CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40334

BIOEQUIVALENCY REVIEW(S)

OFFICE OF GENERIC DRUGS

DIVISION OF BIOEQUIVALENCE

ANDA # 40-334 **SPONSOR:** Gensia Sicor Pharmaceutical, Inc.

DRUG & DOSAGE FORM: Fluorouracil Injection

STRENGTH: 50 mg/mL, 50 and 100 mL Pharmacy Bulk Package Vials

TYPE OF STUDY: **SD** **SDF** **MULT** **OTHER** Waiver Request

STUDY SITE: NA **CLINICAL:** NA **ANALYTICAL:** NA

STUDY SUMMARY:

The waiver of *in vivo* bioequivalence study is granted per 21 CFR § 320.22(b)(1) of Bioavailability/Bioequivalence Regulations.

PRIMARY REVIEWER: Chandra S. Chaurasia, Ph.D. **BRANCH:** I

INITIAL: /S/ **DATE:** 11/3/98

TEAM LEADER: Yih Chain Huang, Ph.D. **BRANCH:** I

INITIAL: [signature] **DATE:** 11/3/98

DIRECTOR, DIVISION OF BIOEQUIVALENCE: Dale P. Conner, Pharm.D.

INITIAL: [signature] **DATE:** 11/4/98

DIRECTOR, OFFICE OF GENERIC DRUGS:

INITIAL: _____ **DATE:** _____

Fluorouracil Injection, USP
50 mg/mL; in 50 and 100 mL
Pharmacy Bulk Package Vials
ANDA # 40-334
Reviewer: Chandra S. Chaurasia

Gensia Sicor Pharmaceutical, Inc
Irvine, CA
Submission Date:
August 31, 1998

Review of a Waiver Request

BACKGROUND

1. The firm has requested a waiver of *in vivo* bioequivalence study requirements for its drug product, Fluorouracil Injection, USP, 50 mg/mL in 50 and 100 mL Pharmacy Bulk Package Vials. The reference listed drug (RLD) is Adrucil® (Fluorouracil Injection, USP)50 mg/mL in 50 and 100 mL Pharmacy Bulk Package Vials, manufactured by Pharmacia and Upjohn's (NDA #81-225, approved August 28, 1991)

2. The drug is indicated for the palliative management of carcinoma of the colon, rectum, breast, stomach and pancreas.

FORMULATION COMPARISON

Components and composition of the test and the reference products are as follows:

Comparison of Formulations		
Ingredient	Test Product (mg/mL)	RLD (mg/mL)
Fluorouracil, USP	50	50
Sodium hydroxide, NF	to adjust pH	to adjust pH
Hydrochloric acid, NF	N/A*	to adjust pH*
Water for Injection	qs to 1 mL	qs to 1 mL

*Gensia Sicor does not utilize Hydrochloric acid to adjust pH of its test product, where as Pharmacia Upjohn uses Hydrochloric acid only if necessary to adjust pH of the RLD.

COMMENTS

1. The drug is classified "AP" in the list of the "Approved Drug Products with Therapeutic Equivalence Evaluation".

2. The test drug product contains the same active and inactive ingredients in the same concentrations as the currently approved listed reference product and is intended solely for administration by injection.

3. The waiver of *in vivo* bioequivalence study requirements may be granted based on 21 CFR § 320.22(b)(1) of the Bioavailability/Bioequivalence Regulations.

RECOMMENDATION

The Division of Bioequivalence agrees that the information submitted by Gensia Sicor Pharmaceuticals, Inc. demonstrates that its Fluorouracil Injection, USP, 50 mg/mL in 50 and 100 mL Pharmacy Bulk Package Vials falls under 21 CFR § 320.22(b)(1) of Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study for Fluorouracil Injection, USP 50 mg/mL in 50 and 100 mL Pharmacy Bulk Package Vials of the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems Gensia Sicor's Fluorouracil Injection, USP 50 mg/mL in 50 and 100 mL Pharmacy Bulk Package Vials bioequivalent to the reference listed product, Pharmacia and Upjohn's Adrucil® 50 mg/mL, 50 and 100 mL Pharmacy Bulk Package Vials.

/S/
Chandra S. Chaurasia
Division of Bioequivalence
Review Branch I

RD INITIALLED YHUANG
FT INITIALLED YHUANG /S/ Date: 11/3/98

Concur /S/ Date: 11/4/98

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

BIOEQUIVALENCY COMMENTS

ANDA: #40-334 APPLICANT: Gensia Sicor Pharmaceutical, Inc

DRUG PRODUCT: Fluorouracil Injection, USP 50 mg/mL; 50 and 100 mL
Pharmacy Bulk Package Vials

The Division of Bioequivalence has completed its review of your application 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