CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-906

Bioequivalence Review(s)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-906 APPLICANT: American Pharmaceutical Partners (APP)

DRUG PRODUCT: progesterone Injection,
50 mg/mL of 10 mL fill in a 10 mL multi-dose vial,

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

Progesterone Injection

50 mg/mL
(10 mL fill in a 10 mL Multi-dose Vial)
ANDA #75-906
Reviewer: Lin-Whei Chuang
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American Pharmaceutical Partners, Inc. (APP)

Submission Date:
June 16, 2000

Review of a Expedited Review Request and a Waiver Request

Background:
Progesterone injection is a sterile solution of progesterone in a suitable vegetable oil available for intramuscular use.

Reference Listed Drug (RLD):
The basis for this ANDA is Progesterone Injection in Sesame Oil manufactured by Steris Laboratories, Inc. (NDA #17362 approved on 1/1/82). No generic progesterone injections are currently available in the market.

Additional RLD:
Progesterone Injection of Lilly (NDA #09238 approved on 1/1/82) is also listed in current *Orange Book* as one of the two RLDs.

Expedited Review Request:
The firm states that there is a market shortage of this drug because: a) Eli Lilly has not manufactured the product for many years; and b) Steris has been placed under a consent decree since 10/16/98 by FDA due to cGMP deficiencies at its manufacturing facilities. Therefore an expedited review is being requested.

Waiver Request:
The firm requests a waiver of the *in-vivo* bioequivalence requirements for its progesterone injection, 50 mg/mL, 10 mL fill in a 10 mL multi-dose vial, based on 21 CFR 320.22(b)(1).

Comparative Formulations:

Ingredients	Test Drug (APP)	RLD (Steris)*
	mg/mL	
Progesterone	50	50
Benzyl Alcohol	100	100
Sesame Oil	q.s.	q.s.

* Source: COMIS and submission by the firm.

Comments:

1. The test drug, progesterone injection, 50 mg/mL, 10 mL fill in a 10 mL multi-dose vial, meets the criteria for waiver of the in-vivo bioequivalence study requirements set forth in 21 CFR 320.22(b)(1):

   a. The test drug product is a parenteral solution solely for administration by injection.

   b. It contains the same active and inactive ingredients in the same concentration as Progesterone Injection manufactured by Steris Laboratories, Inc. approved through NDA #17362.

2. The waiver request for the firm's progesterone injection, 50 mg/mL, 10 mL fill in a 10 mL multi-dose vial, is granted per 21 CFR Section 320.22(b)(1).

3. Regarding the firm's request of an expedited review, the Chemistry Division should be informed that Steris would be distributing progesterone injection by the end of 8/00 (per communication with Office of Compliance through D. Hare).

4. The Office of Compliance has been notified of statement by APP that Eli Lilly has not manufactured the product for many years and, if confirmed, the Eli Lilly product should be moved to the Discontinued Section of the *Orange Book*.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by American Pharmaceutical Partners, Inc. demonstrates that its progesterone Injection, 50 mg/mL of 10 mL fill in a 10 mL multi-dose vial, falls under 21 CFR 320.22 (b)(1). Therefore, the waiver of *in vivo* bioequivalence study requirements for its progesterone, 50 mg/mL of 10 mL fill in a 10 mL multi-dose vial, is granted. The test product is deemed bioequivalent to Progesterone Injection in Sesame Oil manufactured by Steris Laboratories, Inc..

Lin-Whei Chuang 9/14/00

Lin-Whei Chuang
Division of Bioequivalence
Review Branch I

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Concur Date: 9/28/00
Dale Conner, Pharm. D.
Director, Division of Bioequivalence

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