CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 18956/S28

APPROVAL LETTER

D/V

JUL 13 1993

NDA 18-956/S-028

Sterling Winthrop Inc.
1250 Collegeville Road
P.O. Box 5000
Collegeville, Pennsylvania 19426-0900

Attention: Helen Hammes
Associate Director
Project Operations
Drug Regulatory Affairs

Dear Ms. Hammes:

Reference is made to your supplemental new drug application dated January 10, 1990, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Omnipaque (iohexol) Injection.

The supplement provides for a revision in the labeling to include the use of orally or rectally administered Omnipaque 180, 240, and 300 mgI/mL in children for the examination of the gastrointestinal tract.

Reference is also made to your amendments dated February 16, April 17, and June 19, 1990; and August 18, 1992.

We also reference your letter dated June 11, 1993, in which you request that approval of this supplemental application not be contingent upon the approval of S-039, as stated in our approvable letter for this supplement dated June 1, 1993.

We have completed our review of this supplemental application as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling dated August 18, 1992. Accordingly the supplemental application is approved the date of this letter.

Please submit twelve copies of the final printed labeling (FPL) identical to the draft labeling dated August 18, 1992, as soon as possible. Seven of the copies should be individually mounted on heavy weight paper or similar material. The submission should be designated for administrative purposes as "FPL for approved NDA 18-956/S-028." Approval of this submission by FDA is not required before the labeling is used. Marketing of the product with FPL that is not identical to the draft labeling may render the product misbranded and an unapproved drug.

The final printed labeling should include only those labeling revisions provided for in the revised draft labeling dated August 18, 1992 for this supplement, and should not contain labeling revisions under consideration for inclusion in S-039.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

Should there be any questions regarding this communication, please contact Mr. Stephen McCort, Consumer Safety Officer at (301) 443-5818.

Sincerely yours,

/S/

Patricia Love, M.D., M.B.A.
Acting Director
Division of Medical Imaging,
Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
NDA 18-956/S-028
HFD-160/DIVFIL
HFC-130/JAllen with labeling
HFD-80 with labeling
HFD-160/Love
HFD-160/Chow
HFD-161/McCort/Kummerer
Acknowledgements: Jones-06-23-93/Chow-06-23-93/Cheever-06-21-93
drafted by: Steve McCort 6-18-93
F/T by: Jo 07-1-93 18956.S28
Concurrence JC/6/29/93 AEJ/6/23/93 CHOW/6/23/93
SUPPLEMENT APPROVAL

7/1/93

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 18956/S28

APPROVABLE LETTER

NDA 18-956/S-028

JUN 29 1992

Sterling Winthrop Inc.
90 Park Avenue
New York, NY 10016

Attention: Linda Nardone, Ph.D.
Director, Drug Regulatory Affairs

Dear Dr. Nardone:

Reference is made to your supplemental new drug application (NDA) dated January 10, 1990, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the diagnostic radiocontrast agent, Omnipaque (iohexzol) Injection.

The supplement provides for an expansion of the currently approved pediatric labeling whereby Omnipaque administered orally or rectally may be used in children in the examination of the gastrointestinal tract.

We also acknowledge receipt of your amendments and correspondence dated February 16, April 17, and June 19, 1990.

We have completed our review of this supplemental new drug application as amended, and it is approvable. Before the application may be approved, however, we request that you make the following revisions to the draft labeling submitted June 19, 1990:

1. In Section III, the PRECAUTIONS - General section should be revised to read as follows:

2. Despite your request stated in the June 19, 1990 amendment that the data from the European study (N-121) should be factored into the ADVERSE REACTIONS section pertaining to oral pediatric use, it remains our opinion that this open label clinical trial was not adequately controlled to support labeling statements pertaining to safety. The absence of any reported adverse reactions in this study (as well as the absence of laboratory results), brings into question the adequacy of monitoring in the study. For this reason, please revise the ADVERSE REACTIONS subsection pertaining to Children (page 12) to read:

> "In controlled clinical studies involving 58 pediatric patients for examination of the gastrointestinal tract at concentrations of 180 and 300 mgI/mL, the following adverse reactions were reported: diarrhea (36%), vomiting (9%), nausea (5%), fever (5%), hypotension (2%), abdominal pain (2%), and urticaria (2%). In clinical studies an increased frequency and severity of diarrhea was noted with an increase in the administered concentration and dose of the radiocontrast agent."

