patent Nos. RE36481 and RE36520 are being relisted for Zocor (NDA 19-766) pursuant to the decision and related order in Ranbaxy Labs. v. Leavitt, No. 05-1838 (D.D.C. April 30, 2006). The '481 and '520 patents will remain listed in Approved Drug Products with Therapeutic Equivalence Evaluations until any applicable periods of exclusivity pursuant to section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act have been triggered and run, unless the agency's appeal of the decision to the U.S. Court of Appeals for the District of Columbia is decided in the agency's favor before the exclusivity periods have expired. While the patents remain listed, any new or pending ANDA referencing Zocor must contain patent certifications to these patents. For additional information on this matter, please refer to Docket Nos. 2005P-0008 and 2005P-0046.

[View a list of all patent use codes](#)
[View a list of all exclusivity codes](#)

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Patent Use Codes

This page defines the patent use codes.

Code Definition

U-762 TREATMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Office of Generic Drugs

Division of Labeling and Program Support

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Orange Book Data Updated Through September, 2006

Patent and Generic Drug Product Data Last Updated: October 30, 2006

1.3.5.2 Patent Certification

In accordance with Section 505(b)(2)(A)(iv) of the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 355(b)(2)(A)(iv), and FDA regulation 21 C.F.R. § 314.50(i)(1)(i)(4), Dey LP ("Dey") hereby makes the following certification with respect to the unexpired patent that is listed in FDA's electronic publication *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"), updated through June 2006, for the drug Formoterol Fumarate.

Paragraph IV Certification – U.S. Patent No. 6,488,027

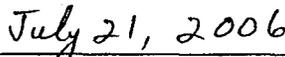
Dey hereby certifies that, in its opinion and to the best of its knowledge, U.S. Patent No. 6,488,027 is invalid and/or will not be infringed by the manufacture, use or sale of the drug product Formoterol Fumarate Inhalation Solution 20 mcg/2 mL for which this Section 505(b)(2) new drug application ("NDA") is submitted.

Statement Concerning Notice to Patent Owner and NDA Holder

In accordance with Section 505(b)(3) of the FDCA, 21 U.S.C. § 355(b)(3), and FDA regulation 21 C.F.R. § 314.52(a), Dey states that it will provide the appropriate notice regarding the above Paragraph IV certification, at the time it receives written notice from FDA that this NDA has been accepted for filing, to: (i) the owner of the patent that is the subject of the certification, or the representative of such owner designated to receive such notice; and (ii) the holder of the new drug application approved under Section 505(b)(1) of the FDCA for the reference listed drug that is the subject of the claims of the pertinent patent, or the representative of such holder designated to receive such notice. In accordance with 21 C.F.R. § 314.52(e), this Section 505(b)(2) NDA will be amended to document said persons' or entities' receipt of said notice.



Imtiaz A. Chaudry, PhD
Senior Vice-President, Scientific Affairs
Dey, LP



Date

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Patent and Exclusivity Search Results from query on Appl No 020831 Product 001 in the OB_Rx list.

Patent Data

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code
020831	001	6488027	MAR 08,2019			

Exclusivity Data

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
020831	001	NCE	FEB 16,2006
020831	001	NPP	JUN 27,2006

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
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3. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.
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5. U.S. Patent Nos. RE36481 and RE36520 are being relisted for Zocor (NDA 19-766) pursuant to the decision and related order in Ranbaxy Labs. v. Leavitt, No. 05-1838 (D.D.C. April 30, 2006). The '481 and '520 patents will remain listed in Approved Drug Products with Therapeutic Equivalence Evaluations until any applicable periods of exclusivity pursuant to section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act have been triggered and run, unless the agency's appeal of the decision to the U.S. Court of Appeals for the District of Columbia is decided in the agency's favor before the exclusivity periods have expired. While the patents remain listed, any new or pending ANDA referencing Zocor must contain patent certifications to these patents. For additional information on this matter, please refer to Docket Nos. 2005P-0008 and 2005P-0046.

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Patent and Generic Drug Product Data Last Updated: July 11, 2006

1.3.5.1 Patent Information

The United States Patents and Trademarks Office has granted the patents listed in Table 1.3.5.1 related to this application. The patents are provided by links in Table 1.3.5.1.

Table 1.3.5.1 United States Patent Numbers and Titles Assigned to Dey, LP for Formoterol Fumarate

PATENT NUMBER	TITLE
6814953	Bronchodilating compositions and methods
6667344	Bronchodilating compositions and methods

Current patent applications listed in Table 1.3.5.2, have been filed with the United States Patents and Trademarks Office related to this submission. Current patent application abstracts are provided by links in Table 1.3.5.2.

Table 1.3.5.2 Formoterol Fumarate Patent Application Numbers and Titles

PATENT APPLICATION NUMBER	TITLE
20050009923	Bronchodilating beta-agonist compositions and methods
20030055026	Formoterol/steroid bronchodilating compositions and methods of use thereof
20020183293	Formoterol/steroid bronchodilating compositions and methods of use thereof

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Patent number '**6814953**' is not currently listed in the Orange Book in the '**OB_Rx**' list.

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents submitted on FDA Form 3542 and listed after August 18, 2003 will have one to three patent codes indicating specific patent claims as submitted by the sponsor and are detailed in the above table.
3. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.
4. *PED and PED represent pediatric exclusivity. Patents with pediatric exclusivity granted after August 18, 2003 will be indicated with *PED as was done prior to August 18, 2003. Patents with *PED added after August 18, 2003 will not contain any information relative to the patent itself other than the *PED extension. Information related specifically to the patent will be conveyed on the original patent only.
5. U.S. Patent Nos. RE36481 and RE36520 are being relisted for Zocor (NDA 19-766) pursuant to the decision and related order in Ranbaxy Labs. v. Leavitt, No. 05-1838 (D.D.C. April 30, 2006). The '481 and '520 patents will remain listed in Approved Drug Products with Therapeutic Equivalence Evaluations until any applicable periods of exclusivity pursuant to section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act have been triggered and run, unless the agency's appeal of the decision to the U.S. Court of Appeals for the District of Columbia is decided in the agency's favor before the exclusivity periods have expired. While the patents remain listed, any new or pending ANDA referencing Zocor must contain patent certifications to these patents. For additional information on this matter, please refer to Docket Nos. 2005P-0008 and 2005P-0046.

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Orange Book Data Updated Through May, 2006

Patent and Generic Drug Product Data Last Updated: July 10, 2006

Patent number '6667344' is not currently listed in the Orange Book in the 'OB_Rx' list.

Additional information:

1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents submitted on FDA Form 3542 and listed after August 18, 2003 will have one to three patent codes indicating specific patent claims as submitted by the sponsor and are detailed in the above table.
3. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.
4. *PED and PED represent pediatric exclusivity. Patents with pediatric exclusivity granted after August 18, 2003 will be indicated with *PED as was done prior to August 18, 2003. Patents with *PED added after August 18, 2003 will not contain any information relative to the patent itself other than the *PED extension. Information related specifically to the patent will be conveyed on the original patent only.
5. U.S. Patent Nos. RE36481 and RE36520 are being relisted for Zocor (NDA 19-766) pursuant to the decision and related order in Ranbaxy Labs. v. Leavitt, No. 05-1838 (D.D.C. April 30, 2006). The '481 and '520 patents will remain listed in Approved Drug Products with Therapeutic Equivalence Evaluations until any applicable periods of exclusivity pursuant to section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act have been triggered and run, unless the agency's appeal of the decision to the U.S. Court of Appeals for the District of Columbia is decided in the agency's favor before the exclusivity periods have expired. While the patents remain listed, any new or pending ANDA referencing Zocor must contain patent certifications to these patents. For additional information on this matter, please refer to Docket Nos. 2005P-0008 and 2005P-0046.

