

COMMITTEE ON MUTAGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COM)

ABILITY OF THE MOUSE LYMPHOMA ASSAY TO DETECT ANEUGENS.

Introduction

1. The mouse lymphoma assay (MLA) is currently recommended as the third *in vitro* assay in Stage 1 of the COM strategy for genotoxicity testing. Some authors have reported that the mouse lymphoma assay can detect, in addition to gene mutations and clastogenicity, information on recombination, deletion and aneuploidy.
2. One COM member has forwarded one pre-publication paper and a pre-publication poster reporting experiments investigating the response of the MLA to aneugens. These are appended at for members use only at Annex 1.

Poster O'Donovan MR et al

3. This study reports results from a number of laboratories which have independently reported negative results for the MLA with colchicine using a 24h exposure, but concurrent positive results with carbendazim and griseofulvin. The authors conclude that the MLA does not detect all aneugens.

Pre-publication paper; Fellows MD et al

4. The authors investigated the mode of action of a number of aneugens in the MLA (taxol, carbendazim, noscipine, econazole, chloral hydrate, diazepam and colchicine) using a 24h exposure period. Increased mutant frequencies were reported at cytotoxic concentrations for econazole, taxol, carbendazim, and chloral hydrate. No increases in mutant frequency were reported for noscipine, diazepam and colchicine. Further investigations using Loss of Heterozygosity (LOH) and FISH were undertaken for taxol and carbendazim. The pattern of results suggested chromosome 11 loss with duplication of the remaining chromosome 11 for these two aneugens. Overall the data suggested that aneugens are only positive when tested up to highly toxic concentrations.

COM Discussion

5. Members are asked whether these data impact on the utility of the MLA as a Stage 1 *in vitro* genotoxicity test.