BIOCOMPATIBILITY TESTING

MHLW to ISO Comparison

	Extraction/Sample Preparation		Methodology		TAT (DAYS)		Sample Requirements	
	MHLW	ISO	MHLW	ISO	MHLW	ISO	MHLW	ISO
Cytotoxicity	24 hrs in EMEM + 10% FBS	24 hrs in EMEM + 5% FBS	Dilute suspension of cells is concurrently plated with extract and incubated for 7 days.	Extract is added to cell monolayer and observed up to 72 hrs.	31	18	2.5g or 150cm^2	1g, 30cm^2 or 15cm^2
Genotoxicology Bacterial Reverse Mutation Test	Exhaustive extract in methanol/acetone with terminal evaporation	50°C / 72 hrs extract in saline & DMSO	Extracts combined with agar and bacteria. Plates incubated for 72 hrs and colonies enumerated.		40	28	10 grams (Pretest) Method 1: TBD Method 2: 1g	0.8g, 24cm^2 or 12 cm^2 (x2)
Genotoxicology – Chromosome Aberration	Exhaustive extract in methanol/acetone with terminal evaporation	50°C / 72 hrs extract in saline & DMSO	Extracts applied to a cell monolayer for up to 20 hrs. Cells harvested and prepared for microscopic examination of gross chromosomal damage.		62		10 grams (Pretest) Method 1: TBD Method 2: 2g	4g, 120cm^2 or 60cm^2 (x2)
Genotoxicology – Mouse Micronucleus	Exhaustive extract in methanol/acetone with terminal evaporation	50°C / 72 hrs extract in saline & sesame oil	The test article extract used to evaluate potential to induce micronuclei formation in bone marrow of CD-1 mice.		55		10 grams (Pretest) Method 1: TBD Method 2: 3g	0.8g, 24cm^2 or 12 cm^2 (x2)
Genotoxicology – Mouse Lymphoma	Exhaustive extract in methanol/acetone with terminal evaporation	50°C / 72 hrs extract in saline & DMSO	Extract evaluated for ability to induce forward mutations at thymidine kinase locus as assayed by colony growth of L5178Y mouse lymphoma cells.		39		10 grams (Pretest) Method 1: TBD Method 2: 2g	4g, 120cm^2 or 60cm^2 (x2)
Hemolysis	Extract exposure for 1, 2 & 4 hrs	Direct exposure for 3 hrs	Extract placed in dilute solution of rabbit blood for 1, 2 & 4 hrs. Optical density is scanned.	Test article placed into dilute solution of rabbit blood for 3 hrs. Optical density is scanned.	32	21	4g, 120cm^2 or 60cm^2 (x6)	4g, 120cm^2 or 60cm^2 (x3)
Complement Activation	Direct contact with NHS for 1 hr. (Sponsor supplied comparison recommended.)		Test and control NHS tested via ELISA plate		25		4g, 120cm^2 or 60cm^2	
Irritation – Intracutaneous	Extraction methods identical		3 rabbits dosed intracutaneously with each extract. Observations & scoring up to 72 hrs. MHLW requires site photos at dosing & scoring periods. Terminal weights recorded.		29		1.2g, 36cm^2 or 18cm^2 (x2)	
Irritation – Primary Skin	Standard extraction	One-inch-square pieces of test article	3 rabbits per extract, at least 2 extracts. Patched 24 hrs, scratched & unscratched skin. Site photos during scoring. Terminal weights recorded.	3 rabbits, patches applied for 4 or 24 hrs, removed and scored.	30		4g, 120cm^2 or 60cm^2 (x2)	2.5cm^2 x 2.5cm^2 (x7)
Sensitization – Guinea Pig Maximization	Exhaustive extract in methanol/acetone with terminal evaporation	50°C / 72 hrs extract in saline & sesame oil	Per extract: 11 test animals plus 6 negative & 6 positive controls run concurrently. Terminal weights recorded.	Per extract: 11 test animals plus 6 negative controls. Positive control validation with 11 animals run every 3 months.	Pretest + 54	47	10 grams (Pretest) Method 1: TBD Method 2: 20g	2g, 60cm^2 or 30cm^2 (x6)
Sensitization – Murine Local Lymph Node	Three options: • standard extraction • exhaustive extract in methanol/acetone • concentrations/dilutions prepared in saline or DMSO	50°C / 72 hrs extract in saline & DMSO or PEG	15 mice per extract or 25 mice for liquids or dissolved solids	15 mice per extract	32	Pretest + 32	Contact lab.	1g, 30cm^2 or 15cm^2 (x6)
Implantation	Preparation methods identical		3 rabbits, either sex. 4-6 test articles can be implanted. Photos at necropsy & pathology evaluation.	3 rabbits, either sex. 4-6 test articles can be implanted.	Same implant duration		~10mm x 3mm (x15)	
Acute Systemic Toxicity	121°C extractions must be performed in an autoclave.	50°C / 72 hrs extract in saline & sesame oil	Necropsy required at study termination. Body weight loss indicative of toxicity if statistically significant between test and control.	Necropsy not required. Body weight loss indicative of toxicity if 3 or more lose greater than 10%.	27		1.6g, 48cm^2 or 24cm^2 (x2)	
Subacute Toxicity (MHLW) Subacute/Subchronic Toxicity (ISO)	Mentions only use of saline as extraction vehicle.	Saline and/or sesame oil can be used.	Rats only. IV dosing for 14 days. Dose of 20 mL/kg.	Mice or rats. Study length and number of doses not outlined. Daily dosing regimen.	105	14-Day: 82 28-Day: 105	20g, 600cm^2 or 300cm^2 (x28)	Mice: 1.6g, 48cm^2 or 24cm^2 Rats: 9g, 270cm^2 or 135cm^2 (x14 or x28)
Pyrogen	Extraction methods identical		Initial test method identical to ISO. 3 rabbits for each continued test (up to 2).	Initial test method identical to MHLW. 5 rabbits used for (only 1) continued test.	26		30g, 900cm^2 or 450cm^2	

Talk to us and find out how our biocompatibility testing services can work for you.

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