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1.3.5.2 Patent Declaration/Certification

Pursuant to 21 CFR 314.53, the appropriate patent declarations and certification are provided on Form 3542a for Patent 6,814,953 and Form 3542a for Patent Number 6,667,344. Form 3542 will be submitted to the Agency should these patents be granted during the application review period or after approval of the submission as required by 21 CFR 314.53.

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EXCLUSIVITY SUMMARY

NDA # 20-007

SUPPL #

HFD # 570

Trade Name Perforomist

Generic Name formoterol fumarate

Applicant Name Dey, L.P.

Approval Date, If Known April 27, 2007 (tentative)

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 questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

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

505(b)(2)

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

YES NO

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

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

Change in dosage form from powder to inhalation solution

d) Did the applicant request exclusivity?

YES NO

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

3 years

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

YES NO

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

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

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 NO

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

NDA# 20-831

Foradil Aerolizer

NDA# 21-592

Foradil Certihaler

NDA#

2. Combination product.

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

YES NO

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

NDA# 21-929

Symbicort

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 NDAs 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 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 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:

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

YES NO

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

YES NO

If yes, explain:

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

YES NO

If yes, explain:

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

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

Investigation #2 YES NO

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

Study DL-052, Study DL-057, Study DL-059 and Study 201-065

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

Investigation #1 YES NO

Investigation #2 YES NO

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

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"):

Study DL-052, Study DL-057, Study DL-059 and Study 201-065

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 # 68,782 YES ! NO
! Explain:

Investigation #2
IND # 68,782 YES ! NO
! Explain:

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

Investigation #1
YES ! NO
Explain: ! Explain:

Investigation #2

YES

Explain:

!

!

! NO

! Explain:

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

YES

NO

If yes, explain:

Name of person completing form: Akilah Green, MS, RN

Title: Senior Regulatory Management Officer

Date: May 11, 2007

Name of Office/Division Director signing form: Badrul A. Chowdhury, MD, PhD

Title: Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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/s/

Badrul Chowdhury
5/11/2007 01:15:31 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 22-007 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: June 29, 2006 Action Date: April 29, 2007

HFD-570 Trade and generic names/dosage form: Formoterol Fumarate 20 mcg/2 mL
Applicant: Dey, L.P. Therapeutic Class: Long acting beta agonist

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: Long-term, twice daily (morning and evening) administration in the maintenance treatment of bronchoconstriction in patients with chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema.

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

Yes: Please proceed to Section A.

No: Please check all that apply: _____ Partial Waiver _____ 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. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

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

Other: _____

Date studies are due (mm/dd/yy): _____

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}

Akilah Green
Senior Regulatory Management Officer

cc: NDA 22-007
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)

Attachment A

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

Indication #2: _____

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

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ 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. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for deferral:

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

Date studies are due (mm/dd/yy): _____

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

Section D: Completed Studies

Age/weight range of completed studies:

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 22-007
HFD-960/ Grace Carmouze

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

(revised 10-14-03)

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/s/

Akilah Green

9/14/2006 11:32:31 AM

DEBARMENT CERTIFICATION

Dey, L.P. hereby certifies that the services of any persons debarred under Section 306(a) or (b) of the Federal Food, Drug and Cosmetic Act were not and will not be used in any capacity in conjunction with this application.

Signed:

Michelle A. Carpenter

Michelle A. Carpenter, JD

Vice President, Regulatory and Clinical Affairs

Date: 5/19/06

CONFIDENTIAL



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-007

DEY, L.P.
2751 Napa Valley Corporate Drive
Napa, California 94558

Attention: Michelle A. Carpenter, JD
Vice President, Regulatory and Clinical Affairs

Dear Ms. Carpenter:

We acknowledge receipt on May 2, 2007 of your May 1, 2007, resubmission to your new drug application for Perforomist (fomoterol fumarate dihydrate) Inhalation Solution 20 mcg/2 mL.

We consider this a complete, class 1 response to our April 27, 2007, action letter. Therefore, the user fee goal date is July 2, 2007.

If you have any questions, call Ms. Akilah, Senior Regulatory Management Officer, at (301) 796-1219.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Chief Regulatory Project Manager
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Akilah Green
5/10/2007 10:54:12 AM

Garcia, Lori

From: Garcia, Lori
It: Friday, April 27, 2007 3:35 PM
'michelle.carpenter@dey.com'
Subject: RE: Vial

I'll be waiting :-)

-----Original Message-----

From: michelle.carpenter@dey.com [mailto:michelle.carpenter@dey.com]
Sent: Friday, April 27, 2007 3:17 PM
To: Garcia, Lori
Cc: antoinette.douglas@dey.com; Gina.Capiaux@dey.com; Elaine.Alambra@dey.com;
Marc.Hefner@dey.com
Subject: Re: Vial

Lori,

It was close, but we just confirmed it fits. I just signed the submission and it will be to you asap.

Regards,

Michelle Carpenter
VP, Regulatory and Clinical Affairs
Compliance Officer
2751 Napa Valley Corporate Drive
Napa, CA 94558
(707) 224-3200 ext. 4750
(707) 224-1364
michelle.carpenter@dey.com

"Garcia, Lori"
<lori.garcia@fda.
hhs.gov>

04/27/2007 11:53
AM

michelle.carpenter@dey.com,
Elaine.Alambra@dey.com,
Gina.Capiaux@dey.com

To

cc

Subject

Vial

How does this work for you??? Of course, you knew we were going to change something...! Think it will fit?

Lori

Vial Body Side #1

Perforomist

Vial Body Side #2

Sterile Solution
For Oral
Inhalation Only

Vial Tab Side #1

Lot #
Exp #

Vial Tab Side #2

Formoterol
Fumarate
Inhalation Solution
20mcg/2mL

Top Vial Tab

Dey

LCDR Lori Garcia, R.Ph.
Regulatory Project Manager
FDA/CDER/OND/DPAP
Bldg. 22, Rm. 3343
10903 New Hampshire Ave
Silver Spring, MD 20993-0002
Phone: (301) 796-1212
lori.garcia@fda.hhs.gov

MEMORANDUM OF TELECON

DATE: April 25, 2007

APPLICATION NUMBER: NDA 22-007

BETWEEN:

Name:	Elaine Alambra	Assoc. Director, Regulatory and Clinical Affairs
	Gina Capiaux, PhD	Sr. Manager, Regulatory Affairs / Clinical
	Michelle Carpenter, JD	VP, Regulatory and Clinical Affairs
	Imtiaz Chaudhry, PhD	Sr. VP, Scientific Affairs
	Kimberly Denis-Mize, PhD	Sr. Manager, Clinical Science
	Antoinette Douglas	Sr. Manager, Regulatory Affairs / CMC
	Mike Rinehart	Director, Clinical Affairs
Phone:	Teleconference	
Representing:	Dey	

AND

Name: Division of Pulmonary and Allergy Products
Lori Garcia, R.Ph.
Peter Starke, M.D.
Prasad Peri, Ph.D.
James Kaiser, M.D.
Lydia Gilbert-McClain, M.D.

SUBJECT: Labeling Revisions

Revised labeling containing the most recent FDA revisions was emailed to Dey prior to the teleconference. The Division requested a teleconference with Dey in order to discuss two major recommended revisions to the label.

1. Deletion of the word " ——— " from the chemical name "formoterol fumarate ——— " in all components of the labeling. FDA explained that this revision was made because the 20 mcg drug product refers solely to formoterol fumarate. The ——— is not taken into account in the 20 mcg dose, and therefore, should not be part of the name. Dey noted that they had not ordered the packaging components yet for their drug product,

so this change will be simple for them to make. Dey committed to provide an agreement to make this change, since it would not be possible to provide revised draft mock-ups for the packaging components prior to the action date for this NDA. This revision will be made to the PI and Med Guide and will be submitted on or before the action date of April 27, 2007.

