Toxicology Testing

Genetic Toxicology Service List

Comprehensive

BioReliance® by SAFC

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Regulatory Battery

BioReliance is a leading provider of services for Genetic Toxicology evaluation to meet global regulatory guidelines. The tables below list the categories and assays required for different regulations.

Product Type	Governing Agency	Guideline	Harmonized Battery	Reference	GLP	Legislation/Regulation
Pharmaceuticals	US FDA (CDER)	ICH S2(R1)	ICH, OECD	**www.fda.gov/opacom/laws/**	21 CFR Part 58	Federal Food, Drug and Cosmetic Act (21 CFR Part 9)
	European Medicines Agency (EMA)	ICH S2(R1)	ICH, OECD	**www.ema.europa.edu**	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	**www.jpma.or.jp/english**	Ordinance No. 21 and 114	Pharmaceutical Affairs Law (Law No. 96, July 31, 2002)
Industrial Chemicals	US Environmental Protection Agency (EPA)	OCSPP	OECD	**www.epa.gov/epahome/lawregs.htm**	EPA 40 CFR Part 792 (TSCA)	Toxic Substances Control Act (TSCA)
	European Chemicals Agency (ECHA)	REACH	OECD	**www.echa.europa.edu**	Directives 2004/9/EC and 2004/10/EC	Council Regulation (EC) No 1907/2006
	Ministry of Economy, Trade and Industry (METI)	CSCL	OECD	**www.meti.go.jp**	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	**www.epa.gov/epahome/lawregs.htm**	EPA 40 CFR Part 150-189(FIFRA)	Federal Insecticide, Fingicide and Rogenticide Act (FIFRA)
	European Chemicals Agency (ECHA)	5.4 Genotoxicity testing	OECD	**www.echa.europa.edu**	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	**www.meti.go.jp**	Act No. 39	Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture (Act No. 117)
Consumer Products	US FDA (CPSC)	see CP SL	OECD	**http://www.cpsc.gov/**	21 CFR Part 58	Consumer Products Safety Commission (CFR Title 16, Chapter IIA)
	EC (SCCP)	SCCP	OECD		Directives 2004/9/EC and 2004/10/EC	Directive (2013/00049), EU 7th Amendment to Cosmetics Directive
Flavors / Food Additives	US FDA (CFSAN)	Redbook 2000 (Sect. IV.C.1) FEMA GRAS	OECD and US EPA	**http://www.cfsan.fda.gov/~redbook/red-ivb2.html**	40 CFR 160, Part 792	Food Additives Amendment (FAA)
	EU EFSA	REACH	OECD	**www.echa.europa.edu**	Directives 2004/9/EC and 2004/10/EC	Council Regulation (EC) No 1334/2008
Fragrances	US FDA	IFRA	OECD	http://www.fda.gov/Cosmetics/ProductsIngredients/Ingredients/ucm388821.htm	21 CFR Part 58	FD&C Act (FFDCA) Federal Food, Drug and Cosmetic Act (21 CFR Part 9)
	EU (SCCS)	REACH	OECD	**www.echa.europa.edu**	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, Australia and NZ	**http://vich.eudra.org/**		
Medical Devices	US FDA (CDRH)	General Memorandum 95-1	OECD	**http://www.fda.gov/MedicalDevices/default.htm**	ISO 10993, Part 3	Federal Food, Drug and Cosmetic Act (21 CFR Part 9)
	EU Member States	Medical Devices Directive	OECD	**http://ec.europa.eu/health/medical-devices/**	Directives 2004/9/EC and 2004/10/EC	Directives 90/385/EEC, 93/42/EEC, 98/79/EC
	Pharmaceuticals and Medical Devices Agency (PMDA)	Notification No. 99	OECD	**http://www.pmda.go.jp/english/**	Ordinance No. 37 and 115	Pharmaceutical Affairs Law (Law No. 96, July 31, 2002)

GLP In Vitro Assays

Bacterial Mutation Assays (Ames)

OECD 471 - *Salmonella / Escherichia coli* Reverse Mutation Assay

This assay detects reverse mutations at histidine genes in *Salmonella typhimurium* or a tryptophan gene in *Escherichia coli*. The bacterial reverse mutation assay, commonly called the Ames assay, typically employs five tester strains (for example, *Salmonella* TA98, TA100, TA1535, and TA1537 and *E. coli* WP2 *uvr*A) each tested with and without S9 activation. Additional or alternate tester strains may be used as described in the OECD and ICH guidelines. Any version of the Ames Assay can be performed with any or all of the strains specified by OECD/ICH.

Regulatory Guidance on Independent Repeat Assays: It is not necessary to conduct an independent repeat assay when the test article is clearly positive or when it is negative (justification is required for OECD, but not ICH). Per both the ICH and OECD guidelines, equivocal results require retesting using an appropriate modification of the experimental design (e.g., dose levels, activation system or treatment method). The inclusion of two independent mutation data sets is incompliance with both OECD and ICH.

Study Phases: Each phase is conducted with the selected tester strains both with and without S9 activation. A preliminary toxicity assay consists of a minimum of eight test article dose levels (one plate per dose) and concurrent vehicle controls. A toxicity-mutation assay consists of a minimum of eight test article dose levels (two replicate plates per dose) and concurrent vehicle and positive controls. A mutation assay consists of a minimum of five test article dose levels (three replicate plates per dose) and concurrent vehicle and positive controls.

Exposure Methods: The plate incorporation method combines the test article and test system in top agar just prior to plating; whereas the preincubation method co-incubates the test article with the test system before mixing with top agar and plating. The preincubation method is considered the more sensitive method for the detection of mutagens, especially for certain classes of chemicals.

