MEMORANDUM

SUBJECT: Atrazine, Probable Cause for Concern with Respect to Adenocarcinomas in Female Rats.

FROM: Herbert Lacayo, Statistician Mission Support Staff Toxicology Branch/HED (TS-769)

TO: Henry Spencer, Ph.D. Section VII Toxicology Branch/HED (TS-769)

THRU: Bertram Litt, Leader, Statistical Team Mission Support Staff Toxicology Branch/HED (TS-769)

THRU: Reto Chief, Chief Mission Support Staff Toxicology Branch/HED (TS-769)

At your request a cursory examination was done of EPL's summary tables (i.e., chronic rat study for Atrazine sponsored by Ciby-Geigy). We found that the adenocarcinoma data (Fig. 1) exhibits a tumor-dose trend significant at less than .00025 using the Cochran-Armitage test (Chi Sq. = 16.6, 1 deg. of freedom)

FIG. 1

Adenocarcinomas of the Mammary Glands in Rats

<table>
<thead>
<tr>
<th>Dose (ppm)</th>
<th>0</th>
<th>10</th>
<th>70</th>
<th>500</th>
<th>1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBA¹</td>
<td>15</td>
<td>15</td>
<td>26</td>
<td>27</td>
<td>35</td>
</tr>
<tr>
<td># Examined</td>
<td>66</td>
<td>64</td>
<td>68</td>
<td>65</td>
<td>64</td>
</tr>
</tbody>
</table>

¹ TBA: Tumor Bearing Animal
MEMORANDUM


FROM: Henry Spencer, Ph.D. Section 7 Toxicology Branch Hazard Evaluation Division (TS-769)

TO: Robert Taylor, Product Manager #25 Herbicide Branch Registration Division (TS-767)

THRU: Albin B. Kocialski, Ph.D. Section Head, Section 7 Toxicology Branch Hazard Evaluation Division (TS-769)

Background:

A previously completed IBT study was found by the registrant to suggest an oncogenic response. However, as the study was subsequently questioned as to its validity, the registrant, Ciba-Geigy Limited, commissioned the present study.

Comments:

There was an apparent increased incidence of both adenocarcinomas and fibroadenomas of the mammary tissues in female rats as reported by the registrant. Although these effects occurred only at the 1000 ppm dosage level (HDT), and the report is of an interim nature, Toxicology Branch considers the interim findings sufficient to warrant the close scrutiny of any additional requests for tolerances until the full study has been submitted and reviewed.
The interim findings reported by the registrant with respect to mammary tumors in females were as follows.

<table>
<thead>
<tr>
<th>Pathologic Findings</th>
<th>Historic Control</th>
<th>Concurrent Control ppm</th>
<th>10 ppm</th>
<th>70 ppm</th>
<th>500 ppm</th>
<th>1000 ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>3/75</td>
<td>0/22</td>
<td>1/5</td>
<td>1/1</td>
<td>0/5</td>
<td>8/25</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>3/75</td>
<td>0/22</td>
<td>0/5</td>
<td>1/1</td>
<td>1/5</td>
<td>3/25</td>
</tr>
</tbody>
</table>