DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 16-831/S-046

ICN Pharmaceuticals
Attn.: Anil K. Hiteshi, RAC
Senior Manager, Corporate Regulatory Affairs
3300 Hyland Avenue
Costa Mesa, CA 92626

Dear Mr. Hiteshi:

Please refer to your supplemental new drug application dated October 24, 2003, received October 27, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Efudex® (fluorouracil) Topical Solution, 5%.

This supplemental new drug application, submitted as changes being effected in 30 days, provides for 1) a new manufacturing site, ICN Puerto Rico, Bo. Mariana, Road 909, Km 1.1, Humacao, Puerto Rico, for the drug product, 2) revisions to the specifications and test methods for fluorouracil drug substance and excipients, made to conform with the current USP monograph and methods, 3) minor site-specific changes to the manufacturing process, 4) elimination of the (b)manufacturing overage of fluorouracil, 5) a new supplier of (b)(4)--------used to produce the closures by the manufacturer, (b)(4)----------, 6) revisions to the specification and test methods for fluorouracil topical solution USP, made to conform with the current USP monograph and methods, and 7) draft labeling (container, carton and package insert) changes reflecting the identity of the new manufacturing site, and making minor editorial and part number revisions, and a strengthened usage warning statement inccorporating a prohibition against intravaginal use.

We completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below.

1) Change "Not for Ophthalmic Use" to "Not for Ophthalmic Use or Intravaginal Use",
2) Add NDC number in accordance with 21 CFR 207.35(b)(3),
3) Delete "Manufactured for:" and reference to previous manufacturer,(b)(4)
4) Correct "excursion" to "excursions",
5) Change part number to ICN system,
6) Replace proprietary name, established name and strength declaration with bar code on top flap (carton only).

The final printed labeling (FPL) must be identical to, and must include the minor editorial revisions indicated in, the submitted labeling (package insert, immediate container and carton labels submitted October 24, 2003). These revisions are terms of the approval of this application.

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 16-831/S-046." Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Mildred A. Wright, Regulatory Project Manager, at (301) 827-2020.

Sincerely,

{See appended electronic signature page}

Norman R. Schmuff, Ph.D.
Chemistry Team Leader (Acting) for the
Division of Dermatologic & Dental Drug Products,
(HFD-540)
DNDC III, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Norman Schmuff

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