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August 1, 1996

VIA FACSIMILE/FEDERAL EXPRESS

Mr. W. Caffey Norman, III
Patton, Boggs & Blow, L.L.P.
2550 M Street, N.W.
Washington, DC 20037
PH: (202) 457-5270

RE: Proposal CL96-0145 to Evaluate 1,1,2-Trichloroethane with Regard to a Proposed HAP Test Rule

Dear Mr. Norman,

The ChemRisk® Division of McLaren/Hart (ChemRisk®) is pleased to submit this brief letter proposal to Patton, Boggs & Blow, L.L.P. (Counsel) in response to a verbal request for proposal from you (Mr. Caffey Norman) on Tuesday, July 30, 1996. It is our understanding that Counsel is seeking consulting services on behalf of certain producers of 1,1,2-trichloroethane (1,1,2-TRI) to evaluate the existing toxicological literature on 1,1,2-TRI as a means of identifying data and/or approaches suitable for satisfying requirements specified in a recently proposed Hazardous Air Pollutant (HAP) Test Rule (61 Fed. Reg. 33178). More specifically, Counsel would like to know the feasibility of using physiologically based pharmacokinetic (PBPK) modeling as a means of filling "data gaps" (i.e., converting oral exposure data to equivalent inhalation exposure data) for 1,1,2-TRI, as well as possibly developing scientific arguments to the effect that extensive testing may not be needed for 1,1,2-TRI due to the possible existence of similar studies found during the review that may not necessarily meet every requirement specified in the proposed rule but may be sufficient none-the-less. It is further understood that the initial evaluation must be completed by September 18, 1996 for presentation to the 1,1,2-TRI producers. The end objective of this first phase of work will be to submit to the USEPA (by October 24, 1996) a proposal describing approaches and/or additional studies regarding 1,1,2-TRI that are deemed appropriate by ChemRisk® and the 1,1,2-TRI producers for fulfilling the requirements of the proposed test rule.

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Any submittal to the USEPA will occur only after a meeting between ChemRisk® and the 1,1,2-TRI producers in which the results of the initial evaluations are discussed and approved. Since this work will occur in a phased manner, only the costs associated with the initial review and those required to attend a one day meeting in Washington, DC are included in this proposal. Following the meeting, a more clear understanding of the proposal to the USEPA (if any) should be identified by the 1,1,2-TRI producers and separate costs for preparing this submittal can then be developed, if necessary.

SCOPE OF WORK

To meet the initial requirements of this project, the following two tasks are proposed:

Task 1: Literature Search/Retrieval/Review

Task 2: Prepare a Brief Summary Report and Present Results at Meeting

For Task 1, ChemRisk® will perform the following activities:

- Review proposed HAP Test Rule and identify key issues/data gaps for 1,1,2-TRI
- Conduct literature search using TOXLINE (contains 16 databases)
- Identify key manuscripts and retrieve
- Review key manuscripts with respect to proposed HAP Test Rule
- Identify possible approaches and studies appropriate for filling data gaps.

For Task 2, ChemRisk® will:

- Prepare a brief summary report that describes the findings from Task 1 and includes recommendations for the 1,1,2-TRI producers
- Participate in a one day meeting in Washington, DC to present results to the 1,1,2-TRI producers.

STAFF QUALIFICATIONS

It is proposed that Dr. Michael Gargas of ChemRisk® serve as a Project Manager and conduct the literature reviews and evaluations, prepare the summary report, and present the findings to the 1,1,2-TRI producers. Additional administrative and junior scientific staff will be utilized only as required to assist Dr. Gargas. Dr. Gargas has extensive experience in developing PBPK models

for volatile chemicals for use in risk assessment and for filling data gaps, as well as extensive interactions with regulatory agencies on behalf of private sector clients (see attached resume). A summary of noteworthy publications and project experience follows:

