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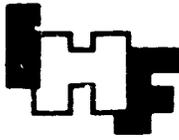
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BEHQ-0993-1063



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INDUSTRIAL HEALTH FOUNDATION, INC.

A NONPROFIT ORGANIZATION FOR THE ADVANCEMENT OF HEALTHFUL WORKING CONDITIONS

34 PENN CIRCLE WEST • PITTSBURGH, PA 15206 • (412) 363-6600

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September 23, 1993

EPA-OTS



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BEHQ-0993-1063

FEDERAL EXPRESS

Document Control Officer
Chemical Information Division
Office of Toxic Substances
Room E-108
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

93 SEP 23 11:55

RE: Notice of Substantial Risk Under TSCA 8(e) for Methylenechloroform (MECO) when Administered by Inhalation to Rats and Mice in an Oncogenicity Study. Addendum to Notices Submitted on May 28, 1992 and April 5, 1993 on Nasal Pathology from a 4-week Exposure.

EPA Docket No.: BEHQ-0990-1063

Attention: Section 8(e) Coordinator

Dear Sir:

The Industrial Health Foundation, Inc. (IHF) submits this notification as agent for and in behalf of the sponsors of the subject study (AlliedSignal, Inc.; Akzo Chemicals, Inc.; Huls America, Inc.; Aceto Corporation; Dussek Campbell, Ltd.; Troy Chemical Company; and Mooney Chemicals, Inc.) in accordance with Section 8(e) of the Toxic Substances Control Act and EPA's statement of Interpretation and Enforcement Policy, 43 Fed. Reg. 1110 (March 16, 1978). The described testing herein was initiated in response to the EPA Final Test Rule for Methylenechloroform (MECO) under section 4 of TSCA (Fed. Reg. 54(176), 37799, September 13, 1990). This study was performed to evaluate the potential for toxic and oncogenic effects of MECO when administered by inhalation to rats for 24 months and mice for 18 months.

The submissions of May 28, 1992 and April 5, 1993 indicated degenerative changes to the olfactory epithelium at 12 and 18 months for mice exposed to MECO. As a result of those findings, the sponsors authorized performance of histopathological evaluation of the nasal turbinates of mice exposed for 4-weeks to 25, 100 and 400 ppm. In the subject 4-week study, these tissues were not initially evaluated as the study was performed primarily as a range-finding study of sublethal doses for the 18-month study and the emphasis was on clinical signs, body weight changes, spleen and liver weight and hematologic findings as these were considered to be the likely prime markers of systemic toxicity.

INDUSTRIAL HEALTH FOUNDATION, INC.

Document Control Officer
U.S. Environmental Protection Agency
September 23, 1993
Page 2

Enclosed is a copy of the narrative portion of the first draft of the pathology report addendum for the 4-week study. The results conclude that compound-related degeneration of the olfactory epithelium of mice was noted in some animals at all exposure levels (Group 1 was control, Group 2 was 25 ppm, Group 3 was 100 ppm and Group 4 was 400 ppm). There may be some minor changes to this draft report as a result of a pathology peer review exercise conducted by EPL. A copy of the narrative portion of the draft of that report is also enclosed, but it appears that the compound-related findings of Pharmacology:LSR were confirmed.

Copies of the full final reports (pathology reports addendum and peer review reports) will be forwarded as soon as possible.

If there are any questions regarding this submission, please contact me at 412/363-6600.

Sincerely,

William E. Rinehart

William E. Rinehart, Sc.D.
President
Agent for Committee on
Toxicology of Methylenechloroform

WER:la

Enclosure

EPL[®]

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.
P.O. BOX 12766, RESEARCH TRIANGLE PARK, NC 27709 (919)544-8061 Fax: (919)544-7289

AUG 30 1993

August 27, 1993

Dr. William E. Rinehart
Industrial Health Foundation
34 Penn Circle West
Pittsburgh, PA 15206

Dear Dr. Rinehart:

Enclosed please find a "draft" bound copy of the pathology report entitled "A 4-Week Inhalation Toxicity Study Methylethylketoxime In Mice - Pathology Peer Review" - PHARMACO::LSR Study No. 90-8249 - EPL Project No. 334-003.

