

# REQUEST FOR APPROVAL TO RELEASE PROPRIETARY TECHNICAL INFORMATION



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|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>1 Complete Section 1. Give this form and 6 copies of your manuscript to your Research Manager. Allow two weeks for processing.</p>                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>TITLE OF MANUSCRIPT: VINYL CHLORIDE METABOLISM AND THE STIMULATION OF SPLENIC LYMPHOCYTE TRANSFORMATION IN MICE</p>                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>AUTHOR(S):</p>                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>TO BE PRESENTED OR DISCLOSED AT:<br/>Give meeting name, place, city: ASPET - 1978, Houston, Texas or IUPHAR - 1978, Paris, France</p>                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>TO BE SUBMITTED FOR PUBLICATION IN:</p>                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| RELATED PATENTS OR DISCLOSURES                                                                                                                                                                                                                                                                                                                             | RELATED PRODUCTS OR PROCESSES                                                                                                                                                                                                                                                                                                                                              | RELATED REPORTS OR PUBLICATIONS                                                                                                                                                                                                                                                                                                                                                                |
| None                                                                                                                                                                                                                                                                                                                                                       | Vinyl Chloride                                                                                                                                                                                                                                                                                                                                                             | In preparation.                                                                                                                                                                                                                                                                                                                                                                                |
| <p>SUGGESTIONS BY AUTHOR FOR POSSIBLE REVIEWERS OF THIS MANUSCRIPT</p>                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>FOR LEGAL ASPECTS (Include Patentability)</p> <p><input type="checkbox"/> INVENTIONS MANAGEMENT</p> <p><input type="checkbox"/> PATENT DEPARTMENT</p> <p><input type="checkbox"/> TRADEMARK SECTION (PATENT)</p> <p><input checked="" type="checkbox"/> LEGAL DEPARTMENT</p> <p><input type="checkbox"/> OTHER</p> <p>NAME _____</p> <p>DEPT. _____</p> | <p>FOR BUSINESS ASPECTS (Include product, the Best of Cost)</p> <p><input checked="" type="checkbox"/> PRODUCT DEPARTMENT</p> <p>NAME Hugh Farber</p> <p>DEPT. Inorganic Chemicals</p> <p><input type="checkbox"/> BUYER</p> <p>NAME _____</p> <p>DEPT. _____</p> <p><input checked="" type="checkbox"/> OTHER</p> <p>NAME Earl Smith</p> <p>DEPT. Inorganic Chemicals</p> | <p>FOR TECHNICAL ASPECTS (Include Environmental Impact)</p> <p><input checked="" type="checkbox"/> HEALTH &amp; ENVIRONMENTAL RES.</p> <p>NAME V. K. Rowe</p> <p>DEPT. Toxicology Research</p> <p><input type="checkbox"/> TECHNOLOGY CENTER</p> <p>NAME _____</p> <p>DEPT. _____</p> <p><input checked="" type="checkbox"/> OTHER</p> <p>NAME T. Torkelson</p> <p>DEPT. Corporate Medical</p> |
| <p>QUESTIONS CONCERNING THIS MANUSCRIPT ARE TO BE DIRECTED TO</p>                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>NAME: R. P. Sharma DEPT: Health &amp; Environmental Research 636-0251</p> <p>BUILDING: 1803 CITY: Midland DATE SUBMITTED: 8-16-77</p>                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>2 Complete Section 2. Secure appropriate departmental approval. Send 1 reviewer, then send this form and six copies of it to CENTRAL REPORT INDEX, BUILDING 566, MIDLAND.</p>                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>DEPARTMENTAL APPROVAL FOR RELEASE</p> <p>I have read this manuscript and approve its release at this time as being in the best interests of The Dow Chemical Company.</p>                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>DEPARTMENTAL SELECTION OF REVIEWERS (See author's suggestions above)</p>                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>APPROVED FOR PUBLICATION ON THE DOW CHEMICAL CO.</p>                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>3 Complete Section 3. Scan the attached manuscript and give your comments and recommendations here. Your remarks will be considered by the Research Director named below and final approval for release will be given by him. Send this form and the manuscript to CENTRAL REPORT INDEX, BUILDING 566, MIDLAND.</p>                                     |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
| COMMENTS                                                                                                                                                                                                                                                                                                                                                   | APPROVE                                                                                                                                                                                                                                                                                                                                                                    | RECOMMENDATIONS                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                            | FOR PUBLICATION ON THE DOW CHEMICAL CO.                                                                                                                                                                                                                                                                                                                                    | <p><input checked="" type="checkbox"/> RELEASE</p> <p><input type="checkbox"/> RELEASE AFTER CHANGES</p> <p><input type="checkbox"/> DO NOT RELEASE</p>                                                                                                                                                                                                                                        |
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| <p>RECEIVED</p> <p>SEP 5 1977</p>                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                |
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VINYL CHLORIDE METABOLISM AND THE STIMULATION OF  
SPLENIC LYMPHOCYTE TRANSFORMATION IN MICE

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We have previously reported that the exposure of mice to vinyl chloride (VC) caused an increase in lymphocyte transformation in splenic cultures and also increased the responsiveness of these lymphocytes to phyto-mitogens. We investigated the role of VC metabolism in these phenomena. Incubation of mice splenic cultures in a VC-atmosphere (1000 ppm) failed to produce any effect. A metabolite of VC, thiodiglycolic acid, produced effects similar to VC exposure in vivo and also increased lymphocyte transformation when added to splenic cultures in vitro. Another metabolite of VC, N-acetyl-S-(hydroxyethyl)cysteine, did not stimulate lymphocyte transformation after in vitro addition. Simultaneous administration of ethanol or phenobarbital with VC decreased this stimulating property. Phenobarbital may have produced its effect either by increasing the hepatic binding of reactive VC metabolite, thus reducing its effective concentration, or by increasing the metabolism of VC through a different pathway. Ethanol has been a known inhibitor of VC metabolism. The results suggested that VC was metabolized to products responsible for increased mitotic activity in splenic lymphocytes. In view of the previous reports that vinyl chloride disease may be an immunological disorder, the evaluation of peripheral lymphocytes in VC-exposed workers is suggested.

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