Protocol*	Assay Description
502	**ICH/OECD protocol - Plate incorporation method:** Preliminary toxicity assay and one mutation assay.
502001	**ICH/OECD protocol - Plate incorporation method with independent repeat:** Preliminary toxicity assay and two mutation assays (initial and confirmatory).
502002	**ICH/OECD protocol - Plate incorporation method with preincubation independent repeat:** Plate incorporation method for preliminary toxicity assay and initial mutation assay. Preincubation method for independent repeat assay.
502005	**OECD protocol - Plate incorporation method:** No preliminary toxicity assay, one mutation assay.
503	**OECD protocol - Plate incorporation method with two trials:** One toxicity-mutation assay and a confirmatory mutation assay.
503001	**OECD protocol – Preincubation method with two trials:** One toxicity-mutation assay and a confirmatory mutation assay.
503005	**OECD protocol - Plate incorporation/preincubation with two trials:** One toxicity-mutation assay (plate incorporation) and a confirmatory mutation assay (preincubation).
504	**OECD protocol – Preincubation method:** Preliminary toxicity assay and one mutation assay.
504001	**ICH/OECD protocol – Preincubation method with independent repeat:** Preliminary toxicity assay and two mutation assays.
507001	**ICH/OECD protocol – Treat and Plate Method with two trials:** One toxicity-mutation assay and a repeat mutation assay. (for compounds containing histidine or tryptophan)

***Specialized protocols for reductive conditions, vapor or gas-phase exposure, and nonstandard S9 activation systems are available upon request.**

In Vitro Mammalian Cell Gene Mutation Assays

OECD 476 - L5178Y TK$^{+/-}$ Mouse Lymphoma Assay

This assay measures induction of mutations at the thymidine kinase (TK) gene in L5178Y mouse lymphoma cells. Preliminary toxicity assay and mutation assay performed with (+S9) and without (-S9) metabolic activation. Mutation assay includes cloning five to eight test article concentrations depending on protocol; three replicate plates per dose for cytotoxicity and mutant selection; concurrent vehicle and positive controls; colony sizing provided for vehicle and positive controls and for mutagenic test articles. For the ICH-compliant protocol 704, an additional non-activation assay with 24 hours continuous exposure is performed if initial 4 hour non-activation exposure is negative. All protocols use soft agar for mutant selection. For ICH-compliant protocols, negative results with S9 activation will not require an independent repeat unless the test article is known to have specific requirements for metabolism. In that case, an independent repeat assay with modified S9 activation will be performed when possible.

Protocol	Assay Description
704	**ICH/OECD protocol - Duplicate cultures per dose level:** Treatments of 4 and 24 hours without S9 and 4 hours with S9.
700	**OECD protocol - Single culture per dose level** Treatment of 4 hours with and without S9.
702	**OECD protocol - Duplicate cultures per dose level** Treatment of 4 hours with and without S9.
702001	**OECD protocol - Duplicate cultures per dose level with independent repeat** Treatment of 4 hours with and without S9.

OECD 476 - CHO/HPRT Gene Mutation Assay

This assay measures induction of mutations at the hypoxanthine-guanine phosphoribosyl transferase (HPRT) gene in Chinese hamster (CHO) cells. Preliminary dose-finding study and mutation assay performed with and without S9 activation. Includes: cloning five test article concentrations; triplicate plates per replicate culture for cytotoxicity and five plates per replicate culture for mutant selection; concurrent vehicle and positive controls. *Other cell lines available, including V79 (please inquire).*

Protocol	Assay Description
782	**OECD protocol - Duplicate cultures per dose level.** Treatment of 5 hours with and without S9.
782001	**OECD protocol - Duplicate cultures per dose level with independent repeat.** Treatment of 5 hours with and without S9.

In Vitro Cytogenetics

OECD 473 - Chromosomal Aberration Assays

This protocol is designed per OECD test guideline 473*. This assay measures chromosomal aberrations and polyploidy in vitro in: human peripheral blood lymphocytes (HPBL), Chinese hamster ovary (CHO) or Chinese hamster lung (CHL) cells and Rat Lymphocytes. Studies performed with (+S9) and without (-S9) metabolic activation, and includes: mitotic inhibition or cell growth inhibition (utilizing relative increase in cell counts) as a measure of toxicity, depending on source of cells. 150 metaphases are scored per culture, 300 per dose level. For ICH-compliant protocols, negative results with S9 activation will not require an independent repeat unless the test article is known to have specific requirements for metabolism. This would usually invoke the use of an external metabolizing system which is known to be competent for the metabolizing/activation of the class of the compound under test.
* Revised OECD guidelines adopted 9/26/14 allow for new and old versions to be employed for a period of 18 months. Designs listed here reflect new requirements. Old designs are available upon request.

Chromosomal Aberrations in Human Peripheral Blood Lymphocytes

Protocol	Assay Description
341	**ICH/OECD protocol (HPBL) -** Treatments of 4 and 20 hours without S9 and 4 hours with S9; cells collected at 20 hours. Numerical and structural aberrations analyzed in a minimum of 3 dose levels in duplicate. Includes mitotic inhibition as a measure of toxicity
331	**ICH/OECD protocol (CHO or CHL) -** Treatments of 4 and 20 hours without S9 and 4 hours with S9; cells collected at 20 hours. Numerical and structural aberrations analyzed in a minimum of 3 dose levels in duplicate. Includes cell growth inhibition, utilizing relative increase in cell counts (RICC) as a primary measure of toxicity and mitotic index as a secondary measure of toxicity.

Chromosomal Aberrations in Rat Lymphocytes

Protocol	Assay Description
140R	**Chromosome Aberrations in Rat Lymphocytes:** In vitro treatments of 4 and 24 hours without S9 and 4 hours with S9; cells collected at 24 hours. Minimum of three dose levels in duplicate with concurrent vehicle and positive controls. Includes mitotic index as a primary measure of toxicity.

OECD 487 - In Vitro Micronucleus Assay

This protocol is designed per OECD test guideline 487*. The assay measures micronucleus formation in vitro, using human TK6 Cells, Chinese hamster ovary (CHO) cells, or human peripheral blood lymphocytes. A specialty assay in EpiDerm™ 3D reconstructed human skin model is also available. Studies are performed with (+S9) and without (-S9) metabolic activation. Studies scored microscopically include an evaluation of the frequency of binucleated cells as a measure of toxicity. Micronucleus studies in CHO cells can be scored using flow cytometry.
* Revised OECD guidelines adopted 9/26/14 allow for new and old versions to be employed for a period of 18 months. Designs listed here reflect new requirements. Old designs are available upon request.

