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Comparative analysis of miniaturized Ames assay variations for substances with ambiguous testing outcomes

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The Ames assay is based on the concept of bacterial reverse gene mutation, and it is proven to be the most widely applied test in mutagenicity assessment. Increasing emphasis is placed on the development of miniaturized versions of the traditional Ames test with an accentuated goal to reduce the necessary amount of test chemicals, reagents, and liver microsomal S9 fraction resulting in a reduction of test animals. The miniaturized assays, especially Ames MPF, facilitate higher throughput by allowing parallel testing of a large number of samples in the compound screening phase. However, these miniaturized assay variations suffer from the lack of regulatory acceptance, which is (at least in part) due to the ambiguity of the results gained with the miniaturized Ames assays versus the traditional method.

Our goal is to provide an insightful picture on the performance of the miniaturized Ames assay variations in the context of testing a selection of chemicals with known equivocal assay outcomes conferred to the traditional Ames test. Herein we present a comparative analysis of the Ames MPF system, the MicroAmes6 assay, and results from the NTP database.

Previous publications showed a good correlation between the agar-plating assays and the Ames MPF system, which we now further corroborate with selected compounds. An important motivation behind our efforts is to show that scaling down is possible without significantly altering the accuracy and sensitivity of the assay. Therefore, we compare in this study the sensitivity of different miniaturized assays with compounds tested false negative elsewhere (in-press to date).

Our experimental results further strengthen the applicability of miniaturized Ames assays in various use cases, for example, early phases of drug development, impurity testing, and additional research and development scenarios. Taken together, our findings indicate that the miniaturized Ames tests provide highly reliable and cost-effective alternatives to the traditional Ames assay for the assessment of mutagenic chemicals.

Keywords:
Ames Test; miniaturized; MPF; MicroAmes; MiniAmes.