Interoffice Communication

To T. G. Grumbles, Houston

From W. D. Broddle, Ph.D., Ponca City

Date October 7, 1983

Subject PROTOCOL DESIGNS FOR ANIMAL SKIN IRRITATION AND INHALATION STUDIES

Action items from the last Conoco Chemical's Product Toxicity Advisory Committee meeting required that I address the above two issues.

Issue No 1: Should rabbit skin irritation studies involve 4 hours or 24 hours of occluded exposure?

At least 95% of all Conoco data involves 24 hours exposure because consumer products generally were tested according to methods applicable to the Federal Hazardous Substance Act (CPSC also endorses 24 hours). The Department of Transportation and recently EPA and OECD switched from a 24-hour to a 4-hour exposure interval. Both Shell Oil and Haskell Laboratories use the 24-hour exposure, even though the irritation readings are usually double that of the 4-hour exposure.

Thus, my recommendation is to continue using the 24-hour exposure for the following reasons:

a) Most Conoco data is from 24-hour exposure and this serves as a historical control.

b) Several important corporate toxicology laboratories are continuing to use 24-hour exposure, especially for consumer-type products.

c) The 24-hour exposure complies with FHSA and would provide data useful for DOT labelling.

Issue No. 2: What concentration level should be used for the 4-hour acute inhalation studies?

Federal agencies consider acute inhalation toxicity to be insignificant and/or do not require product labelling or employee training for chemicals having the following median lethal concentrations (LC_{50}):

	LC_{50}, mg/l
FHSA	> 200
DOT	> 10
EPA	> 20
OSHA	> 20
Haskell Laboratories	> 40
ANSI	> 20
NIOSH	> 100
EEC	> 20
U.N.	> 10

Dr. Roger Keefe, Shell Oil, informed me that they do only limited acute inhalation assays on surfactant materials; instead, Shell toxicologists predict potential inhalation hazards based on prior data of similar chemicals, probable human exposure and physical properties (v.p., b.p., etc.). An acute inhalation study is only done if the above information is not adequate.

Thus, I would recommend the following procedure for determining whether an acute inhalation study is needed for a Chemical's material:

a) The CCPTAC members should evaluate whether acute animal inhalation data is needed to more adequately predict employees and customers health hazards based on historical data, probable human exposure, and physical properties (v.p., etc.) of similar chemicals.

b) If an acute inhalation study is deemed necessary, the following studies should be done:

   i. A pilot study should be conducted to determine whether a minimum chamber concentration of 2 mg/l can be generated for the material. If 2 mg/l is feasible, initiate a 4-hour exposure study with five rats per sex. If at least 2 mg/l cannot be generated, the CCPTAC members must decide whether further testing is needed. Note, the 2 mg/l level was selected because previous testing has shown this concentration to be nearly the maximum attainable in the contract laboratories and 2 mg/l produces a very dense aerosol that sometimes limits visibility through the chamber.

This concludes my remarks, but we can discuss this at the CCPTAC meeting on October 11, 1983.

W. D. Broddle, Ph.D.
Senior Toxicologist

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cc: E. L. DeWhitt, Jr., Ph.D., Ponca City
O. C. Kerfoot, Ponca City
W. L. Groves, Ponca City
J. L. Riddle, Ph.D., Ponca City