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/s/

Lori Garcia
4/26/2007 04:14:28 PM
CSO



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

Memorandum of Facsimile Correspondence

Date: April 26, 2007
To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development
Fax: (707) 224-1364
Phone: (707) 224-3200 x4750
From: Lori Garcia, R.Ph.
Regulatory Management Officer
Division of Pulmonary and Allergy Products
Subject: NDA 22-007: Labeling Revisions

of Pages:

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If you are not 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 received this document in error, please immediately notify us by telephone at (301) 796-2300 and return it to us at FDA, 10903 New Hampshire Ave, Building 22, DPAP, Silver Spring, MD 20993.

Thank you.

NDA 22-007
Dey, L.P.
Perforomist Inhalation Solution

Dear Ms. Carpenter:

The enclosed FDA revised labeling is based upon our review of your revised draft labeling submitted on April 20, 2007, and upon our discussions with you at the teleconference held on April 25, 2007. All agreed-upon changes through April 25, 2007, have been included. Additional FDA recommended revisions are identified by underlining (inserted text) and strike-outs (deleted text).

We request that you submit your revised draft labeling and/or comments by April 27, 2007, 9:00 am EST.

If you have any questions, please contact, Ms. Akilah Green, Senior Regulatory Project Manager, at 301-796-1219.

17 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

Withheld Track Number: Administrative- 1

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/s/

Lori Garcia
4/26/2007 06:22:23 PM
CSO



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

Memorandum of Facsimile Correspondence

Date: April 17, 2007

To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007; labeling comments

of Pages: 4

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Thank you.

_____ have this information in their package inserts. The active control was integral to the study design and is important to the clinician's understanding of the drug's effect. Furthermore, the Agency's request is inconsistent with other package inserts, especially when one considers the package insert for Brovana even includes information on once daily dosing, which was not approved.

FDA Response:

While we note that you did not object to our removal of the comparator arm in the labeling the Agency sent on April 4, 2007, we agree to adding the following sentence, which we have placed in the CLINICAL STUDIES section after the second sentence of the first paragraph: _____

b(4)

4. As explained previously, the onset of bronchodilation information in Section 14.1 (Clinical Studies) was modeled after the reference drug for this 505(b)(2) application (Foradil) and was supported by the Week 12 data from the pivotal study, which is a clinically meaningful timepoint for a COPD maintenance drug. We disagree with the appropriateness of imposing Brovana's statement on Performist given the apparent differences in study design, specifically the serial spirometry timepoints within the hour following the first dose.

FDA Response:

We disagree with your proposed approach. As requested in our previous faxes and at the labeling teleconference of April 2, 2007, provide the requested analyses and complete the requested wording.

If you have any questions, you may contact Ms. Akilah Green, Senior Regulatory Management Officer, at 301-796-1219.

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/s/

Akilah Green
4/17/2007 02:13:49 PM
CSO

Akilah Green
4/17/2007 02:15:57 PM
CSO



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

Memorandum of Facsimile Correspondence

Date: March 26, 2007

To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007; February 28, 2007, meeting minutes

of Pages: 15

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Thank you.



FOOD AND DRUG ADMINISTRATION

Meeting Type: Type A
Meeting Category: Other
Meeting Date and Time: February 28, 2007 2:00-3:00 PM
Meeting Location: Teleconference
Application Number: NDA 22-007
Product Name: formoterol fumarate inhalation solution
Received Briefing Package February 7, 2007
Sponsor Name: Dey, L.P.
Meeting Requestor: Michelle A. Carpenter, JD, VP, Regulatory and Clinical Affairs
Meeting Chair: Elizabeth Dickenson, Office of the Chief Counsel
Meeting Recorder: Akilah Green, MS, RN, Senior Regulatory Management Officer
Meeting Attendees:

FDA Attendees

Elizabeth Dickinson, Office of the Chief Counsel
Nancy Boocker, Director, Division of Regulatory Policy I, Office of Regulatory Policy
Janice Weiner, Regulatory Counsel, Office of Regulatory Policy
Kim Dettelbach, Office of the Chief Counsel
Kim Colangelo, Associate Director of Regulatory Affairs, Office of New Drugs
Akilah Green, Senior Regulatory Management Officer, Office of Drug Evaluation II, Division of Pulmonary and Allergy Products

Sponsor Attendees

Elaine Alambra, Associate Director, Regulatory and Clinical Affairs
Michelle Carpenter, JD, VP, Regulatory and Clinical Affairs

Imtiaz Chaudry, Senior VP, Scientific Affairs

John Kling, Senior VP, Legal

Charles Raubicheck, Legal Counsel, FLH (Frommer Lawrence & Haug, LLP)

1.0 BACKGROUND

The original submission to NDA 22-007 dated June 28, 2006, did not include a certification to the patent for the listed drug. Upon notification by the FDA that Dey did not certify to the patent of the reference listed drug, on July 24, 2006, Dey provided a Paragraph IV certification for U.S. Patent Number 6,488,027, whereby Dey stated that they would provide the appropriate notice regarding the Paragraph IV certification to the Patent and NDA holder when Dey received notice from the FDA that NDA 22-007 was accepted for filing. Subsequently, on September 6, 2006, Dey amended their certification to Patent 6,488,027 from Paragraph IV to Paragraph I, stating that the patent does not claim, or even mention or refer to, the drug formoterol fumarate, or indeed any drug, or an approved use of formoterol fumarate or any other drug. Rather, the 6,488,027 patent claims solely an inhaler device. Dey further stated that alternatively, if patent 6,488,027 can be deemed a method of use patent, the labeling of the formoterol fumarate drug product for which Dey is seeking approval does not include any indication that is claimed or covered by the patent and therefore, in accordance with 21 CFR 314.50(i)(1)(iii), a Statement of Non-Applicable Use is appropriate.

The FDA determined that neither a Paragraph I certification, nor a Statement of Non-Applicable Use was appropriate and contacted Dey to further amend their certification in February 2007. Dey did not agree and submitted a meeting request dated February 7, 2007, to discuss the legal rationale for their Statement of Non-Applicable Use to address U.S. patent number 6,488,027 listed for the reference listed drug Foradil, for NDA 22-007, Formoterol Fumarate Inhalation Solution, 20 mcg/2 mL. The meeting package was included with the meeting request. In a facsimile correspondence dated February 23, 2007, Dey submitted slides, which were presented at the teleconference (attached).

2.0 DISCUSSION

2.1 Agenda Topic 1

U.S. Patent No. 6,488,027 Patent Certification; Statement of Non-Applicable Use

Discussion:

Dey, L.P., began the teleconference with a slide presentation (attached). Dey stated that it is up to the applicant to determine the coverage of the patent and certify to the patent accordingly. Dey believes the patent is a method of use patent and therefore, not applicable to their product. The FDA stated that there is language in the preambles to the regulations regarding reliance on use codes. Dey asserted that they

would delete any reference to ~~_____~~ from the labeling for Dey's. Dey believes the patent is improperly listed as a drug patent and should be a use patent, with a use code. The FDA noted that the agency cautions applicants not to rely on the innovator's patent submissions: they need to see if there are any other patents. But if the patent is a drug product patent and not a use patent, Dey has to file Paragraph III or IV certification. Use patents in the Orange Book are accompanied by use codes and use codes are based on what the innovator tells us (e.g., what the patent claims).

b(4)

Dey stated that they can file a petition to correct the patent and they should not be subject to a 30-month stay. Dey further requested that the FDA help expedite a response from Novartis. The FDA noted that there is not a lot we can do to force Novartis to respond and recommended that Dey spell out exactly what information should be in the Orange Book if they want to file a challenge. Dey stated they want the patent listing to include a use code, or to have the patent de-listed. Dey did not want to withdraw their Non-Applicable Use statement. Dey will move forward with a challenge to Novartis. Dey states that FDA is allowed to make it known that Dey is challenging Novartis' patent. Dey questioned if this issue is not resolved by the April 27, 2006, action date (PDUFA date April 29, 2007), will they receive a tentative approval or a not applicable action. The FDA stated if Dey files a Paragraph III, or IV certification and they have not heard from the patent and NDA holder that there will be no lawsuit, they will get a tentative approval. However, if the NDA contains an incorrect certification the action will be approvable.

