TXR No. 0050263

MEMORANDUM November 8, 2001

SUBJECT: REVISED **Sodium Salt of Aciflourfen** (Tackle™, Blazer™) Quantitative Risk Assessment (Q_1^*) Based On B6C3F1 Mouse Dietary Study Using mg/kg b.w.^$^3/_4$'s/day Cross Species Scaling Factor

P.C. Code 114402

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The unit risk, $Q_1^*(mg/kg/day)^{-1}$, for Sodium Salt of Aciflourfen (Tackle™, Blazer™) is 1.27×10^{-2} in human equivalents based on male mouse liver adenoma and/or carcinoma combined tumor rates. The dose levels used from the 80-week dietary study were 0, 119, 259, and 655 mg/kg/day of Aciflourfen. The corresponding tumor rates were 9/58, 21/60, 16/56, and 40/59, respectively.

Background

On January 13, 1988, the Cancer Peer Review Committee classified Aciflourfen as a Group B2 - probable human carcinogen, and recommended that, for the purpose of risk characterization, a low dose extrapolation model be applied to the experimental animal tumor data

for quantification of human risk (Q_1^*). A Q1* based upon male liver (carcinoma and/or adenoma) tumor rates was generated using mg/kg b.w.$^{2/3}$'s/day cross species scaling factor (Aciflourfen, sodium salt (Tackle), Revised Quantitative Risk Assessment - 80 week B6C3F1 Mouse Dietary Study, B. Fisher, 8/25/93). A subsequent memo was generated to reflect the Agency policy change from use of the $^2/_3$'s to the $^3/_4$'s scaling factor in 1994[1] (REVISED Sodium Salt of Aciflourfen (Tackle™, Blazer™) Quantitative Risk Assessment (Q_1^*) Based On B6C3F1 Mouse Dietary Study Using mg/kg b.w.$^{3/4}$'s/day Cross Species Scaling Factor, L. Brunsman, 8/23/2000, TXR No. 0014296). This memo has been generated to correct the mg/kg/day dose levels in light of the fact that the test material was originally believed to have been a 24% aqueous solution, but is now known to have been pure sodium acifluorfen (Acifluorfen: Request of the Recalculation of the Q_1^*, P. Chin, 11/5/2001).

All unit risks have been converted from animals to humans by use of the $^3/_4$'s scaling factor (Tox_Risk program, Version 3.5, K. Crump, 1994)[1]. For the conversion to human equivalents, weights of 0.03 kg for the mouse, 70 kg for humans were used and the use of 80 weeks for the mouse life-span default were used.

It is to be noted that the Q_1^* $(mg/kg/day)^{-1}$ is an estimate of the upper bound on risk and that, as stated in the EPA Risk Assessment Guidelines, "the true value of the risk is unknown, and may be as low as zero."

Dose-Response Analysis

The statistical evaluation of mortality (Quantitative Risk Assessment for Aciflourfen (TACKLE/BLAZER), H. Lacayo, 10/4/84) indicated a statistically significant increase in mortality with increasing doses of Aciflourfen in male mice. The unit risk, Q_1^*, was obtained by the application of the time-to-tumor Weibull model (Tox_Risk program, Version 3.5, K. Crump, 1994).

Male mice had a significant increasing trend, and significant differences in the pair-wise comparisons of all dose groups with the controls, for liver adenoma and/or carcinoma tumors combined.

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[1]See memo - Deriving Q_1^*s Using the Unified Interspecies Scaling Factor, P.A. Fenner-Crisp, Director, HED, 7/1/94.