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EVALUATION OF ETHYLENIMINE BY THE DOMINANT LETHAL TEST	6
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<i>L.V. Johnston</i>	☐ INTERIM ☒ FINAL	☒ NEW ☐ REVIEW

DESCRIPTIVE SUMMARY WITH CONCLUSIONS:

(Include in this space references to data books, and to earlier related reports, patents and publications.)

The dominant lethal effect of ethylenimine (EI) was evaluated by use of a modified screening procedure of Epstein and Shafner.⁽³⁾ The mutagenic index of EI was lower than the corresponding control value in each week for the duration of this study. Statistical analysis indicated this difference was significant ($p < 0.05$). Thus, under the conditions of this test procedure, the results do not indicate that EI is mutagenic.

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CRI NUMBER

EVALUATION OF ETHYLENIMINE BY THE DOMINANT LETHAL TEST

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H. N. Edwards and T. G. Pullin

INTRODUCTION

The dominant lethal test, a method of mutagenicity testing in mammals, has been recommended by the MRAK Commission⁽¹⁾ as part of required toxicological investigations for clearance of pesticides. This test may also be incorporated into the group of required toxicological investigations of chemicals in the proposed Toxic Substances Act.⁽²⁾ Epstein and Shafner⁽³⁾ and Partington and Bateman⁽⁴⁾ have already tested several environmental pollutants and chemicals using this procedure. According to Schwetz et al,⁽⁵⁾ the most readily detectable mutation in the mouse is the dominant lethal which manifests itself as in utero lethality of embryos developing from gametes in which the mutation has arisen. This procedure reflects mutagenic activity directly induced in male germ cells and excludes systemic drug effects in females. This data may provide one of the simplest means of relating animal induced mutagenic effects to humans. Although extrapolation of data from mice to man involves risk because of the species differences between the two, this technique offers a potential screen for chemical mutagens to which workmen are exposed. This paper presents the results of the screening of one such chemical.

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MATERIALS AND METHODS

The screening procedure described by Epstein and Shafner⁽³⁾ with the exception of two modifications was used to test

ethylenimine (EI; The Dow Chemical Company, Texas Division) on Dublin ICR mice (Flow Laboratories, Dublin, Virginia). The male mice were given a single intraperitoneal injection of 3.8 mg EI/kg body weight. The control group was given the solvent, tricapylin, intraperitoneally. The modifications to the procedure consisted of the use of proven male breeders rather than breeders of unknown mating history and the extension of the tests for a period of nine consecutive weeks after injection rather than eight weeks.

Statistical analyses of the data were conducted under the direction of Dr. E. B. Whorton, Jr., Associate Professor and Director, Medical Education Computer Center, Preventive Medicine and Community Health Biostatistics, University of Texas Medical Branch, Galveston, Texas.

RESULTS

A tabulation of the results of this study is presented in Table 1. The mutagenic index of EI was lower than the corresponding control value in each week for the duration of this study. Statistical analysis using Analysis of Variance procedures (Table 2) indicated this difference was significant ($p < 0.05$). However, this analysis showed there was no significant trend over time and no significant interaction between time and chemical treatment.

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SUMMARY AND CONCLUSIONS

The dominant lethal effect of ethylenimine (EI) was evaluated by use of a modified screening procedure of Epstein and Shafner.⁽³⁾ The mutagenic index of EI was lower than the corresponding control

value in each week for the duration of this study. Statistical analysis indicated this difference was significant ($p < 0.05$). Thus, under the conditions of this test procedure, the results do not indicate that EI is mutagenic.

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TABLE 1
IMPLANTS, RESORPTIONS AND MUTAGENIC INDEX
IN FEMALE MICE BRED WITH EI-TREATED MALES

<u>Week After Administration</u>	<u>Females Bred</u>		<u>Implants</u>		<u>Resorptions</u>		<u>Mutagenic Index**</u>	
	<u>Control</u>	<u>EI*</u>	<u>Control</u>	<u>EI</u>	<u>Control</u>	<u>EI</u>	<u>Control</u>	<u>EI</u>
0 (pre-treatment)	75	45	503	263	22	11	4.37	4.18
1	57	15	385	101	23	3	5.97	2.97
2	87	24	638	224	27	5	4.23	2.23
3	87	24	629	238	36	12	5.72	5.04
4	72	15	590	135	35	6	5.93	4.44
5	69	15	476	86	28	2	5.88	2.33
6	66	15	519	103	25	2	4.82	1.94
7	57	14	333	35	14	1	4.20	2.86
8	57	15	449	146	14	3	3.12	2.05
9	42	15	306	117	11	3	3.59	2.56
TOTAL (9 weeks)	594	152	4,325	1,185	213	37	4.92	3.12

*EI (Ethylenimine; The Dow Chemical Company, Texas Division)

**MI = $\frac{\text{Resorptions}}{\text{Total Implantations}} \times 100$

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TABLE 2

ANALYSIS OF VARIANCE OF DOMINANT LETHAL DATA OF
FEMALE MICE BRED WITH EI-TREATED MALES

<u>Source</u>	<u>df</u>	<u>SS</u>	<u>MS</u>	<u>F ratio</u>	<u>P value</u>
Chemical Treatment	1	534.896	534.896	4.746	<0.05
Time	8	266.149	33.268	0.295	>0.25
Chemical Treat- ment X Time	8	138.394	17.299	0.153	>0.25
Error	482	54312.812	112.682		