CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

80-911

Generic Name: Testosterone Pellets, 75mg

Sponsor: Bartor Pharmacal Company, Inc.

Approval Date: July 13, 1972
## CONTENTS

Reviews / Information Included in this ANDA Review.

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<td>Correspondence</td>
<td>X</td>
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</table>
APPLICATION NUMBER:

80-911

APPROVAL LETTER
Bartor Pharmaceutical Company, Inc.
Attention: Mr. Frank M. Bardani
70 High Street
Rye, New York 10580

Gentlemen:

Reference is made to your abbreviated new drug application dated December 23, 1971, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Testosterone Pellets, 75 mg.

Reference is also made to your communication dated June 12, 1972, enclosing printed labeling.

We have completed the review of this abbreviated new drug application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

The periodic reporting requirements of Section 130.13(b)(4) of the new drug regulations are waived in regard to this application as published in the Federal Register of August 1, 1970.

Any significant change in the conditions outlined in this abbreviated new drug application, requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of section 130.9 of the new drug regulations.

This Administration should be advised of any change in the marketing status of this drug.

The requirement for adequate data to assure the biologic availability is being deferred at the present time. However, our action in approving this application is based upon an understanding that if this requirement is reinstated you will perform the appropriate procedures.
The enclosures summarize the conditions relating to the approval of this application.

Sincerely yours,

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation Project Office
Bureau of Drugs

Enclosures:
Conditions of Approval of a New Drug Application
Records and Reports Requirement

cc:
NYK-DO
Dup
BD-69
BD-67
BD-106
BD-242
BD-100
BD-300
JBacsanyi/JLMeyer/RJWolters
R/D init. by MAClark/JLMeyer/7-7-72
Final typing/rt 7-7-72
Approved

7/11/72
7-10-72
J.Meyer 7/11/72
M.Stele 7/13/72
APPLICATION NUMBER:

80-911

FINAL PRINTED LABELING
TESTOSTERONE PELLETS

DESCRIPTION: Testosterone pellets for subcutaneous implantation: the pellets are cylindrical, 3.2 mm. (1/8 inch) in diameter, and approximately 8 to 9 mm. in length. Each pellet weighs approximately 75 mg., with 75 mg. label claim of testosterone; each pellet is packaged in an individual vial, and is sterile and ready for implantation. Three vials are packaged in one box.

ACTIONS: Testosterone pellets consist of crystalline testosterone. Implanted subcutaneously, the pellets slowly release the hormone for a long-acting androgenic effect.

INDICATIONS: 1. Eunuchoidism and eunuchism; 2. Male climacteric symptoms when these are secondary to testosterone deficiency.

CONTRAINDICATIONS: Contraindicated in persons with known or suspected carcinoma of the prostate and in carcinoma of the male breast.

PRECAUTIONS: Pellet implantation is much less flexible in regard to adjustment of dosage than oral administration of androgens or intramuscular injection of oil solution or aqueous suspensions. Great care is therefore required in estimating the amount to be used.

Prolonged or excessive dosage of androgens may cause retention of sodium and water. Therefore, use cautiously in persons with compromised cardiac reserve or renal disease.

In treating elderly males, avoid stimulation to the point of increasing the nervous, mental, and physical activities beyond the patient's cardiovascular capacity.

If priapism or other signs of excessive sexual stimulation develop, withdraw therapy temporarily.

In the male, prolonged administration or excessive dosage may cause inhibition of testicular function, with resultant oligospermia and decreased ejaculatory volume.

Hypersensitivity and gynecomastia may rarely occur.

PBI may be decreased in patients taking androgens.

In the face of any of the above complications, obviously the effect of such medication should be stopped. The pellets would thus have to be removed in any of these instances. In addition, at times the pellets may slough out. This accident is usually traceable to superficial implantation or to neglect in regard to aseptic precautions.

ADVERSE REACTIONS:
Sodium and water retention
Oligospermia and decreased ejaculatory volume
Priapism
Hypersensitivity and gynecomastia

DOSEAGE AND ADMINISTRATION: The number of testosterone pellets to be implanted depends upon the minimal daily requirement of testosterone propionate determined by a gradual reduction of the amount administered parenterally. The usual ratio is as follows: implant two 75 mg. pellets for each 25 mg. testosterone propionate required weekly. Thus when a patient requires injections of 75 mg. per week, it is usually necessary to implant 450 mg. (6 pellets). With injections of 50 mg. per week, implantation of 300 mg. (4 pellets) may suffice for approximately three months. With lower requirements by injection, correspondingly lower amounts may be implanted. It has been found that approximately one-third of the material is absorbed in the first month, one-fourth in the second month, and one-sixth in the third month. Adequate effect of the pellets ordinarily continues for three to four months, sometimes as long as six months.

HOW SUPPLIED: Pellets of 75 mg. each, one pellet per vial, in box of 3 sterile vials.

BARTOR PHARMACAL CO., INC.
70 High Street, Rye, N.Y. 10580
JUL 13 1972

3 Pellets Sterile

TESTOSTERONE PELLETS N.F.

For subcutaneous implantation

Each pellet contains: 75 mg testosterone

Read accompanying directions carefully.

Caution: Federal law prohibits dispensing without prescription.

Bartor Pharmaceutical Co., Inc.
70 High St., Rye, N.Y. 10580

75 mg brand of testosterone pellets
CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-911

CSO LABELING REVIEW(S)
REVIEW OF ANDA FPL

DATE COMPLETED: 7-3-72

ANDA #: 80-911

F.R. DATE: 8-1-70

CO. NAME: Bartor Pharmacal Co., Inc.
70 High Street
Rye, New York 10580

NAME OF DRUG: Testosterone Pellets, N.F. 75 mg.
(3 vials/box)

DATE OF SUBMISSION: 6-12-72

TYPE OF SUBMISSION: FPL

CLINICAL EVALUATION:

1. Review of Studies: Bioavailability studies are now deferred for this drug.

2. Review of Labeling:

   CONTAINER LABELS: Satisfactory

   PACKAGE INSERT: Satisfactory

CONCLUSION: The FPL for both container and package insert is satisfactory from a medical standpoint.