Protocol	Assay Description
361 *ICH S2(R1) Option*	**In Vitro Micronucleus Assay in TK6 Cells:** Treatments of 3-6 and 27 hours without S9 and 3-6 hours with S9, 9 doses for toxicity assessment, up to 4 dose levels evaluated for MN induction, 4000 cells scored per dose level.
348 *ICH S2(R1) Option*	**In Vitro Micronucleus Assay in HPBL:** Treatments of 4 and 24 hours without S9 and 4 hours with S9, 9 doses for toxicity assessment, minimum of three dose levels evaluated for MN induction, 4000 cells scored per dose level.
368 *ICH S2(R1) Design*	**In Vitro Micronucleus Assay in CHO Cells:** In situ method, treatments of 4 and 24 hours without S9 and 4 hours with S9, 9 doses for toxicity assessment, minimum of three dose levels evaluated for MN induction, and 4000 cells scored per dose level. Scoring by microscopy, with option for flow cytometric evaluation (please inquire).
358	**Reconstructed Skin Micronucleus Assay:** Treatments of up to 6 dose levels in triplicate (score 3).

Options for Mechanistic Analysis in Cytogenetic Assays

FISH and CREST labeling investigate the mode of action for a test article that is positive in a micronucleus assay. FISH and CREST labeling identify whether a micronuclei contains a whole chromosome(s), as a result of an aneugenic mechanism, or a chromosome fragment(s) as a result of a clastogenic mechanism. An aneugenic mechanism may be useful in identifying a threshold, which is very important in the overall risk assessment of a compound.

FISH (Fluorescent in situ Hybridization)

Centromeric labeling of micronuclei by FISH is a cytogenetic technique that is used to detect the presence or absence of centromeric DNA sequences on chromosomes.

Protocol	Assay Description
348FISH	**In Vitro Micronucleus Assay in HPBL with FISH Option Preparation:** Same design as 348, but includes triplicate cultures and slide preparation for FISH analysis.
348FISHselect	**In Vitro Micronucleus Assay in HPBL with FISH Option Preparation in select doses:** Limited treatments and doses as chosen from previous MN assay with positive results. Score all selected doses (triplicate cultures per treatment). Slides prepared for FISH analysis.
FISH_001	**Slide Preparation in HPBL, TK6 or CHO Cells and Analysis:** Slides labeled (stained) for up to 3 treatment conditions. Evaluation of dose level statistically positive for the presence of micronuclei.

* FISH Evaluation can be added to 361 (MN in TK6 cells) without additional preparation (FISH_001 only)

CREST Labeling

CREST uses a human autoimmune antibody that binds to kinetochores of chromosomes across species.

Protocol	Assay Description
348CREST	**In Vitro Micronucleus Assay in Isolated HPBL with CREST Option Preparation:** Similar design as 348, but includes additional culture and slide preparation for CREST option.
348CRESTselect	**In Vitro Micronucleus Assay in HPBL with CREST Option Preparation in select doses:** Limited treatments and doses as chosen from previous MN assay with positive results. Score all selected doses (triplicate cultures per treatment). Slides prepared for CREST option.
368CREST	**In Vitro Micronucleus Assay in CHO Cells with CREST Option Preparation:** Same design as 368, but includes additional culture and slide preparation for CREST option.
368CRESTselect	**In Vitro Micronucleus Assay in CHO Cells with CREST Option Preparation in select doses:** Limited treatments and doses as chosen from previous MN assay with positive results. Score all selected doses, Slides prepared for CREST option.
CREST_004	**In Vitro Micronucleus Option – Anti-Kinetochore Labeling:** Slides stained (from 348) for up to 3 treatment conditions and PCs. Evaluation of dose level(s) statistically positive for the presence of micronuclei.
CREST_001	**In Vitro Micronucleus Option – Anti-Kinetochore Labeling:** Slides stained (from 368) for up to 3 treatment conditions and PCs. Evaluation of dose level(s) statistically positive for the presence of micronuclei.

* CREST Evaluation can be added to 361 (MN in TK6 cells) without additional preparation

Slide Scoring Options

Protocol	Assay Description
150	**Slide Scoring of CHO Cells/Human Lymphocytes:** In vitro chromosome aberration scoring of sponsor-provided slides. One hundred-fifty metaphases per slide.

Morphological Transformation

BALB/3T3 Transformation Assay

This assay detects the ability of a test article to change BALB/3T3 cells from the normal contact-inhibited state to a transformed state characterized by the loss of contact inhibition. Cells that undergo transformation grow into colonies with characteristic morphology and growth characteristics. Preliminary toxicity and definitive assay performed with and without S9 activation. Preliminary toxicity assay includes cloning efficiency in triplicate plates for definitive assay dose selection. Definitive assay includes four dose levels, concurrent positive and negative controls, 15-20 plates per dose level for transformation potential, and three plates per dose level for concurrent cytotoxicity.

Protocol	Assay Description
304	**In Vitro Transformation Assay in BALB/3T3 Cells with and without S9 activation**

In Vitro Syrian Hamster Embryo (SHE) Transformation Assay

This assay detects the ability of a test article to induce preneoplastic changes in primary Syrian hamster embryo cells from a normal contact-inhibited growth to morphologically transformed state colonies characterized by the loss of contact inhibition and normal growth patterns. Cells that undergo transformation grow into colonies with characteristic morphology and growth characteristics. Two study design options are available with dose administration of 24 hours or 7 days. Preliminary toxicity assay performed to establish the dose range and to adjust the target cell seeding density for the definitive assay. Definitive assay includes five dose levels, concurrent negative and positive controls, and 40 plates per dose level for transformation potential.

Protocol	Assay Description
308	**In Vitro Transformation of Syrian Hamster Embryo Cells – 7 Day Exposure**
309	**In Vitro Transformation of Syrian Hamster Embryo Cells – 24 Hour Exposure**
310	**In Vitro Transformation of Syrian Hamster Embryo Cells – 7 day and 24 Hour Exposure**
308001	**Syrian Hamster Embryo (SHE) Cells:** SHE cells prepared from mid gestation (13 days) hamster embryos, which are grown for 24 to 48 hours and cryopreserved. These cells are evaluated for plating efficiency (above 20%), and response toBenzo (a) pyrene and negative control. Frozen cells are available for use in the SHE cell transformation assay frozen at 2.5×10^6 (feeder cells) or 1.0×10^6 (target cells).

GLP In Vivo Assays

In Vivo Cytogenetics

These assays detect damage induced by the test article to alter chromosome structure or interfere with the mitotic apparatus causing changes in chromosome number.

Study Designs

Below are options that fulfill many regulatory requirements, depending on sponsor preference and test article specifics. Each assay will require a dose range finding test (unless data is available from the Sponsor) that is listed on the next page.

OECD 474 - In Vivo Micronucleus Assay

The purpose of the micronucleus test is to identify substances that cause cytogenetic damage, which results in the formation of micronuclei containing lagging chromosome fragments or whole chromosomes (an aneugenic or clastogenic mechanism).

Microscopic Scoring: Mice or rats are used to detect micronuclei in polychromatic erythrocytes in the bone marrow or peripheral blood. Typically, three test article dose levels, concurrent vehicle and positive controls, dose administration followed by one, two, or more bone marrow collection time points, five animals/sex/dose level are used. Plasma or serum collection for demonstration of test article bioavailability available with all *in vivo* studies is available at additional cost. Dose selection is based on a dose range finding test. Assay can be conducted with males only if there is no difference in toxicity between the sexes in the dose range finding assay

Flow Cytometric Scoring: Mice or rats are used to detect micronuclei in polychromatic erythrocytes (PCE) in the bone marrow or in reticulocytes (RET) in peripheral blood. Flow cytometric analysis adds the benefits of automated scoring, increased sample size, and improvements in measurement and cytotoxicity indications. Standard protocols are listed below. Other options and assay designs are listed on the next page. Please inquire for recommendations.

* Revised OECD guidelines adopted 9/26/14 allow for new and old versions to be employed for a period of 18 months. Designs listed here reflect new requirements. Old designs are available upon request.

Protocol #	Assay Description
Mice	
123012	**Mouse bone marrow - ICH/OECD protocol (Microscopic Scoring):** Single administration, two collection time points, vehicle controls at each collection time point, 4000 PCE evaluated per animal, 35 mice/sex. Protocol 123M012: males only
123021	**Mouse bone marrow - ICH/OECD protocol (Microscopic Scoring):** Two administrations, one collection time point, 4000 PCE evaluated per animal, 25 mice/sex. Protocol 123M021: males only
123031FlowPB	**Mouse peripheral blood - ICH/OECD Protocol (Flow Cytometric Scoring):** Repeat doses on three consecutive days, one collection time point, collect 24 hours post last dose. 20,000 RET evaluated per animal, 25 mice/sex.
Rats	
125012	**Rat bone marrow - ICH/OECD protocol (Microscopic Scoring):** Single administration, two collection times, vehicle controls at each collection time point, 4000 PCE evaluated per animal, 35 rats/sex. Protocol 125M012: males only
125021	**Rat bone marrow - ICH/OECD protocol (Microscopic Scoring):** Two administrations, one collection time point, 4000 PCE evaluated per animal, 25 mice/sex. Protocol 125M021: males only
125031FlowPB	**Rat peripheral blood - ICH/OECD Protocol (Flow Cytometric Scoring) - Acute:** Repeat doses on 3 consecutive days with 1 collection time point. Collect 24 hours post last dose. 25 rats/sex, 20,000 RET evaluated per animal.

In Vivo Cytogenetics

Additional Analyses for the In Vivo Micronucleus Assay

Option	**Body temperature monitoring:** Hypothermia and hyperthermia are both known to be associated with production of micronuclei in rodent bone marrow hematopoietic cells, through aneugenesis. A variety of drugs have been shown to raise or lower core body temperature sufficiently to cause micronuclei formation. Implantable temperature transponders may be used to investigate alterations in body temperature

Cytogenetic Analysis Options

As with in vitro assays, FISH and CREST labeling are available to investigate the mode of action for a test article that is positive in an in vivo micronucleus assay.

FISH (Fluorescent in situ Hybridization)

Centromeric labeling of micronuclei by FISH is a cytogenetic technique that is used to detect and localize the presence or absence of specific centromeric DNA sequences on chromosomes.

Protocol	Assay Description
To be used with 123	**Additional Preparation for FISH with In Vivo Micronucleus Assay:** Aneugenic positive control added. Filter bone marrow cells through cellular column. Prepare slides at -30°C for potential FISH.
123FISHselect	**In Vivo Micronucleus Assay in with FISH Option Preparation in select doses:** Definitive assay with select doses. Extra slides prepared for FISH option and stored at -30°.
FISH_002	**In Vivo Micronucleus Option – FISH:** Process slides from cultures selected for FISH analysis. Scoring for centromere positive micronuclei. Evaluate and report FISH data (Mouse Only).

CREST Labeling

CREST uses a human autoimmune antibody that binds to kinetochores of chromosomes across species.

Protocol	Assay Description
To be used with 123 or 125	**Additional Preparation for CREST with In Vivo Micronucleus Assay:** Aneugenic positive control added. Filter bone marrow cells through cellular column. Prepare slides at -30°C for potential CREST.
___CRESTselect	**In Vivo Micronucleus Assay in with CREST Option Preparation in select doses:** Definitive assay with select doses. Extra slides prepared for CREST option and stored at -30°.
CREST_002	**In Vivo Micronucleus Option – Anti-Kinetochore Labeling:** Slides stained. Evaluation pf dose level statistically positive for the presence of micronuclei.

In Vivo Cytogenetics

OECD 475 - Chromosome Aberration Analysis in Rodents

Rodent cytogenetic assays using metaphase analysis measure induction of chromosome aberrations and polyploidy in vivo. Typically, three test article dose levels, concurrent vehicle and positive controls; single dose administration followed by two or more bone marrow collection time points, five animals per sex per dose level for each time point are used. Plasma or serum collection for demonstration of test article bioavailability is available with all in vivo studies at additional cost. Dose selection is based on a dose range finding test. Option for males only is allowed if no difference in toxicity between the sexes is seen in the dose range finding assay.
* Revised OECD guidelines adopted 9/26/14 allow for new and old versions to be employed for a period of 18 months. Designs listed here reflect new requirements. Old designs are available upon request.

