TABLE 11. UNIT RISK ESTIMATES USING THE MOST SENSITIVE END POINT--PREPUTIAL GLAND RESPONSE IN B6C3F1 MALE MICE UNDER VARIOUS ASSUMPTIONS

Case number	Model and statistic used				Exposure equivalance		Unit risk estimate
	Multistage		Mortality corrected Multistage-Weibull				
	MLE	95% upper bound	MLE	95% upper bound	mg/kg	mg/m^2	
1				x		x	1.61×10^{-1}
2			x			x	1.36×10^{-2}
3		x				x	1.25×10^{-1}
4	x					x	3.02×10^{-2}
5				x	x		1.34×10^{-2}
6			x		x		1.13×10^{-3}
7		x			x		1.04×10^{-2}
8	x				x		2.51×10^{-3}

Composite Unit Risk Estimate

Considering the information presented, we feel quite confident that if low-dose linearity holds, the true unit risk lies somewhere between 1×10^{-2} and 1×10^{-1}. Producing a single number from the various estimates presented is a highly subjective undertaking that is open to criticism, no matter what approach is taken.

Applying our best judgment, we believe that the joint unit risk estimate should:

- be based upon epidemiologic studies only;
- use the most extensive data base available;
- give equal weight to the cumulative dose and weighted cumulative dose, as well as relative and absolute forms; and
- use the ML point estimates.

In Table 12, the MLE of unit risk is given for each of the four model types, based on the most complete data set that is common to all models. Not having any rationale for preferring one model over another, we take the geometric mean to obtain a pooled model average. This results in the estimate 2.11×10^{-2}. This estimate, unfortunately, does not take into account the results of the Wong et al. study. A somewhat ad-hoc but reasonable adjustment would be to assume that the ratio of the Rinsky-Ott-Wong studies to Rinsky-Ott for the relative risk cumulative dose model was the same as for other models. Under this assumption, the computed ratio would be multiplied by the pooled model average to obtain a single composite estimate.

Taking the SMR = 100 for the unexposed group, and using the pooled information in the Rinsky-Ott-Wong studies is a reasonable approach to obtaining a joint estimate for cumulative doses. This gives a result of 3.55×10^{-2}, which is obtained from data set VIII and is shown in Table 1. Using this approach,

TABLE 12. RISKS DUE TO LIFETIME 1 PPM BENZENE EXPOSURE BASED UPON COMBINED OTT ET AL. AND RINSKY ET AL. COHORTS, FOLLOWED FROM 1940 TO 1978

Exposure parameter	Model form	
	Relative	Absolute
Cumulative	2.89×10^{-2}	1.96×10^{-2}
Weighted cumulative	2.49×10^{-2}	1.40×10^{-2}

Geometric mean = $(2.89 \times 2.49 \times 1.96 \times 1.4)^{1/4} \times 10^{-2} = 2.11 \times 10^{-2}$.

our correction ratio is estimated to be

$$R = 3.55 \times 10^{-2} \div 2.89 \times 10^{-2} = 1.23$$

The "corrected" joint unit risk estimate is thus

$$u = 2.11 \times 10^{-2} \times 1.23 = 2.60 \times 10^{-2}$$

which we recommend as our single best judgment unit risk estimate.

However, a number of other approaches are possible.

One approach might be to take the geometric mean, 2.66×10^{-2}, of the 21 estimates. However, since the estimates are not random samples from some well-defined population, the rationale for such an approach is not clear.

Another approach that is regarded as "safe" is to take the highest estimate, regardless of the quality of the information on which it is based.

As seen in Table 1, the Wong et al. study gives the highest estimate of risk, 1.04×10^{-1}, with a 95% upper bound of 2.42×10^{-1}. However, much of the

potency associated with this estimate can be attributed to the fact that the non-exposed group had no cases of leukemia. As a result, the increase of risk over controls may be due to an artifact in the data rather than to a true carcinogenic response.

