CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 12209/S038

CORRESPONDENCE

NDA 12-209

DEC 7 1998

ICN Puerto Rico, Inc.
HC01 Box 16625
Bo. Mariana Road 909 Km. 1.1
Humacao, Puerto Rico 07791-9731

Attention: Cheri Jones, M.S., R.A.C.
Director Corporate Regulatory Affairs

Dear Ms. Jones:

Please refer to your Investigational New Drug Application (NDA) submitted pursuant to section 505(i) of the Federal Food, Drug, and Cosmetic Act for Fluorouracil Injection.

We also refer to the November 9, 1998 communication from Lynn DeVenezia-Tobias, Program Manager, Hoffmann-La Roche, Inc., notifying us that the sponsorship of this IND has been transferred to you.

The following principles are applied to changes in ownership of INDs, NDAs and ANDAs:

1. The file reflects the changes actually effected.

2. All third parties (e.g., clinical investigators during the clinical investigation of a new drug) are aware of the change in ownership of this NDA.

3. The responsible persons (applicant, sponsor, agent, official, etc.) are identified, and the necessary commitments are made.

You have fulfilled these requirements, and the transfer of sponsorship of NDA 12-209 is now considered complete.

As sponsor of this NDA, you are responsible for the compliance with the Food, Drug, and Cosmetic Act and the regulations promulgated thereunder. Those responsibilities include reporting any unexpected fatal or life-threatening experiences by telephone or facsimile to this Agency no later than seven calendar days after receipt of the information and the submission of annual progress reports.

12/7/98

Sincerely yours,

/S/

Dotti Pease
Chief, Project Management Staff
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: ORIG. NDA 12-209
Div. File
HFD-150/Project Manager
HFD-92/Sharon Brownewell (Please change in COMIS)
HFD-150/drafter/MPelosi/12-04-98/
R/D init. by: MPelosi/
f/t by: ESugar/12-04-98/

CHANGE IN SPONSORSHIP

NOTE TO HFD-92: PLEASE CHANGE SPONSOR IN COMIS

ICN Pharmaceuticals, Inc.

International Headquarters
ICN Plaza
3300 Hyland Avenue
Costa Mesa, California 92626

Telephone: 714/545-0100
FAX: 714/556-0131
Telex: 67-0413

December 1, 1998

Food and Drug Administration
Division of Oncology Drug Products, HFD-150
Office of Drug Evaluation II
Center for Drug Evaluation and Research
5600 Fishers Lane
Rockville, Maryland 20857

ORIGINAL

NDA NO. 12-209 REF NO. 038
NDA SUPPL FOR SCP

Re: **NDA 12-209 - FLUOROURACIL Injection**
Chemistry, Manufacturing and Controls: New Stopper
SUPPLEMENT - EXPEDITED REVIEW REQUESTED

Ladies and Gentlemen:

In accordance with 21 CFR 314.70(b)(2)(vii), ICN Pharmaceuticals, Inc. (ICN) is submitting herewith a supplemental new drug application to provide for changes in the primary packaging components for FLUOROURACIL Injection.

This supplement provides for a change in the container-closure system. There is a need to change from stopper to stopper because the vendor has discontinued this product line. The proposed stopper is a component of choice for new product development. This stopper is and, as such, does not require the addition of a lubricant, for machinability of the component on the production filling equipment. The component, as received, has a lower particulate, bioburden and endotoxin load than the stopper. The currently approved glass vials and seals remain unchanged.

ICN Pharmaceuticals, Inc. is requesting expedited review of this application. The currently approved stopper, is no longer commercially available. Based on current market demand, ICN will have depleted its inventory of approved stoppers by January 1, 1999. In order to continue to supply this important oncology product to the market without interruption, ICN is requesting expedited review.

In support of the subject changes, this supplement contains schematic drawings, and specifications, and directions for testing for the current and proposed stoppers. A Drug Master File (DMF) authorization letter from the supplier of the proposed stopper is included. Drug product specifications and directions for testing, comparative release and stability data, stability commitment, and stability protocol are also provided. In addition, information is being submitted on the preparation of the stoppers, container-closure integrity validation, and the determination of extractables.

Approvals Sought

The implementation of the proposed changes will provide for an improved closure system.

