CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 75265

CORRESPONDENCE

ANDA 75-265

Spear Pharmaceuticals
Attention: Kim L. Spear, M.D.
13100 Ponderosa Way
Ft. Myers, FL 33907

JAN 13 1998

Dear Sir:

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

NAME OF DRUG: Tretinoin Cream USP, 0.05%

DATE OF APPLICATION: December 2, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: December 5, 1997

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

When submitting applications in the future, it is recommended that applicants follow the accepted format as outlined in the Office of Generic Drugs Policy and Procedure Guide 30-91. A copy of this guidance maybe obtained from the Drug information Branch (301) 827-4573 or from the following web site:

http://www.fda.gov/cder/guidance/index.htm

In addition, you should consider updating your form 356h. A revised copy of this form can be found on the following web site:

http://aosweb.psc.dhhs.gov/forms/fdaforms.htm

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

Should you have questions concerning this application, contact:

Joseph Buccine
Project Manager
(301) 827-5848

Sincerely yours,

/S/

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-265
DUP/Jacket
Division File
Field Copy
HFD-600/Reading File
HFD-610/J.Phillips
HFD-330
HFD-92
HFD-615/M.Bennett
HFD-324/M.Lynch

Endorsement: HFD-615/PRickman, Chief, DDR /S/ date 1/02/98
HFD-615, SMiddleton, CSO date 12/23/97
HFD-629, PSchwartz, Supv. Chem. date
WP FILE X:\NEW\FIRMSNZ\SPEAR\LTRS&REV\75265.ACK
FT/njg/12/22/97
ANDA Acknowledgment Letter!

December 2, 1997

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

Original ANDA Submission
for Tretinoin Cream, USP 0.05% w/w
Spear Pharmaceuticals
Ref: ANDA for 0.025% w/w Strength Submitted Simultaneously with this Application.
Ref: ANDA 75-213 (0.1% w/w)

Dear Mr. Sporn:

Pursuant to the provisions of Section 505 (j)(1) of the Federal Food, Drug, and Cosmetic Act, Title 21 CFR part 314, Subpart C-Abbreviated Applications, Spear Pharmaceuticals hereby submits an Abbreviated New Drug Application for a generic drug product, Tretinoin Cream, USP 0.05%.

The purpose of this submission is to obtain FDA approval for Spear Pharmaceuticals, Inc., to manufacture the topical acne product Tretinoin Cream, USP 0.05% that will be marketed in the USA. This product is the generic equivalent of Retin-A® Cream 0.05%, the reference listed drug which is manufactured and marketed by Ortho Pharmaceutical Corporation., (which was originally the R.W. Johnson Company and is a subsidiary of the Johnson and Johnson Company) under the approved application NDA 17-522 on July 19, 1974.

This application contains comparative *in vitro* release data between the generic formulations and the corresponding reference listed drugs (0.1, 0.05, and 0.025% strengths). In addition, reference is made to our two additional ANDAs [i.e., #75-213 (0.1%) and an ANDA for the 0.025% (simultaneously submitted with this application)] which provide data from two *in vivo* bioequivalence studies evaluated for safety and efficacy that both clearly demonstrated bioequivalence to the corresponding reference listed drugs.

It is our contention that the Spear family of generic Tretinoin Cream products (i.e., 0.1, 0.05, and 0.025% w/w strengths) have met all the requirements that you have proposed which are outlined in your letter (Sporn to Spear; October 15, 1997; a copy of which follows with additional copies presented in Sections VI and XXI of this application) to request a waiver of evidence of *in vivo* bioequivalence for this 0.05% strength.

13100 PONDEROSA WAY ■ FORT MYERS, FLORIDA 33907 ■ 941-936-4665 ■ FAX 941-936-3591

In summary:

- All active and inactive ingredients are qualitatively and essentially quantitatively the same.
- Bracketed *in vivo* studies in humans for the higher and lower strengths have been performed and have demonstrated bioequivalence with respect to safety and efficacy. The safety studies have included evaluations for skin irritation and sensitization as measured by erythema and peeling assessments for the generic vs. reference over the 12 week study period.
- Comparative data have been provided in this application regarding *in vitro* release of all strengths which demonstrates no statistically significant differences in release rates. In addition, physico-chemical properties all compare favorably.

We believe these data are acceptable and consequently, Spear Pharmaceuticals is requesting a waiver of evidence of *in vivo* bioequivalence for this 0.05% (intermediate) product strength.

Our contractor (
the Drug Product.

U.S. Patent 3,906,108 was granted September 16, 1975, to Johnson and Johnson (assignee), of which Ortho Pharmaceutical is a subsidiary. The subject patent specifically claimed [illegible] of Tretinoin that were the subject new drug products previously approved by the FDA. The subject U.S. Patent 3,906,108 is no longer protected under the provisions of the Drug Price Competition and Patent Term Restoration Act.

Spear Pharmaceuticals' generic drug, Tretinoin cream USP 0.05%, is essentially identical to Ortho Pharmaceutical's Retin-A® (Tretinoin, USP) Cream 0.05% concerning the active ingredient and inactive ingredients both qualitatively and quantitatively. The generic product labels and labeling are identical to the labels and labeling currently approved for the marketing of Retin-A® (Tretinoin, USP) Cream 0.05% except for the NDC number, trade name, distributor (*Dist. by Geneva Pharmaceuticals, Inc. Broomfield CO, 80020*), and other labeling information specific to the pioneer drug which is detailed in Section V of this application in a side-by-side analysis.

This ANDA consists of two volumes, each containing the required Table of Contents. Besides the Archival copy and the Review Copy (Two Parts: (1) Review-Pharmacokinetic copy, and (2) Review-Chemistry copy), an additional copy is provided as the "field copy" which contains all the technical sections of the archival copy and has been sent to the Orlando District Office. All required copies contain four (4) sets of draft labeling. The Archival copy bears original signatures on specific required statements and Form FDA 356h.

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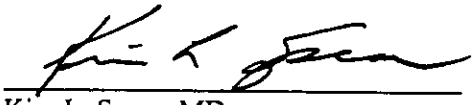
Portions of this submission are considered confidential. Specifically, these are analytical methods validation, processing instructions, and facilities description.

Please address communications related to this ANDA by contacting:

Kim L. Spear, MD, President
Spear Pharmaceuticals
13100 Ponderosa Way
Fort Myers, FL 33907
Tel. (941) 936-5098 or (941) 936-4665
Fax: (941) 936-3591



Kim L. Spear, MD
President,
Spear Pharmaceuticals, Inc.

12/2/97
Date