Another approach that has been suggested is to use as an estimate the single data set model that has the most credibility associated with it. In our opinion, this would be the estimate taken from data set I, Table 3, which is the Rinsky et al. study - weighted cumulative dose relative risk model. This gives a result of 4.10×10^{-2}.

It is apparent that regardless of the method used to obtain the joint unit risk, the resulting answers are relatively consistent, and are close to the original estimate of 2.41×10^{-2}.

Summary

From the slope parameters estimated by Crump and Allen, the unit risk for leukemia due to a lifetime exposure of 1 ppm benzene in the air has been estimated. Using various models and combinations of assumptions and epidemiologic studies, 21 unit risk estimates, ranging from 0.9×10^{-2} to $1. \times 10^{-1}$, were obtained. Based upon the criteria of using the data from all epidemiologic studies with reasonable exposure information and an average value over all the mathematical models believed to be plausible, a combined unit risk estimate of 2.6×10^{-2} was derived. This is taken to be the CAG's best-judgment unit risk, and is only slightly larger than the original estimate of 2.4×10^{-2}, which is based upon far less reliable data.

Unit risks were also obtained from animal studies. However, they are considered to be confirmatory in nature and intrinsically less reliable than those based upon the human response. The inhalation studies that would be preferred due to route similarity tend to give estimates that are an order of

magnitude lower. Gavage studies, although tending to give higher estimates than human, up to about five times in the extreme, are dependent upon a large series of unverifiable assumptions. Thus, while they may be a valid upper bound, they are judged to be overly conservative, based upon the human data.

A more detailed and direct comparison of the human and animal data will be possible in the CAG's final report.

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APPENDIX A

NOTE: Tables referred to in Crump and Allen (1984) have been reproduced exactly. Tables 4, 5, 18, 19, 20, 21, and 22 are not included herein.

Table 1

Observed and Expected Number of Deaths in Ott *et al*. Cohort by Cumulative Dose

Cause	0-5 ppm-yr (1.48)[a] 3533 p-y		5-20 ppm-yr (10.9) 2961 p-y		20-80 ppm-yr (44.8) 3758 p-y		80-200 ppm-yr (125.9) 1790 p-y		200+ ppm-yr (352.9) 1229 p-y		Total (160.04) 13271 p-y	
	O/E	SMR	O/E	SMR	O/E	SMR	O/E	SMR	O/E	SMR	O/E	SMR
All Causes	11/22	50	19/27	70	34/39.8	85	21/19	111	17/19	89	102/127	80
All Malignant Neoplasms	2/3.5	57	9/4.6	196	10/7.4	135	7/3.6	194	3/3.4	88	31/22.5	138
Malignant Neoplasms of Digestive Organs and Peritoneum	0/1.04	0	3/1.4	214	3/2.2	136	3/1.03	291	0/.98	0	9/6.7	134
Malignant Neoplasms of Respiratory System	1/1.07	93	2/1.3	154	4/2.4	167	3/1.2	250	1/1.2	83	11/7.2	153
Leukemia	1/.18	556	0/.202	0	1/.31	323	0/.14	0	0/.13	0	2/.96	208
Other Neoplasms of Lymphatic and Hematopoietic Tissues	0/.28	0	1/.304	329	1/.47	213	0/.23	0	0/.202	0	2/1.5	133

[a] Average exposure in ppm-years

Table 2

Observed and Expected Number of Deaths in Rinsky *et al*. Cohort by Cumulative Dose, Followup from 1940 to 1978