RECOMMENDATIONS: The firm is to be so notified.

J. Bacsanyi, M.D.

cc:
Dup
BD-69
J. Bacsanyi, M.D./kim/7-5-72
APPLICATION NUMBER:

80-911

CHEMISTRY REVIEW(S)
REVIEW OF ANDA

DATE COMPLETED: March 9, 1972  ANDA #: 80-911

F.R. DATE: August 1, 1970

CO. NAME: Bartor Pharmacal Co., Inc.
70 High Street
Rye, New York 10580

NAME OF DRUG: Trade & Generic: Testosterone Pellets N.F., 75 mg. (3 vials/box)

DATE OF SUBMISSION: February 18, 1972

TYPE OF SUBMISSION: ANDA

CLINICAL EVALUATION:

1. Review of Studies:
   a) Bioavailability studies are now deferred for this drug.
   b) Manufacturing data, ingredients of the preparation etc. are to be reviewed by the chemist.

2. Review of Labeling:

   Container label: (final) Satisfactory, except that the zip code number has not been included. This deficiency can be corrected at the time of the next printing.

   Package insert: (draft) Satisfactory, however, it requires the addition of a "HOW SUPPLIED" section.

CONCLUSION: 1. Package insert (draft) requires addition of a "HOW SUPPLIED" section.
2. The zip code number is to be added to the firm's address on the immediate package container at the time of the next printing.
3. Manufacturing data etc. are to be reviewed by the chemist.

RECOMMENDATIONS: Request FPL with the recommended corrections as listed above.

J. Bacsanyi, M.D.

cc:
Dup
BD-69
JBacsanyi/wlb/3-14-72
REVIEW OF RESUBMISSION

DATE COMPLETED: May 17, 1972

ANDA #: 80-911

F.R. DATE: August 1, 1970

CO. NAME: Bartor Pharmaceutical Co., Inc.
70 High Street
Rye, New York 10580

NAME OF DRUG: Trade & Generic: Testosterone Pellets, N.F. 75 mg.
(3 vials/box)

DATE OF SUBMISSION: April 29, 1972

TYPE OF SUBMISSION: Resubmission

CLINICAL EVALUATION:

1. Review of Studies:
   a) Bioavailability studies are now deferred for this drug.
   b) Manufacturing data will be reviewed by the chemist.

2. Review of Labeling:

   Container label: Not submitted. The applicant firm promises inclusion of the zip code number on the label.

   Package insert: Not submitted. The proposed "HOW SUPPLIED" section is satisfactory.

CONCLUSION: 1. Manufacturing data - are to be reviewed by the chemist.
2. Labeling will be satisfactory if the proposed corrections are carried out.

RECOMMENDATIONS: Request FPL.

cc: Dup
    BD-69
    J.Bacsanyi/wlb/5-18-72

J. Bacsanyi, M.D.
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<td>YES [ ] NO [ ]</td>
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<td>if so, what level:</td>
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<tr>
<td>1. Revised labeling per MO's report.</td>
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<td>2. Certification statement from</td>
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<tr>
<td>3. Submit procedures for components, and clarify analysis of pellets.</td>
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<td>4. Clarify use of NF XII and USP XVIII.</td>
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| Purpose of Supplement | | |
|-----------------------| | |

| Pharmacological Category | How Dispensed | |
|--------------------------|---------------||
| Androgen Preparations    | Rx [X]        | O.T.C. [ ]    |

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<td>NO [ ]</td>
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| Satisfactory Probably or Possibly Effective Indications | |
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| (if in labeling)                                       | |
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| Relabeling of drug in commercial channels required? | YES [ ] | NO [ ] |

| so, what level: | |
|-----------------| |
|                  | |

| Remarks | |
|--------| |
| Request FPL while not official is listed in Remington and Merck Index and has several uses in pharmaceutical preparation taken internally.| |
| labels the ampule in addition to , and testing. | |
| DMF - satisfactory details testing and procedures in the | |

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R. Wolters
Name & Address of Applicant (City & State)
Parke, Davis & Company, Inc.
70 High Street
Pye, New York 10580

Name of Drug
Nonproprietary Name
Testosterone

Purpose of Supplement
FPL

Pharmacological Category
Androgen

New Dispensed
RX [X] O.T.C. [ ]

Dosage Form(s)
Pellets

Potency (ies)
75 mg.

Satisfactory Labeling
Date Due Satisfactory (JBacsanyi)

Satisfactory Components, Composition, Manufacturing and Controls
Date Due Active ingredient and drug dosage form comply with USP specs.

Satisfactory Biologic Availability
Date Due Deferred see memo

Is data on current formulation? YES [ ] NO [ ]

Satisfactory Probably or Possibly Effective Indications
(if in labeling)

Date Data Due

Establishment Inspection
All satisfactory see previous Chem. Rev.

Recalls

If relabeling of drug in commercial channels required? YES [ ] NO [ ]

If so, what level:

Remarks

APPEARS THIS WAY ON ORIGINAL

Conclusions approval

RJ Wolters 7/10/72

Reviewer: Signature: Date:
APPLICATION NUMBER:

80-911

ADMINISTRATIVE DOCUMENTS
NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

TO: Press Relations Staff (CE-300)
FROM: Bureau of Drugs

ATTENTION
Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION
□ ORIGINAL NDA □ ABBREVIATED NDA □ SUPPLEMENT TO NDA

CATEGORY
□ HUMAN □ VETERINARY

TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG
Testosterone

Dosage Form
Pellets

How Dispensed
□ RX □ OTC

ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount not declared on label.)

Testosterone 75 mg.