Protocol	Assay Description
108	**ICH/OECD protocol - Mouse bone marrow:** Single administration, two collection time points, vehicle controls at each time point, 200 metaphase cells evaluated/animal, 35 mice/sex. Numerical aberrations evaluated at all dose levels. Protocol 108M: males only
126	**Mouse bone marrow assay for determination of clastogenicity/aneuploidy:** Polychromatic erythrocytes evaluated using immunofluorescent techniques to differentiate micronuclei with and without kinetochores.
107GLP	**ICH/OECD protocol - Rat bone marrow:** Single administration, two collection time points, vehicle controls at each time point, 200 metaphase cells evaluated/animal, 35 rats/sex. Numerical aberrations evaluated at all dose levels. Protocol 107M: males only
139	**Chromosome Aberrations in Rat Lymphocytes:** Repeat-dose oral administration for 5 days, 1 collection time point with subsequent analysis of chromosome damage in the cultured blood cells. Protocol 139M: males only

Dose Range Finding Tests for In Vivo Studies

Each in vivo study requires dose range finding tests to help in the selection of the appropriate dose levels for the definitive study. The dose range finding test includes a modified limit test to determine the maximum tolerated dose (MTD), which will be used as the highest dose in the definitive study, with 2000 mg/kg being the limit dose. The test article will be initially evaluated using 3 male and 3 female in 3 dose groups. In order to further define the MTD, an extensive toxicity test may follow.

Protocol	Assay Description
000M	**Mouse Dose Range Finding Test (Males and females)**
000R	**Rat Dose Range Finding Test (Males and females)**
000RM	**Rat Dose Range Finding Test** (males only)

DNA Damage and Repair

OECD 489 - In Vivo COMET Assay

This assay uses single cell gel electrophoresis to detect and measure single and double-stranded breaks, and alkaline-labile sites in DNA following treatment with a test article. This assay is also known as the COMET assay and may be used as an additional end point on another ongoing animal study or may be run as a separate in vivo study with its own range finding toxicity studies. Normally vehicle, positive and three test article dose levels are used. Routine tissues offered include liver, bladder, peripheral blood, lung, skin, stomach, kidney, bone marrow, spleen and intestine. Other tissues are available. Other options are available to collect Comet DNA damage and Micronucleus cytometric damage from the same animals. Combined COMET and Micronucleus Assay may also be integrated as an endpoint to repeat-dose studies, with and without flow cytometric evaluation for Micronucleus Assay.

Protocol	Assay Description
Mice/Rats	
411/413	**In Vivo Rodent COMET Assay:** Single dose administration, 2 collection times, 150 cells score/dose, 50 animals/sex.
421/423	**In Vivo Rodent COMET Assay:** Triple dose administration, 1 collection time, 150 cells score/dose, 25 animals/sex.
431/433	**In Vivo Rodent Micronucleus and COMET Assay:** Triple dose administration, 1 collection time for Comet and 1 for MN. 5 animals/group/sex, 5 groups. Males only or both sexes
431Flow/433Flow	**In Vivo Rodent Micronucleus and COMET Assay:** Four dose administrations, 1 collection time for Comet and 1 for MN. 5 animals/group/sex, 5 groups. Males only or both sexes. Comet evaluation by microscopy and Micronucleus evaluation by Flow Cytometry.

OECD 486 - In Vivo/In Vitro Unscheduled DNA Synthesis (UDS)

This assay detects repair of DNA in vitro in male rat or mouse hepatocytes collected from animals treated in vivo with test article. Three test article dose levels, concurrent positive and negative controls, single dose administration using 5 animals per dose level with 3 animals per dose evaluated for UDS using auto-radiography, two time points. Dose selection based on dose range finding test.

Protocol	Assay Description
381 *ICH S2 Design*	**Rat Liver UDS Assay:** 40 animals dosed, 30 animals evaluated. 3 dose levels, 1 dose administration, 2 harvests.
383	**Mouse Liver UDS Assay:** 40 animals dosed, 30 animals evaluated 3 dose levels, 1 dose administration, 2 harvests
384	**Mouse Liver UDS Assay:** 45 animals dosed, 30 animals evaluated.
000RM	**Rat Dose Range Finding Test** (males only)

In Vivo Gene Mutation

Pig-a Gene Mutation Assay

The *Pig-a* Gene Mutation Assay is an in vivo assay primarily performed in rats. Gene mutation assays, such as the *Pig-a* assay, provide an advantage for product development and regulatory decision making since they measure the induction of mutations at a specific gene as opposed to measuring overall DNA damage.

Protocol	Assay Description
460033Flow	**Rat peripheral blood - Flow Cytometric Scoring:** 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.
460283Flow	**Rat peripheral blood - Flow Cytometric Scoring:** 28 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.

OECD 488 - Big Blue® Transgenic Rodent Mutation Assay

BioReliance's Big Blue® Transgenic Rodent Mutation (TRM) assay utilizes a novel transgenic animal model bred for specific use in an assay defined by OECD Test Guideline 488, "Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays." This assay allows the measurement of mutations in any tissue including germ cells and has been re-qualified for commercial use. For analysis, Mutation frequency is denoted by dividing the number of mutant plaques over total number of plaques.

Protocol	Assay Description
Mice/Rats	
170/171	**Plaque Counting with Rodent Tissue:** 5 doses (1 vehicle control, 1 positive control, 3 dose levels). 5 male rodents per group. 2 tissues analyzed, 125,000 phage evaluated per tissue; detect 2-fold increase over background with 80% confidence.

Big Blue® Transgenic Rodents

Big Blue® mice and rats are bred to have multiple copies of recoverable target genes integrated into their genome. Big Blue® animals are created by a microinjection of the lambda shuttle vector containing the *cII* gene into the pronucleus of fertilized eggs from either C57Bl/6 mice or Fisher 344 rats. BioReliance has exclusive license to breed these animals which are available commercially.

Protocol	Assay Description
Mice	
BBMM_BL6_HOMO	**Big Blue® C57BL/6 Transgenic Homozygous Mouse:** Both males and females available.
Rats	
BBMR_F344_HOMO	**Big Blue® Fisher 344 Transgenic Homozygous Rat:** Both males and females available..