- Dr. Gargas has published several papers (enclosed) on approaches required for developing PBPK models for volatile chemicals, including 1,1,2-TRI (Gargas *et al.*, 1990, *Inh. Tox.*, 2, 293-319; Gargas *et al.*, 1988, *Toxicol Appl Pharmacol*, 99, 344-353), as well as special techniques for assessing multiple routes of exposure (Gargas, 1990, *J Am Coll Toxicol*, 9, 447-453). Dose route extrapolations may prove useful for filling data gaps for 1,1,2-TRI. Although possibly not readily apparent, a PBPK model for 1,1,2-TRI was developed for the rat in the studies cited above.
- Dr. Gargas has published a paper on estimating certain chemical-specific parameters needed for developing PBPK models in which 1,1,2-TRI data was used (see enclosed Gargas *et al.* 1988, *Toxicol Lett*, 43, 235-256).
- Dr. Gargas and colleagues are currently involved in a project on behalf of the Halogenated Solvents Industry Alliance in which a PBPK model for dichloromethane is being used to fill experimental data gaps identified by the ATSDR without the need for expensive additional studies. This project is being conducted jointly with the ATSDR and is intended to result in a manuscript describing this approach. This approach seems quite relevant to the 1,1,2-TRI evaluation described in this proposal.
- Dr. Gargas and ChemRisk® colleagues completed a project on behalf of the Trichloroethylene Users Group in which a PBPK model was used to demonstrate that the existing SF for trichloroethylene as determined by the USEPA was 10-100-fold overly conservative. This compound is currently being re-evaluated by the Agency.
- Dr. Gargas and colleague presented a refined cancer assessment on vinyl chloride to the USEPA on behalf of CMA. The PBPK modeling approach demonstrated that the existing cancer SF used by the Agency was between 150-1500-fold too conservative. USEPA has withdrawn vinyl chloride from HEAST and is in the process of re-evaluating the SF using the approaches as described in a manuscript that has recently been accepted for publication in *Toxicology and Applied Pharmacology*. (CMA contact: Hasmukh Shah).
- Dr. Gargas is currently serving as a member of the RfD/RfC Working Group for ethylene glycol butyl ether (EGBE), on behalf of the CMA. A PBPK model will be combined with the Bench Mark Dose methodology to determine a new RfD and RfC for EGBE. It is anticipated that this process will result in regulatory criteria between 10 and 100-fold less conservative than that calculated by more standard means. (CMA contact: Susan Lewis).

- Dr. Gargas and colleagues are currently involved with the CMA sponsored risk assessment project on butadiene. A PBPK model describing the dosimetry of butadiene has been refined by ChemRisk® and will be used to propose an alternate SF and risk assessment aimed at countering the assessment anticipated from the USEPA. (CMA contact: Betty Moran).
- Dr. Gargas prepared an evaluation of the cancer SFs for acrylonitrile on behalf of BP Chemicals. This evaluation included a critique of the existing SFs and a proposed refinement that relies on a PBPK modeling approach. The results of these studies are intended to persuade the USEPA to re-evaluate their existing SFs for this compound.
- Dr. Gargas has recently reviewed, critiqued, and will give expert testimony on behalf of the Color Pigments Manufacturer's Association regarding risk assessments performed by the USEPA and reported in the Federal Register on hazardous waste streams specific to the pigment industries. This evaluation uncovered numerous inconsistencies and mistakes made by the Agency and their contractors.

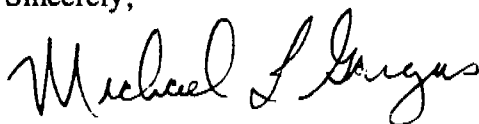
It should also be noted that ChemRisk® already possesses the PBPK modeling code for describing 1,1,2-TRI kinetics in the rat and has extensive optimization software (SIMSOLV®) in-house that may be required for refining future PBPK models for this chemical.

COSTS

It is proposed that Tasks 1 and 2 of this project will be completed for a Lump Sum/Fixed Price cost of \$9,500 in accordance with the enclosed Terms and Conditions. If the scope of work, contract and costs are agreeable to Counsel, please sign and return the enclosed Project Authorization Form so ChemRisk® may begin this important project.

I look forward to working with you on this project. Please do not hesitate to call if you have any questions.

Sincerely,



Michael L. Gargas, Ph.D.
Principal Health Scientist

MLG/rmh

Enclosures

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