APPEARS THIS WAY ON ORIGINAL

NAME OF APPLICANT (Include City and State)

Bartor Pharmacal Company, Inc.
Rye, New York 10580

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY
Androgen

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY
R.J. Wolters
DATE

FORM APPROVED BY
J.L. Meyer
DATE

FD FORM 1442 (7/69) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.
MARCH 21, 1972

BRUCE E. BYER

FOOD AND DRUG ADMINISTRATION
NEW YORK DISTRICT - NYK-050

RE: ABBREVIATED NEW DRUG APPLICATION
80-911 TESTOSTERONE PELLETS

THE DESI PROJECT OFFICE IS PRESENTLY CONSIDERING APPROVAL OF THE SUBJECT ABBREVIATED NEW DRUG APPLICATION. THIS PRODUCT IS MANUFACTURED AND PACKAGED BY BARTOR PHARMACEUTICAL CO., 70 HIGH ST., RYE, NEW YORK.

AS YOU ARE AWARE IN THE ANDA THE FIRM CERTIFIES THAT MANUFACTURING, PACKAGING AND TESTING IS DONE IN CONFORMITY WITH GMP (SEE 130.4 (F) OF THE NEW DRUG REGULATIONS REFERENCE ANDAS, PUBLISHED IN THE FEDERAL REGISTER ON APRIL 24, 1970).

SINCE OUR LAST RECORD OF A COMPLETE CONTROL DRUG INSPECTION OF BARTOR PHARMACEUTICAL WAS IN JULY, 1969, WE ARE REQUESTING AN EVALUATION OF THE FIRM'S PRESENT COMPLIANCE STATUS UNDER GMP AND ITS ABILITY TO COMPLY WITH ANDA AND COMPRENDIUM COMMITMENTS. IF AN INSPECTION IS INDICATED, PLEASE INSPECT AND REPORT RESULTS.
IN YOUR REPLY PLEASE INDICATE WHETHER OR NOT THE ANDA CAN BE APPROVED
BASED UPON THE FIRM'S COMPLIANCE WITH GMP. A RECOMMENDATION TO
WITHHOLD APPROVAL SHOULD BE BASED UPON CRITICAL OR SIGNIFICANT
DEVIATIONS FROM GMP WHICH SHOULD BE LISTED.

I WOULD APPRECIATE A REPLY BY TWX FOLLOWED BY EIR OR MEMO.

PROBLEM CATEGORY: 9

ESTIMATED TIME: 24 HOURS OR AS NEEDED

REPLY REQUESTED BY: APRIL 24, 1972

CHARGE TO: BD-100

CONTACT OFFICER: JACK MEYER, PHONE 301-443-3630

ENDORSE REPORT TO: BD-105

CLEARANCE OFFICER: BRUCE E. BYER

OFFICE OF SCIENTIFIC EVALUATION

PHONE 301-443-4320

CC:
NYK-D50
NYK-F1
BD-100
BD-105
BD-22
BD-69
CA-224
"0-10
"0-69 C/O JACK MEYER
BD-105 C/O BEBYER/MW/3/21/72
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[Docket No. FDC-D-168; NDA No. 3-186 et al.]

CERTAIN ANDROGEN PREPARATIONS

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has evaluated reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following drugs:

1. Perandren Propionate, for Intramuscular Injection, Vials, containing 25 milligrams, 50 milligrams, or 100 milligrams testosterone propionate per milliliter; Ciba Pharmaceutical Co., 550 Merris Avenue, Summit, N.J. 07901 (NDA 7629).

2. Perandren Phenylacetate Intramuscular Repository, Vials, containing 50 milligrams testosterone phenylacetate per milliliter and 1 percent procaine hydrochloride; Ciba Pharmaceutical Company (NDA 8399).

3. Creon Pellets for Subcutaneous Implantation, containing 75 milligrams testosterone per pellet; Schering Corp., 60 Orange Street, Bloomfield, N.J. 07003 (NDA 3613).

4. Halotestin Tablets, contain 10 milligrams, 5 milligrams; or 2 milligrams fluoxymesterone per tablet; The Upjohn Co., 7171 Portage Road, Kalamazoo, Mich. 49002 (NDA 10-511).

5. Ditandren Tablets containing 2 milligrams or 5 milligrams fluoxymesterone per tablet; Ciba Pharmaceutical Co. (NDA 11-124).

6. Ora-Testyl Tablets, containing 2 milligrams or 5 milligrams fluoxymesterone per tablet; E. R. Squibb and Sons Inc., Georges Road, New Brunswick, N.J. 08903 (NDA 11-530).

7. Detatestyl, Sterile Solution, for Intramuscular Injection, containing 250 milligrams testosterone enanthate per milliliter, and in disposable syringes containing 250 mg. testosterone enanthate per syringe; E. R. Squibb and Sons Inc. (NDA 9165).
3. Testosterone propionate is effective for use in men with testicular atrophy in patients with hypogonadism, and for hypogonadism, suppression of adrenocorticosteroids, and for the treatment of anemia associated with hypogonadism, amenorrhea, and anemia associated with surgical or other conditions.

4. Methyltestosterone: Methyltestosterone preparations are in tablet form for oral or by mouth administration.

B. Form of drug. Methyltestosterone is available in tablets, capsules, and solution for intramuscular or subcutaneous injection.

C. Labeling conditions. The labeling of the drug for use in the treatment of women is as follows:

In the female:

1. Methyltestosterone: Methyltestosterone is effective for the treatment of amenorrhea, and for the treatment of amenorrhea associated with hypogonadism, amenorrhea, and anemia associated with surgical or other conditions.

D. Marketing status. Marketing of the drug may continue under the conditions described in items VIII and IX of this announcement except those claims referenced in item IX below may continue to be included in the labeling for the periods stated.

II. Testosterone propionate: for intramuscular injection—A. Effective classification. The Food and Drug Administration has considered the Academy reports, as well as other available evidence, and concludes that:

1. This drug is effective for the treatment of patients with hypogonadism, amenorrhea, and for the treatment of anemia associated with hypogonadism, amenorrhea, and anemia associated with surgical or other conditions.