Genetic Toxicology Endpoints

Many in vivo studies have scoring and evaluation that can be separately added on to the end of the in-life portion of studies. In vivo endpoints may be integrated into general toxicology studies with repeat dosing, as discussed in ICH S2(R1) (length of study is commonly 14 to 28 days, but could be any length). Endpoints can be evaluated by Flow Cytometry, or manual scoring. Entire studies may be conducted within BioReliance's fully accredited animal facility, or added to ongoing animal studies from other facilities. In the case of samples sent to BioReliance from other studies, specific collection procedures and kits are provided. Onsite collection services, for sponsor-run repeat dose animal toxicology studies, are available. There are many options for endpoint assays, including: In Vivo Micronucleus Assay, In Vivo Comet Assay, Chromosome Aberrations and *Pig-a* Assay. Please inquire.

Micronucleus

Protocol	Assay Description
129GLP	**Slide scoring:** Micronucleus evaluation of rodent bone marrow or peripheral blood slides. 2000 cells scored per slide (4000 per animal). Includes staining, evaluation, and summary report.
129FlowPBGLP	**Flow cytometric scoring:** Micronucleus evaluation of samples from whole blood. 20,000 cells scored per sample. Includes summary report.
129FlowPBFGLP	**Flow cytometric scoring:** Micronucleus evaluation of prepared samples (sponsor-provided fixed blood). 20,000 cells scored per sample. Includes summary report.

Chromosome Aberration

Protocol	Assay Description
149	**Slide Scoring:** Evaluation of sponsor-provided slides from rodent bone marrow or cells. 200 metaphases per slide. Includes staining, microscopic evaluation and summary report.

Comet

Protocol	Assay Description
151	**Slide Scoring:** Evaluation of sponsor-provided/prepared rodent bone marrow slides. 150 slides per animal evaluated. Includes evaluation and summary report.
180	**Assay Preparation and Evaluation:** Preparation of tissue, slides and evaluation. 50 cells per slide/100 per animal evaluated. Includes preparation of tissue, processing into slides, electrophoresis, slide evaluation and summary report.
MOCOM	**Mobile Comet Assay Preparation:** Tissue samples processed. Includes preparation of tissue, processing into slides, and electrophoresis.

Pig-a

Protocol	Assay Description
160FlowPB	**Flow Cytometric Scoring:** Evaluation of prepared samples from whole blood. 20,000 cells scored per sample. Includes summary report.

Big Blue®

Protocol	Assay Description
172	**Plaque Counting:** 125,000 phage evaluated per tissue; detect 2-fold increase over background with 80% confidence.

Analytical Chemistry

Analytical support is an important and required part of any GLP assay. Analytical methods must be available or developed before a GLP assay is performed. In addition, stability analysis and dosing formulation verification are available to support Genetic Toxicology assays and protocols. BioReliance offers fully-validated, GLP-compliant equipment, software, and study designs. Our state-of-the-art equipment includes: LC/MS/MS, HPLC, GC, and UV/Vis.

Analytical Method Validation

These studies are available to validate an analytical method for the quantification of the concentration of test article in dosing solutions and in plasma samples.

Protocol	Assay Description
GTCHEM	**Transfer or Full Validation:** Many designs available to evaluate one to multiple vehicles and test articles at one time or later dates. LC/MS/MS, HPLC, GC, and UV/Vis techniques are available.

Dosing Solution Analysis

Dosing solution analysis will be conducted on the day that the samples are prepared, unless stability information allows samples to be analyzed on a different day. Upon preparation for use in each preliminary assay, each definitive assay and each confirmatory assay (as required by protocol design), samples will be collected from the vehicle, least and most concentrated dose formulations.

Protocol	Assay Description
DSA	**Dose and Vehicle Analysis:** Protocols available for every dose in all GLP assay types. LC/MS/MS, HPLC, GC, and UV/Vis techniques are available.

Stability

BioReliance will provide stability analysis of plasma or a test article under desired conditions prior to sample submission.

Protocol	Assay Description
STABIL	**Dose and Storage Condition Analysis of Test Articles:** BioReliance will reanalyze the highest and/or lowest from one set of dosing formulations after at least 3 hours storage at room temperature (15 to 30°C). The stability analysis will be conducted identically to the dosing formulation analysis for that assay, using HPLC or GC.
TKSTABIL	**Plasma or Metabolite Analysis:** BioReliance will determine stability of plasma or metabolites in plasma under the following conditions: bench top, freeze/thaw, long-term frozen, using LC/MS/MS.

Toxicokinetics/Pharmacokinetics (TK/PK)

BioReliance offers a fully validated, state-of-the-art GLP analytical service using Liquid Chromatography–Mass Spectrometry (LC/MS/MS). This powerful technology provides quantitative analysis of chemicals within a given sample, with high sensitivity and selectivity. In addition to its application as a more sensitive analytical process, LC/MS is employed for toxicokinetic (TK/PK) studies.

Protocol	Assay Description
BIOA	**Bioanalysis:** Analysis of plasma samples from in vivo studies on LC/MS/MS
TKA	**TK Analysis Report:** Fully audited report on Bioanalysis , including PK/TK calculations with tables
PLSM	**Plasma Sample Collection:** dose satellite group of animals (3/sex/group/timepoint), collect, process, and ship samples for TK analysis.

Screening Assays

Bacterial Mutation Screening Assays

Salmonella / E. coli Screening Assays

These assays are designed to provide a rapid, low-cost evaluation of developmental materials in limited supply. While not intended for regulatory submission, these assays are predictive of results from regulatory-compliant studies and are a useful tool in the product development process. These assays may employ any or all of the regulatory-required tester strains and each strain is tested with and without S9 activation using duplicate plates per dose level. The test article quantities cited below assume that solubility or workability information is available about the test article in water, dimethyl sulfoxide, ethanol or acetone. While the following protocols represent the more common study designs, BioReliance can customize a screening protocol to meet specific client requirement or available quantity of test article. Please inquire.

