65 RESPIRABLE QUARTZ AND KAOLIN INDUCTION OF APOPTOSIS IN RAT PULMONARY MACROPHAGE NR8383 CELLS. Gao N[1], Keane M[1], Ong T[1], Wallace W[1]. [1]Health Effects Laboratory Division, National Institute for Occupational Safety and Health, Morgantown, WV.

Respirable-sized quartz and kaolin dusts were tested for their induction of apoptosis in the rat pulmonary macrophage NR 8383 cell line. The effects of dust pre-incubation with the dipalmitoylphosphatidylcholine (DPPC) component of pulmonary surfactant on the induction of apoptosis were measured. Occupational exposure to respirable silica quartz dust can result in an acute inflammatory response followed by chronic fibrotic change in the lungs. Kaolin aluminosilicate dust generally is not associated with significant fibrotic lung disease. Pretreatment of dust particles with DPPC is known to suppress some otherwise prompt *in vitro* cytotoxic activities of quartz and kaolin. Apoptosis was measured by two assays: a propidium iodide staining procedure for DNA ploidy analysis using flow cytometry; and an ELISA assay for mono- and oligonucleosomes. Cells challenged in vitro for 6 hours by untreated quartz dust showed a dose-dependent increase in apoptosis, as indicated by both flow cytometry and ELISA assays. Kaolin was less strongly active than quartz in the ELISA assay, and kaolin was active only at high concentrations in the flow cytometry assay. Cells also were challenged over a one- to five-day period by quartz or kaolin at a single concentration. DPPC pretreatment of both dusts delayed their induction of apoptosis as measured by the ELISA assay; partial activity was restored at 3 and 5 days after challenge. Neither DPPC-treated dust showed significant activity in the flow cytometry assay.

66 DETECTION OF GENOME DAMAGES IN WORKERS EMPLOYED IN PESTICIDE PRODUCTION BY COMET ASSAY. Garaj-Vrhovac V[1], Zeljezic D[1]. [1]Institute for Medical Research and Occupational Health, Laboratory for Mutagenesis, Zagreb, Croatia.

Due to widespread use of pesticides concern for their possible threat to human health has been increasing. During the last three decades many toxicological evidences of the mutagenicity and carcinogenicity of several pesticides has been provided. These findings together with the fact that a large population of workers is exposed to such compounds, suggest that the evaluation of their genotoxicity should be extended using different assays available. In our present work we have been tested possible genetic damage on a population of workers occupationally exposed to a mixture of pesticides (atrazine, alachlor, cyanazine, 2,4-dichlorophenoxyacetic acid, malathion) during their production. Cytogenetic evaluation was conducted using the comet assay as relatively new powerful technique for the detection of DNA breaks and damages at alkali sensitive sites according to Singh et al. The extent of DNA migration, presented as the endpoints of the comet assay, was greater in subjects of the exposed group compared to the unexposed subjects chosen from the general population. Lymphocytes of the occupationally exposed subjects manifested higher amount of DNA damage measured by tail length (mean value 50.13 um), compared to the control group (mean value 13.06 um). The mean value of the tail moment calculated for the workers employed in pesticide production was 60.85, whereas in the control group it appeared to be 10.33. All comet data are significantly different ($P<0.001$) for the groups tested. Results suggest that the comet assay, as a rapid method, could be sensitive enough to be used as screening assay in the detection of genome damages caused by long time occupational exposure to pesticides.

67 EFFECT OF CHLOROPHYLLIN ON THE MN-PCE INDUCTION IN PERIPHERAL BLOOD OF MICE EXPOSED TO CHROMIUM TRIOXIDE IN VIVO. García-Rodriguez MC[1], López-Santiago V[1], Altamirano-Lozano MA[1]. [1]Unidad de Investigación en Biologia de la Reproducción, FEZ-Zaragoza, UNAM. México.

Exposure of the human population to toxic environmental compounds has led us to seek natural products that may revert their genotoxic and carcinogenic effects. Chlorophyllin (CHL), a Na and Cu salt of chlorophyll has shown antimutagenic and anticarcinogenic activity without causing toxic effects on live organisms. Chromium is a mutagenic and carcinogenic metal involved in lipid and glucose metabolism, and human exposure is generally to the trivalent (Cr III) or hexavalent (Cr VI) forms. Its genotoxic effects are due, in part, to the fact that Cr (VI) is able to penetrate the cell membrane through a non-specific anion channel, whereas Cr (III) does not readily cross cell membranes. The purpose of this study was to assess the effect of CHL on chromium trioxide induction of micronuclei (MN) in polychromatic peripheral erythrocytes of female CD-1 mice. Animals were treated with a single intraperitoneal dose of 20 mg/kg chromium trioxide, and peripheral blood samples were drawn from the caudal vein every 12 hours for up to 60 hours. Samples were analyzed by the acridine orange technique. Results shown that chromium induces a significant increase in the MN frequency 24 hours after administration, and this increase persisted throughout the observation period (60 hours). Two induction peaks were observed: one 24 hours and the other 48 hours after Cr(III) administration, the latter being greater. Administration of 20 mg/kg of CHL prior to chromium decreased the MN frequency induced by chromium at 24 hours, but showed no effect on the 48 hour peak. This suggests that chromium may induce MN by two different mechanisms, and that CHL exerts its effect on only one of these mechanisms. Alternatively, the effects of CHL may be time-limited in vivo.(Supported by PADEP-UNAM, 500406).

68 UPDATE ON THE SYRIAN HAMSTER EMBRYO (SHE) CELL TRANSFORMATION ASSAY: RESULTS FOR THE PREDICTION ON NTP CARCINOGENS AND FROM THE ILSI/HESI PROGRAM ON ALTERNATIVE CARCINOGENESIS MODELS. Gibson DP[1], Aardema MJ[1], Custer L[2], Isfort RJ[1], LeBoeuf RA[1]. [1]Procter and Gamble Company Cincinnati Ohio 45253-8707. [2]Covance Laboratories Inc. Vienna Virginia 22182.

In 1996, we published the results for 56 chemicals (48 with rodent carcinogenesis data) tested in the pH 6.7 SHE cell transformation assay (Leboeuf et al., Mut. Res. 356, 85-127, 1996). For that group of chemicals the overall concordance was 85%, the sensitivity was 87% and the specificity 83%. Since that time, many other chemicals have been tested, including 24 chemicals tested for the NTP prediction study, nine new chemcials for the ILSI program along with numerous other miscellaneous chemicals. Here we present results for a total of 45 new chemicals which have also been tested in the rodent carcinogenesis bioassay. The updated predictivity for the total database is now (overall concordance is 80%, the sensitivity is 82% and the specificity is 76%). These data, along with the data published previously, bring our SHE cell database up to 93 chemicals. Based on these data, it is concluded that the SHE cell transformation assay has utility for predicting the results of the rodent carcinogenesis bioassay.