CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-297

Bioequivalence Review(s)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:75297 APPLICANT: Zenith Goldline Pharmaceuticals

DRUG PRODUCT: Paclitaxel Injection, 6 mg/mL
5 mL and 25 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,

Dale P. Conner

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

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-297 APPLICANT: Zenith Goldline Pharmaceuticals

DRUG PRODUCT: Paclitaxel Injection 6 mg/mL [100 mg/16.7 mL]

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,

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

Paclitaxel Injection, 6 mg/mL
16.7 mL
ANDA #75-297
Reviewer: Jahnavi S. Kharidia
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Zenith Goldline Pharmaceuticals
Northvale, NJ 07647
Submission Date:
August 13, 1999

Review of an Amendment

Objective:

The firm has a pending Abbreviated New Drug Application for its paclitaxel injection 6 mg/mL [5 mL and 25 mL Vials]. The firm now intends to market a 100 mg vial size [6 mg/mL; 16.7 mL vial] and is requesting a waiver of bioequivalence study requirements for its product. The RLD is Taxol® Injection 6 mg/mL [16.7 mL vial] manufactured by Bristol-Myers Squibb.

Formulation: (Not to be released under FOI)

The test and reference formulations are compared in Table 1.

Table 1. Test and Reference Formulations

Ingredient	Test Product	Taxol®
Paclitaxel	6 mg/mL	6 mg/mL
Polyoxyl		
Dehydrated Alcohol		
Citric Acid		

Comments:

1. The Division of Bioequivalence completed the review of Zenith's earlier application [Paclitaxel Injection 6 mg/mL; 5 mL vial and 25 mL vial]. There were no outstanding bio issues [V:\FIRMSNZ\ZENITH\LTRS&REV\75297W.D97, Review Date: April 7, 1998].

2. The test product contains the same active ingredient in the same concentration and dosage form as the reference product.

3. The proposed product is acceptable under 21 CFR 314.94(a)(9)(iii), which states that an applicant may seek the approval of a drug product that differs from the RLD in preservatives, buffers, or anti-oxidants provided that the applicant identifies and characterizes the differences and provides information demonstrating that the

differences do not affect the safety of the proposed drug product. The proposed product is bioequivalent to the RLD under 21 CFR 320.24(b)(6).

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Zenith Goldline Pharmaceuticals, demonstrates that Paclitaxel Injection, 6 mg/mL [16.7 mL vial] falls under 21 CFR 320.24(b)(6) and 21 CFR 314.94(a)(9) of the Bioavailability/Bioequivalence Regulations. From the bioequivalence point of view, the Division of Bioequivalence deems the Zenith Goldline's Paclitaxel Injection, 6 mg/mL [16.7 mL vial] to be bioequivalent to Taxol® Injection, 6 mg/mL [16.7 mL] manufactured by Bristol-Myers Squibb.

Jahnavi S. Kharidia
Jahnavi S. Kharidia, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALED BDAVIT BMS 9/13/99
FT INITIALED BDAVIT Barbara M Davit Date 9/13/99

Concur: Dale P. Conner Date 9/17/99
Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence

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BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:75297 APPLICANT: Zenith Goldline Pharmaceuticals

DRUG PRODUCT: Paclitaxel Injection, 6 mg/mL
5 mL and 25 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,

Dale P. Conner

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

Paclitaxel Injection, 6 mg/mL
5 mL and 25 mL Vials
ANDA #75-297
Reviewer: Jahnavi S. Kharidia
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Zenith Goldline Pharmaceuticals
Northvale, NJ 07647
Submission Date:
December 30, 1997

Review of a Waiver Request

Objective:

The firm has requested a waiver of bioequivalence study requirements for its product Paclitaxel Injection, 6 mg/mL; 5 mL and 25 mL Vials. Innovator product is Taxol® Injection 6 mg/mL, manufactured by Bristol-Myers Squibb, which is available in 30 mg (5 mL) and 100 mg (16.7 mL) single-dose vials.

The firm is requesting a waiver for 150 mg (25 mL) single dose vial which is different from that of the reference listed drug. To support firm's 150 mg (25 mL) single dose vial, the firm is referring to an approved ANDA Suitability Petition (Docket No. 97P-0058/CP1-approved June 10, 1997) for a new strength of Paclitaxel Injection;150 mg/25 mL submitted by Fujisawa (Please see Attachment A).

Formulation: (Not to be released under FOI)

The test and reference formulations are compared in Table 1.

Table 1. Test and Reference Formulations

Ingredient	Test Product	Taxol®
Paclitaxel	6 mg/mL	6 mg/mL
Polyoxyl 35 castor oil		
Dehydrated Alcohol		
Citric Acid		-

Comments:

1. The test and reference products are an injectable solution in non-aqueous vehicle to be used for IV infusion after dilution in IV fluids.

2. Zenith Goldline and Baker Norton Pharmaceuticals are subsidiaries of the IVAX corporation. The Baker Norton received a tentative approval for its paclitaxel formulation (NDA 20-826). The formulation of paclitaxel injection is the same for both Zenith Goldline Pharmaceuticals and Baker Norton Pharmaceuticals.

3. Waiver of *in vivo* bioequivalence study requirements may be granted based on 21 CFR 320.24(b)(6).

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Zenith Goldline Pharmaceuticals, demonstrates that Paclitaxel Injection, 6 mg/mL; 5 mL and 25 mL Vials falls under 21 CFR 320.24 (b)(6). 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 Zenith Goldline's Paclitaxel Injection, 6 mg/mL to be bioequivalent to Taxol® Injection, 6 mg/mL manufactured by Bristol-Myers Squibb.

Jahnavi S. Kharidia
Jahnavi S. Kharidia, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALED MMAKARY
FT INITIALED MMAKARY Moheb H. Makary Date _____
Moheb H. Makary, Ph.D.
Acting Team Leader, Branch III
Division of Bioequivalence

Concur: Dale P. Conner Date 4/7/98
Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence