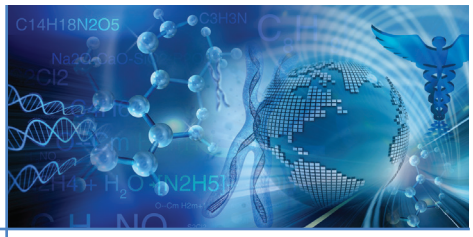
BioReliance

Toxicology Services



Genetic Toxicology Worldwide Regulatory Guidelines

BioReliance's genetic toxicology assays are validated, qualified and conducted according to state-of-the-art global regulations, guidelines, and scientific guidance.

Regulations and Regulatory Guidance

Genetic Toxicology testing is required as part of the hazard assessment process for every type of product intended for human exposure. Specific assays and designs may differ slightly, but each of the below regulations requires the results of a battery of Genetic Toxicology assays to be submitted for approval.

Product Type	Governing Agency	Guideline	Harmonized Battery	GLP	Legislation/Regulation
Pharmaceuticals	US FDA (CDER)	ICH S2(R1)	ICH, OECD	21 CFR Part 58	Federal Food, Drug and Cosmetic Act (21 CFR Part 9)
	European Medicines Agency (EMA)	ICH S2(R1)	ICH, OECD	Directives 2004/9/EC and 2004/10/EC	Eudralex Volume 1: Directive 2001/83/EC
	Japan Pharmaceutical Manufacturers Association (JPMA)	ICH S2(R1)	ICH, OECD	Ordinance No. 21 and 114	Pharmaceutical Affairs Law (Law No. 96, July 31, 2002)
Industrial Chemicals	US Environmental Protection Agency (EPA)	OCSPP	OECD	EPA 40 CFR Part 792 (TSCA)	Toxic Substances Control Act (TSCA)
	European Chemicals Agency (ECHA)	REACH	OECD	Directives 2004/9/EC and 2004/10/EC	Council Regulation (EC) No 1907/2006
	Ministry of Economy, Trade and Industry (METI)	CSCL	OECD	Act No. 39	Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture (Act No. 117)
Agricultural Chemicals	US Environmental Protection Agency (EPA)	OCSPP	OECD	EPA 40 CFR Part 150-189(FIFRA)	Federal Insecticide, Fingicide and Rogenticide Act (FIFRA)
	European Chemicals Agency (ECHA)	5.4 Geno-toxicity testing	OECD	Regulations EU 283/2013, and EU 284/2013	Regulations EU 283/2013, and EU 284/2013
	Ministry of Economy, Trade and Industry (METI)	CSCL	OECD	Act No. 39	Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture (Act No. 117)
Consumer Products (Cosmetics)	US FDA (CPSC)	see CP SL	OECD	21 CFR Part 58	Consumer Products Safety Commission (CFR Title 16, Chapter IIA)
	EC (SCCS)	SCCP	OECD	Directives 2004/9/EC and 2004/10/EC	Directive (2013/00049), EU 7th Amendment to Cosmetics Directive

As a specialty provider with a focus on Genetic Toxicology, BioReliance offers a comprehensive portfolio of GLP assays for regulatory approval needs:

- The latest OECD-compliant designs
- Over 65 years of laboratory operations
- Worldwide expertise and representation on Genetic Toxicology Expert Working Groups
- Fully audited and proficient laboratory
- Large historical database for every assay
- Expert advice and guidance on assay selection
- Clear guidance for managing positive test results

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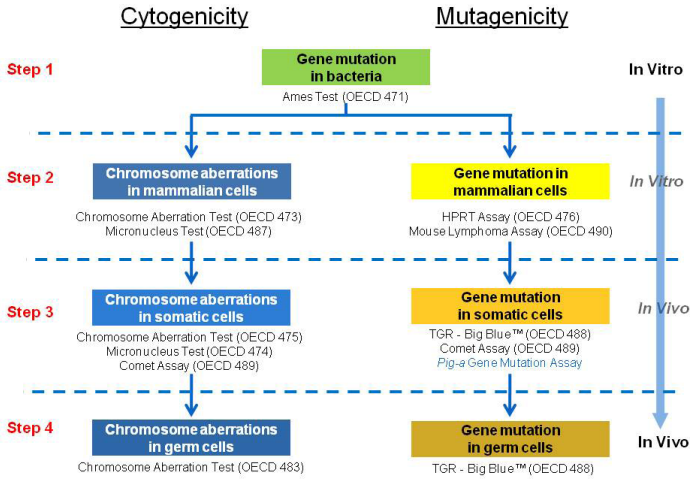
Genetic Toxicology Assays for Regulatory Submission

Product Type	Governing Agency	Guideline	Harmonized Battery	GLP	Legislation/Regulation
Flavors / Food Additives	US FDA (CFSAN)	Redbook 2000 (Sect IV.C.1) FEMA GRAS	OECD and US EPA	40 CFR 160, Part 792	Food Additives Amendment (FAA)
	EU EFSA	REACH	OECD	Directives 2004/9/EC and 2004/10/EC	Council Regulation (EC) No 1334/2008
Fragrances	US FDA	IFRA	OECD	21 CFR Part 58	FD&C Act (FFDCA) Federal Food, Drug and Cosmetic Act (21 CFR Part 9)
	EU (SCCS)	REACH	OECD	Directives 2004/9/EC and 2004/10/EC	Council Regulation (EC) No 1223/2009
Veterinary Medicine	US FDA (CVM)	VICH GL-23	ICH, OECD, EU, US, AU and NZ	21 CFR Part 58	Federal Food, Drug and Cosmetic Act (CPG Sec. 607.100)
Medical Devices	US FDA (CDRH)	General Memoran-dum 95-1	OECD	ISO 10993, Part 3	Federal Food, Drug and Cosmetic Act (21 CFR Part 9)
	EU Member States	Medical Devices Directive	OECD	Directives 2004/9/EC and 2004/10/EC	Directives 90/385/EEC, 93/42/EEC, 98/79/EC
	Pharmaceuticals and Medical Devices Agency (PMDA)	Notifica-tion No. 99	OECD	Ordinance No. 37 and 115	Pharmaceutical Affairs Law (Law No. 96, July 31, 2002)

The required assays for a regulatory submission may differ slightly, but all types of products, whether in development or undergoing a safety/hazard/risk assessment must be tested with a battery of Genetic Toxicology assays. The battery is intended to provide a paradigm for prediction of hazard and if needed follow-up on assays to resolve a positive finding. The specific guidelines are referenced in the preceding table, and below is an overview of assay categories.



Step 1	GLP Genetic Toxicology testing usually begins with an Ames Assay to detect gene mutations in bacteria
Step 2	If further investigation is warranted, needed or required an in vitro assay in mammalian cells is typically chosen. Assays can be selected to assess cytogeneticity (clastogenicity or aneugenicity) or mutagenicity, depending on findings in the Ames assay or specific knowledge from the compound or class of compound.
Step 3	Many regulations require at least one in vivo assay be performed. The assay often is chosen based based on findings from the in vitro assays, and usually continues the investigation with an assay that detects similar types of DNA alteration as observed in the in vitro assays
Step 4	Initially in vivo assays conducted to investigate genotoxicity in somatic cells, but there are some cases where investigation of effects in germ cells is required

For more information please consult information on specific assays, BioReliance's website or a BioReliance representative.

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