



Standard Guide for Development of Micronucleus Assay Standards¹

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1. Scope

1.1 This guide covers minimal criteria which should be met by a micronucleus assay system prior to the development of an ASTM Standard or Guide for the conduct of that assay.

1.2 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Significance and Use

2.1 Micronucleus assays for genetic damage have been developed in many types of eucaryotic cells, both *in vitro* and *in vivo*. The occurrence of micronuclei is indicative of chromosomal damage or mitotic spindle dysfunction.

3. Criteria

3.1 Biology:

3.1.1 The biology of the system should be well understood in terms of (a) cell cycle, (b) metabolic capabilities, (c) culture or growth conditions, and (d) other factors of importance in maintaining a reproducible experimental situation. There should be evidence that micronuclei arise from chromosomal aberrations or chromosome loss or both, and not apoptosis or any other mechanism.

3.2 Time Response:

3.2.1 The “expression time” for micronuclei should be characterized for (a) direct-acting genotoxins and (b) genotoxins requiring metabolic activation.

3.3 Dose Response:

3.3.1 The dose response curves for several classes of genotoxins, over a dose range including both toxic and nontoxic doses, should be known. A rational method for determining the upper and lower doses to be tested should be available.

3.4 Spontaneous Frequency:

3.4.1 The spontaneous frequency of micronuclei should be well characterized and should be stable under the test conditions employed. Major factors affecting the spontaneous incidence of micronuclei should be defined.

3.5 Statistics:

3.5.1 The following statistical criteria should be met:

3.5.1.1 There should be sufficient data to define the major sources of experimental variability (for example, slide to slide, animal to animal), in order to permit rational experimental design,

3.5.1.2 Appropriate statistical methods for analyzing the data should be available,

3.5.1.3 Sufficient data and adequate statistical methods should be available to permit determination of the sample sizes required for adequate statistical power, and

3.5.1.4 The quantitative reproducibility of experimental results between and within experiments should be known.

3.6 Transportability:

3.6.1 There should be sufficient experience with the system in order to know how well the characteristics of the assay are maintained in different laboratories. It should be known whether observer-dependent effects, such as scoring and sample preparation, have been sufficiently controlled among laboratories to ensure uniform interpretation of test data. The influence of factors, such as source of test organism and materials, on experimental outcome should be known. A written description of the techniques required for the conduct of the assay that is adequate to permit a new laboratory with normal experience in genetic toxicology testing to carry out the assay should be available.

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