A final report will be forwarded along with the Quality Assurance Certificate following your review.

Sincerely,



JERRY F. HARDISTY, D.V.M.
Director/Pathologist

JFH:asc
Enclosures
c: Dr. Ward R. Richter

09 SEP 15 11:55

DRAFT

A 4-WEEK INHALATION TOXICITY STUDY
METHYLETHYLKETOXIME IN MICE

PATHOLOGY PEER REVIEW

PHARMACO::LSR STUDY NO. 90-8249

Submitted to:

PHARMACO::LSR
East Millstone, NJ

Submitted by:

Experimental Pathology Laboratories, Inc.
Research Triangle Park, NC 27709

PHARMACO::LSR
PROJECT NO. 90-8249
PEER REVIEW CERTIFICATION

A microscopic peer review was performed of all diagnoses for nasal cavity from all male and female mice from all groups.

Following the review of the microscopic findings reported by the study pathologist the results were discussed and appropriate terminology and diagnoses mutually agreed on. Differences of opinion between the study and reviewing pathologist were resolved with agreement on the final diagnoses. The tables contained in the final report reflect the mutually agreed-upon diagnoses.

JERRY F. HARDISTY, D.V.M.
Diplomate, A.C.V.P.
Reviewing Pathologist
Experimental Pathology
Laboratories, Inc.

WILLIAM L. WOODING, D.V.M., M.S.
Diplomate, A.C.V.P.
Study Pathologist
PHARMACO::LSR

**A 4-WEEK INHALATION TOXICITY STUDY OF METHYLETHYLKETOXIME IN MICE
PATHOLOGY PEER REVIEW****PHARMACO::LSR STUDY NO. 90-8249****NARRATIVE SUMMARY****INTRODUCTION**

A peer review of the histopathology portion of a 4-Week Inhalation Toxicity Study of Methyleneethylketoxime (MEKO) in mice was conducted at PHARMACO::LSR, East Millstone, NJ, by a pathologist from Experimental Pathology Laboratories, Inc. (EPL). The tissues had been previously examined histopathologically by Dr. William L. Wooding, the Study Pathologist, and the data tabulated in draft tables. A copy of the draft tables was provided by PHARMACO::LSR to conduct the peer review of the histopathology data. A summary of the experimental design for the study is presented as follows:

<u>Group Number</u>	<u>Dose Level (ppm)</u>	<u>Number of Animals</u>	
		<u>Male</u>	<u>Female</u>
1	0	10	10
2	25	10	10
3	100	10	10
4	400	10	10

The pathology peer review consisted of the complete review of all slides containing sections of nasal turbinates from all male and female mice in all groups. Slide Review Work Sheets used to document the results of this review are presented in Appendix A. These work sheets

list in animal number order all tissues that were examined by the reviewing pathologist from Experimental Pathology Laboratories, Inc. The work sheets list all diagnoses for the nasal turbinates which were included in the study pathologist's draft histopathology tables for individual animals. The work sheets also record the reviewing pathologist's comments indicating either agreement with the study pathologist's diagnosis or a comment when a difference of opinion was noted.

The results of the review confirmed the study pathologist's results which indicated that compound-related degeneration was present in the olfactory epithelium of the turbinates. The change was characterized by focal degeneration of the olfactory epithelium lining the dorsal meatus of the nasal turbinates of male and female mice at all exposure levels. The changes were most often observed in levels 2 and 3 of nasal turbinates and consisted of a decrease in the cellularity and the number of layers of cells in the olfactory mucosa resulting in a decrease in the overall height of the olfactory mucosa. The degenerative changes also included a decrease in the number of cilia on the surface of the affected epithelium. Although degenerative changes were observed in male and female mice at all exposure levels, the incidence and severity of the changes increased with increasing concentrations of MEKO.