	0-5 ppm-yr (1.20)[a] 19239 p-y		5-20 ppm-yr (11.0) 8098 p-y		20-80 ppm-yr (42.2) 7003 p-y		80-200 ppm-yr (129) 3746 p-y		200-1000 ppm-yr (420.5) 3363 p-y		1000+ppm-yr (1482.5) 437 p-y		Total (70.5) 41886	
	O/E	SMR	O/E	SMR	O/E	SMR	O/E	SMR	O/E	SRM	O/E	SMR	O/E	SMR
All Causes	154/144	107	73/67	109	73/65	112	33/41	80	40/44	91	12/6.6	182	385/368	105
Malignant Neoplasms	28/26	108	15/13	115	7/13	54	5/7.9	63	15/8.8	170	3/1.4	214	73/70.1	104
Digestive Neoplasms	7/7.4	95	4/3.5	114	0/3.5	0	1/2.3	43	2/2.5	80	0/.38	0	14/20	70
Respiratory Neoplasms	8/8.5	94	4/4.4	91	3/4.2	71	3/2.6	115	3/3.03	99	0/.48	0	21/23	91
Leukemia	2/1.2	167	0/.55	0	0/.52	0	0/.32	0	5/.34	1471	1/.051	1961	8/2.98	268
Other Lymphatic and Hematopoietic Neoplasms	2/1.8	[illegible]	0/.87	0	0/.81	0	0/.49	0	1/.52	192	1/.078	1282	4/46	87

[a] Average exposure in ppm-years

Table 3

Observed Deaths, Expected Deaths, SMRs and 95% Confidence Intervals for Lymphatic and Hematopoietic Cancer, Leukemia, and Non-Hodgkin's Lymphopoietic Cancer by Cumulative Occupational Exposure to Benzene

(ppm-months)

Cause of Death (8th ICD)	Variable	Non-exposed	< 180 ppm-months	180-719 ppm-months	720+ ppm-months
Lymphatic and Hematopoietic Cancer (200-209)	Obs.	3	5	5	5
	Exp.	8.68	5.48	3.41	2.85
	SMR	34.6	91.3	146.8	175.2
	95% C.I.	7.1-101.1	29.5-213.3	47.5-343.0	56.7-409.3
Leukemia and Aleukemia (204-207)	Obs.	0	2	1	3
	Exp.	3.40	2.07	1.28	1.09
	SMR	0	96.8	78.2	275.8
	95% C.I.	--	11.7-349.4	2.0-434.4	56.9-806.4
Non-Hodgkin's Lymphopoietic Cancer (200,202-207)	Obs.	2	5	4	4
	Exp.	7.34	4.64	2.89	2.43
	SMR	27.2	107.8	138.4	164.6
	95% C.I.	3.3-79.5	34.9-251.9	37.7-354.0	44.8-421.0

* statistically significant at the 0.05 level

[Lymphatic and hematopoietic cancer includes non-Hodgkin's lymphoma, Hodgkin's disease and leukemia.]

Source: Wong et al. (1983), Table 37

Table 6

Observed and Expected Leukemias
in Rinsky *et al.* Cohort by
Cumulative Exposure; 1950-1978 Followup

Cumulative Exposure in ppm-years (average)	Observed	Expected	SMR	person-years
0-5 (1.29)	2	1.11	180	16890
5-20 (11.0)	0	0.52	0	7092
20-80 (42.2)	0	0.50	0	6591
80-200 (129.0)	0	0.31	0	3557
200-1000 (421)	5	0.32	1560	3075
1000+ (1489)	1	0.049	2040	396

Table 7

Observed and Expected Leukemias
in Rinsky *et al*. Cohort by Cumulative
Exposure Using Revised Exposure Estimates; 1950-1978 Followup

Cumulative Exposure in ppm-years (average)	Observed	Expected	SMR	person-years
0-5 (1.32)	2	1.13	177	17170
5-20 (11.2)	0	0.54	0	7667
20-80 (42.3)	0	0.51	0	6732
80-200 (129)	1	0.30	333	3335
200-1000 (393)	4	0.34	1180	3087
1000+ (1142)	1	0.015	6670	120

Table 8

Observed and Expected Leukemias in Rinsky *et al*. Cohort by Weighted Cumulative Dose; 1940-1978 Followup

Weighted Cumulative Exposure in ppm-years (average)	Observed	Expected	SMR	person-years
0-3 (0.54)	2	1.55	129	24633
3-10 (5.9)	0	0.46	0	5843
10-30 (17.7)	0	0.36	0	4544
30-100 (56.6)	1	0.33	305	3947
100-300 (163.5)	3	0.204	1470	2286
300+ (554.8)	2	0.047	4250	633

