CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75660

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # : 75-660 SPONSOR : Bedford Laboratories

DRUG AND DOSAGE FORM : Milrinone Injection

STRENGTH(S) : 1 mg/mL; 10 mL and 20 mL vials

TYPES OF STUDIES : NA

CLINICAL STUDY SITE(S) : NA

ANALYTICAL SITE(S) : NA

STUDY SUMMARY : **Waiver of bioequivalence studies is granted.**

DISSOLUTION : NA

DSI INSPECTION STATUS

Inspection needed: NO	Inspection status:	Inspection results:
First Generic NO New facility ___ For cause ___ other ___	Inspection requested: (date) Inspection completed: (date)	

PRIMARY REVIEWER : Zakaria Z. Wahba, Ph.D. BRANCH : III

INITIAL : /S/ DATE : 8/10/99

TEAM LEADER : Barbara M. Davit, Ph.D. BRANCH : III

INITIAL : /S/ DATE : 8/10/99

DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.

INITIAL : _____ DATE : 8/23/99

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # : 75-660 SPONSOR : Bedford Laboratories

DRUG AND DOSAGE FORM : Milrinone Lactate Injection

STRENGTH(S) : 1 mg/mL; 50 mL vial

TYPES OF STUDIES : NA

CLINICAL STUDY SITE(S) : NA

ANALYTICAL SITE(S) : NA

STUDY SUMMARY : Waiver of bioequivalence study requirements is granted.

DISSOLUTION : NA

DSI INSPECTION STATUS

Inspection needed: NO	Inspection status:	Inspection results:
First Generic NO New facility ___ For cause ___ other ___	Inspection requested: (date) Inspection completed: (date)	

PRIMARY REVIEWER : Zakaria Z. Wahba, Ph.D. BRANCH : III

INITIAL : ZZW DATE : 5/1/02

TEAM LEADER : Moheb H. Makary, Ph.D. BRANCH : III

INITIAL : MHM DATE : 5/1/02

DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.

INITIAL : DPC DATE : 5/1/02

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-660 APPLICANT: Bedford Laboratories

DRUG PRODUCT: Milrinone Injection, 1 mg/mL; 10 mL and 20 mL Vials

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

Please note that the bioequivalency 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 bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CC: ANDA #75-660
ANDA DUPLICATE
DIVISION FILE
HFD-651/ Bio Drug File
HFD-658/ Reviewer z. Wahba
HFD-658/ Bio team Leader B. Davit

Endorsements:
HFD-658/ Z. Wahba Z.W. 8/10/99
HFD-658/ B. Davit BWD 8/10/99
HFD-650/ D. Conner [signature] 8/23/99

BIOEQUIVALENCY - ACCEPTABLE

submission date: June 29, 1999

OK 1. WAIVER (WAI) Strengths: 1 mg/mL, 10 mL and 20 mL
Outcome: AC

Outcome Decisions: **AC** - Acceptable

Milrinone Injection
1 mg/mL; 10 mL and 20 mL Vials
ANDA #**75-660**
Reviewer: Z.Z. Wahba

Bedford Laboratories
Bedford, OH
Submission Date:
June 29, 1999

REVIEW OF WAIVER REQUESTS

BACKGROUND

1. The firm has requested a waiver of bioequivalence study requirements for its drug product Milrinone Injection, 1 mg/mL; 10 mL and 20 mL Vials. The reference listed drug is Primacor® Injection 1 mg/mL; 10 mL and 20 mL Vials, manufactured by Sanofi-Winthrop.

2. Milrinone Lactate Injection is indicated for the short-term intravenous therapy of congestive heart failure.

FORMULATION

The formulations of Bedford's Milrinone Injection and Sanofi Winthrop's Primacor® Injection, 1 mg/mL are presented below:

Ingredient	Bedford (Amount per mL)	Sanofi Winthrop
Milrinine	1.0 mg	1.0 mg
*Lactic Acid, USP	Adjust pH	Adjust pH
Dextrose Anhydrous, USP	47 mg	47 mg
Sodium Hydroxide, NF	Adjust pH	Adjust pH
Water for Injection	qs to 1.0 mL	qs to 1.0 mL

* The total concentration of lactic acid can vary between {0.95} mg/mL and {1.29} mg/mL.