In addition to the degenerative changes involving the olfactory epithelium, there was an increased incidence of eosinophilic droplets in

the respiratory and olfactory epithelium of exposed male and female mice as compared to control mice. Although the incidence was increased in treated groups, there was no consistent relationship between the incidence or severity of the change and exposure concentration. Although the study pathologist noted this increase in his draft report, he indicated that the presence of these droplets is a common spontaneous finding and because of the lack of a dose response, they were probably unrelated to compound exposure. Since the nasal cavity of mice of this age are not often examined histologically, the statement that these droplets are common spontaneous findings may not be applicable to this study and a probable association with exposure must be considered.

During the review, a few comments were made by the reviewing pathologist concerning the histotechnique. The level of sectioning of nasal turbinates for a few of the animals were inconsistent, resulting in the absence of one or more levels for microscopic examination. The missing sections were most often level 1 or level 3. Although this changes the number examined at each level sectioned, the inconsistent sectioning did not effect the overall interpretation of the data since due to the nature of the compound-related changes more than one level was usually affected.

Following the review of the microscopic changes reported by the study pathologist, the results were discussed and appropriate terminology and diagnoses were agreed upon. Differences of opinion between the study and reviewing pathologist were resolved with agreement

on the final diagnoses. The study pathologist's comments concerning the difference noted by the reviewing pathologist and the action taken to resolve the difference is presented. The study pathologist has indicated either that the data will be updated or indicated no change.

JERRY F. HARDISTY, D.V.M.
Pathologist

Date

JFH:asc

PHARMACO::LSR

PROJECT NO. 90-8249

A 4-WEEK INHALATION TOXICITY STUDY
OF METHYLETHYLKETOXIME IN THE RAT AND MOUSE
PATHOLOGY REPORT ADDENDUM

Performed by: Pharmaco LSR, Inc.
Toxicology Services North America
Mettlers Road, P.O. Box 2360
East Milistone, New Jersey 08875-2360

Submitted to: Industrial Health Foundation, Inc.
34 Penn Circle West
Pittsburgh, Pennsylvania 15206

Attn: Dr. William E. Rinehart

Date: June 18, 1993

0013

A 4-week Inhalation Toxicity Study
of Methylketoxime in the Rat and Mouse
Pathology Report Addendum

0013

A 4-Week Inhalation Toxicity Study
of Methyleneketoxime in the Rat and Mouse
Pathology Report Addendum

Handwritten notes:
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Introduction:

A 4-Week Inhalation Toxicity Study of Methyleneketoxime in the Rat and Mouse was conducted as a pilot study prior to conduct of a chronic inhalation study. The protocol for the 4-Week study did not require that nasal turbinates be examined microscopically. Because of findings in the chronic inhalation study, the sponsor requested that the nasal turbinates from the 4-Week mouse study be examined. The nasal tissue was dehydrated, infiltrated with paraffin, embedded in paraffin, sectioned, mounted on glass slides and stained with hematoxylin and eosin. Four cross sections of nose were prepared. Section 1 included the area between the upper incisor tooth and the incisive papilla; section 2 included the area between the incisive papilla and the first palatal ridge; section 3 included the area between the second palatal ridge and the first upper molar tooth; section 4 included the area between the first upper molar tooth and the nasopharynx.

Results:

Compound-related degeneration was present in the olfactory epithelium of the turbinates at all four levels, sections 1 through 4. There was a dose-related increase in the incidence, although degeneration was not seen at all levels for exposure group 2. The incidence of degeneration of the olfactory epithelium for each level of sectioning is presented below.

Incidence of Degeneration of the Olfactory Epithelium
by
Level of Nasal Section

Sex	Male				Female			
	1	2	3	4	1	2	3	4
Nose/Turbinates 1	0/9	0/10	1/10	3/9	0/10	3/9	3/10	2/10
Nose/Turbinates 2	0/10	3/10	10/10	10/10	0/10	6/10	10/10	10/10
Nose/Turbinates 3	0/10	2/10	7/10	10/10	0/10	6/10	10/10	10/10
Nose/Turbinates 4	0/10	0/10	1/10	8/9	0/10	2/10	6/10	10/10

The degeneration was characterized as a thinning of the epithelium with only a few cell layers present. There was some disorganization with cells arranged haphazardly and with accumulations of cell debris on the epithelium.

Degeneration of respiratory epithelium was present in some levels of some animals but did not appear to be compound-related. The changes

00049

A 4-Week Inhalation Toxicity Study
of Methylethylketoxime in the Rat and Mouse
Pathology Report Addendum

Results (cont.):

were minimal and were not present in a dose-related pattern. Eosinophilic droplets were seen in the olfactory epithelium and respiratory epithelium of some animals. They were more frequent in the olfactory epithelium of compound-treated animals; they were not seen in the controls. However, because the presence of these droplets is a common spontaneous finding and because of the lack of a dose response, they were probably unrelated to compound exposure. All other findings were slight and were not compound-related. They were not unusual as spontaneous findings for mice of this strain and age.

Conclusions:

1. Compound-related degeneration of the olfactory epithelium was present at all exposure levels. There was no NOEL, no observable effect level, demonstrated in this study.
2. There was a dose-related increase in the incidence of epithelial degeneration.
3. All other lesions were spontaneous and unrelated to compound exposure.

William L. Wooding, D.V.M., M.S. Date
Diplomate, A.C.V.P.
Senior Pathologist

Reviewed by: _____
Ward R. Richter, D.V.M., M.S. Date
Diplomate, A.C.V.P.
Vice President and Director of
Pathology

A 4-Week Inhalation Toxicity Study
of Methylethylretoxime in the Rat and Mouse
Pathology Report Addendum

Table I
Incidence Summary of Histopathology Data
Mouse Nasal Turbinates
Preface

KEY:

NOSE/TURB = Nasal Turbinate

*** PATH/TOX SYSTEM OUTPUT ***
A FOUR WEEK INHALATION TOXICITY STUDY
OF METHYLENEDIOXYKETOXIME IN THE RAT AND MOUSE
MICROSCOPIC FINDINGS - INCIDENCE SUMMARY

STUDY NUMBER: 908243A

NUMBER OF ANIMALS AFFECTED

TABLE INCIDENCES	SEX	MALE				FEMALE			
		1	2	3	4	1	2	3	4
GROUP: 10		10	10	10	10	10	10	10	10
GROUP: 1		10	10	10	10	10	10	10	10
GROUP: 2		10	10	10	10	10	10	10	10
GROUP: 3		10	10	10	10	10	10	10	10
GROUP: 4		10	10	10	10	10	10	10	10
GROUP: 5		10	10	10	10	10	10	10	10
GROUP: 6		10	10	10	10	10	10	10	10
GROUP: 7		10	10	10	10	10	10	10	10
GROUP: 8		10	10	10	10	10	10	10	10
GROUP: 9		10	10	10	10	10	10	10	10
GROUP: 10		10	10	10	10	10	10	10	10
GROUP: 11		10	10	10	10	10	10	10	10
GROUP: 12		10	10	10	10	10	10	10	10
GROUP: 13		10	10	10	10	10	10	10	10
GROUP: 14		10	10	10	10	10	10	10	10
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GROUP: 25		10	10	10	10	10	10	10	10
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GROUP: 96		10	10	10	10	10	10	10	10
GROUP: 97		10	10	10	10	10	10	10	10
GROUP: 98		10	10	10	10	10	10	10	10
GROUP: 99		10	10	10	10	10	10	10	10
GROUP: 100		10	10	10	10	10	10	10	10

