

SAFETY AND REGULATORY ACCEPTANCE

- Demonstrated in multiple preclinical models & in human
- One FDA-approved IND & one US Phase-1 trial completed

Study	Animal	Route of Administration	Maximum CLEAR SOL™ Dose in Human Equivalent Dose (HED mg/kg/day)	Dosing regimen	Systemic toxicity	Injection site reaction	Note	
1	Rats	Slow Intravenous injection (15 min infusion)	145 (MTD)	Single dose, rangefinder	Maximally Tolerated Dose (MTD) at 900 mg/kg rat = 145 mg/kg HED	No		
2	Rats	Slow Bolus Intravenous injection (5 min infusion)	121	Daily dosing, repeated for 28 days	No kidney toxicity, while an equivalent dose of <u>SBECD</u> caused <u>renal tubular & cortex vacuolization</u> at 750 mg/kg/day rat	Not up to 75 mg/kg HED	Head-to-head safety comparison with SBECD	
3	Beagle dogs	Slow Intravenous injection (30 min infusion)	83.4	Daily dosing, repeated for 28 days	Well tolerated. No mortality or significant change in BW, vital signs, ophthalmologic exam, EKG, blood chemistry 1:4 animals showed mild hepatic microscopically at 1.5g/day dog	No		
4	Rats	Subcutaneous injection	136	Single dose	No mortality at 843 mg/kg rat	No		
5	Rats	Subcutaneous injection	169	Single dose	Well tolerated, no mortality or significant change in BW, vital signs, ophthalmologic exam, EKG, blood chemistry at 1048 mg/kg rat	minimal reversible injection site reactions	GLP	
6	Human	Subcutaneous injection (abdomen or outer thigh)	3.6 (assuming 60 Kg person)	Single dose	No SAEs & no TEAEs were judged to be serious, and all resolved by the end of the study	Well tolerated	Phase-1 under a US IND, 35 subjects	
7	Human	Oral & topical	All ingredients in CLEAR SOL™ are GRAS and are assumed safe for oral and topical use					