Protocol	Assay Description
501 / 501004	**Ames Abbreviated Standard Assay (2 strains/Plate incorporation method):** Assay employs tester strains TA98 and TA100, two strains that are responsive to a diverse group of mutagens. Each strain is tested at 8 dose levels and the results provide a *quantitative* assessment of the test article's mutagenic activity. Minimum of 90 mg of each test article is required. 501004 is the same as 501 except that dosing is performed using the preincubation method.
501028	**Ames Abbreviated Standard Assay (5 strains/Plate incorporation method) Screening Test:** Assay employs tester strains TA98, TA100, TA1535, TA1537 and WP2 *uvr*A. Each strain is tested at 8 dose levels. A minimum of 225 mg of each test article is required. This protocol is designed for testing test articles with an unknown toxicity profile. 501029 uses same design, but with Preincubation method.
501027	**Ames Abbreviated Standard Assay (5 strains/Plate incorporation method) Screening Test for nontoxic material:** Assay employs tester strains TA98, TA100, TA1535, TA1537 and WP2 *uvr*A. Each strain is tested at 5 dose levels. A minimum of 225 mg of each test article is required. This protocol is designed for testing materials that are expected to be nontoxic, e.g., printer toners.
501007 / 501008	**Mini Ames Assay (2 strains):** Assay employs tester strains TA98 and TA100, using a 6 well format. Each strain is tested at 8 dose levels. A minimum of 20 mg of each test article is required. 501008 employs 5 tester strains (TA98, TA100, TA1535, TA97a and WP2 *uvr*A) with a minimum of 50 mg of each test article required
501009 / 501010	**Micro Ames Assay (2 strains):** Assay employs tester strains TA98 and TA100, using a 24 well format. Each strain is tested at 8 dose levels. A minimum of 5 mg of each test article is required. 501010 employs 5 tester strains (TA98, TA100, TA1535, TA97a and WP2 *uvr*A), with a minimum of 12.5 mg of each test article required.
512	**Ames Spot Test:** The test article is applied in the center of a petri dish and a concentration gradient forms as the test article diffuses into the agar. The results provide a *semi-quantitative* assessment of the test article's mutagenic activity over a limited concentration range. For five strains (TA98, TA100, TA1535, TA1537 and WP2 *uvr*A), a minimum of 110 mg of each material is required.
850	**Ames II:** Assay is a microplate format using TA98 and a mix of novel strains that detect base repair substitutions. Each compound is tested in triplicate at six concentrations, with between 5 and 30 mg required.

In Vitro Mammalian Cell Gene Mutation Screening Assays

Screening Assay Using L5178Y TK$^{+/-}$ Mouse Lymphoma Assay

Protocol	Assay Description
702007	**Screening mouse lymphoma protocol:** This non-GLP assay includes: treatments of 24 hours without S9 and 4 hours with S9. Soft agar method, single cultures.

In Vitro Cytogenetic Screening Assays

Protocol	Assay Description
336	**In Vitro Chromosome Aberration Screening Assay in CHO Cells:** This non-GLP study is designed for rapid cytogenetic evaluation of test articles by measuring chromosome aberration formation in CHO cells. Requires 200 to 400 mg of test article. Treatments of 20 hours without S9 and 4 hours with S9; cells collected at 20 hours. Study conducted with 15 test article concentrations. A minimum of three concentrations scored for aberrations with 100 metaphase scored per concentration. Vehicle controls and positive controls included.
346	**In Vitro Chromosome Aberration Screening Assay in Human Peripheral Blood Lymphocytes:** Similar to protocol 336 except performed in HPBL cells.
360	**In Vitro Micronucleus Assay in TK6 Cells:** Treatments of 3-6 and 27 hours without S9 and 3-6 hours with S9, 9 doses for toxicity assessment, up to 4 dose levels evaluated for MN induction, 2000 cells scored per dose level. Scoring by microscopy.
369	**In Vitro Micronucleus Screening Assay in CHO Cells:** This non-GLP study is designed for rapid cytogenetic evaluation of test articles by measuring micronuclei formation in CHO cells using microscopic scoring. Study performed using 2- or 4-chambered slides. Requires 100 mg of test article. Treatments of 24 hours -S9 and 4 hours +S9; cells collected at 24 hours. Minimum of three dose levels in duplicate cultures with concurrent vehicle and positive controls. Five hundred binucleated cells will be scored for micronuclei per culture and 1000 cells per dose. Design and reporting may be customized to meet screening program needs.
369Flow	**In Vitro Flow Cytometric Micronucleus Screening Assay in CHO Cells:** This non-GLP study is designed for rapid cytogenetic evaluation of test articles in limited supply by measuring micronuclei formation in CHO cells using flow cytometric scoring. Cytotoxicity and anuegenicity measured simultaneously. Treatments of 24 hours -S9 and 4 hours +S9; cells collected at 24 hours.. 10 doses, score at least 3, 10,000 cells scored per sample and 20,000 cells scored per dose.
349	**In Vitro Micronucleus Screening Assay in Human Peripheral Blood Lymphocytes:** This non-GLP study is designed for rapid cytogenetic evaluation of test articles by measuring micronuclei formation in HPBL using microscopic scoring. Requires 125 mg of test article. 5 mL treatments of 24 hours -S9 and 4 hours +S9; cells collected at 24 hours. Minimum of three dose levels in duplicate cultures with concurrent vehicle and positive controls. Five hundred binucleated cells will be scored for micronuclei per culture and 1000 cells per dose. Design and reporting may be customized to meet screening program needs.
349001	**In Vitro Micronucleus Screening Assay in Human Peripheral Blood Lymphocytes:** Similar to protocol 349 except using 1 mL cultures and 50 mg of test article.

Non-GLP In Vitro Assay Options

FISH and CREST Analysis are available for non-GLP assays. For description please see GLP section.

In Vivo Cytogenetics

Protocol	Assay Description
121	**Mouse Bone Marrow Screening Test:** Single administration, two collection times, six doses tested, three doses evaluated, 3 mice/sex/group/time point; 2000 PCE evaluated/animal Protocol 121M: males only
121R	**Rat Bone Marrow Screening Test:** Single administration, two collection times, six doses tested, three doses evaluated, 3 rats/sex/group/time point; 2000 PCE evaluated/animal Protocol 121RM: males only
121Flow	**Mouse Bone Marrow Screening Test:** with Flow Cytometric Analysis

DNA Damage and Repair Assays

In Vitro COMET Assay

This assay uses single cell gel electrophoresis to detect and measure single strand breaks in genomic DNA following treatment with a test article. This assay is appropriate for non-GLP screening. It may be run either in vitro using mammalian cells in culture or in vivo where animals are dosed and cells collected for analysis.

