CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-906

CORRESPONDENCE

AMERICAN PHARMACEUTICAL PARTNERS, INC.

April 20, 2001

ARCHIVAL

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

N/AM

ORIG AMENDMENT

Re: ANDA 75-906
Progesterone Injection, USP
50 mg/mL
10 mL fill in a 10 mL multidose vial
Product Code 260110
Manufacturing Site: Melrose Park, IL

FAX AMENDMENT

Dear Mr. Buehler:

Reference is made to our June 16, 2000 submission of an Abbreviated New Drug Application (ANDA) for Progesterone Injection, USP ANDA # 75-906.

Further reference is a made to a telephone conversation on April 12, 2001 between Frank O. Holcombe, Jr., Ph.D., FDA and Michael Lisjak, APP. In this conversation, Dr. Holcolme requested that American Pharmaceutical Partners, Inc. perform a one-time analysis of the Identification test as described in USP 24 for Progesterone Injection, USP.

The infrared absorption spectra for Progesterone Injection, USP conducted in accordance with USP 24 is provided in **Attachment 1**. The infrared absoption of a dispersion of the residue obtained after extraction exhibits maxima only at the same wavelengths as that of a similar preparation of USP Progesterone RS. Thus the finished product, Progesterone Injection, USP (Lot R100-001 used for the exhibit batch), conforms to the USP identification test.

Furthermore, in compliance with 21 CFR 314.94(d)(5), a true and complete copy (the Field Copy) of this Fax Amendment is being provided to Mr. Raymond Mlecko, District Director, Chicago District Office, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, HFR-MW100, Chicago, IL 60

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www.appdrugs.com

Should you have any questions or require additional information concerning this amendment, please do not hesitate to contact the undersigned at **(708) 547-2365** or Dale Carlson, Associate Director, Regulatory Affairs at **(708) 547-2373**.

Sincerely,

Michael Lisjak
Senior Regulatory Scientist

AMERICAN PHARMACEUTICAL PARTNERS, INC.

April 19, 2001

ARCHIVAL

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

N I KM

ORIG AMENDMENT

Re: ANDA 75-906
Progesterone Injection, USP
50 mg/mL
10 mL fill in a 10 mL multidose vial
Product Code 260110
Manufacturing Site: Melrose Park, IL

FAX AMENDMENT

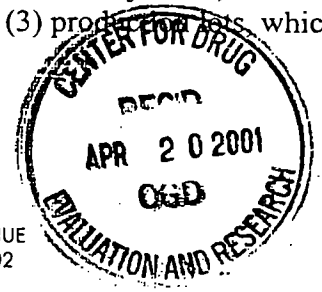
Dear Mr. Buehler:

Reference is made to our June 16, 2000 submission of an Abbreviated New Drug Application (ANDA) for Progesterone Injection, USP ANDA # 75-906.

Further reference is made to an April 19, 2001 telephone call from Michael Lisjak, APP, to Ruby Yu Project Manager, FDA, updating the status of the facility, an outside testing lab that may be used for Preservative Effectiveness Testing (PET) for Progesterone Injection, USP. This laboratory was proposed in American Pharmaceutical Partners, Inc.'s original ANDA 75-906.

On April 16, 2001, APP was informed b y were issued a Form FDA 483 for observations made during an inspection of their testing facility in Kennesaw, GA. In light of this situation, APP contacted Ms. Yu on April 19, 2001 proposing to withdraw from APP's originally submitted ANDA in order to avoid delays in approval of the ANDA. Ms. Yu instructed APP to file a Fax Amendment to the ANDA withdrawing

This correspondence is to formally withdraw as an outside testing lab to conduct PET on Progesterone Injection, USP. Further, APP commits to perform all testing for PET on Progesterone Injection, USP at its Ruby Street, Melrose Park, IL facility for the first three (3) production lots, which is in accordance with APP's proposed stability protocol.



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Furthermore, in compliance with 21 CFR 314.94(d)(5), a true and complete copy (the Field Copy) of this Fax Amendment is being provided to Mr. Raymond Mlecko, District Director, Chicago District Office, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, HFR-MW100, Chicago, IL 60606.

Should you have any questions or require additional information concerning this application, please do not hesitate to contact the undersigned at **(708) 547-2365** or Dale Carlson, Associate Director, Regulatory Affairs at **(708) 547-2373**.