*** PATH/TOX SYSTEM OUTPUT ***
A FOUR WEEK INHALATION TOXICITY STUDY
OF METHYLETHYLKETONE IN THE RAT AND MOUSE
MICROSCOPIC FINDINGS --- INCIDENCE SUMMARY

STUDY NUMBER: 908249A

NUMBER OF ANIMALS - AFFECTED

TABLE INCLUDES SEX ALL GROUP - 1, 2, 3, 4, SCREEN ALL WEEKS - ALL DEATH-ALL, F340=ALL, SUBSET-1	SEX		MALE		FEMALE				
	GROUP	1	2	3	4	1	2	3	4
ORGAN AND FINDING DESCRIPTION	NUMBER	10	10	10	10	10	10	10	10
MOUSE/TURB 4	NUMBER EXAMINED:	10	10	10	10	10	10	10	10
NASOACRIMAL DUCT: ERYTHROCYTES/LEUKOCYTES		5	4	3	5	4	4	5	6
NASOACRIMAL DUCT: SUBMUCOSAL LYMPHOCYTES		5	4	2	5	6	4	4	6
NASOACRIMAL DUCT: EPITHELIAL HYPERPLASIA		2	4	2	4	3	1	1	1
PARANASA STRUS: ERYTHROCYTES/EOSINOPHILIC MATERIAL		1	1	0	0	0	0	0	0
NASAL LUMEN: ERYTHROCYTES/EPITHELIAL CELLS		1	2	0	0	0	0	0	1
OLFAC TORY EPITHELIUM: DEGENERATION		0	0	1	8	0	2	6	10
OLFAC TORY EPITHELIUM: EOSINOPHILIC DROPLETS		0	0	0	0	0	0	0	1
OLFAC TORY EPITHELIUM: EOSINOPHILIC DROPLETS		0	0	0	0	0	0	0	1
OLFAC TORY EPITHELIUM: ACUTE/SUBACUTE INFLAMMATION		0	0	0	0	0	0	0	1

*** END OF LIST ***

0018

A 4-week Inhalation Toxicity Study
of Methyleneketoxime in the Rat and Mouse
Pathology Report Addendum

Table II
Expanded Incidence Summary of Histopathology Data
Mouse Nasal Turbinates
Preface

KEY:

- 1> = Slight
- 2> = Minimal
- 3> = Moderate
- 4> = Marked
- 5> = Severe
- TL> = Total Number of Lesions

NOSE/TURB = Nasal Turbinate

*** PATH/TOX SYSTEM OUTPUT ***
A FOUR WEEK INHALATION TOXICITY STUDY
OF METHYLETHYLOXIME IN THE RAT AND MOUSE
MICROSCOPIC FINDINGS --- EXPANDED INCIDENCE SUMMARY

STUDY NUMBER: 908249A

--- NUMBER OF ANIMALS AFFECTED ---

TABLE INCLUDES
SEX: ALL GROUPS 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833, 834, 835, 836, 837, 838, 839, 840, 841, 842, 843, 844, 845, 846, 847, 848, 849, 850, 851, 852, 853, 854, 855, 856, 857, 858, 859, 860, 861, 862, 863, 864, 865, 866, 867, 868, 869, 870, 871, 872, 873, 874, 875, 876, 877, 878, 879, 880, 881, 882, 883, 884, 885, 886, 887, 888, 889, 890, 891, 892, 893, 894, 895, 896, 897, 898, 899, 900, 901, 902, 903, 904, 905, 906, 907, 908, 909, 910, 911, 912, 913, 914, 915, 916, 917, 918, 919, 920, 921, 922, 923, 924, 925, 926, 927, 928, 929, 930, 931, 932, 933, 934, 935, 936, 937, 938, 939, 940, 941, 942, 943, 944, 945, 946, 947, 948, 949, 950, 951, 952, 953, 954, 955, 956, 957, 958, 959, 960, 961, 962, 963, 964, 965, 966, 967, 968, 969, 970, 971, 972, 973, 974, 975, 976, 977, 978, 979, 980, 981, 982, 983, 984, 985, 986, 987, 988, 989, 990, 991, 992, 993, 994, 995, 996, 997, 998, 999, 1000.

