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# 40 C.F.R. § 798.5195

## Mouse biochemical specific locus test.

(a) *Purpose.* The mouse biochemical specific locus test (MBSL) may be used to detect and quantitate mutations originating in the germ line of a mammalian species.

(b) *Definitions.* (1) A biochemical specific locus mutation is a genetic change resulting from a DNA lesion causing alterations in proteins that can be detected by electrophoretic methods.

(2) The germ line is comprised of the cells in the gonads of higher eukaryotes, which are the carriers of the genetic information for the species.

(c) *Reference substances.* Not applicable.

(d) *Test method*—(1) *Principle.* The principle of the MBSL is that heritable damage to the genome can be detected by electrophoretic analysis of proteins in the tissues of the progeny of mice treated with germ cell mutagens.

(2) *Description.* For technical reasons, males rather than females are generally treated with the test chemical. Treated males are then mated to untreated females to produce F1 progeny. Both blood and kidney samples are taken from progeny for electrophoretic analysis. Up to 33 loci can be examined by starch-gel electrophoresis and broad-range isoelectric focussing. Mutants are identified by variations from the normal electrophoretic pattern. Presumed mutants are bred to confirm the genetic nature of the change.

(3) *Animal selection*—(i) *Species and strain.* Mice shall be used as the test species. Although the biochemical specific locus test could be performed in a number of in bred strains, in the most frequently used cross, C57BL/6 females are mated to DBA/2 males to produce (C57BL/6 × DBA/2) F1 progeny for screening.

(ii) *Age.* Healthy, sexually-mature (at least 8 weeks old) animals shall be used for treatment and breeding.

(iii) *Number.* A decision on the minimum number of treated animals should take into account possible effects of the test chemical on the fertility of the treated animals. Other considerations should include:

(A) The production of concurrent spontaneous controls.

(B) The use of positive controls.

(C) The power of the test.

(4) *Control groups*—(i) *Concurrent controls.* An appropriate number of concurrent control loci shall be analyzed in each experiment. These should be partly derived from matings of untreated animals (from 5 to 20 percent ofthe treated matings), although some data on control loci can be taken from the study of the alleles transmitted from the untreated parent in the experimental cross. However, any laboratory which has had no prior experience with the test shall produce a spontaneous control sample of about 5,000 progeny animals and

a positive control (using 100 mg/kg ethylnitrosourea) sample of at least 1,200 offspring.