Sincerely,

Michael Lisjak
Senior Regulatory Scientist

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date FEB 21 2001

From Consumer Safety Officer, Investigations & Preapproval Compliance Branch/DMPQ (HFD-324)

Subject Recommendations, **(AMENDED to include ANDA 75-906)**

To Pat Beers-Block, Chief
Review Support Branch, HFD-632

Applicant: American Pharmaceutical Partners, Inc
2045 North Cornell Ave.
Melrose Park, ILL

Mfger: American Pharmaceutical Partners, Inc.
2020 Ruby St.
Melrose Park, ILL
CFN 1450022

Division of Manufacturing and Product Quality (DMPQ) has completed a review of the PAI EIR for the subject ANDAs. The EIR covers an inspection that was conducted at the applicant's manufacturing and testing site from November 1 - December 14, 2000.

DMPQ does not concur with the District's recommendation to withhold approval of these ANDAs. Our nonconcurrence is based on our review of the reponse received from American Pharmaceutical Partners, Inc. dated January 12, 2001. This response appears to adequately address the GMP concerns cited during the November 1, 2000 et al inspection and in CHI-DO's January 11, 2001 warning letter.

A copy of the EIR, Exhibits and APP's responses are attached for your review. If you have questions, please contact me at (301)-827-0065.

Note a review of EES shows that CHI-DO also covered ANDA 75-906 during the November 1, 2000 et al EI. DMPQ's recommendation for ANDA 75-906 is approve.

American Pharmaceutical Partners, Inc.

Randall L. Woods

Randall L. Woods

Attachments sent with original memo include - EIR, Exhibits and APP response

AMERICAN PHARMACEUTICAL PARTNERS, INC.

ARCHIVAL

February 1, 2001

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

FDA DRUG AMENDMENT

Re: ANDA 75-906
Progesterone Injection, USP
50 mg/mL
10 mL fill in a 10 mL multidose vial
Product Code 260110
Manufacturing Site: Melrose Park, IL

AMENDMENT

Dear Mr. Buehler:

Reference is made to our June 16, 2000 submission of an Abbreviated New Drug Application (ANDA) for Progesterone Injection, USP ANDA # 75-906. Reference is also made to the Minor Amendment dated January 24, 2001.

American Pharmaceutical Partners, Inc. (APP) is submitting this Amendment to revise the test method, SOP # , entitled "Test Method for the Determination of Impurities in Progesterone Injection, USP". This test method, provided in the original ANDA on pages 000 00630 – 000 00638, is being amended to include a blank solution to facilitate the identification of possible peaks (C and D). The relative retention times and typical chromatograms for the d peaks C and D, are included in the revised SOP, provided in **Attachment 1**.

Furthermore, in compliance with 21 CFR 314.94(d)(5), a true and complete copy (the Field Copy) of this Amendment is being provided to Mr. Raymond Mlecko, District Director, Chicago District Office, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, HFR-MW100, Chicago, IL 60606.

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AMERICAN PHARMACEUTICAL PARTNERS, INC.

ARCHIVAL

January 24, 2001

ORIG AMENDMENT

N/AM

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

Re: ANDA 75-906
Progesterone Injection, USP
50 mg/mL
10 mL fill in a 10 mL multidose vial
Product Code 260110
Manufacturing Site: Melrose Park, IL

MINOR AMENDMENT
FOR
CHEMISTRY, LABELING AND MICROBILOGY DEFICIENCIES

Dear Mr. Buehler:

Reference is made to our June 16, 2000 submission of an Abbreviated New Drug Application (ANDA) for Progesterone Injection, USP ANDA # 75-906. Reference is also made to the attached January 2, 2001 Deficiency Letter for this application, which is provided immediately after this letter.

American Pharmaceutical Partners, Inc. (APP) is submitting this Amendment in response to each of the comments made in the deficiency letter dated January 2, 2001. For ease of review, each of the reviewer's observation is provided in bold, followed by APP's response. Final Printed Labeling (FPL) is included in this response along with a separate binder containing twelve (12) copies of the FPL.

Furthermore, in compliance with 21 CFR 314.94(d)(5), a true and complete copy (the Field Copy) of this Major Amendment is being provided to Mr. Raymond Mlecko, District Director, Chicago District Office, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, HFR-MW100, Chicago, IL 60606.