Table 9

Observed and Expected Leukemias
in Rinsky *et al*. Cohort by Exposure in
Ten-Year Window; 1940-1978 Followup

ppm-years accumulated 12.5 to 2.5 years prior to age category (average)	Observed	Expected	SMR	person-years
0-2 (0.15)	3	2.025	148	27106
2-5 (3.2)	0	0.145	0	2474
5-10 (7.3)	0	0.131	0	2178
10-50 (23.6)	0	0.309	0	4939
50-200 (104.5)	1	0.249	401	3671
200+ (471.1)	4	0.103	3880	1518

Table 10

Observed and Expected Leukemias in
Ott *et al*. Cohort by Weighted Cumulative Exposure

Weighted Cumulative Exposure in ppm-years (average)	Observed	Expected	SMR	person-years
0-3 (.635)	1	.31	321	5416
3-10 (5.94)	0	.199	0	2218
10-30 (18.8)	1	.19	518	2533
30-100 (51.8)	0	.17	0	2056
100+ (153)	0	.089	0	1054

Table 11

Observed and Expected Leukemias in
Ott *et al*. Cohort by Exposure in Ten-Year Window

ppm-years accumulated 12.5 to 2.5 years prior to age category (average)	Observed	Expected	SMR	person-years
0-2 (.115)	1	.44	229	6192
2-5 (3.42)	0	.052	0	800
5-10 (7.18)	0	.066	0	882
10-50 (25.3)	1	.21	488	2903
50-200 (101)	0	.17	0	2105
200+ (263)	0	.032	0	395

Table 12

Results of Fitting Relative Risk Model
Using Cumulative Dose

Data Set	Parameter Estimates: a (background) MLE	b (Slope of Dose Response) (ppm-years)$^{-1}$ 95% Lower	MLE	95% Upper	Goodness of Fit: Chi-sq.	d.f.	p-value
I Rinsky *et al.* (followup from 1950 Table 6)	.87	.0074	.023	.051	5.0	4	.29
II Rinsky *et al.*, (followup from 1940, Table 2)	.82	.0069	.023	.051	5.0	4	.29
III Rinsky *et al.* (revised exposures, Table 7)	.88	.0080	.029	.065	3.3	4	.50
IV Rinsky *et al.* (Table 6) and Ott *et al.* (Table I)	1.2	.0035	.013	.031	4.8	4	.31
V Same as IV except two questionable cases added	1.7	.0020	.0092	.023	2.6	4	.63
VI Wong (Table 3 SMR=50 assumed for unexposed)	0.5	.00039	.047	.11	2.4	2	.30
VII Rinsky *et al.* (Table 6) Ott *et al.* (Table I) and Wong (Table 3)	.57	.012	.033	.072	11.7	8	.16
VIII same as VII except SMR=100 assumed for unexposed	1.0	.0070	.016	.029	9.5	9	.49

Table 13

Results of Fitting Absolute Risk Model
Using Cumulative Dose

Data Set	Parameter Estimates: a (background) MLE	b (Slope of Dose Response) $(ppm\text{-}years)^{-1}$ 95% Lower	MLE	95% Upper	Goodness of Fit: Chi-sq.	d.f.	p-value
I Rinsky *et al.* (followup from 1950, Table 6)	5.9×10^{-6}	8.3×10^{-7}	2.0×10^{-6}	3.9×10^{-6}	5.2	4	.27
II Rinsky *et al.* (followup from 1940, Table 2)	7.9×10^{-6}	7.6×10^{-7}	1.8×10^{-6}	3.6×10^{-6}	5.1	4	.28
III Rinsky *et al.* (revised exposures, Table 7)	6.0×10^{-6}	1.0×10^{-6}	2.5×10^{-6}	4.9×10^{-6}	4.0	4	.41
IV Rinsky *et al.* (Table 6) and Ott *et al.* (Table I)	1.4×10^{-5}	5.9×10^{-7}	1.6×10^{-6}	3.1×10^{-6}	5.1	4	.28
V Same as IV except two questionable cases added	4.5×10^{-5}	5.8×10^{-7}	1.7×10^{-6}	3.3×10^{-6}	2.8	4	.59

