

Molecular Dosimetry of Vinyl Chloride

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Research Report and Budget Request

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Research Report

Year 1 (1996-1997 Budget)

The laboratory portion of this project began this spring by sending teams of 3-4 of our laboratory personnel to New Jersey to collect tissues and liver cell types from rats that were exposed to 0, 10, 100, or 1100 ppm vinyl chloride (VC) for 1-20 days. Procedures were rather difficult during the first set of necropsies, but went much better for subsequent procedures after we sent an additional person and shipped up our own centrifuge. We were able to harvest good yields of cells and tissues for the experiment as a whole. It was unfortunate that the [^{14}C]-VC experiment was the first to come off, as this was the least smooth running of all. Even so, adequate numbers of cells were able to be harvested to meet our objectives.

We are currently isolating DNA from the 4-week hepatocytes, as these are the most plentiful cells. A new immunoaffinity chromatograph-GC/MS method is replacing our previous low pressure strong cation exchange-GC/MS method for the analysis of ethenoguanine. After this shakedown, we will begin working with the [^{14}C]-VC liver cells. Parallel to this effort will be the analysis of urines for excretion of ethenoadenine using immunoaffinity chromatography and LC-MS. Likewise, we will begin examining the major DNA repair pathway for VC DNA adducts including methyl purine glycosylase (MPG) and AP-endonuclease (AP).

Year 2 (1997-1998 Budget)

During Year 2 we will continue to work up the many samples collected in New Jersey. Priority will be given to establishing exposure response relationships, identifying cell-specific differences in DNA repair, determining effects of exposure on endogenously formed DNA adducts, and doing initial studies related to incorporating these data into a PB/PK risk assessment model. We are also developing new methods for the $^1\text{N},2$ -ethenoguanine adduct, which has never been characterized *in vivo*.

Year 3 (1998-1999)

We expect to complete this research during the third year. At this time, we will have analyzed all of the relevant tissues and cells for DNA adducts, will establish the role of defects in DNA repair and the effect of induction of DNA repair on exogenous and endogenous DNA adducts, and incorporate these data into a biologically-based risk assessment model.

Research Budget

My understanding of the funding available for this project is that between \$50,000-75,000 will be available per year for three years. The cost of this research project will greatly exceed this, with personnel costing ~\$140,000 this year. However, since VC has been and continues to be one of the chemicals that we are investigating under our NIEHS Superfund Basic Research Program Project, I can offset part of the cost, providing that the CMA agrees to share acknowledgement with NIEHS. Should we need additional [¹⁴C]-VC exposures, they can be done at UNC, since the EOIC has agreed to fund new research that includes funds to set up a small nose-only exposure system for similar studies on ethylene oxide. Thus, we can maximize our future research dollars to fund critical studies. We need to move forward as fast as possible, as the EPA has already developed a new risk assessment on VC that suggests increased risk compared to their previous estimates. The new assessment incorporates metabolism data, but not information on DNA adducts or DNA repair. Finally, we incurred major expenses during the four trips to New Jersey that were not included in Year 1's budget. These are listed under sample collection in the budget.

1997-1998 Budget request

Sample collection		\$20,695
Travel expenses	\$8172	
Shipping	752	
Supplies	11771	
Research budget		\$66,500
Personnel	35000	
Supplies	24000	
LC-MS/MS time (\$25/hr)	2500	
Travel	3000	
Equipment maintenance agreements	2000	
TOTAL BUDGET REQUEST		\$87,195