

ILSI RISK SCIENCE INSTITUTE**FAXED**
7/15/96

International Life Sciences Institute

Robert Venezia
Chemical Manufacturers Association
1300 Wilson Blvd.
Arlington, VA 22209

July 15, 1996

VIA FACSIMILE

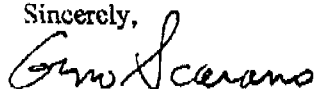
Dear Mr. Venezia:

It was a pleasure speaking with you this morning. Per our conversation, attached are a fact sheet and a list of working group members for our project on the Use of Non-Tumor Data in Cancer Risk Assessment. I am happy to hear that the CMA Vinyl Chloride Health Committee has expressed an interest in this activity. Please share this information with the Committee.

Genotoxicity data have been used historically as part of hazard identification (i.e., to classify carcinogens as genotoxic or nongenotoxic) but not as part of the dose-response assessment to quantitatively estimate cancer risk. The current scientific and regulatory climate is such that the use of endpoints other than tumors to quantitatively estimate cancer risk is on the horizon. This project was initiated to address the question of whether and how genotoxicity data should be used as part of a cancer risk assessment. A component of the project includes the development of cancer risk assessments for four chemicals using genotoxicity and other data, and following the draft revisions to the U.S. EPA cancer risk assessment guidelines. Partial funding for the project has been provided by the American Petroleum Institute (API) and the U.S. EPA. We are seeking further funding from a variety of sources from both the private and public sectors.

At your request, I would be pleased to submit a full proposal to the CMA Vinyl Chloride Health Committee. Please call me at 202-659-3306 if you have any questions.

Sincerely,



Gino Scarano, Ph.D.
Senior Scientist

cc: Dr. Jeffery Foran, Executive Director, RSI

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FACT SHEET

Using Non-Tumor Data in Cancer Risk Assessment

The current scientific and regulatory climate is such that the use of data on additional endpoints to supplement and refine cancer risks obtained using tumor incidence is on the horizon. This project was initiated to address the question of whether and how genotoxicity and other data should be used as part of a cancer risk assessment.

A small working group of distinguished scientists was convened by the ILSI Risk Science Institute (RSI). The working group agreed that the qualitative and quantitative inclusion of endpoints other than tumors in a cancer risk assessment is an issue worthy of investigation. Examples of non-tumor endpoints that might be utilized include genotoxicity data (mutagenicity, DNA adduct formation, etc), cell proliferation data, and cell death data. The working group suggested that the goal of this project - to determine how to use genotoxicity and other ancillary data along with tumor data in a cancer risk assessment - should be pursued initially through the use of case studies. These case studies will likely involve the development of cancer dose-response relationships for four substances: aflatoxin, benzene, butadiene, and vinyl chloride. Each case study may include the following:

1. A cancer potency estimate derived following the existing U.S. EPA cancer risk assessment guidelines.
2. An estimate derived following the proposed revisions to the U.S. EPA cancer risk assessment guidelines using the LED_{10} for tumor response (lower limit on the dose causing a 10% tumor response) as the "point of departure" (i.e., the starting point from which to extrapolate to the low dose-response region).
3. An estimate derived by choosing a point of departure from endpoints other than tumors (i.e., DNA adduct formation, *in vivo* mutation data, cell proliferation data, etc.). The endpoint must be mechanistically linked to the observed tumor response.
4. An estimate derived by using biologically-based dose response modeling, if adequate data are available.

Individuals will be identified who will be asked to generate first drafts of the case studies by the fall of 1996. Upon completion of the drafts, authors, reviewers and the working group will meet (likely in late 1996/early 1997) to review the case studies and to discuss their implications for quantitative cancer risk assessment. The product of this project is anticipated to be a report published in the peer-reviewed literature or a stand-alone monograph on the quantitative application of genotoxicity data in cancer risk assessment. RSI staff will manage the project and coordinate preparation of the final report.

For more information on this project, please call Dr. Gino Scarano (202-659-3306).

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CMA 118953

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