Sumary of pharmacokinetic and toxicity studies with luciferase / coelenterazine

Coelenterazine

Study	Test material	Test animals	Outcome	Notes
IV pharmacokinetics	Coelenterazine	Dogs - Beagle n= 3 M	mean maximum plasma concentrations 77733 ng/mL at 0.033 hour post-dose. The mean plasma exposure from time zero to 24hr (AUC0-last)) 14707 ng.h/mL. Plasma coelenterazine below LOQ at 24Hr	Single iv dose 20mk/kg, concn 20mg/L. Target dose vol 1mL/lg
Oral pharmacokinetics	Coelenterazine	Dogs - Beagle n= 3 M	mean maximum plasma concentrations for Coelenterazine 6.61 ng/mL at 0.5 hour post-dose. AUC0-last 25.3 ng.h/mL. mean absolute oral bioavailability 0.0172% Plasma coelenterazine below LOQ at 24Hr	Single oral gavage dose 200mk/kg, concn 40mg/L Target dose vol 5 mL/kg
14 oral gavage	Coelenterazine 1.0 mg/kg/day	Rat n=11	No observed toxicity	
14 day I.p.	Coelenterazine 1.0 mg/kg/day	Mouse n=6	No observed toxicity	
Acute eye irritation	Coelenterazine 1.0 mg/eye	Rabbit n=4	No significant irritation	
Acute dermal irritatrion	Coelenterazine 1.0 mg	Rabbit n=4	No significnat irritation	

Study	Test material	Test animals	Outcome	Notes
In vitro micronucleus screening assay	Coelenterazine	Chinese hamster ovary (CHO-WBL) cells in presence and absence of S9	Negative up to 50mcg/ml	Study No: 139-0002
In vitro micronucleus screening assay	Coelenterazine	Chinese hamster ovary (CHO-WBL) cells in presence and absence of S9	Negative up to 500mcg/ml minimal cytotoxicity below 70mcg/ml	Study No: 139-0004
In vitro chromosomal aberration	Coelenterazine	Chinese hamster ovary (CHO-WBL) cells in presence and absence of S9	no significant increase of the percentage of cells with structural or numerical aberrations compared to the solvent control at any dose level up to 60 mcg/ml	Study No: 139-0005

Study	Test material	Test animals	Outcome	Notes
Mouse Bone Marrow Micronucleus Assay	Coelenterazine	mouse	Negative up to 2000 mg/kg	Study No: 130-0008
mini-Ames mutagenicity	Coelenterazine	S typhimurium (TA98, TA100) in the presence or absence S9	Negative up to the highest dose 1000 µg/plate	Study No.: 139-0001
mini-Ames mutagenicity	Coelenterazine	S typhimurium (TA98, TA100) in the presence or absence S9	Negative up to the highest dose 1000 µg/plate	Study No.: 139-0003

Study	Test material	Test animals	Outcome	Notes
Ames mutagenicity	Coelenterazine	S typhimurium (TA98, TA100, TA1535 and TA1537) and E coli WP2 uvrA, pKM101, in the presence or absence S9	Negative up to the highest dose 5000 µg/plate	Study No 139-0006

Renilla luciferase + Coelenterazine

Study	Test material	Test animals	Outcome	Notes
Acute oral toxicity	Renilla luciferase + Coelenterazine 5g/kg	Rat n=5m, 5f	LD50>5g/kg	No deaths observed

Study	Test material	Test animals	Outcome	Notes
Acute dermal irritatrion	Renilla luciferase + Coelenterazine	Rabbit n=6	No significant irritation	
Acute dermal irritatrion	Renilla luciferase + Coelenterazine	Rabbit n=5	No significant irritation	

Luminous food as consumed

Study	Test material	Test animals	Outcome	Notes

Study	Test material	Test animals	Outcome	Notes
Acute Oral toxicity	Luminous lollipop	KM Mouse (SPF) M&F n= not identifed	LD50>15g/kg	No deaths observed
Acute Oral toxicity	Luminous cream	KM Mouse (SPF) M&F n= not identifed	LD50>10g/kg	No deaths observed