ORGAN/TISSUE EXAMINED	SEX:										SEX:									
	MALE					FEMALE					MALE					FEMALE				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
*** TOP OF TEST **																				
ROSE/TURB 1																				
BASOPHILIC DUST ERYTHROCYTES/EOSINOPHILIC MATERIAL	9	10	10	9	10	10	10	10	10	10	9	10	10	9	10	10	10	10	10	10
1>	5	5	5	4	1	5	5	2	1	5	5	5	4	1	5	5	2	1	5	5
2>	0	2	1	1	2	1	0	2	1	0	2	1	0	0	0	0	0	0	0	0
3>	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TL>	5	8	6	5	3	6	5	4												
BASOLACRIMAL DUCT EPITHELIAL CELLS	1>	1	0	0	0	3	1	0	1	0	1	0	1	0	1	0	1	0	1	0
1C>	1	0	0	0	1	2	1	1	0											
1J>	0	0	0	1	2	1	1	1	0											
1L>	0	0	0	1	2	1	1	1	0											
SUBEPITHELIAL MINERALIZATION	1>	1	1	2	2	1	1	3	2											
2>	0	0	1	0	0	0	0	0	0											
3>	0	0	1	3	2	1	1	3	2											
TL>	1	1	3	2	1	1	3	2												
AMYLOIDOSIS	1>	0	0	0	0	0	0	1	1											
2>	0	0	0	0	0	0	0	0	0											
3>	0	0	0	0	0	0	0	0	0											
TL>	0	0	0	0	0	0	0	0	0											
BASAL TUMOR EOSINOPHILIC MATERIAL/ERYTHROCYTES	1>	0	0	0	0	0	0	0	1	1										
2>	0	0	0	0	0	0	0	0	0											
3>	0	0	0	0	0	0	0	0	0											
TL>	0	0	0	0	0	0	0	0	0											
DEFACATORY EPITHELIUM: EOSINOPHILIC DROPLETS	1>	0	1	0	0	0	0	0	1	0										
1L>	0	1	0	0	0	0	0	0	1	0										
DEFACATORY EPITHELIUM: DEGENERATION	1>	0	0	1	0	0	0	0	0	0										
2>	0	0	0	2	0	0	2	1	1	2										
3>	0	0	0	1	0	1	0	1	1	0										
TL>	0	0	1	3	0	3	0	3	2	2										
ACUTE/SUBACUTE INFLAMMATION	2>	0	0	0	1	0	0	0	0	0										
1L>	0	0	0	1	0	0	0	0	0	0										
RESPIRATORY EPITHELIUM: EOSINOPHILIC DROPLETS	1>	0	0	2	1	0	1	1	1	1										
2>	0	1	0	0	0	1	1	0	0	0										
TL>	0	1	2	1	0	2	1	2	1											
RESPIRATORY EPITHELIUM: DEGENERATION	1>	0	0	1	0	0	0	0	0	0										
2>	0	0	3	0	0	0	0	0	0	2										
TL>	0	0	4	0	0	0	0	0	0	2										

*** PATH/TOX SYSTEM OUTPUT ***
A FOUR WEEK INHALATION TOXICITY STUDY
OF METHYLETHYLETUOXIME IN THE RAT AND MOUSE
MICROSCOPIC FINDINGS -- EXPANDED TREATMENT SUMMARY

