

CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:
21-248**

**CHEMISTRY REVIEW/EA FONSI/MICROBIOLOGY
REVIEW**

Division of Oncology Drug Products
Review of Chemistry, Manufacturing and Controls

AUG 14 2000

NDA #: 21,248 CHEM. REVIEW #: 2 REVIEW DATE: 7-16-2000

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGN DATE</u>
Original	3-27-2000	3-28-2000	4-3-2000
BL	6-27-2000	6-28-2000	
BC	6-26-2000	6-27-2000	
BC	7-19-2000	7-20-2000	
NC	7-12-2000	7-13-2000	
BZ	7-11-2000	7-12-2000	
BC	7-18-2000	7-19-2000	

NAME & ADDRESS OF APPLICANT: Cell Therapeutics, Inc.
201 Elliott Ave. W. 400
Seattle, WA 98119

DRUG PRODUCT NAME:

Proprietary: TRISENOX
Nonproprietary/USAN: Arsenic trioxide
Code Name/#:
Chem. Type/Ther. Class: 1-P

PHARMACOL. CATEGORY/INDICATION:

Treatment of acute promyelocytic
leukemia (APL)

DOSAGE FORM/STRENGTHS:

1 mg/mL

ROUTE OF ADMINISTRATION:

Intravenous

MANUFACTURER:

Spillman

Division of Oncology Drug Products
Review of Chemistry, Manufacturing and Controls

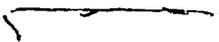
JUN 20 2000

NDA #: 21,248 CHEM. REVIEW #: 1 REVIEW DATE: 6-20-2000

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGN DATE</u>
Original	3-27-2000	3-28-2000	4-3-2000

NAME & ADDRESS OF APPLICANT: Cell Therapeutics, Inc.
201 Elliott Ave. W. 400
Seattle, WA 98119

DRUG PRODUCT NAME:

Proprietary:  proposed
Nonproprietary/USAN: TBD
Code Name/#:
Chem. Type/Ther. Class: 1-P

PHARMACOL. CATEGORY/INDICATION:

Treatment of acute promyelocytic leukemia (APL)

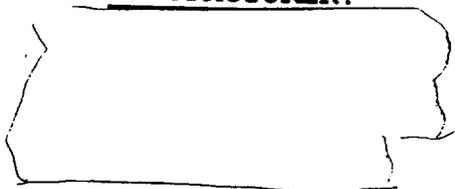
DOSAGE FORM/STRENGTHS:

1 mg/mL

ROUTE OF ADMINISTRATION:

Intravenous

MANUFACTURER:



CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR WEIGHT:

As₂O₃, MW = 197.8, Arsenic trioxide
CAS 1327-53-3

SUPPORTING DOCUMENTS:

[Redacted]

CONSULTS:

<u>Consult</u>	<u>Status</u>	<u>Comments</u>
EES	Acceptable	Only [Redacted] manufacturer in [Redacted] is pending for inspection. Other [Redacted] sites for [Redacted] manufacture and testing are found to be acceptable.
Microbiology	Acceptable	Submitted on 3/29/00
Trademark	Pending	
Environment Assessment	Categorical exclusion	Acceptable
USAN	Pending	

REMARK/COMMENTS:

Adequate CMC information has been submitted for this orphan drug which is used to treat acute promyelocytic leukemia (APL). Several minor deficiencies which are related to [Redacted] and [Redacted] studies need be resolved by the applicant.

CONCLUSIONS AND RECOMMENDATIONS:

The NDA is recommended for approval from a chemistry manufacturing and control perspective. The CMC deficiencies listed in the Draft Letter to the applicant will be sent as an information request. Response to the questions should be provided as soon as possible

See attached review notes and draft deficiency letter.

[Redacted Signature] 6/20/00
Xiaohong Chen, Ph.D., Review Chemist

[Redacted Signature] 6/20/00
Chengyi Liang, Ph.D., Review Chemist

[Redacted]

6/20/00

Eric Duffy, Ph.D.
Chemistry Team Leader...