Table 14

Results of Fitting Relative Risk Model
Using Weighted Cumulative Dose

Data Set	Parameter Estimates: a (background) MLE	a 95% Lower	b (Slope of Dose Response) $(ppm\text{-}years)^{-1}$ MLE	b 95% Upper	Goodness of Fit: Chi-sq.	d.f.	p-value
I Rinsky *et al.* (Table 8)	.180	.025	.079	.17	2.0	4	.74
II Rinsky *et al.* (Table 8) and Ott *et al.* (Table 10)	1.05	.014	.048	.108	6.3	9	.71

Table 15

Results of Fitting Absolute Risk Model
Using Weighted Cumulative Dose

Data Set	Parameter Estimates: a (background) MLE	b (Slope of Dose Response) (ppm-years)$^{-1}$ 95% Lower	MLE	95% Upper	Goodness of Fit: Chi-sq.	d.f.	p-value
I Rinsky *et al.* 1940-1970 followup (Table 8)	9.0×10^{-6}	2.2×10^{-6}	5.2×10^{-6}	9.9×10^{-6}	2.1	4	.72
II Rinsky *et al.* (Table 8) and Ott *et al.* (Table 10)	9.1×10^{-6}	1.6×10^{-6}	4.1×10^{-6}	8.0×10^{-6}	6.0	9	.74

Table 16

Results of Fitting Relative Risk Model
Using "Window" Dose

Data Set	Parameter Estimates: a (background) MLE	b (Slope of Dose Response) (ppm-years)$^{-1}$ 95% Lower	MLE	95% Upper	Goodness of Fit: Chi-sq.	d.f.	p-value
I Rinsky *et al.* (Table 9)	1.11	.017	.051	.107	2.2	4	.70
II Rinsky *et al.* (Table 9) and Ott *et al.* (Table II)	1.3	.011	.035	.076	5.1	10	.88

Table 17

Results of Fitting Absolute Risk Model
Using "Window" Dose

	Parameter Estimates				Goodness of Fit		
	a (background)	b (Slope of Dose Response) $(ppm\text{-}years)^{-1}$					
Data Set	MLE	95% Lower	MLE	95% Upper	Chi-sq.	d.f.	p-value
I Rinsky *et al.* (Table 9)	4.5×10^{-6}	1.5×10^{-6}	3.8×10^{-6}	7.5×10^{-6}	2.3	4	.68
II Rinsky *et al.* (Table 9) and Ott *et al.* (Table 11)	1.7×10^{-5}	1.2×10^{-6}	3.1×10^{-6}	8.7×10^{-6}	5.0	10	.89

Table 23

Doses Corresponding to Increased Risk of 10^{-6}
in Rodent Inhalation Studies

Data Sets	Multistage Model	
	MLE	95% Lower Limit
Bioassays from Goldstein *et al.* (1980)	(Dose units = ppm/8 hr day)	
Leukemia, male rats	Inf.	.379E-2[a]
Leukemia, male mice	2.041	.776E-2
Bioassays from Maltoni *et al.* (1983)	(Dose units = ppm/8 hr day)	
Leukemia, both sexes, rats	.314E-1	.955E-2
Zymbal gland or nasal cavity carcinoma or leukemia, both sexes, rats	.375E-2	.233E-2

