BioReliance

Toxicology Services

Enhance your 3R Strategy

Replacement, Reduction, Refinement

There is an increased emphasis in the field of toxicology on services that moderate testing with animals. BioReliance provides an innovative mindset towards the 3Rs (replacement, reduction, refinement) and today offers the most comprehensive testing program for genetic toxicology and carcinogenicity to enhance your strategy.

BioReliance's History Supports the 3Rs

- The concept of the 3Rs, first proposed by Russell and Burch in mid 1950s[1], has led to a paradigm shift in the field of toxicology away from whole animal testing to in vitro approaches.
- Since inception, BioReliance has been at the forefront of the 3R movement. In the 1950s, what was then Microbiological Associates supplied commercial cell cultures and performed in vitro safety testing on the first polio vaccines.
- In the 1990s, BioReliance worked with NTP to validate the first transgenic models for carcinogenicity testing
- Today BioReliance solidifies our position as a 3R leader with a comprehensive offering of 3R methods for genetic toxicology and carcinogenicity testing and most recently with the introduction of the novel 3D Reconstructed Human Skin Micronucleus Assay.
- BioReliance furthers the 3Rs through involvement in key external groups including the ILSI-HESI Genetic Toxicology Technical Committee, and as a founding member of the new ASCCT Society (The American Society of Cellular and Computational Toxicology)

Innovations for 3R Programs

In Vitro 3D Human Skin Micronucleus Assay—a novel method for testing the genotoxicity of dermal exposures, including cosmetics.

On February 27, 2003, EU member states enacted The 7th Amendment of the EU Directive 76/768/EEC. This amendment requires cosmetics manufacturers and distributors to provide certain product information for the safety of the end user. This amendment prohibits testing of finished cosmetic products and cosmetic ingredients on animals (testing ban), and prohibits marketing of finished cosmetic products and ingredients included in cosmetic products which were tested on animals (marketing ban in EU member countries).[2] The ban on in vivo genotoxicity testing for these products was made effective in March 2009. The final deadline for implementation of this ban occurred on March 11, 2013.

The 3D human skin micronucleus assay provides the first genotoxicity tissue model testing approach for use as a follow-up for chemicals/drugs that are positive in the standard in vitro genotoxicity assays.

BioReliance's Comprehensive 3R Services

Replacement

- Standard In Vitro Genotoxicity Assays
- In Vitro Micronucleus Assay in 3D Reconstructed Skin Models
- High through-put 96 well screening tests
- In Vitro Cell Transformation Assays

Reduction

- *Pig-a* In Vivo Gene Mutation Assay
- Standard In Vivo Genotoxicity Assays
- Combined Micronucleus and Comet Assay
- Integrated genotoxicity endpoints in repeat dose studies
- 26-week Transgenic Carcinogenicity Assays
- Big Blue Transgenic In Vivo Mutation Assay

Refinement

- Euthanex® - Quick and painless Euthanasia of small laboratory animals

BioReliance offers the most comprehensive commercial offerings adhering to the 3Rs

All Animal Testing for Cosmetic products banned in the EU, effective March 11, 2013

References

1 Russell, W.M.S and Burch, R.L. The principles of humane experimental technique. Methuen, 1959 Print, 2008 digitized.

2 "DIRECTIVE 2003/15/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 February 2003 amending Council Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products. <http://ec.europa.eu/consumers/sectors/cosmetics/files/doc/200315/200315_en.pdf>"

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Selected Assays for 3R Testing Programs