The frequency rate of these reactions, particularly with regard to diarrhea, are in line with those currently reported for the adult population for oral pass-through examinations.

3. In Section III, under INDIVIDUAL INDICATIONS AND USAGE, Oral Use, Dosage and Administration, please add the word "undiluted" in the "Adults" subsection as follows:

Please submit, as an amendment to the supplemental application, revised draft labeling for our review. Should additional information relating to the safety and effectiveness of this drug product become available, further revision of the labeling may be required.

Within ten days after the date of this letter, you are required to amend the supplemental application, or notify us of your intent to file an amendment, or follow one of the other alternatives under 21 CFR 314.110. In the absence of such action, the Food and Drug Administration may take action to withdraw the supplemental application.

If you have any questions, please contact:

Ms. Susan Kummerer
Consumer Safety Officer
Telephone: (301) 443-5963

Sincerely,

/S/ 6/26/92

Wiley A. Chambers, M.D.
Acting Director
Division of Medical Imaging,
Surgical and Dental Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

CC: Original NDA
HFC-130
HFD-82
HFD-100
HFD-735
HFD-160/DivDir/Chambers
HFD-160/SMO/Jones AE Jones 6/25/92
HFD-160/MO/Chow Howard 6/22/92
HFD-160/SChem/Sheinin
HFD-160/SPharm/De Witt
HFD-160/SCSO/Cheever
HFD-160/CSO/Kummerer SK 6.23.92
Huntley 6/22/92 KH
Approvable
AE 6/26/92

D/6

NDA 18-956/S-028

Sterling Winthrop Inc.
1250 Collegeville Road
P.O. Box 5000
Collegeville, Pennsylvania 19426-0900

JUN - 1 1993

Attention: Helen Hammes
Associate Director
Project Operations
Drug Regulatory Affairs

Dear Ms. Hammes:

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The supplement provides for a revision in the labeling to include the use of orally or rectally administered Omnipaque 180, 240, and 300 mgI/mL in children for the examination of the gastrointestinal tract.

Reference is also made to your amendments dated February 16, April 17 and June 19, 1990, and August 18, 1992.

We have completed our review of this supplemental application as amended including the submitted draft labeling dated August 18, 1992, and it is approvable. Before the application can be approved, however, we request that the package insert be revised as detailed in our letter dated December 11, 1992. A copy of that letter is enclosed for your reference.

Within 10 days after the date of this letter, you are required to amend the application, or notify us of your intent to file an amendment, or follow one of the other options under 21 CFR 314.10. In the absence of such action FDA may take action to withdraw the application. The changes indicated above cannot be legally implemented until you have been notified in writing that the application is approved.

We remind you of your commitment to revise the **ADVERSE REACTIONS** section of the Omnipaque package insert within 60 days of the approval of S-031, S-032, S-033 and S-034, as stated in your letter dated January 18, 1993.

Should there be any questions regarding this communication, please contact, Stephen McCort, Consumer Safety Officer at (301) 443-5818.

Sincerely yours,

/S/ 5/28/93

Paula Botstein, M.D.
Acting Director
Division of Medical Imaging
Surgical and Dental Drug Products
and
Deputy Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: FDA Letter Dated December 11, 1992

cc:
NDA 18-956/S-028
HFD-160/DIVFIL
HFC-130
HFD-80
HFD-160/Botstein
HFD-160/Chow
HFD-161/McCort/Kummerer
Acknowledgements: Jones-04-28-93/Cheever-04-13-93/Chow-04-19-93
F/T by: AChapman 05-06-93
Revised by: McCort
Revised F/T by: AChapman 05-19-93
SUPPLEMENT APPROVABLE

5/21/93