involving dietary exposure to sodium saccharin, is likely to be responsible for the formation of rat urinary bladder tumors in chronic animal feeding studies. Chronic dietary exposure to sodium saccharin at appropriate levels leads to urothelial hyperplasia and subsequent bladder tumors in rats. However, silica microcrystals are found in the urinary bladder of rats fed sodium saccharin and these are absent in rats fed propoxur.

Miles Inc. recently reported on the results of a preliminary scanning electron microscopy study designed to determine if silica crystalline deposits occur in the urinary bladders of propoxur-treated rats and their possible role in inducing hyperplasia and tumors as mediated by the diet and urinary pH. No silica crystalline deposits were observed. The registrant has maintained its previous position of a non-genotoxic mechanism for propoxur-induced cell proliferative response in the rat bladder, but added that propoxur may act like a mitogen (that is, it promotes increased cell division, but does not, by itself, alter cell DNA). It is not known whether a complex interaction of weak or moderate genotoxic activity, cell proliferation and cytotoxicity in the urinary bladder results in tumor formation, or whether cell proliferation alone can cause this effect. Miles Inc. has indicated that it is studying whether there are genotoxic effects in the urinary bladder. In the absence of this information, which might indicate a threshold effect, and for purposes of this risk assessment, EPA has used the linear multistage model that it typically uses.

The Agency has received data from Miles Inc. which indicates the elevated incidence (8/48 or 16.7 percent) of uterine carcinomas observed at 5,000 ppm in a 2–year rat study was within the range (0/50 to 10/50) observed for historical control groups in a series of 32 chronic feeding studies in rats. The overall incidence of uterine carcinomas and/or adenocarcinomas was 163/2,107, or 7.7 percent.

Until propoxur is reviewed again by the Carcinogenicity Peer Review Committee and concludes differently, propoxur remains classified as a B2 carcinogen for which the carcinogenic potency has been quantified at 3.7×10^{-3} $(mg/kg/day)^{-1}$.

B. Exposure

The estimates of exposure for Pest Control Operators (PCOs), Residential Applicators (RAs), and residents of treated homes are discussed below and displayed in Table 1 below.

1. *Applicator exposure.* The main routes of human exposure to propoxur are through dermal contact with and inhalation of residues. Residues may be found on surfaces to which propoxur has been applied. However, propoxur may volatilize or evaporate during and following application, and be deposited onto other, untreated interior surfaces of a building. Inhalation exposure occurs from contact with propoxur vapors or dust during and following application of propoxur products. PCOs and RAs are exposed primarily during the mixing, loading, and application of propoxur products to the interior or around the exterior of buildings. Kennel workers and pet owners are exposed while treating animals. Residents of treated buildings are exposed to airborne and surface residues following application. EPA assessed human exposure to propoxur using data obtained from several sources, including studies submitted by Miles Inc. in response to the 1987 DCI, data from the technical literature, and surrogate data. The exposure data and the related estimates are discussed below.

a. *Crack and crevice study of PCO exposure.* Crack and crevice treatments are among the most popular propoxur uses for indoor pest control. In response to the December 14, 1987 Data Call-in (DCI) requirement, Miles Inc. submitted an acceptable crack and crevice study of PCO exposure (Ref. 4), in which Miles Inc. monitored the dermal and inhalation exposures of three PCOs as they treated five homes each. In this study, PCOs used a compressed air sprayer to apply a wettable powder formulation of propoxur, diluted to 1.1 percent active ingredient (a.i.), to cracks and crevices and as a limited broadcast treatment. The PCOs wore chemical-resistant gloves, cotton/polyester coveralls over a long sleeved shirt and long pants, and leather boots. Dermal exposure was monitored using gauze patches inside and outside clothing. Levels of residues on PCOs' hands were measured using an ethanol handwash. Inhalation exposure was measured by using personal sampling devices located in the applicator's breathing zone. (Inhalation exposure was found to be negligible compared to dermal.)

(1) *Wettable powders.* To estimate PCO exposure to wettable powders, EPA supplemented the crack and crevice data with additional assumptions as follows: the average PCO weighs 70 kg, works 8 hours per day over a 20–year working-life of a 70–year life-span, and handles 924 oz. a.i. per year. Dermal absorption was assumed to be 50 percent. Dermal exposure was estimated at 5.2×10^{-3} mg/kg/day (Ref. 5).

(2) *Ready-to-Use (RTU) liquids.* EPA determined that RTU liquid products are applied at rates similar to the wettable powder formulations, and residues are not expected to be higher or more persistent than those from the wettable powder formulation. For this reason, EPA determined the results of the crack and crevice exposure assessment for wettable powders should be used to estimate PCO exposure during application of RTU liquids (Refs. 5, 6 and 7). Thus, exposure was estimated at 5.2×10^{-3} mg/kg/day.

b. *Granular bait study.* Granular baits are formulated as dry pellets, usually containing 2 percent propoxur. They can be scattered on paper, pasteboards, or on the floor at a rate of about 4 oz per 500 to 1,000 square feet areas. Baits are used near baseboards, in closets, under sinks and refrigerators, around structures, patios, sidewalks and other places where insects may be. Miles Inc. submitted an acceptable study of PCO exposure to granular products. In this study, PCOs wore gloves, long-sleeved shirts, cotton trousers, and baseball caps over normal clothing which consisted of denim or cotton trousers, long-sleeved shirts and shoes while applying 2 percent granular baits by hand to a 2 to 3 foot wide band around driveways, sidewalks, patios, and flower beds, at the prescribed label rate of 4 oz per 1,000 square feet (0.08 oz. a.i./1000 sq. ft.). The granules were applied by three PCOs, each of whom carried a 5 pound carton of the bait in one hand while scattering the material with the other hand. Dermal exposure was measured using gauze patches worn both inside and outside the clothing and on the front of the cap. Hand exposure was measured from an ethanol handwash. Airborne residues were determined by drawing air from the breathing zone through filters using calibrated personal sampling pumps. Propoxur residues were not detected in most of the samples analyzed for dermal or respiratory exposure. Similarly, propoxur was not detected in hand washes after removal of the protective gloves. Because of the large numbers of samples with non-detectable values, EPA determined under these conditions that the exposure would be negligible for PCOs (Refs. 6, 7, and 8).

c. *Aerosol pet spray study.* A number of pressurized aerosol spray products are formulated for use directly on dogs and cats. The amount of a.i. in the products varies from 0.25 percent to 1 percent propoxur. In response to the 1987 DCI requirement, Miles Inc. submitted an acceptable aerosol pet spray study (Ref. 10). In this study, exposures of five workers using a 0.025 percent aerosol spray of propoxur were measured at each of three different