Specifically, we are seeking approval for the following:

1. FLUOROURACIL Vials in the proposed primary packaging components, which consist of a glass vial with a stopper which has

2. Continuation of the currently approved expiry period of 15 months.

Commitment

We commit to placing the first three batches of FLUOROURACIL Injection packaged with the stopper on routine long-term stability, to monitor the stability for the length of the expiration dating period, and to report the results in the Annual Report in accordance with 21 CFR § 314.81(b)(2).

All other information remains unchanged from that submitted in the Original NDA and supplements thereto.

The information contained in this supplement is **CONFIDENTIAL** and is not to be disclosed to any person outside the Food and Drug Administration without prior notification and written consent from ICN Pharmaceuticals, Inc.

ICN Pharmaceuticals, Inc. acquired ownership of NDA 12-209 from Hoffmann-La-Roche, Inc. This transfer of NDA was effective November 9, 1998, and was communicated to the agency in a letter dated November 18, 1998. FLUOROURACIL Injection is currently manufactured by for ICN Pharmaceuticals, Inc.

In conformance with 21 CFR §314.71(b), and as indicated at the end of this letter, an identical field copy of this supplement has been prepared for simultaneous submission to the New Jersey District Office of the FDA. The undersigned hereby certifies that the copy submitted to the District Office is identical to that submitted to the Division of Oncology Drug Products.

ICN Pharmaceuticals, Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

Please feel free to contact the undersigned at (800) 548-5100, extension 3057, or via e-mail: ahiteshi@icnpharm.com, or facsimile (714) 641-7287 if you have any questions concerning this supplement.

Sincerely,
ICN PHARMACEUTICALS, INC.

Anil K. Hiteshi, R.A.C.
Senior Manager, Corporate Regulatory Affairs

Attachments

CC: Virginia A. Pate - HLR
Desk Copy: Maureen A. Pelosi, CSO

Field Copy: Ms. Regina Brown
Pre-Approval Program Director
Food and Drug Administration
120 North Central Drive
North Brunswick, NJ 08902

ICN

ORIGINAL

N Pharmaceuticals, Inc.

International Headquarters
ICN Plaza
3300 Hyland Avenue
Costa Mesa, California 92626

Telephone: 714/545-0100
FAX: 714/556-0131
Telex: 67-0413

November 18, 1998

SUPPL NEW CORRESP

Food and Drug Administration
Division of Neuropharmacological Drug Products, HFD-120
Office of Drug Evaluation I
Center for Drug Evaluation and Research
1451 Rockville Pike, Woodmont II Building
Rockville, Maryland 20852

Re: NDA 12-209—Fluorouracil Injection
TRANSFER OF NDA OWNERSHIP

Dear Sir/Madam:

ICN Puerto Rico, Inc., a wholly-owned subsidiary of ICN Pharmaceuticals, Inc. (ICN), with offices at 3300 Hyland Avenue, Costa Mesa, CA 92626, acknowledges and accepts ownership of the referenced NDA for Fluorouracil Injection from Roche Products, Inc., Bo. Mariana, State Road 909, Km. 1.1, HC01 Box 16626, Humacao, Puerto Rico 00791, effective November 09, 1998.

With the transfer of ownership of the referenced NDA, all rights and responsibilities have been transferred to ICN. A complete copy of the approved application, including NDA supplements and other required records, as well as all correspondence to and from the Agency regarding this application, has been provided to ICN.

manufacture and package the approved drug product for ICN until such time as a manufacturing supplement is submitted and approved for an ICN manufacturing site.

It is ICN's intention to utilize existing inventories of printed packaging materials before revisions are implemented to indicate ICN as distributor of the product.

Current finished drug supply is being transferred to ICN, who will act as marketer of this product.

Any adverse Drug Experience Reports received by

will be forwarded to ICN Pharmaceuticals, Inc., for further evaluation and processing.

CENTER FOR DRUG EVALUATION AND RESEARCH

NOV 24 1998

RECEIVED HFD-120

All future communications regarding this application should be forwarded to my attention at 3300 Hyland Avenue, Costa Mesa, California 92626; or by e-mail: cjones@icnpharm.com; phone (800) 548-5100, extension 5031; or FAX (714) 641-7287.

Sincerely,
ICN PUERTO RICO, INC.

Cheri Jones, M.S., R.A.C.
Director Corporate Regulatory Affairs

cc: Anthony J. Corrado, Associate Director, Drug Regulatory Affairs HLR U.S.
Frankie Santana, President and General Manager, Roche Product, Inc.