[a] .379E-2 means $.379 \times 10^{-2}$

Table 24

Doses Corresponding to Increased Risk of 10^{-6} in Rodent Gavage Studies

Data Sets	Model: Multistage MLE	Multistage 95% Lower Limit	Multistage-Weibull MLE	Multistage-Weibull 95% Lower Limit
NTP Bioassays (Dose units = mg/kg body wt.)				
Zymbal gland carcinoma, male rats	.576E-3[a]	.383E-3	.555E-3	.341E-3
All squamous cell carcinomas, male rats	.444E-3	.339E-3	.394E-3	.300E-3
Zymbal gland carcinoma, female rats	.348E-3	.238E-3	.333E-3	.216E-3
All squamous cell carcinomas, female rats	.797E-3	.479E-3	.804E-3	.430E-3
Squamous cell carcinoma of preputial gland, male mice	.297E-3	.123E-3	.113E-2	.955E-4
All squamous cell carcinomas, male mice	.690E-3	.129E-3	.660E-1	.103E-3
Alveolar/bronchiolar carcinoma, male mice	.427E-3	.238E-3	.338E-3	.186E-3
Lymphoma, NOS, male mice	.742E-3	.357E-3	.527E-3	.227E-3
All squamous cell carcinomas, female mice	1.883	.132E-2	1.716	.107E-2
Mammary gland carcinoma, NOS, female mice	.442E-3	.270E-3	.339E-3	.227E-3
Alveolar/bronchiolar carcinoma, female mice	.545E-3	.366E-3	.333E-3	.213E-3
Lymphoma, female mice	.167E-2	.271E-3	INF.	.401E-3
Bioassays from Maltoni *et al.* (1983) (Dose units = mg/kg body wt.)				
Leukemia, male rats	.708	.128E-2		
All tumors, male rats	.532	.736E-3		
Zymbal gland carcinoma, female rats	.840E-3	.519E-3		
Leukemia, female rats	INF.	.269E-2		
All tumors, female rats	.295E-3	.190E-3		
Leukemia, both sexes, rats	.399E-2	.178E-2		
All tumors, both sexes, rats	.905E-3	.386E-3		

[a] [illegible] 10^{-3}

CRUMB — APPENDIX A

DATA AND MODEL PARAMETERS FOR ANIMAL STUDIES

This appendix summarizes the data and models used to estimate cancer risks from three long-term rodent bioassays: Goldstein et al. (1980), Maltoni et al. (1983), and NTP (1983). For the time-to-response multistage-Weibull model applied to the NTP data (pages A24-A35), time is measured in weeks and the tumor indicator variable has the following interpretation:

1: Death without carcinogenic response of interest;

2: Death with carcinogenic response of interest.

Data from Goldstein *et al*. (1980)

Species and Sex: Sprague-Dawley rats, male

Endpoint: Leukemia

Exposure Route: Inhalation

Doses (ppm/8 hr day)	0	75	225
# affected	0	1	0
# at risk	67	40	45

Multistage Model -

Chi-square Goodness-of-Fit Statistic: 2.819

Degrees of Freedom: 2

p-value: .2419

Maximum Likelihood Parameter Estimates:

q_0 = .660E-2

Linear term corresponding to 95% upper limit on risk (q_1^*): .264E-3

Data from Goldstein *et al*. (1980)

Species and Sex: AKR, C57BL, and CD-1 mice, male

Endpoint: Leukemia

Exposure Route: Inhalation

Doses (ppm/8 hr day)	0	75	225
# affected	0	0	2
# at risk	210	50	160

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .699E-1

Degrees of Freedom: 2

p-value: .9661

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = 0$

$q_2 = .240E-6$

Linear term corresponding to 95% upper limit on risk (q_1^*): .129E-3

Data from Maltoni *et al*. (1983)

Species and Sex: Sprague-Dawley rats, male and female

Endpoint: Leukemia

Exposure Route: Inhalation

Doses (ppm/8 hr day)	0	241
# affected	1	2
# at risk	365	193

Multistage Model -

Chi-square Goodness-of-Fit Statistic: -

Degrees of Freedom: -

p-value: -

Maximum Likelihood Parameter Estimates:

q_0 = .274E-2

q_1 = .318E-4

Linear term corresponding to 95% upper limit on risk (q_1^*): .105E-3

Data from Maltoni et al. (1983)