Protocol	Assay Description
400	**In Vitro Mammalian Cell COMET Assay in CHO, TK6, V79, or HPBL cells** Also available with Caco2, Human Keratinocytes, Hela cells, and SHE cells.

Other high throughput cytotoxicity and apoptosis endpoints such as ATP and Caspase-3/7 activation assay can be added to determine mechanism.

GreenScreen Assay

Protocol	Assay Description
801	**GreenScreen HC:** Assay is a microplate format using the human TK6 cell line. The line links the regulation of the human GADD45a (Growth Arrest and DNA Damage) gene to the production of Green Fluorescent Protein (GFP). Combined +/- S9

Morphological Transformation Assays

Protocol	Assay Description
320	**Bhas-42 Initiator and Promoter Cell Transformation Assay** 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). 6-well format. Also available as just initiator assay (320I) or promoter assay only (320P)
321	**Bhas-42 Initiator and Promoter Cell Transformation Assay** Same as protocol 320, but in 96-well format.
310nGLP	**In Vitro Transformation of Syrian Hamster Embryo Cells –** 7 day and 24 Hour Exposure
308nGLP	**In Vitro Transformation of Syrian Hamster Embryo Cells –** 7 Day Exposure
309nGLP	**In Vitro Transformation of Syrian Hamster Embryo Cells –** 24 hour Exposure
311	**In Vitro Transformation of Syrian Hamster Embryo Cells –** Preliminary range finder for 7 days, followed by definitive assay, treatment with a transformation initiator (TPA) prior to test article treatment.

In Vivo Gene Mutation

Protocol	Assay Description
460033FlowNGLP	**Rat peripheral blood - Flow Cytometric Scoring:** 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.
460283FlowNGLP	**Rat peripheral blood - Flow Cytometric Scoring:** 28 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.

Medical Device Testing

A series of in vitro genetic toxicology and cytotoxicity assays are available for the testing of medical devices and biomaterials. Assays conform to ISO 10993 Part 3 Guideline. Volume discounts are provided for multiple samples tested concurrently.

Bacterial Mutation Assays

Medical Device *Salmonella / E. coli* Reverse Mutation Assays

Protocol	Assay Description
502201	**Biocompatibility testing of Medical Devices - Screening test:** Bacterial mutation assay using a single dose level with each of two extracts.
502200	**Biocompatibility testing of Medical Devices - Full test:** Bacterial mutation assay using multiple dose levels with each of two extracts.

In Vitro Mammalian Cell Gene Mutation Assays

Medical Device L5178Y $TK^{+/-}$ Mouse Lymphoma Assays

Protocol	Assay Description
702201	**Biocompatibility testing of Medical Devices - Screening test:** Mouse lymphoma assay using a single dose level of each of two extracts.
702200	**Biocompatibility testing of Medical Devices - Full test:** Mouse lymphoma assay using multiple dose levels of each of two extracts.

In Vitro Cytogenetic Assays

Medical Device Chromosome Aberration Assays

Protocol	Assay Description
331201	**Biocompatibility testing of Medical Devices - Screening test:** In vitro chromosome aberration assay in CHO cells using a single dose level of each of two extracts.
331200	**Biocompatibility testing of Medical Devices - Full test:** In vitro chromosome aberration assay in CHO cells using multiple dose levels of each of two extracts.
341201	**Biocompatibility testing of Medical Devices - Screening test:** In vitro chromosome aberration assay in HPBL using a single dose level of each of two extracts.
341200	**Biocompatibility testing of Medical Devices - Full test:** In vitro chromosome aberration assay in HPBL using multiple dose levels of each of two extracts.

In Vivo Cytogenetic Assays

Medical Device In Vivo Micronucleus Assays

Mice and Rats are used to detect micronuclei in polychromatic erythrocytes in the bone marrow of animals treated with saline and vegetable oil extracts of a medical device or biomaterial. One or two collection times, vehicle controls at each collection time point, 2000 PCE evaluated per animal, 5 animals/sex/dose. Dose range finding test may be required with each extract. Volume discounts are provided for multiple samples tested concurrently.

In Vivo Micronucleus Assays for Medical Devices

Protocol	Assay Description
Mice/ Rats	
123201/ 125201	**Biocompatibility testing of Medical Devices - Screening test:** Mouse/Rat micronucleus assay using one administration of single high dose of each of two extracts. Includes two harvest time points.
123202/ 125202	**Biocompatibility testing of Medical Devices - Screening test:** Mouse/Rat micronucleus assay using two administrations of a single high dose level of one extract. Includes one harvest time point.
123203 125203	**Biocompatibility testing of Medical Devices - Screening test:** Mouse/Rat micronucleus assay using two administrations of a single high dose level of each of two extracts. Includes one harvest time point.
123200 125200	**Biocompatibility testing of Medical Devices - Full test:** Mouse/Rat micronucleus assay using one administration of three dose levels of each of two extracts. Includes two harvest time points.

Primary DNA Damage Assays

Unscheduled DNA Synthesis Assays for Medical Devices

Protocol	Assay Description
380201	**Biocompatibility testing of Medical Devices - Screening test:** UDS assay in primary rat hepatocytes using a single dose level of each of two extracts.
380200	**Biocompatibility testing of Medical Devices - Full test:** UDS assay in primary rat hepatocytes using multiple dose levels of each of two extracts.

Cytotoxicity

Protocol	Assay Description
375001	**Agar Diffusion:** Agar diffusion for cytotoxicity (Dental Material).
375002	**Agar Overlay:** Cytotoxicity Assessment of Medical Devices using Agar Overlay method.
375003	**Direct Contact:** Direct contact test for cytotoxicity (Dental Material).
375004	**Filter Diffusion:** Filter diffusion test for cytotoxicity (Dental Material).
375005	**MEM Elution:** Cytotoxicity Assessment of Medical Devices using MEM Elution method.
375006	**Neutral Red Uptake (NRU):** Cytotoxicity Assessment of Medical Devices using Neutral Red Uptake.
375007	**Colony Growth Inhibition (CGI):** Cytotoxicity Test by reduction in colony formation

Information and Ordering

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