



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

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OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP 2F2707/FAP 2H5355. Cyromazine (Larvadex®).  
Addendum to Previous Review, Dated 12/17/84 Re:  
Review of Additional Information and Comments  
Submitted by Ciba-Geigy.

TOX Chem. No. 167 R

TO: Timothy A. Gardner, Product Manager #17  
Registration Division (TS-767C)

FROM: Edwin R. Rudd, Section Head  
Section II, Toxicology Branch.  
Hazard Evaluation Division (TS-769C)

THRU: William L. Burnam, Deputy Chief  
Toxicology Branch  
Hazard Evaluation Division (TS-769C)

Background:

In a previous memorandum from Edwin R. Rudd to Timothy A. Gardner, dated December 17, 1984, a preliminary review of Ciba-Geigy's responses to issues related to the Larvadex® 2-year chronic feeding/oncogenicity study in rats and the oncogenicity study in mice was submitted -- pending concurrence by and additional discussion with the Toxicology Branch pathologist, Dr. L. Kasza, who was unavailable at that time. Subsequent consultation with Dr. Kasza now permits an updating of the previous memorandum.

Toxicological Considerations:

2-Year Chronic and Oncogenicity Study with CGA-72662 Technical in Albino Rats (IRDC Study No. 382-081).

Dr. L. Kasza has confirmed that the requested microscopic slides for kidneys for all animals in this study have been submitted to him. He has furthermore concurred with the conclusions presented in the previous memorandum, dated December 17, 1984. All previously outstanding issues relating to this study are now resolved. This rat chronic feeding/oncogenicity study is classified as Core-Minimum. The NOEL for this study is 30 ppm. The LOEL is 300 ppm. Effects observed at the LOEL were decreased mean body weights and

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possibly decreased mean food consumption. An oncogenic potential for Larvadex® was not demonstrated in this study at dosage levels up to and including 3000 ppm.

Oncogenicity Study with CGA-72662 in Albino Mice (IRDC Study No. 382-082).

Review of Ciba-Geigy's responses to Toxicology Branch (TB) concerns on the mouse oncogenicity study is not yet completed. Dr. L. Kasza has indicated that written commentary is required from Dr. J. Hardisty, the pathologist who reviewed the slides in this study, before TB can complete its review of this study. The written commentary was requested about 2 months ago and has not yet been received. Dr. Kasza will phone Dr. Hardisty and again request the written commentary.

NOTE:

Review of Ciba-Geigy's responses to the teratology issues is being dealt with entirely by Larry Chitlik.

cc: Dr. L. Kasza (TOX)  
Dr. O. E. Paynter (HED)

OPP:HED:TOX:E.RUDD:sh 1/9/85 X77395 #10-D20

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**END**