- CC:
- Orig. NDA 21-248
- HFD-150 Division File
- HFD-150/XChen
- HFD-150/CLiang
- HFD-150/EDuffy
- HFD-150/DSpillman
- HFD-810/Directors

MAY - 2 2000

REVIEW FOR HFD-150
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGISTS REVIEW #1 OF NDA 21-248
24 April 2000

A. 1. NDA 21-248

APPLICANT: Cell Therapeutics, Inc.
201 Elliott Avenue, West
Suite #400
Seattle, WA 98119

2. PRODUCT NAMES: (arsenic trioxide injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is intended for intravenous infusion.

4. METHODS OF STERILIZATION:

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE
INDICATION:

The drug product is indicated for the treatment of acute promyelocytic leukemia (APL).

B. 1. DATE OF INITIAL SUBMISSION: 27 March 2000

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW: 19 April 2000

C. REMARKS:

D. CONCLUSIONS: The application is recommended for approval, pending the applicant's commitment to provide the data indicated in "List of Microbiology Comments" post-approval.

/S/
24 April 2000
Paul Stinavage, Ph.D.
PAC 5/2/00

cc: Original NDA 21-248
HFD-805/Stinavage/Consult File
HFD-150/Div File/E. Duffy/C. Liang/D. Spillman

Drafted by: P. Stinavage, 24 April 2000
R/D initialed by P. Cooney

Spillman

AUG 18 2000

REVIEW FOR HFD-150
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #2 OF NDA 21-248
14 August 2000

A. 1. NDA 21-248 BZ

APPLICANT: Cell Therapeutics, Inc.
201 Elliott Avenue, West
Suite #400
Seattle, WA 98119

2. PRODUCT NAMES: (arsenic trioxide injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is intended for intravenous infusion.

4. METHODS OF STERILIZATION:

[Redacted]

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE
INDICATION:

The drug product is indicated for the treatment of acute promyelocytic leukemia (APL).

B. 1. DATE OF INITIAL SUBMISSION: 27 March 2000

2. DATE OF AMENDMENT: 11 July 2000 (Subject of this Review.)

3. RELATED DOCUMENTS:

[Redacted]

4. ASSIGNED FOR REVIEW: 14 August 2000

C. REMARKS:

[Redacted]

D. CONCLUSIONS: This submission provides the data requested in Microbiologist's Review #1 dated 24 April 2000. The application is recommended for approval on the basis of sterility assurance.

/S/
August 2000
Paul Stinavage, Ph.D.
PK 8/18/00

cc: Original NDA 21-248
HFD-805/Stinavage/Consult File
HFD-150/Div File/E. Duffy/C. Liang/D. Spillman/X. Hong

Drafted by: P. Stinavage, 24 April 2000
R/D initialed by P. Cooney

MAY - 2 2000

REVIEW FOR HFD-150
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #1 OF NDA 21-248
24 April 2000

A. 1. NDA 21-248

APPLICANT: Cell Therapeutics, Inc.
201 Elliott Avenue, West
Suite #400
Seattle, WA 98119

2. PRODUCT NAMES: (arsenic trioxide injection)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is intended for intravenous infusion.

4. METHODS OF STERILIZATION:

[Redacted]

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE
INDICATION:

The drug product is indicated for the treatment of acute promyelocytic leukemia (APL).

B. 1. DATE OF INITIAL SUBMISSION: 27 March 2000

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS:

[Redacted]

4. ASSIGNED FOR REVIEW: 19 April 2000

C. REMARKS:

[Redacted]

D. CONCLUSIONS: The application is recommended for approval, pending the applicant's commitment to provide the data indicated in "List of Microbiology Comments" post-approval.

/S/
24 April 2000
✓ Paul Stinavage, Ph.D.
PAC 5/2/00

cc: Original NDA 21-248
HFD-805/Stinavage/Consult File
HFD-150/Div File/E. Duffy/C. Liang/D. Spillman

Drafted by: P. Stinavage, 24 April 2000
R/D initialed by P. Cooney