Dey requested that the FDA work with them as they submit their petition to correct the patent and questioned how long they have to amend their certification to Paragraph IV if a Statement of Non-Applicable Use is not appropriate. The FDA stated Dey has to allow enough time for Novartis to respond within 45 days of receipt of Dey's notice of a Paragraph IV certification, unless Dey obtains a statement in writing from Novartis that they will not sue and allow the immediate approval of NDA 22-007.

3.0 ISSUES REQUIRING FURTHER DISCUSSION

There were no issues requiring further discussion.

4.0 ACTION ITEMS

Action Item/Description	Owner	Due Date
Submit a petition to correct Patent No. 6,488,027	Dey	ASAP

5.0 ATTACHMENTS AND HANDOUTS

The slides Dey, L.P., presented at the teleconference are attached.

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Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

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/s/

Akilah Green

3/25/2007 10:15:46 PM



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

Memorandum of Facsimile Correspondence

Date: April 13, 2007

To: Michelle A. Carpenter
V. P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Carol Hill, MS
Regulatory Project Manager
Division of Pulmonary and Allergy Products

Subject: NDA 22-007; Labeling Revisions

of Pages: 16

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Thank you.

NDA 22-007

Dey, L.P.

Perforomist Inhalation Solution

We have reviewed the labeling text for Perforomist Inhalation Solution, submitted April 10, 2007, including the Package Insert and Medication Guide. We have made revisions to your proposed Package Insert (attached). Comments and requests regarding the Package Insert are embedded in the document and highlighted. Please submit all labeling, including the Package Insert, Medication Guide, and carton and container labeling by April 20, 2007. Include all supplementary analyses that support the new labeling.

If you have any questions, you may contact, Ms. Akilah Green, Senior Regulatory Project Manager, at 301-796-1219.

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✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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/s/

Carol F. Hill
4/13/2007 02:48:06 PM
CSO

MEMORANDUM

To: Akilah Green, MS, BSN, RN
Division of Pulmonary and Allergy Products

From: Iris Masucci, PharmD, BCPS
for Study Endpoints and Label Development (SEALD) Team, OND

Date: April 5, 2007

Re: Comments on draft labeling for Perforomist (formoterol fumarate)
inhalation solution
NDA 22-007

We have reviewed the proposed label for Perforomist (FDA version dated 3-23-07 and the sponsor's response) and offer the following comments. These comments are based on Title 21 of the Code of Federal Regulations (201.56 and 201.57), the preamble to the Final Rule, labeling Guidances, and FDA recommendations to provide for labeling quality and consistency across review divisions. We recognize that final labeling decisions rest with the review division after a full review of the submitted data.

GENERAL COMMENTS

- The PLR regulations state that any FDA-approved patient information (e.g., a Medication Guide) either follow the last section of the prescribing information or accompany it as a separate document. If the Medication Guide is an accompanying document, it need not be (but may be) a numbered subsection under "17 Patient Counseling." If it is to be a continuous document with the professional labeling intended to be torn off given to patients, then it would be section "17.6 Medication Guide." The lone approval in PLR format that included a Medication Guide thus far (trade name Soliris) did not assign a numbered subheading to the Medication Guide.

HIGHLIGHTS

b(4)

- "PERFOROMIST™ (formoterol fumarate ——— Inhalation Solution"

This line must contain both the dosage form and route of administration. Please consider whether "inhalation solution" is adequate here or if we need to specify that it is for oral inhalation use.

- The year of initial U.S. approval must be filled in upon approval.

Indications and Usage

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/s/

Iris Masucci
4/5/2007 02:20:07 PM
DDMAC REVIEWER

Laurie Burke
4/6/2007 02:06:08 PM
INTERDISCIPLINARY



DEY, L.P.
2751 Napa Valley Corporate Drive
Napa, CA 94558
TEL. (707) 224-3200 FAX (707) 224-1364

13 April 2007

Food and Drug Administration
Center for Drug Evaluation and Research
Badrul Chowdhury, MD, PhD, Division Director
Division of Pulmonary and Allergy Drug Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

Re: New Drug Application 22-007/A023
PERFOROMIST™ Inhalation Solution
Response to FDA 29 March 2007 Fax: Post-Marketing Study Commitment
Comments

Dear Dr. Chowdhury,

Dey is responding to the Agency's facsimile dated 29 March 2007 regarding post-marketing commitments for NDA 22-007. Dey provided responses to the Agency's comments via e-mail to Ms. Akilah Green on 30 March 2007 and is now submitting the responses to the NDA as requested.

This information is being submitted electronically on 1 CD with a total file size of approximately 1 MB. In addition, the content of the index-md5.txt file is provided as an appendix as well as original signatures for the following documents:

- Cover Letter
- Form FDA 356h

The submission is virus free. All files have been scanned using McAfee VirusScan Enterprise, version 7.1.0. Please contact Marc Hefner at 707-224-3200 x2056 for electronic support.

If you have any questions, please do not hesitate to contact me at 707-224-3200 x4750, 707-396-0039 (cell) or Elaine Alambra at 707-224-3200 x3426.

Sincerely,

Michelle A. Carpenter, JD
Vice President, Regulatory and Clinical Affairs



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

Memorandum of Facsimile Correspondence

Date: March 29, 2007

To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007; regarding post-marketing commitments

of Pages: 4

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Thank you.

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NDA 22-007
Perforomist Inhalation Solution

Dear Ms. Carpenter:

We have reviewed your submission dated January 25, 2007, to NDA 22-007 for Perforomist Inhalation Solution and have the following comments:

We have reconsidered our request for sensitivity analyses of certain primary endpoints in trials DL-052 and DL-057 (Refer to our December 13, 2006, facsimile correspondence). It is acceptable for you not to submit these analyses.

At this time we ask that you submit post-marketing study commitments as listed below:

- 1. To conduct a postmarketing multiple-dose safety and tolerability study with one or more doses and one or more dose levels of Perforomist Inhalation Solution in children with asthma and/or obstructive airway disease (Refer to comment 3.a. of our December 13, 2006, facsimile correspondence). We do not agree that the data submitted in the NDA address this issue. The data presented in NDA 22-007 in subjects with asthma consist of single-dose, dose-finding trials in a small number of subjects, including only 44 at the proposed labeled 20 mcg dose and below. The entire pediatric asthma age range was not explored. In addition, propose relevant dates for the study:**

Protocol Submission Date:
Study Start Date:
Final Report Submission Date:

- 2. To conduct a postmarketing multiple-dose safety and efficacy study with one or more doses and one or more dose levels of Perforomist Inhalation Solution in children 12 years of age and younger presenting with an acute exacerbation of asthma. You have agreed to conduct this study with the following study dates:**

Protocol Submission Date: March 27, 2009
Study Start Date: July 27, 2009
Final Report Submission Date: November 27, 2011

In your submission you requested confirmation that completion of this study would qualify NDA 22-007 for an additional six months of marketing exclusivity beyond the 180-days

We are not clear as to whether you are referring to Pediatric exclusivity after completion of pediatric studies in response to a Written Request or marketing exclusivity after completion of a full clinical development program for an indication. We are open to both possibilities, although the safety and efficacy study to which you refer would not alone be sufficient for either. We

b(4)

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encourage you to pursue development of Perforomist Inhalation Solution for _____ and will be happy to discuss further the elements of such a plan. b(4)

We acknowledge your commitment for the following study as part of your pharmacovigilance plan and ask that you include it in your Postmarketing Study Commitments:

3. A multicenter, randomized, placebo-controlled, large, simple safety study to evaluate the effects of long term use of Perforomist Inhalation Solution in patients with COPD. The objective of this trial would be to determine the risk of fatal and life-threatening respiratory events associated with the long term use of Perforomist Inhalation Solution in patients with COPD. You have agreed to conduct this study with the following study dates:

Protocol Submission Date:	February 27, 2008
Study Start Date:	June 27, 2008
Final Report Submission Date:	June 27, 2012

I may be reached at 301-796-1219 for any questions.