NUMBER OF ANIMALS AFFECTED

TABEL IDENTIFIER	SEX GROUP	MALE				FEMALE			
		1	2	3	4	1	2	3	4
17 ALL GROUP 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100									
ORGAN/TISSUE EXAMINED	NUMBER EXAMINED	10	10	10	10	10	10	10	10
17 FROM PREVIOUS PAGE **	17	0	1	2	0	0	1	0	1
18 FROM PREVIOUS PAGE **	18	0	1	4	2	0	3	5	2
19 FROM PREVIOUS PAGE **	19	0	0	1	8	0	2	5	7
20 FROM PREVIOUS PAGE **	20	0	2	7	10	0	6	10	10
21 FROM PREVIOUS PAGE **	21	0	0	0	3	0	0	5	3
22 FROM PREVIOUS PAGE **	22	0	1	0	0	0	1	1	0
23 FROM PREVIOUS PAGE **	23	0	1	0	3	0	1	6	3
24 FROM PREVIOUS PAGE **	24	0	0	0	0	0	0	0	0
25 FROM PREVIOUS PAGE **	25	0	1	1	1	0	2	4	0
26 FROM PREVIOUS PAGE **	26	0	1	0	1	0	2	4	3
27 FROM PREVIOUS PAGE **	27	0	0	0	0	0	1	1	0
28 FROM PREVIOUS PAGE **	28	0	2	1	2	0	2	9	3
29 FROM PREVIOUS PAGE **	29	0	0	0	0	0	1	0	0
30 FROM PREVIOUS PAGE **	30	0	0	0	0	0	1	0	0
31 FROM PREVIOUS PAGE **	31	0	0	0	0	0	1	0	0
32 FROM PREVIOUS PAGE **	32	0	2	2	2	1	0	3	3
33 FROM PREVIOUS PAGE **	33	2	1	0	2	3	2	2	1
34 FROM PREVIOUS PAGE **	34	3	1	1	1	0	2	0	2
35 FROM PREVIOUS PAGE **	35	5	4	3	5	4	4	5	6
36 FROM PREVIOUS PAGE **	36	2	1	0	1	1	0	0	0
37 FROM PREVIOUS PAGE **	37	1	2	2	3	2	4	5	5
38 FROM PREVIOUS PAGE **	38	2	1	0	1	3	2	0	1
39 FROM PREVIOUS PAGE **	39	5	4	2	5	6	4	4	6
40 FROM PREVIOUS PAGE **	40	0	1	1	0	2	0	0	0
41 FROM PREVIOUS PAGE **	41	2	3	1	4	1	1	1	1
42 FROM PREVIOUS PAGE **	42	2	4	2	4	3	1	1	1
43 FROM PREVIOUS PAGE **	43	0	1	0	0	0	0	0	0
44 FROM PREVIOUS PAGE **	44	1	0	0	0	0	0	0	0
45 FROM PREVIOUS PAGE **	45	1	1	0	0	0	0	0	0

** CONTINUED ON NEXT PAGE **

*** PATH/TOX SYSTEM OUTPUT ***
A FOUR WEEK INHALATION TOXICITY STUDY
OF METHYLETHYLEKLOXIME IN THE RAT AND MOUSE
MICROSCOPIC FINDINGS --- EXPANDED INCIDENCE SUMMARY

STUDY NUMBER: 908249A
NUMBER OF ANIMALS AFFECTED

SEX	MALE				FEMALE			
	1	2	3	4	1	2	3	4
GROUP:	10	10	10	10	10	10	10	10
NUMBER:	10	10	10	10	10	10	10	10
ORGAN/TISSUE EXAMINED								
*** FROM PREVIOUS PAGE ***								
NOSE/TURB 4								
RAJAL TURB 1								
RAJAL TURB 2								
RAJAL TURB 3								
RAJAL TURB 4								
RAJAL TURB 5								
RAJAL TURB 6								
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ORGAN/TISSUE EXAMINED
 OULCAGORY EPITHELIUM DEGENERATION
 OULCAGORY EPITHELIUM EOSINOPHILIC DROPLETS
 RESPIRATORY EPITHELIUM DEGENERATION
 RESPIRATORY EPITHELIUM EOSINOPHILIC DROPLETS
 GULCAGORY EPITHELIUM ACUTE/SUBACUTE INFLAMMATION

** END OF LIST **

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