



Genetic Toxicology

microScreens
GLP

**For smarter and more
efficient lead optimization
and genotoxicity testing,
Midwest BioResearch
is on your bench.**

From discovery through development, Midwest BioResearch has the testing capabilities to evaluate a large number of compounds plus the experience to perform GLP testing within a strict regulatory environment.

*We're on **your** bench.*



MBR's microAmes Screens For Predicting the GLP Regulatory Ames Test

MBR's microAmes uses approximately 5-10 mg of test article while mimicking the regulatory Ames format. Based on our years of experience with the microAmes screen, results are accurate and delivered in two weeks or less from receipt of compound.

By using the ICH-compliant *Salmonella* and *E. coli* tester strains, MBR's screen accurately predicts the full Ames—an industry first.

Other companies' mutagenicity screens do one or more of the following:

- Use genetically modified Ames strains or use other test systems
- Use only two tester strains
- Do not use *E. coli* strains
- Do not use a liver S9 fraction or proper activation protocols
- Use liquid-based formats
- Use larger quantities of material

MBR's screen is similar to full plate Ames:

- Uses five ICH-compliant *Salmonella/E. coli* tester strains
- Uses liver S9 activation systems
- Uses agar format
- Measures colony formation, cytotoxicity and compound precipitation

Our microAmes screen thus provides the industry's most robust and accurate screen for Ames mutagenicity, the gold standard in mutagenicity evaluations.

MBR also offers structure-toxicity interpretation and provides strategic advice to help companies act quickly on suspected genotoxicity impurities or drug candidates.

Features include:

- Predictive for GLP regulatory Ames Test
- 5-10 mg requirement
- Turnaround in 2 weeks or less from compound receipt
- Cost-effective and competitive pricing
- Experience with S9 fractions from a variety of species
- Expert actionable advice based on our 10+ years in applying microAmes screening format

MBR's microClastogenicity Screens For Predicting Regulatory Clastogenicity Tests

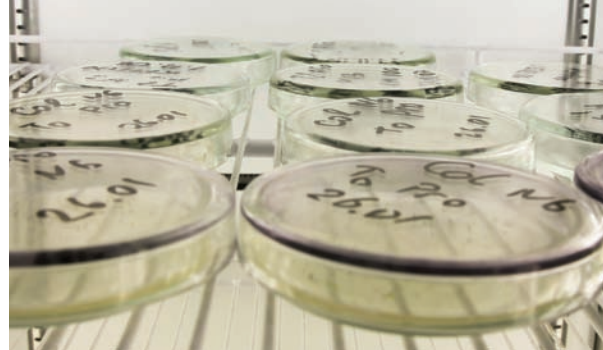
Screening for potential mutagenicity in bacteria is one step in determining a molecule's genotoxicity potential. The other step is to test for clastogenic effects in a mammalian system. Regulatory assays used to evaluate mammalian clastogenicity include the *in vitro* chromosome aberration test and the *in vivo* micronucleus assay.

MBR offers microClastogenicity screens that identify DNA-damaging and aneugenic compounds. Our screens are excellent predictors of the regulatory ICH-compliant *in vitro* mammalian chromosome aberration assay and *in vivo* micronucleus assay. Our screens use approximately 10 mg of compound to detect clastogenicity via the presence of micronuclei formed during cell division. MBR's micronized version measures cytotoxicity as per current draft OECD guidelines for the *in vitro* micronucleus assay and evaluates compound precipitates, important parameters in genotoxicity assessments. Comparison of MBR's microClastogenicity screen data with the classical chromosome aberration and micronucleus tests indicate that MBR's screens predict the outcome of the regulatory clastogenicity tests.

We have experience with a variety of cell types in miniature environments. We routinely use human peripheral blood lymphocytes, TK6, CHO and mouse lymphoma cells.

Features include:

- Excellent predictor of the regulatory *in vitro* chromosome aberration and *in vivo* micronuclei tests
- 10 mg required
- Turnaround in 2 weeks or less from compound receipt
- Cost-effective and competitive pricing
- Expert actionable advice based on our 10+ years in applying microClastogenicity screening technology to drug discovery projects



GLP Genetic Toxicology Assays

Ames

The *Salmonella/E. coli* mammalian microsomal reverse mutation assay (Ames test) has been shown to detect various classes of mutagenic chemicals. Our tests are run with and without an exogenous metabolic activation system using either the plate incorporation or preincubation assay. The *Salmonella typhimurium* strains used contain mutations in the histidine operon and thus are histidine auxotrophs (*his-*). The *Escherichia coli* strain used in this assay contains mutations in the tryptophan operon and thus is a tryptophan auxotroph (*trp-*). When these cells are grown on minimal media containing a trace amount of histidine or tryptophan, only those cells that revert to prototrophy (*his+* or *trp+*) are able to grow and form colonies.

MBR has experience with a variety of molecules and with S9 metabolic activation systems from a number of species.

Regulatory Standards

Our regulatory genotoxicity tests are conducted in compliance with U.S. Food and Drug Administration (FDA) Good Laboratory Practice (GLP) regulations; CFR Title 21, Part 58 and in general accordance with the International Conference on Harmonisation (ICH) guidelines S2A and S2B and the Organization for Economic Cooperation and Development (OECD).

In Vitro Clastogenicity

Clastogenicity testing assesses the ability of compounds to induce chromosomal aberrations or micronuclei in cultured cells with and without an exogenous metabolic activation system and with short and/or long-term incubations. Our *in vitro* mammalian cell assays can evaluate the ability of a test article to induce structural changes in the genetic material of the cell. Chromosome alterations are often associated with cancer; therefore, a chromosomal aberration assay is used as an appropriate test for detecting potential mutagens and carcinogens.

MBR has experience with a number of cell types, including human peripheral blood lymphocytes and CHO cells.

In Vivo Micronucleus

The micronucleus assay is a test for clastogenic agents that interfere with normal mitotic cell division. Micronuclei are small chromatin bodies consisting of entire chromosomes and/or acentric chromosome fragments that lag behind at mitotic anaphase. At telophase, these chromosomes and/or fragments are not segregated to either daughter nucleus and form single or multiple micronuclei in the cytoplasm. During maturation of erythroblasts to erythrocytes, the nucleus is extruded. Micronuclei, if present, persist in the cytoplasm of these anucleate cells. Test articles affecting spindle-fiber function or formation as well as clastogenic agents can be detected through micronucleus induction.

MBR has experience evaluating micronuclei from a number of mammalian species.



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