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MEMORANDOM

SUBJECT: Update of Quantitative Risk Assessment for Banner/Tilt

TO: Alan Katz, Toxicoligist
TOX/HED/OPP

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SUMMARY

This memo updates the initial Quantitative Risk Assessment (see the Tox Branch Peer Review of Banner/Tilt and an undated Risk Assessment to Hank Jacoby, from Bertram Litt). This update, as requested by the Peer Review Committee, contains a revised tumor count by Alan Katz, an updated Peto Trend Test, and a new Q* based on a time to tumor analysis (Weibul182). The Peto Test indicates a significant dose related trend (p < .0001). Based on the Weibull time to tumor model, the new Q* is 7.87×10^{-2} (mg/kg/day)$^{-1}$ in human equivalent (versus 3×10^{-2} for the Q* based on the multistage model). As a result, the calculated risk, stated in the Litt memo, is marginally increased.

DATA and ANALYSIS

Alan Katz removed five male mice (# 26,79,145,149,180) from the analysis due mainly to autolysis. The actual raw data (time of death and liver tumor findings) is stored in the Stat. Team's Banner/Tilt file.

Table 1 contains the time intervals used in the trend test, together with the results of trend analysis.

TABLE 1

Peto Trend Test: Time Intervals and Significance Values

Week	Dose (ppm)				Sig. Values
	0	100	500	2500	
0 – 52	0/2	0/5	2/4	1/8	.51
53	2/12	0/11	3/11	4/9	.018
54 – 78	5/9	3/11	1/10	14/15	.0001
79 – 92	3/9	1/9	3/6	11/11	.0001
93 – 104	6/7	3/7	4/9	4/5	.25
105	12/24	7/20	12/21	14/14	.0001
TOTAL	28/63	14/63	25/61	48/62	.0001

The $Q^*(7.87 \times 10^{-2})$ in human eqivalent is derived from the Weilbull82 program as follows:

1. For a given time of 104 weeks, and the fixed risk level of 10^{-6} the associated .95 lower confidence bound on the dose was 1.27654×10^{-2} ppm.

2. Assuming linearity, Q^* in ppm is derived by:

$$Q^* = Risk/Dose$$

$$= 7.87 \times 10^{-4} \ (ppm)^{-1}$$

3. The human equivllent is then approximately :

$$Q^*(human) = 100 \times Q^*$$

sb/hl