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TOXICOLOGICAL STUDIES WITH POLYCHLORINATED BIPHENYLS

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In 1966 (Sweden) and in 1967 (USA) polychlorinated biphenyls (PCB's) were detected in certain birds and in other samples taken from the environment. Since that time, numbers of other reports have been published which indicate that the PCB's have been found in other samples of fish, birds, water, etc.

Polychlorinated biphenyls are manufactured in this country under the name Aroclors by the Monsanto Company and in Europe and Japan under such trade names as Phenochlor and Clophen. Aroclors are manufactured by replacing one or more of the 10 hydrogen atoms in biphenyl with chlorine atoms. Theoretically, there are about 210 compounds which can be made by different substitutes. Biphenyl is chlorinated to a certain percent of the molecular weight. Thus, an Aroclor is a mixture of compounds, not a single chemical entity.

There were very few data in 1966 to indicate possible toxicological hazard from long term ingestion or exposure to small quantities of the PCB's. Therefore, a number of toxicity studies was started.

The polychlorinated biphenyls (PCB's) investigated were Aroclor 1242 (biphenyl chlorinated to 42% by weight), Aroclor 1254 (chlorinated to 54%) and Aroclor 1260 (chlorinated to 60%). These compounds are not very toxic acutely. The oral LD_{50}'s in the rat are about 2 to 10 g/kg.

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Preliminary (30-day) feeding studies in rats were conducted. When fed at 1000 ppm in the diet, there were decreases in food consumption and rate of gain of body weight. At 300 ppm in the diet, there was no apparent effect from Aroclor 1254 or 1260, but there were slight (but not statistically significant) decreases in food consumption and rate of weight gain from 1242.

More extensive studies were then started. These included two-year feeding studies in rats and dogs, three-generation reproduction studies in rats, reproduction studies in chickens and teratogenic studies in rats. Feeding levels selected were 1, 10 and 100 ppm. The two-year rat feeding study was started with sufficient animals for interim sacrifices at 3, 6 and 12 months. Seventy animals per group (35 males and 35 females) were fed the full two-year period. A two-year dog feeding study was started with eight dogs (four males and four females per group). In both of the two-year studies, body weights, food consumption, hematology, clinical chemistry studies (BUN, glucose, SAP, SGPT and SGOT), organ weights, histology of 25 to 30 organs and tissues, and the saving of frozen tissues for chemical analyses were included.

In the rat studies, after 24 months, the liver weights and liver to body weight or brain weight ratios were significantly elevated in animals fed 100 ppm of the three Aroclors. Histologic examination of the livers from the groups fed 100 ppm revealed several animals

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with vacuolar change, indicative of fatty degeneration. Specific fat stains confirmed the presence of fat in these vacuoles. Focal hypertrophy and focal hyperplasia were also found in the livers from some of these animals. All other parameters at 100 ppm and all parameters at 1 or 10 ppm were normal.

There were no effects in dogs fed Aroclor 1242 or 1254 for 24 months at 1, 10 or 100 ppm. Dogs fed Aroclor 1260 at 100 ppm showed increased serum alkaline phosphatase activity and increased liver weights. At 1 or 10 ppm of Aroclor 1260, no effects were observed in the dogs.

In the three-generation studies weanling rats were fed the compounds in the diet until 100 days of age, at which time they are allowed to mate. Pups from the second litter were used as parents of each succeeding generation. Mating indices, fertility indices, incidences of pregnancy and incidences of parturition were recorded for parental animals, as well as body weights, reactions and pathology. Live birth indices, survival indices (at 24 hours and 5 days) and lactation indices for progeny were calculated.

There were low mating indices and decreased survival of pups at 100 ppm Aroclor 1242 and decreased survival of pups at 100 ppm Aroclor 1254. There were no effects at 1 or 10 ppm Aroclor 1242 or 1254 or at 1, 10 or 100 ppm Aroclor 1260.

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White Leghorn chickens were fed Aroclor 1242, Aroclor 1254 or Aroclor 1260 at 1, 10 or 100 ppm in the diet. Effects on the chickens as well as on egg production, hatchability of the eggs and physical characteristics of the eggs were determined.

The body weights of males fed Aroclor 1242 at 10 or 100 ppm and of males and females fed Aroclor 1254 at 100 ppm were slightly lower than the weights of control chickens. Their food consumption also was low. Some birds died showing evidence of malnutrition.

Egg production in hens fed Aroclor 1242 at 100 ppm or Aroclor 1254 at 100 ppm was much lower than the egg production of the control group. There was poor hatchability of eggs from hens fed Aroclor 1242 at 10 ppm. None of the eggs hatched from hens fed Aroclor 1242 at 100 ppm or Aroclor 1254 at 100 ppm.

There were no significant differences in specific gravity among eggs from treated or from control hens. The egg shells, however, from hens fed Aroclor 1242 at 10 or 100 ppm or fed Aroclor 1254 at 100 ppm were not as thick as the shells of eggs from hens fed the control diet.

Therefore, the ingestion of Aroclor 1242 at 1 ppm, Aroclor 1254 at 10 or 100 ppm or Aroclor 1260 at 1, 10 or 100 ppm caused no apparent effects on the mature chickens or on their eggs, including hatchability and physical characteristics of the eggs. However, the chickens fed Aroclor 1242 at 10 or 100 ppm or Aroclor 1254 at 100

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ppm did not produce as many eggs as the chickens fed the control diet. The eggs from these three groups of chickens had thin shells and did not hatch well after incubation.

An additional reproduction study in chickens was conducted with 1242 at levels of 2, 4 and 8 ppm. In general, there were no effects attributable to Aroclor 1242 with the possible exception of slightly decreased hatchability at 8 ppm.

Teratogenicity studies in rats were conducted with all three Aroclors. The oral dosage levels were 10 and 30 mg/kg/day. Administration was from day 6 through day 15 of gestation. The results showed no evidence of teratogenic effects.

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