

201-14539



NCIC HPV

Sent by: Mary-Beth
Weaver

06/06/2003 02:01 PM

To: NCIC HPV, moran.matthew@epa.gov

cc:

cc:

Subject: Environmental Defense comments on 2-Chloropyridine (CAS#
109-09-1)



Richard_Denison@environmentaldefense.org on 06/06/2003 10:54:38 AM

To: oppt.ncic@epamail.epa.gov, hpv.chemrtk@epamail.epa.gov, Rtk Chem/DC/USEPA/US@EPA, Karen
Boswell/DC/USEPA/US@EPA, sjbarbee@archchemicals.com
cc: lucierg@msn.com, kflorini@environmentaldefense.org, rdenison@environmentaldefense.org

Subject: Environmental Defense comments on 2-Chloropyridine (CAS# 109-09-1)

(Submitted via Internet 6/6/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov,
boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and
sjbarbee@archchemicals.com)

Environmental Defense appreciates this opportunity to submit comments on
the robust summary/test plan for 2-Chloropyridine (CAS# 109-09-1).

The test plan and robust summaries for 2-chloropyridine (2-PC1) were
prepared by Arch Chemicals. 2-PC1 is an oily substance used in the
synthesis of pharmaceutical and agricultural chemicals. It is also used in
the synthesis of pyrithione-based biocides for use in cosmetics and various
pharmaceutical products. The sponsor states that 2-PC1 is not sold to
individual consumers, but no information is provided on its presence as a
residual contaminant or to establish that it is absent from any consumer
products, pharmaceuticals or agricultural chemicals. Likewise no
information is provided on environmental releases, so we are not able to
evaluate environmental or human exposures. The sponsor states that
exposures in the workplace are tightly controlled, but no information is
provided on workplace monitoring or industrial practices designed to
protect workers from exposure to this toxic and mutagenic substance.

The test plan proposes studies on repeat dose, reproductive and
developmental toxicity because no data are available on those endpoints. We
agree with this proposal and we also recommend that the sponsor conduct
water stability studies, as no such studies are currently available.
Overall the test plan and robust summaries are informative and
well-written. Specific comments are as follows:

1. The sponsor uses ECOSAR predictions to provide data on all ecotoxicity
endpoints. While this approach is acceptable, the sponsor should provide
information in the robust summaries on the analogs of 2-PC1 used to
generate the ECOSAR predictions.

2. 2-PC1 is resistant to biodegradation as evidenced by multiple studies.
The sponsor also claims, based on scientific judgment, that 2-PC1 is
resistant to hydrolysis. While this contention is likely correct, 2-PC1 is
a hazardous substance, so we recommend that water stability studies be
conducted so that this endpoint is addressed with experimental data.

3. The acute toxicity studies, while not conducted under GLP, are sufficient
to demonstrate that 2-PC1 is toxic via multiple routes of exposure, so we
agree with the sponsor that no additional acute toxicity studies are
needed.

4. 2-PC1 is genotoxic in a variety of in vitro and in vivo tests, and its

2003 JUN - 6 PM : 32

RECEIVED
OPPT/CBIC

genetic toxicity in all these systems appears to be highly dependent on metabolic activation. Does the sponsor have any information on the nature of the mutagenic metabolites and how those metabolites interact with genetic constituents? If so, this information should be provided in the test plan and robust summaries. Although not formally required by the HPV program, mechanistic data are very helpful for assessing exposure-response relationships in the workplace, the general environment and following exposures related to use of consumer products.

5. There are no available data on 2-PCl for the repeat dose, reproductive and developmental toxicity endpoints. We agree with the sponsor's proposal to conduct those studies. However, the sponsor did not indicate the route of exposure to be used. We recommend either the oral or inhalation route of exposure.

Thank you for this opportunity to comment.

George Lucier, Ph.D.
Consulting Toxicologist, Environmental Defense

Richard Denison, Ph.D.
Senior Scientist, Environmental Defense