Akilah Green,
Senior Regulatory Management Officer

3
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/s/

Akilah Green
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RA Received

3-29-07 Mf

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Elaine
Alambra/Dey_Labs/Merck-Gen/Merck

03/30/2007 02:21 PM

To Akilah Green
cc Imtiaz Chaudry/Dey_Labs/Merck-Gen/Merck@Merck, Michelle Carpenter, Antoinette
Douglas/Dey_Labs/Merck-Gen/Merck@Merck, Gina Latanya Porter/Dey_Labs/Merck-Gen/Merck@Merck
bcc
Subject NDA 22-007, Performist Inhalation Solution: Postmarketing Study Commitments

Ms. Green,

Please see the information below in anticipation of Monday's (2 April 2007) teleconference .

Postmarketing Study Commitments

1. Dey agrees to conduct a postmarketing safety and tolerability study with one or more doses and one or more dose levels of Performist Inhalation Solution in children with asthma and/or obstructive airway disease. The proposed study design is a 2-week, placebo or active controlled study with Performist Inhalation Solution BID in approximately 100 patients 12 years of age and younger. We proposes the following relevant dates:

Protocol Submission Date:	January 31, 2008
Study Start Date:	April 30, 2008
Final Report Submission Date:	July 30, 2009

The proposed study design is a 2-week, placebo or active controlled study with FFIS 20mcg/2mL BID in approximately 100 patients 12 years of age and younger.

2. Dey agrees to conduct a postmarketing safety and efficacy study with one or more doses and one or more dose levels of Performist Inhalation Solution in children 12 years of age and younger presenting with an acute exacerbation of asthma. We agree to conduct this study with the following study dates:

Protocol Submission Date:	March 27, 2009
Study Start Date:	July 27, 2009
Final Report Submission Date:	November 27, 2011

3. Dey agrees to conduct a postmarketing multicenter, randomized, placebo-controlled, simple safety study to evaluate the effects of long-term use of Performist Inhalation Solution in patients with COPD. The objective of this trial would be to determine the risk of fatal and life-threatening respiratory events associated with the long-term use of Performist Inhalation Solution in patients with COPD. We agreed to conduct this study with the following study dates.

Protocol Submission Date:	February 27, 2008
Study Start Date:	June 27, 2008
Final Report Submission Date:	June 27, 2012

Additionally, Dey appreciates the Agency's encouragement to develop this product for use in
Specifically, for _____

b(4)

Does the Agency agree?

If Dey successfully replicates the data from postmarketing commitment #2 above, will that support a label

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

Memorandum of Facsimile Correspondence

Date: March 23, 2007

To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007; *Page 8 of Labeling FAX*

of Pages: 30

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Thank you.

NDA 22-007

Perforomist Inhalation Solution

We have reviewed the labeling text for Perforomist Inhalation Solution, submitted February 13, 2007, including the Package Insert, Medication Guide, and carton and container. FDA has made numerous revisions to your proposed labeling (attached). The following comments refer to the Package Insert and carton and container labeling. The comments are not exhaustive, but are meant to clarify the major issues addressed in the revisions. There may be additional edits and suggested changes upon further review of the label within the Agency. Please submit revised labeling and any questions by March 28, 2007.

Package Insert

General Comments

1. The proprietary name "Perforomist" is acceptable. We have inserted your proprietary name in the appropriate locations of the attached labeling.
2. We have revised and/or added subsections based on the various Physician Labeling Rule guidances for label content and format. Please consider these changes preliminary, as further changes are likely. All changes are subject to final FDA review, for example, to ensure that the Highlights fit on ½ page.
3. Note that in several sections we have asked you to propose new language or add missing information. In each instance, the request or missing information is highlighted.
4. Your proposed package insert contains information specific to _____
_____. This specific information is not appropriate in the labeling for Perforomist, and has been removed. b(1)
5. We have made an effort to ensure that all statements in the Medication Guide have counterparts in, and coordinate with, the Package Insert.

Comments by section

HIGHLIGHTS

6. We have revised the "Highlights" section to reflect the information from within the labeling that we feel is most important for practitioners. The "ADVERSE REACTIONS" section will require modification to include the events in a revised table of adverse events from trial 201-065. In the comments below, we request a new table of adverse reactions not contingent on treatment relationship.

27 Page(s) Withheld

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_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Akilah Green
3/23/2007 04:26:33 PM
CSO

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: February 28, 2007

TO: Badrul Chowdhury, M.D., Director
Division of Pulmonary and Allergy Products

VIA: Akilah Green, Regulatory Project Manager
Division of Pulmonary and Allergy Products

FROM: Jeanine Best, M.S.N., R.N., P.N.P.
Patient Product Information Specialist
Division of Surveillance, Research, and Communication Support

THROUGH: Toni Piazza-Hepp, Pharm.D., Deputy Director
Division of Surveillance, Research, and Communication Support

SUBJECT: OSE/DSRCS Review of Medication Guide for formoterol fumarate inhalation solution, NDA 22-007

Background and Summary

DEY, LP submitted a NDA June 28, 2006, for formoterol fumarate inhalation solution, NDA 22-007, a long-action beta₂-adrenergic agonist (LABA), "for the long-term, twice daily (morning and evening) administration in the maintenance treatment of bronchoconstriction in patients with Chronic Obstructive Pulmonary Disease including chronic bronchitis and emphysema." Submitted labeling included Full Prescribing Information (FPI) and a Patient Package Insert (PPI).

On December 13, 2006, the review division sent an information request to the sponsor that included a request for a revised FPI with a Boxed Warning and the submission of a Medication Guide (MG) to replace the PPI for consistency with other LABA products. The sponsor was told to use the recently approved Brovana (arformoterol tartrate) labeling as a guide.

The sponsor submitted a revised FPI and a MG on January 25, 2007.

OSE/DSRCS was consulted to review the MG.

Comments and Recommendations

1. See the attached Medication Guide (marked and clean copies) for our suggested revisions. We have made the MG consistent with the revised draft FPI and/or made suggestions for inclusion of important information in the FPI. The sponsor did submit a MG that was nearly

identical to the Brovana MG, but the formoterol draft FPI does not contain identical information that is in the Brovana PI. A MG must be consistent with its approved professional labeling [208.20(a)(2)].

2. For the FPI we have the following revisions:
 - a) **Highlights of Prescribing Information:** revise “See 17 for PATIENT COUNSELING INFORMATION – and FDA approved patient labeling” to “See 17 for PATIENT COUNSELING INFORMATION – and Medication Guide” [per 201.57(a)(14)]
 - b) Section 17.5, revise heading “FDA – Approved Patient Labeling” to “Medication Guide”.

Comments to the review division in the attached Medication Guide are **bolded, underlined and italicized**. Please call us if you have any questions.

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/s/

Jeanine Best
2/28/2007 03:03:11 PM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
2/28/2007 03:44:53 PM
DRUG SAFETY OFFICE REVIEWER



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

Memorandum of Facsimile Correspondence

Date: April 5, 2007

To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007; labeling comments

of Pages: 19

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Thank you.

