



PHYSICIANS
COMMITTEE
FOR
RESPONSIBLE
MEDICINE

5100 WISCONSIN AVENUE, N.W., SUITE 400
WASHINGTON, DC 20016
T: (202) 686-2210 F: (202) 686-2216
PCRM@PCRM.ORG WWW.PCRM.ORG

201-16528

December 21, 2006

Steven Johnson, Administrator
US Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

2007 JAN 24 AM 8:18
RECEIVED
DPPT CBIC

Subject: Comments on the HPV test plans for the Monoazo and Related Pigments

Dear Administrator Johnson:

The following comments on the Color Pigment Manufacturers Association (CPMA) test plans for Monoazo and Related Pigments are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

CPMA submitted these test plans, including one test plan for 6-Amino-4-chloro-m-toluenesulfonic acid (2B Acid (CAS RN 88-51-7) and 2-Aino-5-chloro-p-toluenesulfonic acid (C Amine) (CAS RN 88-53-9), one test plan for C.I Pigment Red 49 (Barium) (Red 49) (CAS RN 1103-38-4), and one test plan for C.I. Pigment Red 48 (Calcium) (Red 48 Calcium) (CAS RN 7023-61-2), C.I. Pigment Red 48 (Barium) (Red 48 Barium) (CAS RN 7585-41-3), and C.I. Pigment Red 52 (Calcium) (Red 52) (CAS RN 1785-29-22), in June 2006. While we support the general conclusions of the test plans, we have several suggestions for all three test plans as well as the plans individually which merit consideration by the sponsors and the EPA.

CPMA has used thoughtful toxicology in constructing these test plans, first by grouping related pigments and also by using analogous chemicals with available data that can be used to fill HPV program endpoints when the test chemicals themselves do not have available data.

Often in order to show the extent of similarity of category chemicals, sponsors may construct a table comparing the known properties of the test chemical and any analogs. CPMA has started to do this in the test plans, but perhaps an organized table, with more physicochemical, ecological, or toxicity data, if available, in a side-by-side display, would be helpful in determining the similarities of the three chemicals. Even modeled data for each property and chemical would be useful, such as that available for the Red 48/52 Pigments as stated on page 7 on that test plan.

It appears that for all of these test plans, guideline repeat dose/reproductive/developmental studies, or long-term feeding studies that measured reproductive and developmental toxicity endpoints are available for the test chemical or surrogates. However, the robust summaries would be significantly enhanced if that available data were discussed in the specific context of the developmental toxicity endpoint in the robust summaries themselves. Information pertaining to the endpoint in question should always be clearly delineated in the appropriate robust summaries to prevent any confusion in regard to actual data available and in order to prevent the duplication of animal tests.

These pigment test plans also make use of analogous pigments to fulfill HPV program endpoints. It would be helpful for reviewers of the test plan if CPMA were to somehow clarify the nomenclature of the analogs used, especially in test plan text and study summaries. For example, in the plan for Red 49, the chemicals D & C Red #9 and C.I. Pigment Red 53 appear to be used interchangeably, but it isn't clear if they are in fact the same chemical. Additionally, in the robust summaries, in some cases the chemical name is given as the test substance and in some cases the common name is listed along with the test substance. In order to properly review the available data, it would be helpful to list common and chemical names for each test substance if available.

Specific comments on the Red 48/Red 52 test plan:

- Some structural differences between the proposed analog (Red 57) and the test chemicals may lead readers to question the appropriateness of the analog, based on differences in solubilities of the chemicals. Accordingly, only the water solubility for the analog, Red 57, is given. In constructing a comparison table as we suggest above, we suggest that the sponsor generate real or modeled solubility values on the test chemicals, to support the use of the Red 57 analog. Further, in order to determine the physiological relevance of using the Red 57 analog, it may also be prudent as other sponsors have done to conduct a hydrolysis study at physiologically-relevant pH, in order to determine if the test chemicals and the analog will behave similarly in mammalian systems. Results of a similar nature might support the appropriateness of using Red 57 as analog for mammalian toxicity endpoint purposes.

Specific comments on the 2B Acid and C Amine test plan:

- We echo the sentiment of the above comment here. In order to improve the acceptability of the proposed analog, 4B Acid, we suggest that bench solubility and/or hydrolysis studies be conducted or modeled as appropriate.
- The sponsor also states that 2B Acid and C Amine are closed-system intermediates. If this is in fact the case, we suggest that CPMA provide information regarding this status.

This test plan is an example of the thoughtful toxicology that is needed to be consistent with the EPA's stated goal of maximizing the use of existing data in order to limit additional animal testing and to avoid a mere box-checking approach to the HPV program. Thank you for your attention to these comments. We may be reached at 202-686-2210, ext. 335, or via e-mail at kstoick@pcrm.org with any further questions.

Sincerely,

Kristie M Stoick, M.P.H.
Research Analyst

Chad B. Sandusky, Ph.D.
Director of Research