2. This drug is probably effective for postmenopausal osteoporosis.

3. This drug is probably effective for improvement in the treatment of patients with hypogonadism, amenorrhea, and for the treatment of anemia associated with hypogonadism, amenorrhea, and anemia associated with surgical or other conditions.

4. Testosterone propionate lacks substantial evidence of effectiveness for treatment of patients with hypogonadism, suppression of adrenocorticosteroids, and for the treatment of anemia associated with hypogonadism, amenorrhea, and anemia associated with surgical or other conditions.
C. Labeling conditions. 1. The label bears the statement "Caution: Federal law prohibits dispensing without prescription."

2. The drug is labeled to comply with all requirements of the Act and regulations. Its labeling bears adequate information for safe and effective use of the drug and is in accord with the guidelines for uniform labeling published in the Federal Register of February 6, 1970. The "indications" section of the labeling is as follows:

**Indications**

In the male:

1. Postmenopausal osteoporosis. Androgens are without value in primary therapy but may be of value as adjunctive therapy. Equal or greater consideration should be given to diet, calcium balance, physiologic, and corrective health-promoting measures.

2. Postmenopausal osteoporosis. Androgens may be without value in primary therapy, but may be of value as adjunctive therapy. Equal or greater consideration should be given to diet, calcium balance, physiologic, and corrective health-promoting measures.

3. Radiation of adenogen-reactive, adenogen, inoperable mammary cancer in women who are more than 1, but less than 5 years postmenopausal or who have been proven to have hormone-dependent tumors, as shown by previous beneficial responses to castration.

**Marketing status.** Marketing of the drug may continue under the conditions described in Items VIII and IX of this announcement except those claims referenced in Item VII below may continue to be included in the labeling for the periods stated.

**Postmenopausal osteoporosis.** Androgens may be without value in primary therapy, but may be of value as adjunctive therapy. Equal or greater consideration should be given to diet, calcium balance, physiologic, and corrective health-promoting measures.

**V. Pergonal androgynates for intramuscular therapy—A. Effectiveness classification.** The Food and Drug Administration has considered the Academy report, as well as other available evidence, and concludes that:

1. This drug is effective for contraceptive purposes when these are secondary to testosterone deficiency and of mammary cancer.

2. This drug is probably effective for osteoporosis (postmenopausal).

3. This drug is possibly effective for anabolic effect in fracture after surgery and injury in convalescence to oppose catabolic action of cortisone.

4. Testosterone phenylacetate lacks substantial evidence of effectiveness for prophylaxis of hypogonadism, menorrhagia, and metrorrhagia.

**VII. Form of drug.** Testosterone phenylacetate preparations are suitable for intramuscular administration.

**Labeling conditions.** 1. The label bears the statement "Caution: Federal law prohibits dispensing without prescription."
and submit to the FDA and the Advisory Committee on元宝 Administrative data to provide substantial evidence of effectiveness. To be acceptable for consideration in support of the effectiveness of a drug, such data must be well-organized, include data from adequate and well-controlled clinical investigations (identified for ready review) as described in §130.12(a)(9) of the regulations published in the Federal Register of May 8, 1970 (35 FR. 7559). Carefully conducted and documented clinical studies obtained under controlled or partially controlled situations are not acceptable as a sole basis for the establishment of the effectiveness of a drug. Such studies may be considered on their merits for correlative support of efficacy and evidence of safety.

VIII. Previously approved applications. 1. Each holder of a "previously approved" new drug application (i.e., an application which became effective on the basis of safety prior to Oct. 10, 1962) for such drug is requested to seek approval from the Commissioner of Food and Drugs, Washington, D.C., 20204, by submitting supplemental information:

a. Adequate data to assure the biologic availability of the drug in the formulation which is marketed. For preparations containing sustained action, timed release, or other delayed or prolonged effect, the data should show that the drug is available at a rate of release which is safe and effective. If such data are not included in the application, specific reference to this may be made.

b. Adequate data to assure the biologic availability of the drug in the formulation which is marketed. For preparations containing sustained action, timed release, or other delayed or prolonged effect, the data should show that the drug is available at a rate of release which is safe and effective. If such data are not included in the application, specific reference to this may be made.

c. 60 days for updating information.

3. Marketing of the drug may continue until the supplemental applications submitted in accordance with the provisions of paragraphs 1 and 2 are acted upon, provided the Commissioner of Food and Drugs approves the supplemental applications and the Commissioner of Food and Drugs does not notify the applicant that the further marketing of the drug is not permissible. If the Commissioner of Food and Drugs determines that no further marketing of the drug is permissible, he will notify the applicant in writing and the drug must be removed from the market.

IX. New applications. 1. Any other person who distributes or dispenses a drug which is intended for which the drug is not effective, as described under A above, should submit an appropriately new drug application meeting the conditions specified in §130.40 (1), (2), (3), and (4) of the Federal Register of April 29, 1970 (35 FR. 7554). Such applications should include proposed labeling which is in accord with the labeling conditions described herein and adequate data to assure the biologic availability of the drug in the formulation which is marketed or proposed for marketing.

II. Distribution of any such preparation currently on the market without an approved new drug application may be continued under the conditions specified in §130.40 (1), (2), (3), and (4) of the Federal Register of April 29, 1970 (35 FR. 7554). Such applications should include proposed labeling which is in accord with the labeling conditions described herein and adequate data to assure the biologic availability of the drug in the formulation which is marketed or proposed for marketing.

3. Distribution of any such preparation currently on the market without an approved new drug application may be continued under the conditions specified in §130.40 (1), (2), (3), and (4) of the Federal Register of April 29, 1970 (35 FR. 7554). Such applications should include proposed labeling which is in accord with the labeling conditions described herein and adequate data to assure the biologic availability of the drug in the formulation which is marketed or proposed for marketing.

4. The application submitted under the conditions described in §130.40 (1), (2), (3), and (4) of the Federal Register of April 29, 1970 (35 FR. 7554). Such applications should include proposed labeling which is in accord with the labeling conditions described herein and adequate data to assure the biologic availability of the drug in the formulation which is marketed or proposed for marketing.

