GE Rat-Feeding Study and EPA PCB Cancer Reassessment

While there is no credible evidence that PCBs cause cancer in humans (based on numerous human epidemiological studies), EPA regulates PCBs as "probable human carcinogens" based on results from rat-feeding studies.

In the past, EPA has used data from a study involving Aroclor 1260 to calculate a Cancer Slope Factor of 7.7 $(mg/kg/day)^{-1}$ and applied this factor to all PCBs, regardless of composition, in risk calculations. This practice was inconsistent with the totality of feeding study data, which indicated that other, less chlorinated PCB mixtures would have lower cancer potency. However, the previous rat-feeding studies were performed following different protocols, including different rat strains, numbers of animals, dose levels, feeding periods, et al. These differences made study-to-study comparisons problematical, even though the diagnosis of the pathology from the previous studies was later determined by a pathology working group.

In order to overcome these shortcomings, GE has sponsored a comprehensive rat-feeding study, involving the four major Aroclors (1016, 1242, 1254 and 1260) that were used in the production of electrical equipment and that represent over 90% of total PCBs sold in this country. The study was carried out at Battelle Laboratories, Columbus, Ohio. In developing the protocol, we sought guidance from scientists from EPA and the National Toxicology Program, the U.S. Government group that conducts such studies for government agencies, and we followed EPA's guidelines for Good Laboratory Practices.

There were multiple dosage levels for male and female Sprague Dawley rats. Rats were killed at different time points in order to study the development of lesions in the liver and other target organs, and to study the retention of PCBs in various tissues on a congener-specific basis. A pathology working group was convened to review the liver pathology and provide a consensus opinion to the toxicology laboratory. The interim analytical work was part of an effort to relate the development of tumors to the build-up of PCBs (on a congener basis) in the animals. For each dose group, we also tested the animals for neurological effects after one year of treatment.

The results of the study are as follows:

- Liver tumors were increased in all female rats except lowest dose (50 ppm) 1016 and only in the high-dose group of 1260 in males. Thyroid tumors were observed in male rats, but did not follow a dose response.

- Tumorigenic response was generally less than observed in previous studies.

- Mammary Gland tumors were generally reduced in treated female rats compared to controls.

GE Rat-Feeding Study and EPA PCB Cancer Reassessment (Continued)

- No evidence of Neurotoxicity.
- PCB-exposed female rats (most affected by liver toxicity) significantly outlived untreated rats.

These data were provided to U.S. EPA in order that they might be considered as part of EPA's ongoing reassessment of the cancer potency of PCBs. Details of the study and its results were reviewed by EPA's Scientific Advisory Panel in May, 1996. The Battelle-GE study was hailed by EPA, environmentalists and scientific reviewers as an excellent study, filling important data gaps, and carried out in a way to ensure credibility and acceptance.

Subsequent to the Advisory Panel meeting in May, EPA released its reassessment of the carcinogenic potency of PCBs, replacing the old slope factor of 7.7 $(mg/kg/day)^{-1}$ with a range of 0.07-2.0 $(mg/kg/day)^{-1}$, incorporating data from both the old studies and the new study. EPA advises risk assessors to consider the route of exposure in applying the range of slope factors to PCBs found in the environment. For example, if the exposure route is through fish or soil consumption, the slope factor of 2.0 should be used; for drinking water or inhalation of soluble or volatile congeners, resp., a factor of 0.4 should be used. If the environmental mixture contains no more than 0.5% (by weight) of pentachloro- (or higher) congeners, the factor of 0.07 can be used. Thus, a reduction in slope factor of about 4 to 100 might be justified, depending on the circumstances.

These changes reduce concerns about cancer risk of PCBs, and also provide the opportunity to lower costs of clean-up of contaminated wastes without incurring additional risks.

c:sbh/holdingstmnt.docs