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**M E M O R A N D U M**

**TO:** Gary Patterson, Ph.D., Chief  
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**FROM:** Anna M. Fan, Ph.D., Chief *AMF*  
Pesticide and Environmental Toxicology Section

**DATE:** October 30, 1997

**SUBJECT:** Comments on the Department of Pesticide  
Regulation's Draft Risk Characterization  
Document for Pentachlorophenol

Thank you for the opportunity to review the Department of Pesticide Regulation's (DPR) draft risk characterization document for pentachlorophenol (PCP). The document is well-written, focuses on exposure conditions specific for California, and presents a scientifically justified assessment of health risks for humans potentially exposed to this chemical. Inclusion of the review of the published literature and a detailed discussion of relevant toxicological and epidemiological data and issues results in a comprehensive characterization of the current health risks.

In general, the Office of Environmental Health Hazard Assessment (OEHHA) staff support DPR staff's estimates of carcinogenic and noncarcinogenic risks. We provide the following comments to be considered in finalizing the report:

1. Acute Margin of Exposure (MOE) calculation

The acute MOE was derived from a developmental gavage study in rats (see page 82). The developmental "NOEL" identified in this study was 5.8 mg/kg-day based on skeletal and soft tissue anomalies observed at 15 mg/kg-day and higher doses. On page vi an acute toxicity study in rats is described and discussed from which a "NOEL" of 0.6 mg/kg is



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identified based on the decreased level of the thyroid hormone thyroxin at 1.8 mg/kg. An explanation should be provided why this study (with a NOEL lower than 5.8 mg/kg-day) was not chosen for calculating risk from acute exposure.

2. Cancer Risk Assessment

DPR based its cancer risk assessment on the endpoint hemangiosarcomas in female mice. From the same experiment, OEHHA, in preparing its Public Health Goal document for PCP, selected adenocarcinomas and carcinomas in male mice as the endpoint, which gives a five times more health-conservative estimate of the cancer risk. The rationale for using hemangiosarcomas is that this is a lethal cancer that may be more relevant to human carcinogenesis. The rationale for using adenocarcinomas and carcinomas is that it showed a more statistically significant trend. DPR estimated the cancer risk to highly exposed workers at  $7.7 \times 10^{-6}$ . If DPR had used a cancer potency based on adenocarcinomas and carcinomas in male mice, the estimated cancer risk to these individuals would have been  $4 \times 10^{-5}$ . Presenting this alternative cancer risk estimate in the risk characterization document would provide a range of potential risks that might be helpful to risk managers in developing mitigation measures.

3. Structure-Activity Relationship (SAR)

Characterization of PCP's potential for carcinogenicity could be broadened by briefly addressing carcinogenicity of other structurally related compounds such as phenol and hexachlorobenzene.

4. Weighing Evidence of Hazard

It might be helpful if DPR added a paragraph on "Weighing Evidence of Carcinogenicity," with narrative descriptors reflecting overall ranking of PCP carcinogenicity in relation to the quantitative assessment of carcinogenic risk for humans.

5. Relevance of the Available Toxicological Data to the Products on the Market

There is sufficient information provided in the draft document on the composition of different PCP products used in animal tests. However, this information is distributed throughout the text and is difficult to locate. It might be helpful if the PCP products used for testing in key toxicological studies were compared in one section to the PCP products currently on the market.

6. Additional Citation

With regard to the mechanism of action of PCP as an uncoupler of oxidative phosphorylation (page 15), recent scientific literature should be cited, such as Bartstad, A., Peyton, D. and P. Smejtek (1993), "AHA-heterodimer of a class-2 uncoupler: pentachlorophenol," *Biochem. et Biophys. Acta* 1140:262-270.

7. Chemical Structure of Related Compounds

It would be helpful if the structure of TECHQ and possibly other related compounds (such as HpCDD and HxCDD) were given on page 12. These abbreviations are used on page 14, but it is not easy to find the definitions which are on page 11.

8. NOAEL versus NOEL

DPR may consider using "NOAEL" instead of "NOEL" when toxicological endpoints refer to adverse effects, for example, malformations.

9. Footnote

On page 20 (footnote), replace "connote" with "denote."

Gary Patterson, Ph.D., Chief  
October 30, 1997  
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We hope these comments are helpful to you in finalizing the risk characterization document for PCP. If you have any questions, please contact me or Dr. Michael DiBartolomeis at (510) 540-3063.

cc: Michael J. DiBartolomeis, Ph.D.  
William Vance, Ph.D.