5. The application submitted under the conditions described in §130.40 (1), (2), (3), and (4) of the Federal Register of April 29, 1970 (35 FR. 7554). Such applications should include proposed labeling which is in accord with the labeling conditions described herein and adequate data to assure the biologic availability of the drug in the formulation which is marketed or proposed for marketing.

The manufacturer, packer, or distributor of any drug application which is not submitted within the time specified in paragraph 1 or 2 above, is subject to regulatory proceedings.

X. Exception from periodic reporting. The periodic reporting requirements of §§130.35(a) and 130.35(b)(4) are waived in regard to applications approved for these drugs solely for the conditions of use for which the drugs are regarded as effective as described herein. The reporting requirements of §§130.35(a) and 130.35(b)(1), (2), and (3) are not waived by this exemption and all other requirements of the Food and Drugs Administration are continued.

XI. Opportunity for a hearing. A. The Commissioner of Food and Drugs proposes to issue an order under the provisions of section 503(c) of the Federal Food, Drug, and Cosmetic Act withdrawing approval of any new drug application submitted which is not approved and may be required, including results of animal and clinical testing, to show whether the drug is safe and effective.

A copy of the NAS-NCI report has been furnished to each firm referred to above. Any other interested person may obtain a copy by contacting the appropriate office named above.

Communications forwarded in response to this announcement should be identified with the reference number.
DESI 3158 and be directed to the attention of the following appropriate office and unless otherwise specified be addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Md. 20852:

Requests for Hearing (identify with docket number): Hearing Clerk, Office of General Counsel (GC-1) Room 6-82, Parklawn.

Supplements (identify with NDA number): Office of Marketed Drugs (BD-200), Bureau of Drugs.

Original abbreviated new-drug applications (identify as such): Office of Marketed Drugs (BD-200) Bureau of Drugs.

All other communications regarding this announcement:

Special Assistant for Drug Efficacy Study Implementation (BD-201), Bureau of Drugs.


This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 503, 52 Stat. 1050-53, as amended; 21 U.S.C. 502, 503) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 2.150).

Dated: July 6, 1970.

SAM D. FOX,
Associate Commissioner for Compliance.

[F.R. Doc. 70-8902; Filed, July 31, 1970; 8:47 a.m.]
NEW DRUG APPLICATION (DRUGS FOR HUMAN USE)  
(Title 21, Code of Federal Regulations, § 130.4)  

Name of applicant: BARTOR PHARMACAL CO., INC.  
Address: 70 High St, Rye, New York 10580  
Date: Dec. 23, 1971  

Name of new drug: TESTOSTERONE PELLETS  

☐ Original application (regulation § 130.4).  
☐ Amendment to original, unapproved application (regulation § 130.7).  
☐ Abbreviated application (regulation § 130.4(f)).  
☐ Amendment to abbreviated, unapproved application (regulation § 130.7).  
☐ Supplement to an approved application (regulation § 130.9).  
☐ Amendment to supplement to an approved application.  

The undersigned submits this application for a new drug pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act. It is understood that when this application is approved, the labeling and advertising for the drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application; and if the article is a prescription drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the drug will contain the same information for its use, including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant warnings, hazards, contraindications, side effects, and precautions, as that contained in the labeling which is part of this application in accord with § 11.106(b) (21 CFR 11.106(f)). It is understood that all representations in this application apply to the drug produced until an approved supplement to the application provides for a change or the change is made in conformance with other provisions of § 130.9 of the new-drug regulations.

Attached hereto, submitted in the form described in § 130.4(e) of the new-drug regulations, and constituting part of this application are the following:

1. Table of contents. The table of contents should specify the volume number and the page number in which the complete and detailed item is located and the volume number and the page number in which the summary of that item is located (if any).

2. Summary. A summary demonstrating that the application is well-organized, adequately tabulated, statistically analyzed (where appropriate), and coherent and that it presents a sound basis for the approval requested. The summary should include the following information: (In lieu of the outline described below and the evaluation described in Item 3, an expanded summary and evaluation as outlined in § 130.4(d) of the new-drug regulations may be submitted to facilitate the review of this application.)

a. Chemistry.
   i. Chemical structural formula or description for any new-drug substance.
   ii. Relationship to other chemically or pharmacologically related drugs.

b. Description of dosage form and quantitative composition.

c. Scientific rationale and purpose the drug is to serve.

d. Reference number of the investigational drug notice(s) under which this drug was investigated and any notice, new-drug application, or master file of which any contents are being incorporated by reference to support this application.

e. Preclinical studies. (Present all findings including all adverse experiences which may be interpreted as accidental or not drug-related. Refer to date and page number of the investigational drug notice(s) or the volume and page number of this application where complete data and reports appear.)

f. Pharmacology (pharmacodynamics, endocrinology, metabolism, etc.).

ii. Toxicology and pathology: Acute toxicity studies; subacute and chronic toxicity studies; reproduction and teratology studies; miscellaneous studies.

c. Clinical studies. (All material should refer specifically to each clinical investigator and to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found.)

i. Special studies not described elsewhere.

ii. Dose-range studies.

iii. Controlled clinical studies.

iv. Other clinical studies (for example, uncontrolled or incompletely controlled studies).

v. Clinical laboratory studies related to effectiveness.

vi. Clinical laboratory studies related to safety.

vii. Summary of literature and unpublished reports available to the applicant.

