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MONSANTO BIOHAZARDS COMMITTEE

Minutes of a Meeting

February 17, 1984

The next item on the agenda was a report by Dr. Levinskas on the dioxin problem. He wished us to examine a protocol that had been set for the study of acute dioxin toxicity in animals. Dr. Levinskas indicated in an earlier meeting that he planned to study the toxicology of 2,3,7,8 TCDD, a number of dioxin isomers plus a number of dibenzofurans in three species, the guinea pig (most sensitive), the rat (intermediate sensitivity), and the hamster (low sensitivity), as well as evaluating their causation of chloracne in the rabbit. The pathological studies he outlined in this protocol seemed reasonable. The Committee felt that the measurements proposed should give some clues regarding the cause of death. He was advised to investigate the possibility that the thymus atrophy observed may be indirect and may be mediated by the adrenal cortex.

Dr. Levinskas also reported on the dioxin research at CIIT, which was described by Dr. Bob Neal, the Director, in a letter to Dr. Roush. Some questions being investigated are: 1) whether TCDD is acting as a complete carcinogen, i.e. inducer and promoter, or merely a promoter. In mouse fibroblasts 3T3 10T1/2 cell line in which TCDD does not induce malignant transformation, TCDD is a potent promoter, some 10,000 times more potent than phorbol myristate.

Another CIIT investigator is studying the proliferative effect of TCDD in epithelial tissues (Bill Greenlee). He demonstrated involvement of hydrocortisone in the proliferative response produced in human skin cells and he has shown that TCDD has a profound effect on the binding of Epidermal Growth Factor (EGF) to its plasma membrane receptors which facilitates the breakdown of cyclic AMP.

The effect of TCDD on the immune system is being studied by Dr. Jack Dean at CIIT. Preliminary data indicate adult exposure of 1 and 10 µg/kg in these B6C3F1 mice produce significant decrease in thymus weights, spleen cellularity, antibody plaque-forming cell responses, and mitogenic responses to T- and B-lymphocyte mitogens.