EFFECTS OF THE ANTIOESTROGEN TAMOXIFEN ON THE CELL CYCLE KINETICS OF THE HUMAN MAMMARY CARCINOMA CELL LINE, MCF-7. A.E.Lykkesfeldt[1], J.K.Larsen[2], I.Christensen[2] and P.Briand[1], [1]The Fibiger Laboratory and [2]The Finsen Laboratory, Copenhagen, Denmark.

The effects of tamoxifen (10^{-6}M) on MCF-7 cells adapted to growth at 0.5% foetal calf serum have been studied. Growth curves have been determined by cell counting, whereas the distribution of cells in the different cell cycle phases and the growth fraction have been measured by flow cytometry. We find that tamoxifen inhibits growth, reduces the proportion of cells in S-phase and increases the proportion in G1-phase. The growth fraction in the control culture is 97% whereas the growth fraction in a culture treated 6 days with tamoxifen is 60%. After 10 days treatment with tamoxifen the majority of the cells detach and die, but colonies of cells continue to grow in the presence of tamoxifen. The distribution of these cells in the different cell cycle phases is close to that found in an exponentially growing control culture.

A FOLLOW-UP STUDY OF WORKERS IN MANUFACTURE OF MCPA(2 METHYL-4 CHLOROPHENOXYACETIC ACID) IN DENMARK.

Elsebeth Lynge. Danish Cancer Registry, Copenhagen, Denmark.

Two case-control studies from Sweden show an excess risk of soft tissue sarcomas in men exposed to phenoxyacetic acids in general and/or chlorophenols. One Swedish study also showed an excess risk of malignant lymphomas. Furthermore, an excess number of soft tissue sarcomas has been observed in the U.S.A. from cohorts of workers in the manufacture of 2,4,5-T. Taken together, these observations indicate a carcinogenic effect of exposure to 2,4,5-T and/or impurities in the herbicide. The main phenoxyacetic acids in agricultural use are, however, MCPA and 2,4-D. One of the Swedish case-control studies showed an excess risk for soft tissue sarcomas following exposure to these two types of phenoxy acids exclusively. Due to their widespread use, further information on the possible carcinogenic effect of these two herbicides is warranted. In Kemisk Værk Køge, Denmark, the manufacture of 2,4-D was commenced in 1947. MCPA was introduced in 1948 and has been the predominant product since 1950. In 1951-55 small quantities of 2,4,5-T were produced based on purchased 2,4,5-trichlorophenol. Some 490 men and 209 women have been employed in the plant since 1947. Included in the cohort are also some 80 men who have been employed in the manufacture of MCPA and 2,4-D in three other Danish plants. The cohort was followed-up to 1 January 1983. An excess risk of soft tissue sarcomas, malignant lymphomas and stomach cancer is tested.

ENHANCEMENT OF SPECIFIC ANTITUMOUR IMMUNITY IN MICE FED WITH A DIET ENRICHED IN VITAMIN A ACETATE. M.Malkovský, C.Doré, R.Hunt, L.Palmer, P.Chandler and P.B.Medawar Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, U.K.

Age-matched male CBA mice on conventional or vitamin A acetate (VAA) diet (Nature 302, 328, 1983) were immunized with irradiated,cloned, 3-methylcholanthrene- or Harvey sarcoma virus-induced (McSa-1 or HT3-2.1) sarcoma cells and challenged with viable corresponding or unrelated syngeneic sarcoma cells two weeks later. The survival of the specifically immunized mice on the VAA diet was significantly prolonged in comparison with all control groups of mice as assessed using log-rank tests. Moreover, the specific immunization markedly decreased the incidence of tumours after the McSa-1 (but not HT3-2.1) challenge in a group of mice on the VAA diet (5%) as compared with the equivalent group on the control diet (50%). The VAA diet or immunization itself or together did not influence natural killer cell activity. However, specific T-cell-mediated cytotoxicity after *in vivo* priming and *in vitro* boosting with sarcoma cells was increased in VAA-fed mice. Although, we believe, this marginal increase in cytotoxicity does not itself explain the strikingly increased resistance to tumour transplants in preimmunized mice on the VAA diet in comparison with pre-immunized mice on the control diet, this data provides direct support for the hypothesis that the anticancer action of VAA is mediated through an immunological process.