Species and Sex: Sprague-Dawley rats, male and female

Endpoint: Zymbal gland or nasal cavity carcinomas or leukemia

Exposure Route: Inhalation

Doses (ppm/8 hr day)	0	241
# affected	4	14
# at risk	365	193

Multistage Model -

Chi-square Goodness-of-Fit Statistic: -

Degrees of Freedom: -

p-value: -

Maximum Likelihood Parameter Estimates:

q_0 = .110E-1

q_1 = .267E-3

Linear term corresponding to 95% upper limit on risk (q_1^*): .428E-3

Data from Maltoni et al. (1983)

Species and Sex: Sprague-Dawley rats, male

Endpoint: Leukemia

Exposure Route: Gavage

Doses (mg/kg body wt)	0	50	250
# affected	0	0	4
# at risk	28	28	33

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .145

Degrees of Freedom: 2

p-value: .9304

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = 0$

$q_2 = .200E-5$

Linear term corresponding to 95% upper limit on risk (q_1^*): .783E-3

Data from Maltoni et al. (1983)

Species and Sex: Sprague-Dawley rats, male

Endpoint: All tumors

Exposure Route: Gavage

Doses (mg/kg body wt)	0	50	250
# affected	2	1	8
# at risk	28	28	33

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .519

Degrees of Freedom: 1

p-value: .4713

Maximum Likelihood Parameter Estimates:

q_0 = .529E-1

q_1 = 0

q_2 = .353E-5

Linear term corresponding to 95% upper limit on risk (q_1^*): .136E-2

Data from Maltoni *et al*. (1983)

Species and Sex: Sprague-Dawley rats, female

Endpoint: Leukemia

Exposure Route: Gavage

Doses (mg/kg body wt)	0	50	250
# affected	1	2	1
# at risk	30	30	32

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .577

Degrees of Freedom: 2

p-value: .7484

Maximum Likelihood Parameter Estimates:

q_0 = .445E-1

Linear term corresponding to 95% upper limit on risk (q_1^*): .372E-3

Data from Maltoni et al. (1983)

Species and Sex: Sprague-Dawley rats, female

Endpoint: Zymbal gland carcinoma

Exposure Route: Gavage

Doses (mg/kg body wt)	0	50	250
# affected	0	2	8
# at risk	30	30	32

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .527E-1

Degrees of Freedom: 2

p-value: .9739

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = .119E-2$

Linear term corresponding to 95% upper limit on risk (q_1^*): .192E-2

Data from Maltoni et al. (1983)

Species and Sex: Sprague-Dawley rats, female

Endpoint: All tumors

Exposure Route: Gavage

Doses (mg/kg body wt)	0	50	250
# affected	6	10	21
# at risk	30	30	32

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .741E-2

Degrees of Freedom: 1

p-value: .9315

Maximum Likelihood Parameter Estimates:

q_0 = .227

q_1 = .339E-2

Linear term corresponding to 95% upper limit on risk (q_1^*): .526E-2

Data from Maltoni *et al*. (1983)

Species and Sex: Sprague-Dawley rats, male and female

Endpoint: Leukemia

Exposure Route: Gavage

Doses (mg/kg body wt)	0	50	250
# affected	1	2	5
# at risk	58	58	65

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .326E-1

Degrees of Freedom: 1

p-value: .8562

Maximum Likelihood Parameter Estimates:

q_0 = .191E-1

q_1 = .251E-3

Linear term corresponding to 95% upper limit on risk (q_1^*): .561E-3

Data from Maltoni *et al*. (1983)

Species and Sex: Sprague-Dawley rats, male and female

Endpoint: All tumors

Exposure Route: Gavage

Doses (mg/kg body wt)	0	50	250
# affected	8	11	29
# at risk	58	58	65

Multistage Model -

Chi-square Goodness-of-Fit Statistic: -

Degrees of Freedom: -

p-value: -

Maximum Likelihood Parameter Estimates:

q_0 = .148

q_1 = .110E-2

q_2 = .266E-5

Linear term corresponding to 95% upper limit on risk (q_1^*): .259E-2

Data from NTP (1983)

Species and Sex: F344/N rats, male

Endpoint: Zymbal gland carcinoma

Exposure Route: Gavage

Doses	0	50	100	200
# affected	2	6	10	17
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .144E-2