3. Evaluation of safety and effectiveness. a. Summarize separately the favorable and unfavorable evidence for each claim in the package labeling. Include references to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found.

b. Include tabulation of all side effects or adverse experience, by age, sex, and dosage formulation, whether or not considered to be significant, showing whether administration of the drug was stopped and showing the investigator's name with a reference to the volume and page number in the application and any documents incorporated by reference where the complete data and reports may be found. Indicate those side effects or adverse experiences considered to be drug-related.

c. Copies of the label and all other labeling to be used for the drug (a total of 32 copies if in final printed form, 4 copies if in draft form).
8. A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug. Included in this description should be full information with respect to any new-drug substance and to the new-drug dosage form, as follows:

a. A description of the physical facilities including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.

b. A description of the qualifications, including educational background and experience, of the technical and professional personnel who are responsible for assuring that the drug has the safety, identity, strength, quality, and purity of the drug.

c. The methods used in the synthesis, extraction, isolation, or purification of any new-drug substance. When the specifications and controls applied to such substance are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperatures, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the substance may be specified.

d. Precautions to assure proper identity, strength, quality, and purity of the raw materials, whether active or not, including the specifications for acceptance and methods of testing for each lot of raw material.

e. Whether or not each lot of raw materials is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.

f. If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new-drug substance or the new-drug dosage form, his statement identifying each person who will perform any part of such operations and designating the part; and a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls in his part of the operation.

g. Method of preparation of the master formula records and individual batch records and manner in which these records are used.

h. The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new drug, including any special precautions observed in the operations.

i. Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

j. Number of individuals checking weight or volume of each individual ingredient entering into each batch of the drug.

k. Whether or not the total weight or volume of each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the formula card and, if so, at what stage and by whom it is done.

l. Precautions to check the actual package yield produced from a batch of the drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in the event of an unexplained discrepancy.

m. Precautions to assure that each lot of the drug packaged with the proper label and labeling, including provisions for labeling storage and inventory control.
n. The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components. If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

o. An explanation of the exact significance of the batch control numbers used in the manufacturing, processing, packaging, and labeling of the drug, including the control numbers that appear on the label of the finished article. State whether these numbers enable determination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch if its recall is required.

p. A complete description of, and data derived from, studies of the stability of the drug, including information showing the suitability of the analytical methods used. Describe any additional stability studies undertaken or contemplated. Stability data should be submitted for any new-drug substance, for the finished dosage form of the drug in the container in which it is to be marketed, including any proposed multiple-dose container, and if it is to be put into solution at the time of dispensing, for the solution prepared as directed. State the expiration date(s) that will be used on the label to preserve the identity, strength, quality, and purity of the drug until it is used. (If no expiration date is proposed, the applicant must justify its absence.)

q. Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product.

An application may be refused unless it includes adequate information showing that the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the drug are adequate to preserve its identity, strength, quality, and purity in conformity with good manufacturing practice and identifies each establishment, showing the location of the plant conducting these operations.

9. Samples of the drug and articles used as components, as follows: a. The following samples shall be submitted with the application or as soon thereafter as they become available. Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assay:

i. A representative sample or samples of the finished dosage form(s) proposed in the application and employed in the clinical investigations and a representative sample or samples of each new-drug substance, as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

ii. A representative sample or samples of finished market packages of each dosage form of the drug prepared for initial marketing and, if any such sample is not from a commercial-scale production batch, such a sample from a representative commercial-scale production batch; and a representative sample or samples of each new-drug substance as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

iii. A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new-drug substance and other assayed components of the finished drug: Provided, however, That samples of reference standards recognized in the official U.S. Pharmacopoeia or The National Formulary need not be submitted unless requested.

b. Additional samples shall be submitted on request.

c. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new-drug application to which it relates.

d. There shall be included a full list of the samples submitted pursuant to Item 9a; a statement of the additional samples that will be submitted as soon as available; and, with respect to each sample submitted, full information with respect to its identity, the origin of any new-drug substance contained therein (including for the case of new-drug substances, a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays. Include for any reference standard a complete description of its preparation and the results of all laboratory tests on it. If the test methods used differed from those described in the application, full details of the methods employed in obtaining the reported results shall be submitted.

e. The requirements of Item 9a may be waived in whole or in part on request of the applicant or otherwise when any such samples are not necessary.

f. If samples of the drug are sent under separate cover, they should be addressed to the attention of the Bureau of Medicine and identified on the outside of the shipping carton with the name of the applicant and the name of the drug as shown on the application.

10. Full reports of preclinical investigations that have been made to show whether or not the drug is safe for use and effective in use.

a. An application may be refused unless it contains full reports of adequate preclinical tests by all methods reasonably applicable to a determination of the safety and effectiveness of the drug under the conditions of use suggested in the proposed labeling.

b. Detailed reports of the preclinical investigations, including all studies made on laboratory animals, the methods used, and the results obtained, should be clearly set forth. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the underlying data are available for inspection.

The animal studies may not be considered adequate unless they give proper attention to the conditions of use recommended in the proposed labeling for the drug such as, for example, whether the drug is for short- or long-term administration or whether it is to be used in infants, children, pregnant women, or women of child-bearing potential.

c. Detailed reports of any pertinent microbiological and in vitro studies.

d. Summarize and provide a list of literature references (if available) to all other pertinent preclinical information known to the applicant, whether published or unpublished, that is pertinent to an evaluation of the safety or effectiveness of the drug.

II. List of investigators. a. A complete list of all investigators supplied with the drug including the name and post office address of each investigator and, following each name, the volume and page references to the investigator's report(s) in this application and in any documents incorporated by reference, or the explanation of the omission of any reports.

b. The unexplained omission of any reports of investigations made with the new drug by the applicant, or
submitted to him by an investigator, or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources, whether or not it would bias an evaluation of the safety of the drug or its effectiveness in use, may constitute grounds for the refusal or withdrawal of the approval of an application.

