several carcinogenicity studies, the Agency has concluded that dichlorvos meets the criteria for a Group C (possible human) carcinogen. Dichlorvos has been shown to induce forestomach tumors in mice and leukemia in rats. Results from acute/ short-term, subchronic and chronic toxicity studies have shown dichlorvos to be a potent inhibitor of plasma, red blood cell and brain cholinesterase in several mammalian species, and to produce cholinergic signs.

In the Notice initiating the Special Review, EPA estimated cancer risks for those individuals potentially exposed to dichlorvos through dietary and nondietary (i.e. inhalation and dermal contact) routes. Since that time, EPA has determined that it is not appropriate to extrapolate from oral carcinogenicity data for estimation of excess individual cancer risks for exposure by the dermal and inhalation routes. Therefore, cancer risk estimates for workers and residents exposed to dichlorvos by the dermal and inhalation routes are not included in this revised risk assessment. EPA only estimated excess individual lifetime cancer risks for dietary exposure to the general population.

Dietary exposure to dichlorvos residues may occur as a result of use on a variety of sites, including greenhouse food crops, mushroom houses, bulkstored and packaged or bagged nonperishable processed and raw food, commercial food processing plants, groceries, eating establishments, and direct animal treatment. Some of these exposures and resulting risks may be eliminated due to voluntary cancellations or cancellation of uses related to the revocation of the FAR for packaged or bagged nonperishable processed food; however, since these actions are not final yet, for purposes of this document, EPA will assume that these uses will continue. EPA estimates dietary cancer risks from registered uses of dichlorvos to be 4.4 x 10-6. The major source of this estimated risk is from consumption of bulk, packaged or bagged nonperishable raw and processed food treated with dichlorvos (3.4 x 10⁻⁶).

In addition to registered uses of dichlorvos, naled provides an additional source of dietary risk from dichlorvos. Naled, an insecticide, is metabolized to dichlorvos by plants. As a result, the Agency felt it appropriate to characterize the total risk from dichlorvos even though naled itself is not under Special Review. The combined dietary cancer risk from dichlorvos is 5.1 x 10⁻⁶ which includes risk directly from dichlorvos (4.4 x 10⁻⁶) and from naled-derived dichlorvos (7.2 x 10^{-7}).

EPA completed a series of exposure assessments in 1987 for the Registration Standard and PD 1 that estimated the exposure to individuals mixing, loading and applying dichlorvos, as well as to those reentering areas treated with dichlorvos. These estimates were based on the best available data, which in most cases were exposure data derived from other pesticides applied in a similar manner as dichlorvos. Additional exposure data have been submitted since that time and the Agency has determined that revisions to the original assessments are appropriate based on these new data. EPA has revised its original exposure estimates for several uses of dichlorvos, including: Crack and crevice application, greenhouses, mushroom houses, dairy barns and milk rooms, household aerosol and total release fogger products.

Red blood cell, plasma and brain cholinesterase inhibition and/or cholinergic signs are the basis for the short-term, intermediate, and long-term MOE estimates. For pesticides, EPA classifies occupational/residential exposure patterns as short-term (1 to 7 days), intermediate (1 week to several months per year), or long-term (a substantial portion of the lifetime). These scenarios could vary by region or from year-to-year depending on the severity of the pest problem. Separate NOELs were selected from acute (0.5 mg/kg/day), subchronic (0.1 mg/kg/day), and chronic (0.05 mg/kg/day) toxicity studies to estimate MOEs for varying durations of exposure. Margins of exposure are outlined in Table 1 in Unit II. of this document for individuals reentering treated facilities and for individuals exposed during the application of dichlorvos. Most of the MOEs are below the level which the Agency believes is protective of public health (100).

B. Effects of Concern

1. *Carcinogenicity*. EPA has determined that the risk criteria for carcinogenicity as set forth in 40 CFR 154.7 (a)(2) has been exceeded for dietary exposure. Based on the studies described below, EPA has classified dichlorvos as a Group C (possible human) carcinogen (Ref. 1).

i. Hazard identification. In July 1987, the Office of Pesticide Program's Carcinogenicity Peer Review Committee (CPRC) classified dichlorvos as a Group B2 (probable human) carcinogen, based primarily on the results of National Toxicology Program (NTP) studies in mice and rats. Since that time, EPA has reevaluated the carcinogenic potential of dichlorvos and concluded that dichlorvos is a Group C (possible human) carcinogen. The basis for that determination is summarized below.

(a) Mouse study. Dichlorvos was administered by gavage to B6C3F1 mice (60/sex/group) for 103 weeks (5 days/ week) using corn oil as the vehicle (Ref. 2). Doses were 0, 10, or 20 mg/kg/day for male mice and 0, 20, or 40 mg/kg/ day for females. Administration of dichlorvos to female mice was associated with a statistically significant dose-related trend and statistically significant increase in squamous cell forestomach papillomas and combined squamous cell forestomach papillomas and carcinomas at the high-dose. The forestomach tumors were outside the historical control range. In male mice, an increase in squamous cell forestomach papillomas was associated with a significant dose-related trend, but was not statistically significant by pairwise comparison at either dose level. No other tumor types were identified in this study. No malignant squamous cell tumors were found in the historical controls.

(b) Rat study. Dichlorvos was administered, with corn oil as the vehicle, by gavage to F344 rats (60/sex/ group) for 103 weeks (five days/week) (Ref. 3). The dosages were 0, 4, or 8 mg/ kg/day. The study resulted in a statistically-significant increase in mononuclear cell leukemia in males by pairwise comparison at both dosage levels. The increase in leukemia also exhibited a statistically significant positive dose-related trend. There was an increased incidence of lung adenomas in high-dose male rats which was significant only for a dose-related trend. In addition, dichlorvos administration was associated with a statistically significant increased incidence of mammary gland adenomas and all mammary gland tumors at the low-dose only (by pairwise comparison) in rats. However, the incidence of lung adenomas and mammary gland tumors were within the historical control range.

(c) Reexamination of cancer classification. The FIFRA Scientific Advisory Panel (SAP) reviewed the CPRC's Group B2 cancer classification and concluded that dichlorvos should be classified as a Group C (possible human) carcinogen since: (1) only benign tumors were induced by dichlorvos; (2) they were not doserelated; and (3) dichlorvos was not mutagenic in *in vivo* assays (although it was mutagenic in several *in vitro* test systems with and without metabolic activation) (Ref. 4).