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THE AMES MPF 98/100 ASSAY: NOVEL MUTAGENICITY TESTING IN LIQUID MICROPLATE FORMAT USING *S. TYPHIMURIUM* TA98 AND TA100

Sini Flückiger-Isler

Markus Kamber

Xenometrix, Allschwil, Switzerland

Genetic toxicity testing has moved towards the earlier stages of drug discovery in order to identify genotoxic liabilities of new compounds in the pipeline. Scaled-down versions of the original Ames plate incorporation test using the *S. typhimurium* strains TA98 (frameshifts) and TA100 (base-pairs) are often used for this purpose. Because in early development many compounds are available in very small quantities, a liquid microplate version with these strains was developed to decrease compound consumption and to increase the through-put of the assay.

TA98 is already successfully used in the Ames II assay, in combination with TAMix, a mixture of strains to detect base-pair mutations. TA100 with its high spontaneous reversion rate was as yet not suitable for the microplate format with its 48-well limit.

We were able to decrease the spontaneous reversion rate of TA100 to a level low enough to be used in the microplate format without loss of sensitivity. The mutagenic response to 13 reference compounds, examined in TA100 and in the Ames II TAMix cultures, resulted in comparable results: Seven compounds were stronger mutagenic in TA100 than in TAMix, and both strains showed similar responses with one compound. One compound had a weaker effect in TA100. As expected, one compound was detected by TAMix only and three chemicals showed no mutagenic activity in both strains.

The new Ames MPF 98/100 test by Xenometrix using a liquid format and 384-well microplates offers a time and cost-effective pre-regulatory alternative to the plate incorporation method. As both assays use the same *Salmonella* strains, TA98 and TA100, results can be compared with existing data sets. The new test kit including ready-to-use media and bacteria enables rapid screening of a large number of compounds and consumes six times less test substances and consumables than the plate incorporation method, and reduces hands-on time.

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7768 Service Center Drive • West Chester OH 45069

Phone: 513.770.1991

Toll Free: 866.783.3797

Fax: 513.573.9241

Email: info@aniara.com

www.aniara.com