12. Full reports of clinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the drug is safe and effective for use as suggested in the labeling.

b. An application may be refused unless it includes substantial evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

c. Reports of all clinical tests sponsored by the applicant or received or otherwise obtained by the applicant should be attached. These reports should include adequate information concerning each subject treated with the drug or employed as a control, including age, sex, conditions treated, dosage, frequency of administration of the drug, results of all relevant clinical observations and laboratory examinations made, full information concerning any other treatment given previously or concurrently, and a full statement of adverse effects and useful results observed, together with an opinion as to whether such effects or results are attributable to the drug under investigation and a statement of where the underlying data are available for inspection. Ordinarily, the reports of clinical studies will not be regarded as adequate unless they include reports from more than one independent, competent investigator who maintains adequate case histories of an adequate number of subjects, designed to record observations and permit evaluation of any and all discernible effects attributable to the drug in each individual treated and comparable records on any individuals employed as controls. An application for a combination drug may be refused unless there is substantial evidence that each ingredient designated as active makes a contribution to the total effect claimed for the drug combination. Except when the disease for which the drug is being tested occurs with such frequency in the United States as to make testing impractical, some of the investigations should be performed by competent investigators within the United States.

d. Attach as a separate section a completed Form FD-1639, Drug Experience Report (obtainable, with instructions, on request from the Department of HEW, Food and Drug Administration, Bureau of Drugs (BD-200) Rockville, Maryland 20852), for each adverse experience or, if feasible, for each subject or patient experiencing one or more adverse effects, described in Item 12c, whether or not full information is available. Form FD-1639 should be prepared by the applicant if the adverse experience was not reported in such form by the investigator. The Drug Experience Report should be cross-referenced to any narrative description included in Item 12c. In lieu of a FD Form 1639, a computer-generated report may be submitted if equivalent in all elements of information with the identical enumerated sequence of events and methods of completion; all formats proposed for such use will require initial review and approval by the Food and Drug Administration.

e. All information pertinent to an evaluation of the safety and effectiveness of the drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commercial marketing (for example, outside the United States), or reports in the scientific literature, involving the drug that is the subject of the application and related drugs. An adequate summary may be acceptable in lieu of a reprint of a published report which only supports other data submitted. Reprints are not required of reports in designated journals, listed in §130.38 of the new-drug regulations, about related drugs; a bibliography will suffice. Include any evaluation of the safety or effectiveness of the drug that has been made by the applicant's medical department, expert committee, or consultants.

f. If the drug is a combination of previously investigated or marketed drugs, an adequate summary of pre-existing information from preclinical and clinical investigation and experience with its components, including all reports received or otherwise obtained by the applicant suggesting side effects, contraindications, and ineffectiveness in use of such components. Such summary should include an adequate bibliography of publications about the components and may incorporate by reference information concerning such components previously submitted by the applicant to the Food and Drug Administration.

g. The complete composition and/or method of manufacture of the new drug used in each submitted report of investigation should be shown to the extent necessary to establish its identity, strength, quality, and purity if it differs from the description in Item 6, 7, or 8 of the application.

13. If this is a supplemental application, full information on each proposed change concerning any statement made in the approved application.

Observe the provisions of §130.9 of the new-drug regulations concerning supplemental applications.
§ 130.4 (f)

(1) Abbreviated new-drug applications. Such applications shall contain:

(i) Satisfactory information of the kinds described in items 1 (table of contents), 4 (label and all other labeling), 5 (Rx or OTC statement), and 6 (components) of the new-drug application form FD-358H, and in lieu of full information described under items 7 and 8 (composition and methods, facilities, and controls), brief statements that:

(ii) Identify the place where the drug will be manufactured, processed, packaged, and labeled and the name of the supplier of the active ingredients;

(iii) Identify any person other than the applicant who performs a part of those operations and designate the part;

(iv) Include certifications from the applicant and from any person identified in subdivision (iii) of this subparagraph that the methods used in, and the facilities and controls used for, the manufacture, processing, packaging, and holding of the drug are in conformity with current good manufacturing practice in accordance with Part 133 of this chapter;

(v) Assure that the drug dosage form and components will comply with the specifications and tests described in an official compendium, if such article is recognized therein, or, if not listed or if the article differs from the compendium drug, that the specifications and tests applied to the drug and its components are adequate to assure their identity, strength, quality, and purity.

(vi) Outline the methods used in, and the facilities, and controls used for, the manufacture, processing, and packing of the drug.

(vii) Labeling that is in accord with the labeling conditions described in the finding that an abbreviated new-drug application is sufficient.

(viii) If the drug finding so specifies for the formulation intended for marketing, data adequate to assure the biological availability of the drug. For preparations claiming sustained action, time-release, or other delayed or prolonged effect, such data should show that the drug is available at a rate of release that will be safe and effective.

(ix) Any information available to the applicant, including preclinical or clinical data developed by the applicant or by other persons on behalf of the applicant, on adverse effects of the drug that is not reflected in the labeling.

(x) Additional information that may be required for the approval of the application as specified in a written communication from the Food and Drug Administration.

(xi) The signature of the applicant or responsible official or agent on a completed form FD-358H.

Appears this way on original
CENTER FOR DRUG
EVALUATION AND
RESEARCH

APPLICATION NUMBER:

80-911

CORRESPONDENCE
February 18, 1972

Drug Efficacy Study Implementation
Project Office (DESI)
Attention: Dr Paul A. Bryan, Director
Bureau of Drugs BD69
Food & Drug Administration
5600 Fisher's Lane
Rockville, Md 20852

RE: Abbreviated NDA approval for Testosterone pellet implants

Dear Sir:

Since Aug. 25, 1971, we have finally been steered correctly to you and form 356H for an abbreviated NDA on Testosterone pellet implants for human use.

As you know, this preparation is over 30 years old and has been marketed by Schering Corp. as Oretone Pellets (Implants). I had been active with them in this development.

Bartor Pharmacal wishes to market this preparation under the generic name with considerable cost saving.

Most important, is the dire need for these pellets, for Dr Robert Greenblatt's use. He is at the University of Georgia Medical School, Dep't of Endocrinology, Augusta, Georgia. He has been waiting for the past 12 months. Dr Greenblatt is involved in an NIH grant project.

We would therefore appreciate an A.N.D.A. number, as soon as possible, that we may process our pellets.

I'm submitting an original and two copies of the ANDA covering form 356H. I would appreciate your expediting the processing of this application.