COMMENTS

1. The test drug product contains the same active and inactive ingredients in the same strength and dosage form as the currently approved listed reference products.

2. Waiver of in vivo bioequivalence study requirements may be granted based on 21 CFR 320.22(b)(1).

RECOMMENDATION

The Division of Bioequivalence agrees that the information submitted by Bedford Laboratories, demonstrates that Milrinone Injection, 1 mg/mL; 10 mL and 20 mL Vials, falls under 21 CFR 320.22 (b)(1). The waiver of in vivo bioequivalence study for the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test injectable formulation 1 mg/mL to be bioequivalent to Sanofi-Winthrop's Primacor® Injectable, 1 mg/mL.

/S/

Zakaria Z. Wahba, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALLED BDAVIT BZW 8/10/99
FT INITIALLED BDAVIT /S/ Date: 8/10/99

Concur: /S/ Date: 8/23/99
Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence

Milrinone Lactate Injection
1 mg/mL; 50 mL/50 mL Vial
ANDA #75-660
Reviewer: Z.Z. Wahba

Bedford Laboratories
Bedford, OH
Submission Date:
September 12, 2000

STUDY AMENDMENT

BACKGROUND

- On 06/29/99, the firm has requested a waiver of bioequivalence study requirements for its drug product Milrinone Lactate Injection, 1 mg/mL; 10 mL and 20 mL Vials. The DBE reviewed the submission and the waiver request was granted for the firm's Milrinone Lactate Injection, 1 mg/mL; 10 mL and 20 mL Vials (DBE review date: 08/23/99).

- In the present submission, the firm submitted an amendment to provide for an additional 50 mL vial size to its Milrinone Lactate Injection, 1 mg/mL; 10 mL and 20 mL Vials.

- The reference listed drug is Primacor® Injection 1 mg/mL; 10 mL, 20 mL and 50 mL Vials, manufactured by Sanofi-Winthrop.

- Milrinone Lactate Injection is indicated for the short-term intravenous therapy of congestive heart failure.

FORMULATION

The formulations of Bedford's Milrinone Lactate Injection and Sanofi Winthrop's Primacor® Injection, 1 mg/mL are presented below:

Ingredient	Bedford (Amount per mL)	Sanofi Winthrop (Amount per mL)
Milrinone	1.0 mg	1.0 mg
Dextrose Anhydrous, USP	47 mg	47 mg
*Lactic Acid, USP	Adjust pH	Adjust pH
Sodium Hydroxide, NF	Adjust pH	Adjust pH
Water for Injection	qs to 1.0 mL	Qs to 1.0 mL

* The total concentration of lactic acid can vary between {0.95} mg/mL and {1.29} mg/mL.

COMMENTS

1. The test drug product contains the same active and inactive ingredients in the same strength and dosage form as the currently approved listed reference product.

2. Waiver of in vivo bioequivalence study requirements may be granted based on 21 CFR 320.22(b)(1).

RECOMMENDATION

The Division of Bioequivalence agrees that the information submitted by Bedford Laboratories, demonstrates that Milrinone Lactate Injection, 1 mg/mL; 50 mg/50 mL Vial, falls under 21 CFR 320.22 (b)(1). The waiver of in vivo bioequivalence study for the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test injectable formulation 1 mg/mL to be bioequivalent to Sanofi-Winthrop's Primacor® Injectable, 1 mg/mL.

/S/

Zakaria Z. Wahba, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALLED MMAKARY mmm
FT INITIALLED MMAKARY /S/ Date: 5/1/02

Concur /S/ Date: 5/1/02

Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence