CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 090304

BIOEQUIVALENCE REVIEW

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	90304
Drug Product Name	Dactinomycin for Injection, USP
Strength(s)	0.5 mg per vial
Applicant Name	Bedford Laboratories
Address	300 Northfield Road Bedford, OH 44146
Applicant's Point of Contact	Molly Rapp, Director, Ben Venue Labs
Contact's Telephone Number	(440) 201-3576
Contact's Fax Number	(440) 439-6080
Original Submission Date(s)	December 28, 2008
Submission Date(s) of Amendment(s) Under Review	NA
Reviewer	Saeid Raofi
OUTCOME DECISION	**ACCEPTABLE**

Review of Waiver Request

1. EXECUTIVE SUMMARY

Bedford Laboratories has filed an ANDA for its product, Dactinomycin for Injection, 0.5 mg per vial referencing Cosmegen® from Ovation Pharms as the reference listed drug (RLD) (NDA #50682). The firm requests a waiver of *in vivo* bioequivalence study requirements for its test product in accordance with 21 CFR 320.22 (b)(1). The Division of Bioequivalence (DBE) concludes that the test product is qualitatively (Q1) and quantitatively (Q2) the same as the RLD and therefore recommends that the waiver be granted.

2. TABLE OF CONTENTS

3. SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Dactinomycin for Injection USP 0.5 mg per vial
Reference Product	Cosmegen® 0.5 mg per vial
RLD Manufacturer[1]	Ovation Pharms
NDA No.	50-682
RLD Approval Date	Prior to January 1, 1982
Indication[1]	COSMEGEN, as part of a combination chemotherapy and/or multi-modality treatment regimen, is indicated for the treatment of Wilms' tumor, childhood rhabdomyosarcoma, Ewing's sarcoma and metastatic, nonseminomatous testicular cancer. COSMEGEN is indicated as a single agent, or as part of a combination chemotherapy regimen, for the treatment of gestational trophoblastic neoplasia. COSMEGEN, as a component of regional perfusion, is indicated for the palliative and/or adjunctive treatment of locally recurrent or locoregional solid malignancies.

3.2 History

Controls: None

Protocols: None

ANDAs:

62350 (b) (4) Review is not traceable

[1] Physicians' Desk Reference, 2008

3.3 PK/PD Information

Food Effect	Not applicable
Tmax	Not applicable
Metabolism	Results of a study in patients with malignant melanoma indicate that Dactinomycin (^{3}H actinomycin D) is minimally metabolized, is concentrated in nucleated cells, and does not penetrate the blood-brain barrier.
Excretion	Approximately 30% of the dose was recovered in urine and feces in one week.
Half-life	36 hrs
Drug Specific Issues (if any)	COSMEGEN should not be given at or about the time of infection with chickenpox or herpes zoster because of the risk of severe generalized disease which may result in death. Reports indicate an increased incidence of second primary tumors (including leukemia) following treatment with radiation and antineoplastic agents, such as COSMEGEN. Multi-modal therapy creates the need for careful, long-term observation of cancer survivors. COSMEGEN may cause fetal harm when administered to a pregnant woman. This drug is **HIGHLY TOXIC** and both powder and solution must be handled and administered with care COSMEGEN is extremely corrosive to soft tissue, it is intended for intravenous use. Inhalation of dust or vapors and contact with skin or mucous membranes, especially those of the eyes, must be avoided.

3.4 Comments:

1. The test product is an injection and contains qualitatively (Q1) and quantitatively (Q2) the same active and inactive ingredients as the reference listed drug.

2. Dactinomycin for injection is a lyophilized powder for injection by the intravenous route or by regional perfusion after reconstitution.

4. RECOMMENDATIONS

The Division of Bioequivalence (DBE) agrees that the information submitted by Bedford Laboratories demonstrates that Dactinomycin for Injection, 0.5 mg per vial meets the requirements of Section 21 CFR § 320.22 (b)(1). The DBE recommends the waiver of in vivo bioequivalence testing be granted. Accordingly bioequivalence testing should not be undertaken.

5. Appendix

Formulation **NOT TO BE RELEASED UNDER FOI**

Ingredient	Function	Test product (amount per vial)	RLD (amount per vial)
Dactinomycin, USP	Active	0.5 mg	0.5 mg
Mannitol, USP	(b) (4)	20 mg	20 mg
(b) (4)			

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 90304

APPLICANT: Bedford Laboratories

DRUG PRODUCT: Dactinomycin for Injection, USP
0.5 mg per vial

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Barbara M. Davit, Ph.D., J.D.
Acting Director,
Division of Bioequivalence II
Office of Generic Drugs
Center for Drug Evaluation and Research

6. OUTCOME PAGE

Completed Assignment for 90304 ID: 6735

Reviewer: Raofi, Saeid **Date Completed:**
Verifier: **Date Verified:**
Division: Division of Bioequivalence
Description: Injection waiver

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
6735	12/28/2007	Other	Waiver Injectable	1	1
				Bean Total:	1

DIVISION OF BIOEQUIVALENCE 2 REVIEW COMPLEXITY SUMMARY

Injection Waiver Applications

Solubility Study	1
Injection Waiver Study Total	*1*

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/s/

Saeid Raofi
11/5/2008 10:27:02 AM
BIOPHARMACEUTICS

Kuldeep R. Dhariwal
11/5/2008 10:31:36 AM
BIOPHARMACEUTICS

Barbara Davit
11/23/2008 03:58:21 PM
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