C.c. Dr. R. Greenblatt

Yours truly,

Frank Bardani
President

P.S. When originally submitted incorrectly under an IND in triplicate, two copies were returned---but Washington kept the original. Consequently, a few of the original sheets were replaced with copies.
Harbor Pharmaceutical Co., Inc.
Attention: Mr. Frank Barzanti
70 High Street
Rye, New York 10580

Gentlemen:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NAME of DRUG: Testosterone Pellets

DATE of APPLICATION: December 23, 1971

DATE of COVER LETTER: February 18, 1972

DATE of RECEIPT: February 23, 1972

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the NDA number shown above.

Sincerely yours,

[Signature]

Marvin Seife, M.D.
Director
Division of Active Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NBK-60
Dcp
BD-69
BD-67
BD-22
BD-310
JLMeyer/whb/2-29-72
Ack.
Barter Pharmacal Company, Inc.
Attention: Mr. Frank Bardani
70 High Street
Rye, New York 10580

Gentlemen:

Reference is made to your abbreviated new drug application dated December 23, 1971, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Testosterone Pellets, 75 mg.

We have completed the review of this abbreviated new drug application and have the following comments regarding the proposed labeling:

1. Container label: The zip code should be included in the address. This may be done at the time of the next printing.

2. Package insert: A HOW SUPPLIED section should be added.

Other information required by section 130.4(f) of the regulations:

1. Certification statements from ___________ and ___________ that the methods used in, and the facilities and controls used for the ___________ of the drug are in conformity with current good manufacturing practice in accord with Part 133 (21 CFR) of the regulations.

2. Procedures that assure that the drug dosage form and components will comply with the specifications and tests described in an official compendium if such article is recognized therein, or, if not listed or if the article differs from the compendium drug, that the specifications and tests applied to the drug and its components are adequate to assure their identity, strength, quality and purity.

In addition, submit the procedures used by ___________ and clarify ___________ statement that the analysis will be performed on ___________.
3. It is noted that you refer to N.F. XII and U.S.P. XVII in several places in this abbreviated new drug application. Please clarify.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife, M.D.
Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NYK-D0
Dup.
BD-67
BD-69
BD-22
BD-242
J Bacsanyi/JLMeyer/RJWolters 3-23-72
R/D init. MClark/JLMeyers 3-27-72
Final Typing/rf 3-29-72
Rev w/f

P.Wolfer 3-31-72 J. Bacsanyi 4-1-972
SMeyer 4/3/72
Dr Marvin Seife, Director  
Division of Actions Implementation  
Drug Efficacy Study Implementation Project Office  
Bureau of Drugs  

April 29, 1972  

RE: Additional information supplemental to Abbreviated  
NDA 80-911 -- your letter 4/4/72

Dear Sir:

We submit the following in response to your inquiry above:

Labeling:
1. Since labels are preprinted for control number inclusion, we will include the Zip Code with the address - 10580.
2. The package insert will have the following added:
   "HOW SUPPLIED - Pellets of 75 mg. each, one pellet per vial, in a box of 3 sterile vials."

Other information required by section 130.4(f) of regulations:
1. Certification statements from ________ attesting conformity to GMP in accord with Part 133 (21 CFR) of the regulations are attached.
   2. and 3. (are answered in the final part of this letter).
   A supplementary letter from ________ explains the

The original ________ letter refers to "Estradiol and other similar type products," e.g. Testosterone. This was submitted when both items were requested for clearance prior to the advice of HEW to submit Testosterone separately. We have enclosed a modified and more pertinent letter from ________ for clarification.

2. To erase any ambiguity of commitments in the Abbreviated NDA, Bartor Pharmacal assures that the drug dosage form and components do and will comply with the specifications and tests described in an official compendium, if such article is recognized therein, as to identity, strength, quality and purity.

Bartor, aside from submitted protocols from reliable U.S. suppliers, will run and will have run the following procedures for all components, as:

Testosterone - NF XIII Pg 687 ALL TESTS
Stearic Acid - USP XVIII Pg 683 ALL TESTS, except Chromatographic Testosterone Pellet Implants - NF XIII Pg 683 ALL TESTS
Stability data furnished and run by Bartor, ________ indicates adequacy of quality and purity as well as identity with reference.

______ purchased only from ________ will have the following tests run by Bartor (attached). Bartor Pharmacal assures that ________, not in official compendium as such, meets the requirements of identity, strength, quality & purity.
3. We wish to update our monogram references to the NF XIII and USP XVIII (for the NF XII and USP XVII) wherever mentioned—
for whatever specifics have been mentioned in the original submission.
Paragraph number 2 last mentioned in this letter, makes more specific references with pertinent page numbers.

We appreciate your willingness to process this submission as promptly as possible. Thank you for your co-operation and courtesies on behalf of your staff on the telephone.

Yours truly,

Frank Bardani, President

Cc. John Accardi
consulting Chemist
Riker Pharmaceuticals Company, Inc.
Attention: Mr. Frank Bardani
70 High Street
Rye, New York 10580

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Testosterone Pellets, 75 mg.

Reference is also made to your communication dated April 29, 1972, enclosing revised labeling and manufacturing information.

We have completed the review of this abbreviated new drug application as submitted with draft labeling. However, before the application may be approved, it will be necessary for you to submit final printed labeling. The labeling should be identical in content to the draft copy.

Please submit twelve copies of the printed labeling.

Sincerely yours,

[Signature]

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NYK-D0
Dup
BD-69 BD-67 BD-106 BD-242
JBacsanyi/JMeyer/RWolters 5-22-72
R/D init. JMeyer 5-25-72
Final typing/rt 5-26-72
Approvable

M. Clarke 5/31/72
June 12, 1972

Drug Efficacy Implementation
Project Office (DESI)
Att: Dr. Paul A. Bryan Director
Food & Drug Administration
5600 Fisher Lane
Rockville, Md. 20852

Ref: Nda-911 Letter of May 31, 1972

Dear Sir:

Enclosed printed labeling as you requested in your letter of May 31, 1972

Yours Truly

Frank M. Bardani
Pres.

RECEIVED 11-COPY
PHOTOSTATS MADE
FOR DUP____TRIP_____

RECEIVED
BUREAU OF DRUGS
JUN 14 1972