NDA 22-007

Perforomist Inhalation Solution

We have reviewed the labeling text for Perforomist Inhalation Solution, submitted March 28, 2007, including the Package Insert, Medication Guide, and carton and container. FDA has made revisions to your proposed labeling (attached). The following comments refer to the Package Insert, Medication Guide, and carton and container labeling. The comments are meant to clarify the major issues addressed in the April 2, 2007, labeling teleconference and subsequent revisions. There may be additional edits and suggested changes upon further review of your response to this facsimile. Please submit revised labeling and any questions by April 11, 2007.

Package Insert

General Comments

1. We have accepted your proposed changes, where appropriate.
2. We have made further revisions to the HIGHLIGHTS, CONTENTS, and FULL PRESCRIBING INFORMATION sections/subsections based on the various Physician Labeling Rule guidances for label content and format. For example, several subsection headings have been changed from numbered subsections to bolded but not numbered.
3. We accept the capitalization of your trade name, Perforomist in the Package Insert and Medication Guide. Please accept all changes with capitalization, but note that there may be instances in the text where revisions have been made to wording where the trade name is not capitalized.

Comments by section

HIGHLIGHTS

4. We have included the lack of an indication for use in children as an important limitation to use.
5. We have revised the "ADVERSE REACTIONS" section to include the events in a revised table of adverse events from trial 201-065.

FULL PRESCRIBING INFORMATION: CONTENTS

6. We have revised and removed various subsection headings not required to be listed.

FULL PRESCRIBING INFORMATION

ADVERSE REACTIONS

7. We have rearranged the "ADVERSE REACTIONS" section to be consistent with the Guidance on the content and format of this section. The standardized language that clinical trial information cannot be directly compared across drugs has been placed at the beginning of the Clinical Trials Experience subsection, but before the results of the COPD studies.
8. Results from the 12-week trial have been consolidated into one paragraph, and a sentence containing generalized warning/precaution language that is already present in the labeling has been removed.
9. We have renamed Table 1 as "adverse reactions" because it includes events for which a reasonable basis of association with Performist exists. We have rearranged the order of reactions listed in Table 1 in descending order of frequency.

USE IN SPECIFIC POPULATIONS

10. Section 8.5 has been modified to be consistent with the CLINICAL STUDIES section regarding efficacy (see our comments for the CLINICAL STUDIES section).

CLINICAL PHARMACOLOGY

Systemic Safety and Pharmacokinetic / Pharmacodynamic Relationships subsection

11. Verify that the replaced standard deviation for the potassium value is — or replace with a corrected value. We have rounded laboratory values and standard deviations to whole numbers. b(4)

Electrophysiology subsection

12. Verify that the ~~—~~ beats per minute is correct. b(4)

Tachyphylaxis / Tolerance subsection

13. The tachyphylaxis/tolerance subsection has been extensively reworded to convey the essential message.

CLINICAL STUDIES

14. We have revised the description section of the study to clearly describe the patients enrolled and the primary endpoint.
15. Verify the numbers of patients who completed the study, and add percents, as highlighted.

16. Insert the correct percent of patients who experienced cardiovascular events, as highlighted.
17. Regarding the y-axis for Figures 1 and 2, keep the y-axis as currently shown in the figures. However, move the legends to within the margins of the figures.
18. We have added standardized language regarding age, gender, and racial subgroup analyses to be consistent with the Guidance on the content and format of this section, and revised the Geriatric Use subsection accordingly.
19. Provide an analysis of the early bronchodilator effects of Perforomist using the following guidelines, and complete the areas highlighted:
 - a. Use observed data.
 - b. Base the analysis on the first dose of Perforomist on Day 1, not following the Week 12 dose.
 - c. For each subject, determine the time at which the subject achieves a 15% increase from baseline in FEV₁ via interpolation. Provide your algorithm of the calculation of the onset time. Repeat this analysis for 12% increase with an increase of 200 ml or more, and for peak effect.
 - d. Provide a figure and summary statistics, including mean, median, lower and upper quartiles, on the distribution of onset times as described above, and for peak effect. Provide the number of patients treated with Perforomist who did not reach a 15% increase in FEV₁ on Day 1.

PATIENT COUNSELING INFORMATION

20. We have removed the numbering for subsection headings.

Medication Guide

21. Since all adverse reactions in the ADVERSE REACTIONS section should be represented in the listing of possible side effects, add vomiting to the listing of possible side effects on page 3.

Carton and Container

22. Remove the phrase " _____ " from the container labeling. This would be consistent with the current (version 4) Peforomist foil label.

b(4)

23. Capitalize the trade name on the carton and container labeling as it is in the Package Insert and Medication Guide.

If you have any questions, you may contact, Ms. Akilah Green, Senior Regulatory Management Officer, at 301-796-1219.

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/s/

Akilah Green

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**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

Memorandum of Facsimile Correspondence

Date: March 1, 2007

To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007

of Pages: 3

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Thank you.

NDA 22-007

We are reviewing your submission dated June 28, 2006, and we have the following comment and requests for information:

1. The Pharmaceutical Development Report, "report-pdr-716b.pdf", does not mention FFIS lots C037 or C051, which are cited as batches used in DL-052 and DL-057, respectively, in the reports for these trials.
 - a. Clarify any discrepancies between the Pharmaceutical Development Report and the final reports of all clinical trials in FFIS lots used.
 - b. Provide information about all clinical lots, consistent with the information already provided about clinical lots in the Pharmaceutical Development Report in Tables 9.1.1 and 9.1.2.

If you have any questions, you may contact Ms. Akilah Green, Senior Regulatory Management Officer, at 301-796-1219.

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/s/

Akilah Green
3/1/2007 02:04:28 PM
CSO



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

Memorandum of Facsimile Correspondence

Date: February 16, 2007
To: Elaine Alambra
Company: Dey, L.P.
Fax: (707) 224-1364
Phone: (707) 224-3200 ext. 3426
From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products
Subject: NDA 22-007
of Pages: 4

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Thank you.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-007

Dey, L.P.
2751 Napa Valley Corporate Drive
Napa, California 94558

Attention: Michelle A. Carpenter, JD
Vice President, Regulatory and Clinical Affairs

Dear Ms. Carpenter:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for formoterol fumarate inhalation solution

We also refer to your February 7, 2007, correspondence, received February 8, 2007, requesting a meeting to discuss the legal rationale for Dey's statement of non-applicable use for the reference listed drug Foradil.

Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type A meeting as described in our guidance for industry titled *Formal Meetings with Sponsors and Applicants for PDUFA Products* (February 2000). The meeting is scheduled for:

Date: February 28, 2007
Time: 2:00-3:00 PM
Phone Arrangements: Dey to provide CALL-IN NUMBER AND PASSCODE

CDER Participants: Elizabeth Dickinson, Regulatory Counsel, Division of Regulatory Policy II, Office of Regulatory Policy
Nancy Boocker, Director, Division of Regulatory Policy I, Office of Regulatory Policy
Janice Weiner, Regulatory Counsel, Office of Regulatory Policy (tentative)
Kim Dettelbach, Regulatory Counsel, Office of Regulatory Policy (tentative)
Kim Colangelo, Associate Director of Regulatory Affairs, Office of New Drugs
Akilah Green, MS, RN, Senior Regulatory Management Officer

NDA 22-007

Page 2

If you have any questions, call Ms. Akilah Green, Senior Regulatory Management Officer, at (301) 796-1219.

Sincerely,

{See appended electronic signature page}

Sandy Barnes
Chief Regulatory Project Manager
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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this page is the manifestation of the electronic signature.**

/s/

Akilah Green
2/16/2007 04:25:02 PM
Signed for Sandy Barnes

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; White Oak 22; Mail Stop 4447)

DATE RECEIVED: Dec. 5, 2006
DATE OF DOCUMENT: Nov. 16, 2006

DESIRED COMPLETION DATE:
Feb. 28, 2007
PDUFA Date: Apr. 29, 2007

OSE REVIEW #:
2006-901

TO: Badrul Chowdhury, M.D.
Director, Division of Pulmonary and Allergy Products
HFD-570

THROUGH: Alina Mahmud, RPh, MS, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Deveonne Hamilton-Stokes, RN, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME:
Perforomist
(Formoterol Fumarate Inhalation Solution)
20-mcg/2 mL

SPONSOR: Dey, L.P.

