EXHIBIT #
8A

February 2, 1975

Trip Report

On January 31, 1975; Drs. Richter, Levinskas and myself met with Drs. Squire and Kimbrough at the National Cancer Institute in Bethesda, Maryland. The purpose of this meeting was to review the slides and data from a 23 month oral feeding study with Aroclor 1260 in rats that was conducted by Dr. Kimbrough while at the E.P.A. In her study, 200 female rats (Sherman strain) were fed 100 ppm of Aroclor 1260 in the diet for 21 months, while 200 female rats of the same strain served as controls and were fed Purina Rat Chow. The Sherman Rat is a random-bred animal derived from the Osborn Mendel Strain. The animals were 21-26 days of age when the study began, and were sacrificed after 23 months on the study. Therefore, there was a 2 month recovery period at the end of the study in which the test material was removed from the diet. The details of the experimental design, procedures and results that were forwarded to Dr. Levinskas are attached. In summary, Dr. Kimbrough found a rather high incidence of hyperplastic (nodular hyperplasia) and neoplastic (hepatomas, carcinomas) lesions in the liver of the test animals. The slides were subsequently reviewed by Dr. Robert Squire, Head of the Tumor Pathology Branch of The National Cancer Institute, who concurred with her findings, although, the terminology he used in classification of the lesions varied slightly from Dr. Kimbrough's. In this regard, it was his impression that all hyperplastic nodules should be regarded as "pre-cancerous lesions" and the term "hepatomas"

Bishop Ex # 8-A
CK 6-29-87

SCM 023633

000043

00042

HARTOLDMON0020159

be deleted and re-classified as carcinomas or neoplastic nodules. This classification system was based on a Liver Tumor Workshop that was held on Dec. 11-13, 1974 in Silver Springs, Maryland which was attended by a small group of pathologists from the regulatory agencies, research laboratories and industry.

In view of Dr. Kimbrough's findings, additional sections of liver from a 2-Year Oral Feeding Study With Aroclor 1260, in rats, conducted at Industrial Bio-Test were processed and evaluated. In this study, there was a 3, 8 and 14 month interim sacrifice which enabled one to determine the approximate time of onset of the liver changes. No interim sacrifices were conducted in Dr. Kimbrough's study. The additional slides prepared at Bio-Test were examined by Dr. Richter and a tabulation of the liver findings are attached. These slides were reviewed by Drs. Kimbrough and Squire at our meeting. Although there was some disagreement on the terminology used in classification of the lesions, it was apparent that the incidence and severity of liver lesions (hyperplasia, nodular hyperplasia and neoplastic changes - carcinomas) was greater in Dr. Kimbrough's study when compared with the results of the Bio-Test Study, even though the same level of test material was administered in the diet. There are two possible explanations for this difference:

1.) The strain of rat. When questioned, Dr. Kimbrough had no information on the spontaneous incidence of hyperplastic or neoplastic liver lesions in the Sherman strain. However, the incidence of spontaneous liver cell hyperplasia would appear to be extremely low since this finding was reported in only 4 controls. The incidence of liver hyperplasia among control rats of the Bio-Test study was also very low. The incidence of spontaneous hyperplastic liver nodules reached 20% in the Fischer Rat

HARTOLDMON0020160

and in some of the other strains.

2.) Sex difference. On the basis of our studies and those of other investigators in rats and mice, it was found that the incidence of hyperplastic and neoplastic liver lesions are much higher in females.

The results of the liver tumor workshop are to be published in the near future and will include the participants. The views of this group, regarding classification of hyperplastic and neoplastic liver lesions is based on the pathogenesis of such lesions in rats that have been induced by known carcinogens such as the nitrosoamines and 2 - acetylaminoflorine (2-AAF). The adoption of this terminology and classification system by the scientific community will have widespread implications regarding assessment of safety of chemicals and drugs currently on test and those previously studied.

Attached are Dr. Richter's comments in regard to Dr. Kimbreugh's findings.

D. E. Gordon

Donovan E. Gordon, D. V. M., Ph. D.
Dipl., Am. College Vet. Path.

SCM 023635
000045
00044

HARTOLDMON0020161