CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75184

BIOEQUIVALENCY REVIEW(S)

DW

Paclitaxel Injection
30 mg/5 mL, 150 mg/25 mL & 300 mg/50 mL
ANDA #**75-184**
Reviewer: Z.Z. Wahba
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Baker Norton
(Immunex)
Miami, FL
Submission Date:
June 15, 1999

REVIEW OF WAIVER REQUESTS

BACKGROUND

1. Immunex submitted a waiver request for paclitaxel injection, 30 mg/5 mL on July 22, 1997. Immunex transferred the ownership of this ANDA to Baker Norton. The request for the waiver was granted (review dated 12/31/97, reviewed by M. Park, Ph.D.).

2. Later, the firm reformulated its product (paclitaxel injection, 30 mg/5 mL) and requested a waiver for the reformulated product. The firm replaced with citric acid. Dr. Mary Fanning had previously determined that the presence of citric acid in similar test formulations does not pose a safety concern. The formulation was found acceptable by the Division of Bioequivalence (review dated 04/27/99, reviewed by K. Dhariwal, Ph.D.).

3. The changes in formulation are acceptable.

4. In this submission, the firm is providing additional information in support of waiver requests for two additional dose formulations.

FORMULATION COMPSITION

Baker Norton's formulations for its drug products paclitaxel injection, 30 mg/5 mL, 150 mg/24 mL and 300 mg/50 mL, are included in this report (Attachment #1 and #2).

RECOMMENDATION

The Division of Bioequivalence agrees that the information submitted by Baker Norton demonstrates that its paclitaxel injection, 30 mg/5 mL, 150 mg/24 mL and 300 mg/50 mL fall under 21 CFR 314.94 (a)(9)(iii) and 320.24(b)(6) of Bioavailability/ Bioequivalence Regulations. From the bioequivalence point of view, the Division of Bioequivalence deems the test formulation

to be bioequivalent to Taxol® injection, 30 mg/5 mL, 150 mg/24 mL and 300 mg/50 mL marketed by Bristol Myers Squibb.

/S/

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

RD INITIALED B.DAVIT BMD 7/9/99
FT INITIALED B.DAVIT /S/ Date 7/9/99

Concur: /S/ Date 7/12/99
Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-184 APPLICANT: Baker Norton

DRUG PRODUCT: Paclitaxel Injection, 30 mg/5 Ml, 150 mg/25 mL and 300 mg/50 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,

/S/

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

Paclitaxel Injection
30 mg/ 5 mL
ANDA #75-184
Reviewer: Kuldeep R. Dhariwal
File name: 75184W.499

Immunex
(Baker Norton)
Seattle, WA
Submission Date:
April 2, 1999

Review of a Waiver Request

Immunex submitted waiver request for paclitaxel injection, 30 mg/ 5 mL on July 22, 1997. Immunex transferred the ownership of this ANDA to Baker Norton. Moo Park reviewed the submission and the waiver was granted on December 31, 1997. The Division of Chemistry communicated deficiencies to the firm on March 6, 1998. This amendment is response to Chemistry deficiencies. The firm has reformulated its product and therefore the waiver request is reviewed again by DBE.

Chemistry deficiency #7: Please demonstrate that the [redacted] acts as a buffer (exception excipient) in your non-aqueous formulation of paclitaxel injection. Alternatively, reformulate the paclitaxel product without the glycine hydrochloride.

Firm's response: Baker Norton recognizes that [redacted] is not a compendial product, and we understand the Agency's concern. We have therefore reformulated the paclitaxel product with citric acid, a USP grade material commonly used in the industry. Citric acid is known to be an acidifying/buffering agent and is included on the list of substances generally recognized as safe (GRAS). It is included in the FDA's IIG for human use in injections.

Reviewer's comments: 1. Citric acid, which does not appear in the Taxol® formulation (RLD), is acceptable since it is an exception excipient for parenterals. Dr. Mary Fanning has previously examined the issue of the presence of citric acid in similar test formulations and determined that this excipient does not pose a safety concern.

2. **NOT TO BE RELEASED UNDER FOI:** The Agency has accepted citric acid in several generic paclitaxel injections.

Chemistry deficiency #8: [redacted] in the formulation of Paclitaxel injection concentrate should conform with Polyoxyl 35 Castor oil NF monograph specifications.

Firm's response: As per our response to deficiency #7 above, this component is being replaced with which conforms to the Polyoxyl 35, Castor Oil NF monograph specifications.

Reviewer's comments: Acceptable.

FORMULATION: **Not to be released under FOI**

Ingredient	Test	Reference
	mg per mL	
Paclitaxel	6	6
Polyoxyl 35, Castor Oil, NF	527	527
Citric Acid, anhydrous, USP	2	--
Dehydrated Alcohol, USP	49.7% (v/v)	49.7% (v/v)

Comments:

Changes in formulation are acceptable. Waiver can be granted.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Baker Norton demonstrates that its paclitaxel injection, 6 mg/mL falls under 21 CFR 314.94 (a)(9)(iii) and 320.24(b)(6) of Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study requirements for paclitaxel injection, 6 mg/mL of the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test formulation to be bioequivalent to Taxol® injection, 6 mg/mL marketed by Bristol Myers Squibb.

/S/

Kuldeep R. Dhariwal, Ph.D.
Review Branch II
Division of Bioequivalence

RD INITIALED S.NERURKAR
FT INITIALED S.NERURKAR /S/ Date 4/23/1999

Concur: /S/ Date 4/27/99
Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-184 APPLICANT: Baker Norton

DRUG PRODUCT: Paclitaxel Injection, 30 mg/5 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,

/S/

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