NDA#: 22-007

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Perforomist. This is considered a final decision. However, if 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 approvals of other proprietary or established names from the signature date of this document.
2. DDMAC finds the proprietary name Perforomist acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Nancy Clark, Project Manager, at 301-796-1187.

Division of Medication Errors and Technical Support
Office of Surveillance and Epidemiology
HFD-420; WO22; Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: December 7, 2006
NDA#: 22-007
NAME OF DRUG: **Perforomist**
(Formoterol Fumarate Inhalation Solution)
20 mcg/2 mL
NDA SPONSOR: Dey, L.P.

NOTE: This review contains proprietary and confidential information that should not be released to the public.

I. INTRODUCTION

This consult was written in response to a request from the Division of Pulmonary and Allergy Products, for an assessment of the proprietary name "Perforomist" regarding potential name confusion with other proprietary or established drug names. Please refer to consult number 2006-137 for comments regarding labels and labeling.

PRODUCT INFORMATION

Perforomist is a selective beta-2 adrenergic bronchodilator indicated for the maintenance treatment of bronchoconstriction in patients with Chronic Obstructive Pulmonary Disease (COPD), including chronic bronchitis and emphysema. Perforomist will be available in unit-dose vials containing 2 mL (20 mcg) of Formoterol. The usual dosage is 20 mcg every 12 hours orally inhaled via a nebulizer.

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,iv} for existing drug names which sound-alike or look-alike to "Perforomist" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database^v and Clinical Pharmacology^{vi} were also conducted. The Saegis^{vii} Pharma-In-Use database was searched for drug names with potential for confusion. 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

ⁱ MICROMEDEX Integrated Index, 2006, 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 1998-2006, and the electronic online version of the FDA Orange Book.

^{iv} Phonetic and Orthographic Computer Analysis (POCA)

^v WWW location <http://www.uspto.gov>.

^{vi} Clinical Pharmacology, online version available at <http://cpip.gsm.com>

^{vii} Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

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, Perforomist. Potential concerns regarding drug marketing and promotion related to the proposed name were 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, Perforomist.
2. The Expert Panel identified a total of thirteen names and the word Performist that were thought to have potential for confusion with Perforomist. Of these thirteen names, eight were not reviewed further due to the lack of significant look-alike and/or sound-alike similarities to Perforomist in addition to differentiating product characteristics that may include: indication for use, product strength, usual dosage, route of administration, frequency of administration, dosage form, prescriber population, patient population, product unavailability and/or area of marketing. The names not reviewed are as follows: Prepair per, Preparation H, Preferin Eye, Prometh Fortis, Proferrin-Forte, Proparacaine, Propranolol and Centrum Performance. In addition, the word Performist was not reviewed further because it is loosely used to refer to a performer and is not listed in a dictionary. DMETS found that five names warranted further evaluation based on their potential for confusion with Perforomist. These products are listed in Table 1 (see next page), along with the dosage forms available and usual dosage.

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

Product Name	Established name, Dosage form(s)	Usual adult dose	Other
Perforomist	Formoterol fumarate 20 mcg/2 mL Inhalation solution	20 mcg every 12 hours orally inhaled via a nebulizer	N/A
Proferdex	Iron Dextran Injection	Inject intramuscularly or intravenously once daily; Dose dependent on patients laboratory test results	LA
Primatene Mist	Epinephrine 0.22 mg Aerosol	One inhalation, then wait at least one minute. If relieved, use once more. Do not use again for at least 3 hours	LA
Perfosfamide***	No addition info available	No dosing info available	LA
Perifosine (found on internet)	Oral Tablets	<u>Loading dose:</u> 150 mg by mouth every 6 hours x 4 doses on first day. <u>Maintenance dose:</u> 100 mg/day by mouth On days 1-28. Course repeats every 28 days in the absence of disease progression	LA
Porfiromycin***	Porfiromycin	No additional information available at this time	SA/LA

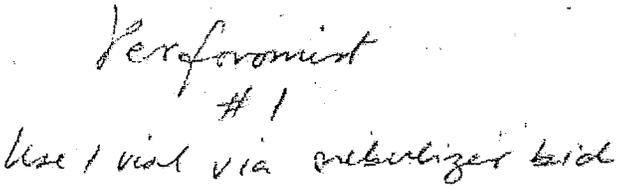
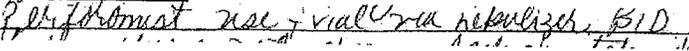
*** Note: This review contains proprietary and confidential information that should not be released to the public.***

b(4)

B. 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 Perforomist 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 122 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 prescription were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Perforomist (see below). 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
<p>Outpatient RX :</p> 	<p>Perforomist #1 Use 1 vial via nebulizer BID</p>
<p>Inpatient RX # :</p> 	

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.

C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name "Perforomist", the Expert Panel's primary concerns relating to look-alike and sound-alike confusion with Perforomist are Proferdex, Primatene Mist, Perfosfamide, Perifosine and Porfirmycin.

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 misinterpretations were misspelled/phonetic variations of the proposed name, Perforomist.

Although the following names below may look and/or sound similar to Perforomist, they will not be

reviewed due to the reasons as follows:

- Perfosfamide*** (Pergamid) _____

b(4)

- Perifosine i _____

- Porfiromycin*** (Promycin) _____

The names that will be further reviewed are as follows:

1. Proferdex was identified as having look-alike similarities to Perforomist when scripted. Proferdex, iron dextran, is indicated for the treatment of iron deficiency anemia in patients who cannot take iron by mouth.

Proferdex and Perforomist may look similar because the first 6 letters look very similar when scripted (see example below). Both names share the same letters (P, f, r) in the same positions which contribute to their similar appearance. However, Proferdex contains 9 letters and Perforomist contains 11 letters which helps to lengthen the name and provide a visual difference. In addition the upstroke letter "d" near the end of Proferdex helps to distinguish it from Perforomist.

Proferdex
Perforomist

Both drugs share an overlapping dosage form (solution). However, Proferdex and Perforomist differ in indication for use (anemia vs. bronchoconstriction), strength (50 mg/mL vs. 20 mcg/2 mL), route of administration (intramuscular or intravenous vs. oral via nebulizer), and frequency of administration (once daily vs. every 12 hours). Furthermore, the usual dose for Proferdex is dependent on a patient's ferritin, red blood cells and other tests; so the dose will vary, whereas the usual dose for Perforomist remains constant at 20 mcg.

DMETS believes that the lack of convincing orthographic similarities and the above-mentioned product differences will aid in minimizing the risk of confusion and error between Proferdex and Perforomist.

2. Primatene Mist was identified as a name with a similar appearance to Perforomist when scripted. Primatene Mist is an over the counter medication used for the treatment of mild asthma and congestion.

Primatene Mist and Perforomist may look similar as they both begin with "P" and they both end with "-mist" (see example top of next page). However, the upstroke "t" near the end of Primatene Mist and the downstroke of the "f" near the beginning of Perforomist may help to differentiate the names.

*** Note: This review contains proprietary and confidential information that should not be released to the public.***

*Primatene mist
Perforomist*

Both drugs share a similar indication for use (mild asthma vs. bronchoconstriction) and a similar route of administration (oral inhalation vs. oral inhalation via nebulizer). However, the differentiating product characteristics between Primatene Mist and Perforomist include strength (none vs. 20 mcg/2 mL), dosage form (aerosol vs. solution), frequency of administration (every 3 hours as needed vs. every 12 hours), prescription status (over-the-counter vs. prescription) and usual dose (1 inhalation vs. 20 mcg every 12 hours via nebulizer). Furthermore, Primatene Mist is mainly self prescribed by patients and most doctors do not prescribe Primatene Mist to patients with asthma. Also, the likelihood that a prescriber will include "...via nebulizer" in the directions for use for Perforomist may help further to distinguish the name. Therefore, DMETS believes the risk of confusion between Primatene Mist and Perforomist is minimal.

