BORDEN SERVICES COMPANY
"QUALITY BUSINESS SOLUTIONS"

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Hasmukh Shah, Ph.D.
Manager, Vinyl Chloride Panel
Chemical Manufacturers Association
1300 Wilson Blvd.
Arlington, VA 22209

Dear Has:

ILSI's RSI group has initiated a project to use genotoxicity data in cancer risk assessment. Vinyl Chloride will be one of the case studies. (See attached)

Our Vinyl Chloride Health Committee may want to discuss this, if they haven't already, in the most recent conference call which I missed.

Sincerely,

Mark A. Gruenwald
Associate Director

/cac

Attachment

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*on essential elements, dose selection in chronic rodent bioassays, microbial risk assessment, human variability, and other issues is completed and disseminated.*

*In this issue of* RSI Update *we highlight two new RSI projects on genotoxicity and reproductive/developmental toxicity. These projects, like many others at RSI, should provide benefits to individuals and organizations seeking improved, balanced, and reliable scientific input on issues of public interest and concern. We would like to hear from you whenever you draw on the results of RSI projects, for whatever reason. When our work is of value to you, your feedback in turn will be of great value to us.*

*Jeffery A. Foran, Ph. D.*

## New Projects

### *Use of Genotoxicity Data in Cancer Risk Assessment*

Historically, genotoxicity data have been used 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 RSI project was initiated to address the question of whether and how genotoxicity data should be used as part of a cancer risk assessment.

A small working group of distinguished scientists convened by RSI agreed that the qualitative and quantitative use of endpoints other than tumors (DNA adduct formation, cell proliferation data, in vitro and in vivo genotoxicity data including mutagenicity, among others) in a cancer risk assessment is an issue worthy of investigation. The working group suggested that the goal of this project—to determine how to use genotoxicity and other information in a cancer risk assessment—should be pursued initially through the use of case studies. These case studies will involve the development of cancer risk estimates for four substances: aflatoxin, benzene, butadiene, and vinyl chloride. Each case study will include the following:

- a cancer risk estimate derived following the 1986 U.S. EPA cancer risk assessment guidelines,
- a cancer risk estimate derived following the proposed revised U.S. EPA cancer risk assessment guidelines using the $LED_{10}$ for tumor response (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), and
- a cancer estimate derived by choosing a point of departure from endpoints other than tumors (i.e., DNA adduct formation, in vivo mutation data, etc.) that are mechanistically linked to the observed tumor response.

Expert scientists identified by the working group will be asked to generate first drafts of the case studies by September 1996. Upon completion of the drafts, authors, reviewers, and the working group will meet (likely in late 1996) 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 as a stand-alone monograph on the quantitative application of genotoxicity data in cancer risk assessment. Contact: Dr. Gino Scarano at RSI.

### *Methods for Assessing Sperm Parameters*

Regulatory agencies are in the process of revising test guidelines for reproductive toxicity studies, and are proposing the addition of assessments of sperm parameters including motility, morphology, and counts. While these assessments can provide valuable information for the determination of potential reproductive toxicity, the methods for conducting the assessments have not been well developed. In addition, there is disagreement about the optimal collection site for obtain-