



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

010663

NOV 18 1993

NOV 18 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: 1-Naphthaleneacetic acid: Determination of the Adequacy of Metabolism Data

P.C. Code: 056002
Submission: S449377
MRID Nos: 00004942 and 05008052
DP Barcode: D195517

FROM:

Timothy F. McMahon, Ph.D., Pharmacologist
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

11/7/93

TO:

Susan Jennings / PM 72
Special Review and Reregistration Division (7508W)

THRU:

Yiannakis M. Ioannou, Ph.D., Section Head
Review Section I, Toxicology Branch II
Health Effects Division (7509C)

J. M. Ioannou 11/16/93

and

Marcia Van Gemert, Ph.D., Branch Chief
Toxicology Branch II
Health Effects Division (7509C)

M. Van Gemert 11/17/93

Registrant: not stated

Action Requested: Determination of the adequacy of metabolism data submitted previously for 1-naphthaleneacetic acid.

10F2



Recycled/Recyclable
Printed with SoyCanada Ink on paper that
contains at least 50% recycled fiber

010663

Data Summary:

Two published studies on the metabolism of 1-naphthaleneacetic acid were submitted to Toxicology Branch II for determination of the adequacy of the submitted data under the current metabolism guidelines. In one study (published in *Xenobiotica* 7, 695-706, 1977), eleven species (including female Wistar rats) were examined for metabolism of 1-naphthaleneacetic acid. Three female rats were given a single oral dose of 100 mg/kg 14-C 1-naphthaleneacetic acid, and radioactivity in urine collected and analyzed for total radioactivity as well as urinary metabolites. An additional study was conducted in bile cannulated rats given intraperitoneal doses of 5, 25, 50, 250, and 500 mg/kg (no. of rats per dose not specified) where urinary and biliary metabolites were also characterized. In the second study (published in *J. Agr. Food Chem.* 14: 532-535, 1966) 2 male Osborne-Mendel rats per dose were administered 1-naphthaleneacetic acid at dose levels of 0.1, 1.0, 100, and 250 mg/kg, and urinary and fecal radioactivity collected. Urinary metabolites were characterized, and additional work was also done on bile duct cannulated rats for identification of biliary metabolites.

The submitted studies as summarized above do not, by strict definition, fulfill the §85-1 data requirement for the following reasons:

- 1) No repeat oral dose group in either study.
- 2) No feces data for the female rat study
- 3) Inadequate number of rats per dose group
- 4) Inadequate mass balance for the female rat study

While it is apparent that several deficiencies exist in each of the submitted studies in relation to the current §85-1 guidelines, it is also apparent from review of the existing data that significant new information on the disposition of 1-naphthaleneacetic acid would not be obtained from conduct of additional studies to satisfy these deficiencies. The metabolism of this class of compounds has been well characterized in the literature, and these compounds are invariably conjugated with either glycine or glucuronic acid. In addition, there is no evidence to suggest that 1-naphthaleneacetic acid is mutagenic or carcinogenic as judged by the data available in the Toxicology one-liner database. Therefore, no additional metabolism data are requested for 1-naphthaleneacetic acid at this time. The Agency reserves the right, however, to request additional studies should significant toxicity of 1-naphthaleneacetic acid be discovered.

2