CPA
CHLOROBENZENE PRODUCERS ASSOCIATION
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White Paper on para-Dichlorobenzene

para-Dichlorobenzene (also known as 1,4-dichlorobenzene, p-dcb or para) has been used around the world for 40 years as an effective moth control agent to protect clothing from destructive insects. It is also used as a space deodorant, as an intermediate in the manufacture of an engineering plastic and in a number of lower volume applications. Para has been widely tested to determine whether it poses risks to humans, and in particular, to determine whether it poses a risk of cancer.

The U.S. Environmental Protection Agency (EPA) has reviewed the scientific evidence addressing the health effects of para as part of a comprehensive risk assessment. This assessment led to an EPA regulatory decision that serves as a model of sound scientific decision making. EPA is the only agency to date that has made a regulatory decision based on an assessment of the entire body of scientific data on para.

After EPA evaluated the large body of evidence in 1987, received comments from the Science Advisory Board, and obtained public comment, it decided not to regulate para as a "probable" human carcinogen. Instead, it decided a less restrictive regulation was warranted and classified the substance as only a "possible" human carcinogen. EPA thus determined that the conflicting and questionable animal studies provided only limited evidence of carcinogenicity.

EPA and its independent Science Advisory Board reviewed a large body of conflicting studies and prepared an authoritative scientific review of the evidence regarding para, which can be a useful guide for state regulators. EPA's assessment shows the following:

- Para is not genotoxic -- a factor that is very important in deciding whether animal cancer studies are relevant to humans.
- Para did not cause cancer in a rodent study using the inhalation route of exposure, which is the primary route of exposure for humans.
- When para was inserted with corn oil directly into the stomachs of mice and rats in a 1980-1982 National Toxicology Program (NTP) study, cancer was observed. However, the results were interpreted by EPA as not constituting an indication of probable carcinogenicity to humans, for the reasons summarized below.
    - The only tumors reported in the rat study were kidney tumors in the male rats, which do not appear to be relevant to humans. There were no tumors in female rats. EPA noted that these male rat kidney tumors have been linked to a protein present in male rats, but not found in humans (or at significant levels in female rats). EPA further noted with respect to these rat tumors that a mechanism of carcinogenesis of little relevance to humans "is a probable and sound scientific explanation [for these tumors] that has been developed from a large body of mechanistic and pharmacokinetic studies on this chemical."

DSW 136668

STLCOPCB4036628

- EPA also found that too high a dose of para had been injected into the rats reported as developing tumors in the NTP bioassay (above the maximum tolerated dose), making the high dose results questionable. Without the high dose results, the rat study would be negative.

- EPA concluded that the mouse liver tumors (the only mouse tumors in the NTP study) could be ascribed "diminished toxicological significance," because of the extremely high background cancer rate in the particular mouse strain used and because of potential confounding effects of the corn oil in which the para was mixed.

- EPA also questioned the method of inserting para and corn oil directly into the stomachs of the NTP test animals, a method not comparable to human exposure.

- EPA noted that chemicals structurally similar to para did not cause cancer in animal studies.

- Finally, EPA observed that there is no evidence of para-induced cancer in humans.

After weighing all this evidence and assessing the risk to humans, EPA decided not to regulate para as a "probable" human carcinogen because there was only limited evidence of carcinogenicity. Instead, based on the weight of the evidence, the federal agency concluded that para was only a "possible" human carcinogen, and established a maximum contaminant level goal for para in drinking water at 0.075 milligrams per liter -- a level which EPA concluded was "the level at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety."

The same suggestive animal studies that led EPA to classify para as a "possible" carcinogen in 1987 were used by the International Agency for Research on Cancer (IARC) that same year to classify para as a "possible" carcinogen as well. IARC did not classify para as a "probable" carcinogen. The EPA terminology for the "possible" category is Group C; the IARC terminology is Group 2B.

In 1989 the National Toxicology Program, a research arm of the Department of Health and Human Services, listed para in its *Fifth Annual Report on Carcinogens.* NTP explained that the listing of para was essentially the same as reporting the results of the NTP rodent study (which EPA had rejected as proof of probable carcinogenicity in humans) and that the listing did not reflect a consideration of the mechanism of cancer formation or other evidence regarding the relevance of the NTP study to humans. NTP has further explained that the category in the *Annual Report* in which it placed para is a list of possible or potential carcinogens based only on positive animal studies and that, in contrast, decisions by regulatory agencies involve a complete risk assessment, like the one performed by EPA.

Although all three of these agency decisions concluded that para is a "possible" carcinogen, only EPA assessed the entire body of scientific data to reach a regulatory decision on para. Its more extensive assessment of the evidence should be used as a model for sound scientific decision making by other regulatory agencies on this issue.

October 1990

DSW 136669