food consumption, and increased kidney and liver weight ratios at the 400-ppm dose level.

2. A 3-month feeding study in dogs fed diets containing 0, 2, 10, 50, and 1,500 ppm with a NOEL for red blood cell cholinesterase inhibition of 2 ppm (equivalent to 0.05 mg/kg/day) and a NOEL for systemic effects of 50 ppm (equivalent to 1.25 mg/kg/day) based on tremors and decreased food consumption in females at the 1,500-ppm dose level.

3. A 1-year feeding study in dogs fed diets containing 0, 5, 20, or 125 ppm with a NOEL for cholinesterase inhibition of less than 5 ppm (equivalent to less than 0.18 mg/kg/day) based on decreased brain and red blood cell cholinesterase at the 5-ppm dose level and a systemic NOEL of less than 5 ppm based on decreased liver weight in females at the 5-ppm dose level.

4. A two-generation reproduction study in rats fed diets containing 0, 1, 15, or 65 ppm (equivalent to 0/0, 0.08/0.09, 1.2/1.3, or 5.46/6.04 mg/kg/day for males/females) with a tentative reproductive NOEL of 15 ppm based on decreased fertility in the F1b and F2a, and F2b matings: decreased pup weight during the lactation period for both sexes and generations and decreased live births in the F2b litters.

5. A developmental toxicity study in rats given gavage doses of 0, 3, 6, or 18 mg/kg/day with no developmental toxicity observed under the conditions of the study. The NOEL for maternal toxicity was established at 6 mg/kg/day; rats fed 18 mg/kg/day (lowest-effect level) displayed hypersensitivity, tremors, and unsteady gait.

6. A developmental toxicity study in rabbits given gavage doses of 0, 10, 20, or 40 mg/kg/day from day 7 to day 19 of gestation with a developmental NOEL of 20 mg/kg/day based on significant reduction in fetal weight at the 40- mg/kg/day dose level. The maternal NOEL was established at 10 mg/kg/day based on body weigth decrement at 20 mg/kg/day dose level.

7. A 2-year chronic feeding/carcinogenicity study in rats fed diets containing 0, 5, 25, or 100 ppm (equivalent to 0, 0.25, 1.25, or 5.0 mg/kg/day) with a systemic NOEL of 25 ppm based on increased female mortality, decreased male body weight gain, anemia in males and increased leukocytes in male and female rats at the 100-ppm dose level. The NOEL for cholinesterase inhibition was established at 5 ppm based on cholinesterase inhibition at the 25-ppm dose level. In male rats, there were dose-related trends for (1) spleen hemangiosarcomas (malignant tumors associated with connective tissue, and blood and lymph vessels); (2) combined spleen hemangioma (benign tumors) and hemangiosarcoma; and (3) combined spleen hemangioma and hemangiosarcoma, and skin hemangiosarcoma. Furthermore, there were significant pair-wise comparisons between control and the high dose (100 ppm) for spleen (hemangioma/hemangiosarcoma) and in the combined tumors of spleen and skin hemangioma/hemangiosarcoma and lymph angioma/angiosarcoma (benign and malignant tumors made up of lymph vessels). There was also a significant difference by pair-wise comparison between the control and low dose (5 ppm) for (1) lymph angiosarcoma, (2) combined lymph angioma and angiosarcoma, and (3) combined spleen and skin hemangioma/hemangiosarcoma and lymph angioma/angiosarcoma. There were no significant tumor increases in female rats.

8. A 78-week carcinogenicity study in B6C3F1 mice fed diets containing 0, 25, 100, or 200 ppm (equivalent to 0, 3.75, 15, or 30 mg/kg/day). In male mice there were significant dose-related increased trends for (1) combined lung adenoma and/or adenocarcinoma, (2) for lymphoma, and (3) for the combined group of lymphoma, reticularsarcoma, and leukemia. In female mice there were significant dose-related trends for (1) liver carcinoma and for (2) combined liver adenoma and/or carcinoma.

9. Dimethoate is regarded as a mutagenic compound based on the results of studies designed to determine gene mutation and structural chromosome aberrations. Dimethoate is a bacterial mutagen and shows equivocal results for gene mutations in mammalian cells. It produces clastogenic effects in several studies in vitro and in vivo, and there are suggestive results for dominant lethal effects. The National Toxicology Program has concluded that dimethoate is a mutagenic compound based on its testing for gene mutation and chromosomal aberrations.

Dimethoate has been classified as a possible human carcinogen (category C) by the Office of Pesticide Programs' Health Effects Division's Carcinogenicity Peer Review Committee. The Peer Review Committee supports this classification based on the appearance of equivocal hemolymphoreticular tumors in male mice, the compound-related (no dose response) weak effect of combined spleen (hemangioma and hemangiosarcoma), skin (hemangiosarcoma), and lymph (angioma and angiosarcoma) tumors in male rats, and positive mutagenic activity associated with dimethoate.

The Peer Review Committee concluded that the lung tumors seen in male mice were not biologically significant tumors related to compound administration, since there were no statistically significant differences based on pair-wise comparisons with controls and each dose level. The incidence of lung tumors in the control groups was variable, and there was a high background level of these tumors. The increase in lymphoma observed in male mice in the high-dose group was of borderline statistical significance by pair-wise comparison with controls. The incidence of lymphoma in mice is also common and variable. The Committee agreed that the increased incidence for the combined hemolymphoreticular tumors in male mice is compound related but could only classify this incidence as equivocal. The incidence of hemolymphoreticular tumors in male mice was relatively low and consistent with historical control, only occurred in one sex (males), and was evident only in the high-dose group.

The Committee concluded that in female mice there were no significant pair-wise comparisons, there was only the trend with combined tumors, and the combined incidence was similar to historical controls. In addition, there also was no evidence of precursor lesions to carcinogenicity. Regarding the carcinogenicity study in rats, the Committee concluded that although there were significant pair-wise comparisons at the low and high doses for all tumors combined, these tumors did not indicate much more than a weak effect.

EPA has concluded that dimethoate poses no greater than a negligible cancer risk to humans; therefore, the Agency has chosen to use reference dose calculations to estimate dietary risk from dimethoate residues. The reference dose (RfD) for dimethoate is established at 0.0005 mg/kg body weight/day. The RfD is based on a NOEL of 0.05 mg/kg bwt/day for brain cholinesterase inhibition from a 2-year feeding study in rats and an uncertainty factor of 100. The anticipated residue contribution (ARC) for the general population from published uses and the proposed use on asparagus utilizes 21 percent of the RfD. The ARC for the subgroup most highly exposed, nonnursing infants, utilizes 41 percent of the RfD based on published uses and the proposed use on asparagus. The dietary risk assessment indicates that there is no appreciable risk from the establishment of the proposed tolerance for asparagus.