Assay Name	Protocol Number	Test System	Assay Design	Gram TA Required
Screening Assays				
Ames Abbreviated	501	Salmonella strains (TA98, TA100)	Plate incorporation, 8 dose levels, 5 mg/plate max., neg. and pos. controls, ±S9	90 mg
Ames II	850	Salmonella strains (TA98, TAMix)	6 dose levels, 1000 µg/mL high dose, neg. and pos. controls, ±S9, in triplicate	6 mg
Abbreviated Mouse Lymphoma Assay (MLA)	702007	TK gene in mouse lymphoma cells	treatments of 4 hours +S9 and 24 hours -S9, 15 doses, 6 cloned	400 mg
In Vivo Micronucleus Assay	121	Bone Marrow	Single administration, 2 collection times, 6 doses tested, 3 doses evaluated, 3 mice/sex/group/time point, 2000 PCE evaluated/animal in mice	1.5 g
Pig-a Gene Mutation Assay	460033FlowNGLP.BTL	Rat Peripheral Blood	3 daily doses, 3 harvests. 6 male rats per group, 3 dose groups plus vehicle and positive control. 1-3 million RET and 100 million RBC scored per sample. Non-GLP	50 g
Chromosome Aberration Assay	336	CHO cells	Duplicate cultures, treatments of 4 hours +S9 and 20 hours -S9, 15 doses, score 3, 100 metaphases scored per dose, aberrations not classified (3 treatment avail. Upon request) - No range finder	300 mg
In Vitro Micronucleus Assay	349	HPBL	5 mL cultures, treatments of 4 hours +S9 and 24 hours -S9, 15 doses, score 3, 500 cells scored, in duplicate	300 mg
In Vitro Comet Assay	400	HPBL, CHO, TK6, or V79	4 hour treatment, 8 dose levels, highest dose-5000 µg/mL, duplicate cultures, ±S9, 50 cells scored per slide	300 mg
Bhas-42 Initiator and Promoter Cell Transformation Assay	320	Bhas-42 cells	Preliminary range finder for 7 days, followed by definitive assay consisting of 3 days dosing for initiator assay and 10 days dosing for promoter assay (total 21 days)	300 mg
GLP In Vitro Assays				
Ames Assay	502	Salmonella/E. coli strains†	OECD - Preliminary toxicity assay, 1 replicate/dose - 1 mutagenicity assay, 3 replicates/dose	900 mg
Mouse Lymphoma Assay	704	TK gene in L5178Y mouse lymphoma cells	ICH/OECD - preliminary toxicity assay, 1 trial, treatments of 4 hours +S9 and 4 and 24 hours -S9, 2 cultures/dose	3.5 g
CHO/HGPRT Gene Mutation Assay	782	HGPRT gene in CHO cells	OECD - preliminary toxicity assay, treatments of 5 hours ±S9, 1 trial, 2 cultures/dose	1.5 g
Chromosomal Aberration Assay	331	CHO or CHL	ICH/OECD - preliminary toxicity assay, treatments of 4 hours +S9 and 4 and 20 hours -S9, 20 hour collection. Minimum 3 dose levels in duplicate scored for chromosome aberrations. RICC as primary and mitotic index as secondary measure of toxicity.	1 g
In Vitro Micronucleus Assay	348	HPBL	OECD - preliminary toxicity assay, treatments of 4 hours +S9 and 4 and 24 hours -S9, 24 hour collection, 9 doses, score minimum of 3, 2000 cells scored per dose level	1 g
Reconstructed Skin Micronucleus Assay (RSMN)	358	EpiDerm 3D skin	Preliminary toxicity assay, 2-3 days of treatments of up to 6 dose levels in triplicate (score 3)	TBD
Micronucleus Assay	368	CHO Cells	Preliminary toxicity assay, treatments of 4 hours +S9 and 4 and 24 hours -S9, 24 hour collection, score minimum of 3 dose levels for micronucleus induction, 2000 cells scored per dose level	200 mg
GLP Study Options				
In Vitro Micronucleus Option - Anti-Kinetochore Labeling	CREST_001.BTL	Slides	Slides stained for up to 3 treatment conditions and PCs. Evaluation of dose level(s) statistically positive for the presence of micronuclei	N/A
In Vitro Micronucleus Option - Fluorescent In Situ Hybridization (FISH)	FISH_001.BTL	Slides	Slides labeled (stained) for up to 3 treatment conditions. Evaluation of dose level statistically positive for the presence of micronuclei	N/A
GLP In Vivo Assays				
In Vivo Micronucleus Assay	123012.BTL	Mouse Bone Marrow	Single administration, 2 collection time points, 2000 PCE evaluated per animal, 35 animals/sex	3.5 g
	125012.BTL	Rat Bone Marrow		23 g
Metaphase Analysis	107GLP	Rat Bone Marrow	Single administration, 2 collection time points, 100 metaphases evaluated/animal. 35 animals/sex	24.5 g
	108	Mouse Bone Marrow		3.5 g
Pig-a Gene Mutation Assay	460033Flow.BTL	Rat Peripheral Blood	3 daily doses, 3 harvests. 6 male rats per group, 3 dose groups plus vehicle and positive control. 1-3 million RET and 100 million RBC scored per sample.	50 g
In Vivo Rodent Comet Assay®	421	Mouse tissue	Triple dose administration, 1 collection time, 25 animals/sex	7.2 g
	423	Rat tissue		50.75 g
In Vivo Rodent Micronucleus and Comet Assay	431	Mouse tissue only for Comet, Blood or tissue for MN	Triple dose administrations, 1 collection time for Comet and MN (5 animals/group/sex, 5 groups)-Males and females	7.25 g
	433	Rat tissue only for Comet, Blood or tissue for MN	Triple dose administrations, 1 collection time for Comet and MN (5 animals/group/sex, 5 groups)-Males and females	50.5 g

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