

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
21-272

MICROBIOLOGY REVIEW

REVIEW TO HFD 110
OFFICE OF NEW DRUG CHEMISTRY
Microbiology Staff, HFD-805
Microbiologist's Review #3 of Supplement
March 28, 2001

- A. 1. **NDA:** 21-272/N-BI
2. **APPLICANT/SPONSOR:** United Therapies Corporation
68 T.W. Alexander Dr.
Research Triangle Park, NC 27709
- Contact:** Dean Bunce
Associate Director,
Regulatory Affairs
919-485-8350
5. **MANUFACTURING SITE:** _____
6. **DRUG PRODUCT NAME**
Proprietary: Uniprost (UT-15)
Nonproprietary: Triprostinol Sodium (applied for)
Drug Priority Classification: Standard
7. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Subcutaneous injection
 - 1.0, 2.5, 5.0, and 10 mg/mL
8. **METHOD(S) OF STERILIZATION:** _____
9. **PHARMACOLOGICAL CATEGORY AND/OR PRINCIPLE INDICATION:**
pulmonary arterial hypertension
- B. 1. **DOCUMENT/LETTER DATE:** August 11, 2000
2. **RECEIPT DATE:** August 14, 2000
3. **CONSULT DATE:** August 16, 2000
4. **DATE OF AMMENDMENT:** February 19, 2001 (Subject of this review)
5. **ASSIGNED FOR REVIEW:** March 28, 2001

6. **SUPPORTING/RELATED DOCUMENTS:**

Review #1 of this supplement was completed on October 26, 2000. A deficiency letter was sent on November 6, 2000. A teleconference was held on February 1, 2000 with Dean Bunce and several representatives of United Therapeutics Corporation to discuss the vials.

C. **REMARKS: Uniprost (UT-15) has been designated as an orphan drug for the treatment of pulmonary arterial hypertension. The following is a review of the applicant's responses to the microbiology deficiencies listed in the first review.**

D. **CONCLUSIONS: The submission is recommended for approval from the standpoint of microbial product quality.**

S

Stephen E. Langille, Ph. D.

cc: Original **NDA-21-272**
HFD-110/Division File
HFD-110/Chem./Advani
HFD 805/Consult File/Langille
Drafted by S. Langille c:reviews/21-272r3
Initialed by P. Cooney

2 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

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

/s/

Stephen Langille
4/19/01 11:33:10 AM
MICROBIOLOGIST

Peter Cooney
4/19/01 01:40:09 PM
MICROBIOLOGIST

REVIEW TO HFD 110
OFFICE OF NEW DRUG CHEMISTRY
Microbiology Staff, HFD-805
Microbiologist's Review #2 of Supplement
March 5, 2001

- A. 1. **NDA:** 21-272/N-000-C
2. **APPLICANT/SPONSOR:** United Therapies Corporation
68 T.W. Alexander Dr.
Research Triangle Park, NC 27709
- Contact:** Dean Bunce
Associate Director,
Regulatory Affairs
919-485-8350
5. **MANUFACTURING SITE:** _____
6. **DRUG PRODUCT NAME**
Proprietary: Uniprost (UT-15)
Nonproprietary: Triprostinol Sodium (applied for)
Drug Priority Classification: Standard
7. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Subcutaneous injection
 - 1.0, 2.5, 5.0, and 10 mg/mL
8. **METHOD(S) OF STERILIZATION:** _____
9. **PHARMACOLOGICAL CATEGORY AND/OR PRINCIPLE INDICATION:**
pulmonary arterial hypertension
- B. 1. **DOCUMENT/LETTER DATE:** August 11, 2000
2. **RECEIPT DATE:** August 14, 2000
3. **CONSULT DATE:** August 16, 2000
4. **DATE OF AMMENDMENT:** November 10, 2000
5. **ASSIGNED FOR REVIEW:** November 15, 2000
6. **SUPPORTING/RELATED DOCUMENTS:**

Review #1 of this supplement was completed on October 26, 2000. A deficiency letter was sent on November 6, 2000. A teleconference was held on February 1, 2000 with Dean Bunce and several representatives of United Therapeutics Corporation to discuss the _____ vials. In a letter to the FDA dated February 19, 2001, United Therapeutics Corporation agreed to _____ all vials during commercial production of UT-15.

- C. REMARKS: Uniprost (UT-15) has been designated as an orphan drug for the treatment of pulmonary arterial hypertension. The following is a review of the applicant's responses to the microbiology deficiencies listed in the first review.**
- D. CONCLUSIONS: The submission is recommended for approval from the standpoint of microbial product quality.**

IS

Stephen E. Langille, Ph. D.

cc: Original NDA-21-272
HFD-110/Division File
HFD-110/Chem./Advani
HFD 805/Consult File/Langille
Drafted by S. Langille c:reviews/21-272r2
Initialed by P. Cooney

E. REVIEW NOTES:

5 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

/s/

Stephen Langille
3/6/01 09:14:48 AM
MICROBIOLOGIST

Peter Cooney
3/6/01 01:41:09 PM
MICROBIOLOGIST

FR0MM
OCT 26 2000

REVIEW TO HFD 110
OFFICE OF NEW DRUG CHEMISTRY
Microbiology Staff, HFD-805
Microbiologist's Review #1 of Supplement
October 24, 2000

- A. 1. **NDA:** 21-272
2. **APPLICANT/SPONSOR:** United Therapies Corporation
68 T.W. Alexander Dr.
Research Triangle Park, NC 27709
- Contact:** Dean Bunce
Associate Director,
Regulatory Affairs
919-485-8350
5. **MANUFACTURING SITE:** _____
6. **DRUG PRODUCT NAME**
Proprietary: Uniprost (UT-15)
Nonproprietary: Triprostinol Sodium (applied for)
Drug Priority Classification: Standard
7. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Subcutaneous injection
 - 1.0, 2.5, 5.0, and 10 mg/mL
8. **METHOD(S) OF STERILIZATION:** _____
9. **PHARMACOLOGICAL CATEGORY AND/OR PRINCIPLE INDICATION:**
pulmonary arterial hypertension
- B. 1. **DOCUMENT/LETTER DATE:** August 11, 2000
2. **RECEIPT DATE:** August 14, 2000
3. **CONSULT DATE:** August 16, 2000
4. **DATE OF AMMENDMENT:**
5. **ASSIGNED FOR REVIEW:** August 22, 2000
6. **SUPPORTING/RELATED DOCUMENTS:**

- C. REMARKS: **Uniprost (UT-15) has been designated as an orphan drug for the treatment of pulmonary arterial hypertension.**
- D. CONCLUSIONS: **The submission is approvable pending resolution of microbiological deficiencies. Specific comments regarding the process are provided in "E. Review Notes" and "List of Microbiology Deficiencies and Comments".**

SL / 10-24-00
Stephen E. Langille, Ph. D.

SL 10/26/00

cc: Original **NDA-21-272**
HFD-110/Division File
HFD-110/Chem./Advani
HFD 805/Consult File/Langille
Drafted by S. Langille v:microrev\# 21-272r1
Initialed by P. Cooney

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