Degrees of Freedom: 1

p-value: .9706

Maximum Likelihood Parameter Estimates:

q_0 = .407E-1

q_1 = .174E-2

q_2 = .712E-6

Linear term corresponding to 95% upper limit on risk (q_1^*): .261 E-2

Data from NTP (1983)

Species and Sex: F344/N rats, male

Endpoint: All squamous cell carcinomas

Exposure Route: Gavage

Doses	0	50	100	200
# affected	0	10	8	16
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: 5.530

Degrees of Freedom: 3

p-value: .1493

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = .225E-2$

Linear term corresponding to 95% upper limit on risk (q_1^*): .295E-2

Data from NTP (1983)

Species and Sex: F344/N rats, female

Endpoint: Zymbal gland carcinoma

Exposure Route: Gavage

Doses	0	25	50	100
# affected	0	5	5	14
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: 1.302

Degrees of Freedom: 2

p-value: .5220

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = .287E-2$

$q_2 = 0$

$q_3 = .310E-7$

Linear term corresponding to 95% upper limit on risk (q_1^*): .421E-2

Data from NTP (1983)

Species and Sex: F344/N rats, female

Endpoint: All squamous cell carcinomas

Exposure Route: Gavage

Doses	0	25	50	100
# affected	0	1	4	6
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .478

Degrees of Freedom: 1

p-value: .4890

Maximum Likelihood Parameter Estimates:

q_0 = .444E-25

q_1 = .125E-2

q_2 = .893E-6

Linear term corresponding to 95% upper limit on risk (q_1^*): .209E-2

Data from NTP (1983)

Species and Sex: $B6C3F_1$ mice, male

Endpoint: Squamous cell carcinoma of the preputial gland

Exposure Route: Gavage

Doses	0	25	50	100
# affected	0	3	18	28
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: 3.874

Degrees of Freedom: 2

p-value: .1446

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = .337E-2$

$q_2 = .567E-4$

Linear term corresponding to 95% upper limit on risk (q_1^*): .811E-2

Data from NTP (1983)

Species and Sex: $B6C3F_1$ mice, male

Endpoint: All squamous cell carcinomas

Exposure Route: Gavage

Doses	0	25	50	100
# affected	0	4	20	37
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: 1.814

Degrees of Freedom: 2

p-value: .4046

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = .145E-2$

$q_2 = .131E-3$

Linear term corresponding to 95% upper limit on risk (q_1^*): .773E-2

Data from NTP (1983)

Species and Sex: $B6C3F_1$ mice, male

Endpoint: Alveolar/Bronchiolar carcinoma

Exposure Route: Gavage

Doses	0	25	50	100
# affected	5	11	12	14
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: 1.250

Degrees of Freedom: 2

p-value: .5354

Maximum Likelihood Parameter Estimates:

q_0 = .137

q_1 = .234E-2

Linear term corresponding to 95% upper limit on risk (q_1^*): .421E-2

Data from NTP (1983)

Species and Sex: $B6C3F_1$ mice, male

Endpoint: Lymphoma, NOS

Exposure Route: Gavage

Doses	0	25	50	100
# affected	3	5	6	10
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .440E-1

Degrees of Freedom: 1

p-value: .8341

Maximum Likelihood Parameter Estimates:

q_0 = .639E-1

q_1 = .135E-2

q_2 = 0

q_3 = .234E-7

Linear term corresponding to 95% upper limit on risk (q_1^*): .280E-2

Data from NTP (1983)

Species and Sex: $B6C3F_1$ mice, female

Endpoint: All squamous cell carcinomas

Exposure Route: Gavage

Doses	0	25	50	100
# affected	0	0	1	7
# at risk	50	50	50	50

Multistage Model -

Chi-square Goodness-of-Fit Statistic: .123

Degrees of Freedom: 3

p-value: .9890

Maximum Likelihood Parameter Estimates:

$q_0 = 0$

$q_1 = 0$

$q_2 = 0$

$q_3 = .150E-6$

Linear term corresponding to 95% upper limit on risk (q_1^*): .760E-3