**APPEARS THIS WAY
ON ORIGINAL**

Appendix A

Perforomist prescription study results

Outpatient Written	Inpatient Written	Verbal
Perforomist	Performoist	Performerace
Perforomist	Perforomist	Performaris
Performist	Perforomist	Performeris
Perforomist	Perforomist	Performerance***
Performist	Performist	Performaris
Performist	Perforomist	Performerance
Perforomist	Perforomist	Proforma
Perforomist	Perforomist	Proformeris
Perforomist	Periforomist	Performerest
	Perforomist	Performeras
	Perforomist	Performerest
	Periforomist	Performeris
		Proformerist
		Performist
		Perforomist

***On participant in the verbal study commented: "for erectile dysfunction?"

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/s/

Deveonne Hamilton-Stokes
2/7/2007 11:19:45 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
2/7/2007 02:53:48 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
2/7/2007 03:33:21 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
2/7/2007 04:49:49 PM
DRUG SAFETY OFFICE REVIEWER



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

Memorandum of Facsimile Correspondence

Date: February 2, 2007

To: Michelle A. Carpenter
V.P., Regulatory Affairs and Clinical Development

Fax: (707) 224-1364

Phone: (707) 224-3200 x4750

From: Akilah Green, MS, RN
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007

of Pages: 4

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Thank you.

Your NDA is currently under review, and we have the following requests for information. Provide your response as soon as possible, preferably by February 9, 2007.

1. For trial 201-065, explain the differences in FEV₁ values among the various summaries of FEV₁ from section-1-15-report-body.pdf (see table).

Table. Mean FEV₁ from various sections of trial 201-065 section-1-15-report-body.pdf

Table from report	term for timepoint	Treatment		
		FFIS	FA	Placebo
14.1.3	baseline prebronchodilator	1.35 n=123	1.30 n=114	1.36 n=114
14.2.1.1.1	baseline	1.32 n=123	1.28 n=114	1.32 n=114
14.2.2.3.1	baseline trough	1.46 n=123	1.39 n=1.31	1.34 n=114

2. The plan for randomization of subjects into the open-label period of DL-059 is unclear. We note the following:
 - a. The protocols for DL-059 dated April 14, 2004, and February 22, 2005, do not contain information on the randomization of subjects into the open-label period. In fact, the Study Time and Events schedule does not contain an entry for randomization into the open-label period of the trial.
 - b. The statistical plan for the DL-059 open-label period dated August 20, 2005, states: "Approximately 690 adult patients with a medical diagnosis of COPD are randomized in a 2:1:1:1 ratio to the FFIS 20 mcg group (continuing with twice-daily FFIS 20 mcg in the open-label extension), the Foradil® 12 mcg group (continuing with twice-daily FFIS 20 mcg in the open-label extension), the Foradil® 12 mcg group (continuing with twice-daily Foradil® 12 mcg in the open-label extension), and the placebo group (continuing with FFIS 20 mcg in the open-label extension)." This plan was not changed in the amended plan of November 7, 2005.

Provide the detailed original plan for randomization and any amendments that were made to it. Clarify how individual treatment assignments were made from subjects in the double-blind period of DL-059 into the open-label period of DL-059.

3. For trial DL-056, provide the following information separately for glucose, potassium, pulse rate, and the ECG parameters QTcB and QTcF:
 - a. Summary statistics (i.e., mean with standard deviation, median, and range) at each time point, including predose and post-dose time points, separately for Foradil® and for each dose level of FFIS.

- b. Figures representing the mean and range over time, including predose and post-dose time points, separately for Foradil® and for each dose level of FFIS.
4. For trial DL-056, provide the total numbers and identities of subjects, with respect to treatment received and time point, whose QTcB changed after treatment by >60 msec or exceeded 500 msec. Repeat this for QTcF.
5. For trial DL-056, provide datasets of individual subject data for all serum laboratory values, pulse rate, and the ECG parameters QTcB and QTcF including, at least, variables for treatment received and time point.
6. For each clinical trial that used a placebo, provide the following information or provide its location in the NDA.
 - a. The exact chemical constituents, and their amounts, for each placebo treatment.
 - b. Details as to the physical measures that were used to blind placebo treatment. Details should include but may not be limited to appearance of the placebo and labels used in shipping.

If you have any questions, you may contact Ms. Akilah Green, Senior Regulatory Management Officer, at 301-796-1219.



**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II**

Memorandum of Facsimile Correspondence

Date: January 29, 2007

To: Gina Caprio
Associate Director, Regulatory Affairs

Company: Dey, L.P.

Fax: (707) 224-1364

Phone: (707) 224-3200 ext. 3306

From: Akilah Green, RN, MS
Senior Regulatory Management Officer
Division of Pulmonary and Allergy Products

Subject: NDA 22-007

of Pages: 4

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Thank you.

NDA 22-007
formoterol fumarate

We are reviewing your submission dated June 28, 2006, and we have the following labeling comments and requests for information:

General comments:

1. Indicate whether the labeling reflects the total volume of hold-up in the tip of the LDPE vial.
2. Evaluate and provide the consistency of recovered volume from the LDPE vial.
3. Revise the established name to "Formoterol Fumarate Dihydrate" in all labeling, and include the established name with the first occurrence of the proprietary name in the How Supplied/Storage and Handling Section.
4. Revise the storage statement to state "After dispensing to the patient: Store at 2° to 25° (36° F to 77° F) for up to 3 months on all labels."
5. Revise the statement "For Inhalation Only" to "For Oral Inhalation Only" on all labeling.

Package Insert:

6. Provide the mean nebulization times and flow rate of the nebulizer in the Description section.
7. Specify the Total Volume of the LDPE vial in the Description section.
8. Revise the dosing frequency from "twice daily" to " _____ " to reduce confusion. **b(4)**
9. For the Package Insert and Patient Package Insert, include a statement in the Dosage and Administration and How Supplied sections indicating "Do not take by mouth" and "Contents of any partially used container should be discarded." The container and top, due to their small size, pose a danger of choking to young children.

Carton and container labeling:

10. Revise the background and lettering on the foil pouch, including storage conditions and established name, for better legibility.
11. Assure the established name is at least ½ the size of the proprietary name pursuant to 21 CFR 201 (g) (2).

12. Increase the prominence of the product strength, as it is currently overshadowed by the Trade Name and “2 mL” statement. This strength (20 mcg) is of great importance, as the currently marketed Foradil contains 12 mcg of formoterol.
13. Delete the ~~_____~~ Currently this presentation is larger than the product strength. Additionally, it is duplicative since the volume is presented in conjunction with the strength. b(4)
14. Revise the “Dispense Date” and “Use by” box. As currently presented, there is no space for the entry of a dispensing date. Furthermore, the “Use by” box is referenced throughout the labeling. Thus, consider the deletion of the “Dispense date” statement since it is not relevant. The previous sentence (Discard three months after dispense date) describes the “Use by” date.
15. The picture of the individual vial illustrates embossing on both sides, which has been found to result in illegibility of the text in post-marketing reporting. Therefore, emboss the established name and strength on one side of the body of the vial to help patients and practitioners identify the vial content. These data are currently embossed on the tab of the vial. The tab space can then include the tradename, route of administration, lot, and expiration.

If you have any questions, you may contact Ms. Akilah Green, Senior Regulatory Management Officer, at 301-796-1219.

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

/s/

Akilah Green
1/29/2007 01:58:12 PM
CSO