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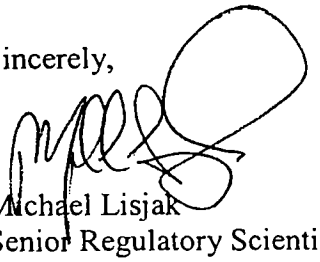
1/31/01

Should you have any questions or require additional information concerning this application, please do not hesitate to contact the undersigned at **(708) 547-2365** or Mitchall Clark, Vice President, Regulatory Affairs at **(708) 547-3618**.

Sincerely,



Michael Lisjak
Senior Regulatory Scientist

AMERICAN PHARMACEUTICAL PARTNERS, INC.

ARCHIVAL

June 16, 2000

EXPEDITED REVIEW REQUESTED

Gary Buehler, Acting Director
Office of Generic Drugs
Metro Park North II, HFD-600, Room 150
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855-2773

This Submission Contains Microbiological & Sterility Assurance Information

Re: Progesterone Injection, USP 50 mg/mL
10 mL fill in a 10 mL multidose vial
(Code 260110)
Manufacturing Site: Melrose Park, IL
Number of Volumes: 4 Volumes

ORIGINAL ANDA

Dear Mr. Buehler:

This Abbreviated New Drug Application is submitted in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355) to seek marketing clearance for Progesterone Injection, USP. The referenced listed drug is Progesterone Injection, USP manufactured by Steris Laboratories, Inc.

American Pharmaceutical Partners, Inc., would like to request an expedited review of this ANDA based on the following:

> The Orange Book lists two other approved manufacturers of Progesterone Injection, USP; Steris and Eli Lilly. Eli Lilly has not manufactured the product for many years which until recently left only Steris as the supplier of this drug product. However, on October 16, 1998, Steris was placed under a consent decree by the FDA following an inspection which found significant cGMP deficiencies at its manufacturing facility. Since this time, Steris has not been able to manufacture the product causing a market shortage of this important drug.

American Pharmaceutical Partners, Inc., will manufacture this product in manufacturing facilities located at 2020 Ruby Street, Melrose Park, IL. This application contains all the information required describing the chemistry, manufacturing and control of Progesterone Injection, USP 50 mg/mL (10 mL fill in a 10 mL multidose vial). This application contains a request for the waiver of *in vivo* bioequivalence studies. **This application also contains microbiology and sterility assurance information, which is**

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provided in Section XXII. For the reviewer's convenience, a copy of the product labeling (package insert) is also provided in Section XXII.

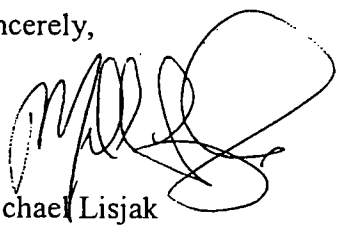
The application has been formatted according to the information in the Guidance for Industry: Organization of an ANDA, dated February 1999. An executive summary explaining the organization of this application is included after the cover letter. The application consists of 4 volumes.

American Pharmaceutical Partners, Inc., is filing an archival copy (blue folder) of the ANDA that contains all the information required in the ANDA and a technical review copy (red folder) which contains all of the information in the archival copy with the exception of the bioequivalence section (Section VI). Three copies of the analytical methods validation section are included in red folders. Four copies of the draft labeling are included in both the archival and the review copies. A separate copy of the bioequivalence section is provided in an orange folder. The bioequivalence section consists of a request for a waiver from the need to conduct a bioequivalence study.

Furthermore, in compliance with 21 CFR 314.94(d)(5), a true and complete copy (the Field Copy) of this abbreviated application is being provided to Mr. Raymond V. Mlecko, District Director, Chicago District, Food and Drug Administration, 300 S. Riverside Plaza, Suite 550 South, Chicago, Illinois 60606. We certify that the field copy is a true and complete copy of the Abbreviated New Drug Application.

Should you have any questions or require additional information concerning this application, please do not hesitate to contact the undersigned at **(708) 547-2365** or Nancy Bauer, Associate Director, Regulatory Affairs at **(708) 547-2381**.

Sincerely,



Michael Lisjak
Regulatory Scientist