UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

NOV 3 1999

MEMORANDUM

SUBJECT: Section 18 - Specific Exemption Request for Use of Paraquat Dichloride in California (99-CA-48) to Control Weeds in Artichokes

FROM: James J. Jones, Director
Registration Division

TO: Susan B. Hazen, Deputy Director
Office of Pesticide Programs

I. APPLICANT'S REQUEST:

Applicant: California Department of Pesticide Regulation

Chemical: Paraquat dichloride

Product: Gramoxone Extra Herbicide (EPA Reg. No. 10182-280), manufactured by Zeneca Ag. Products

Site: Artichokes

Pests: Various weeds and grasses

Rate: A maximum of 3 ground applications at a rate of 1.28 to 3.2 pints of product, equivalent to 0.4 to 1 lb. a.i., per acre per year. Maximum of 3.2 pints of product (1.0 lb ai) per acre per year. No application may be made within 1 day of harvest.

Use season: Year round

Acres: 6,000

Emergency Condition: Simazine has been used in the past to control the subject pests. With the imminent cancellation of simazine, the industry purchased all existing stocks. The growers have now depleted the existing stocks of simazine. Since simazine has always been available, the artichoke growers do not have economic numbers that reflect a crop loss due to unavailability of simazine.

II. BACKGROUND:

This is the first emergency exemption submitted for use of paraquat dichloride on artichokes. Tolerances have been established (40 CFR 180.205) for residues of paraquat in numerous commodities. Tolerances have also been established for fat, kidney, meat, and meat byproducts for cattle, goats, hogs, horses, poultry and sheep as well as tolerances for eggs and milk. An IR4 petition (7E4857) which includes this use on artichokes is currently scheduled for completion the first quarter of 2000. A RED for paraquat dichloride was published August 1997.

III. EPA EVALUATION

An acute reference dose (acute RfD) of 0.03 milligrams per kilogram per day (mg/kg/day) has been identified for females 13+ years old and the general population including infants and children. For females 13+ the acute RfD is based on the maternal no observable adverse effects level (NOAEL) of 3 mg/kg/day derived from the combined results of two developmental studies in rats. The effects of concern are delayed ossification of the forelimb and hindlimb digits. The maternal NOAEL of 3mg/kg/day has also been identified as the endpoint of concern for the acute RfD for the general population including infants and children. The effects of concern are based on clinical signs of toxicity, decreased body weight gain, and respiratory distress and histopathology of the lungs An uncertainty factor (UF) of 100 (10 x for inter-species extrapolation and 10 x for intra-species variability) is appropriate. The **10 x** FQPA Safety factor to account for enhanced sensitivity of infants and children [as required by FFDCA § 408 (b)(2)(C)] was reduced to **1 x** for acute exposures. The acute Population Adjusted Dose (aPAD) is a modification of the acute RfD to accommodate the FQPA Safety Factor. The aPAD is equal to the acute RfD divided by the FQPA Safety Factor. Therefore, for females 13+ years old and the general population including infants and children the dietary aPAD is 0.03 mg/kg/day.

The NOAEL of 3.0 mg/kg/day derived from the combined results of two developmental studies in rats was identified as the short - and intermediate-term endpoints for dermal exposures. At lowest observable adverse effects level (LOAEL) of 5.0 mg/kg/day, there were clinical signs of toxicity, decreased body weight gain, and lung histopathology. A 0.3% dermal absorption rate should be used in risk assessments.

EPA has established the chronic RfD for paraquat at 0.0045 mg/kg/day. The chronic RfD is based on the NOAEL of 0.45 mg/kg/day from a one year oral study in dogs. At the LOAEL of 0.93 mg/kg/day the effects were chronic pneumonitis. An UF of 100 (10 x for inter-species extrapolation and 10 x for intra-species variability is appropriate. The **10 x** FQPA Safety factor to account for enhanced sensitivity of infants and children [as required by FFDCA § 408 (b)(2)(C)] is not applicable because the endpoint used in deriving the chronic RfD is based on chronic pneumonitis (not developmental or neurotoxic effects) in

adult dogs after chronic exposure and thus are not relevant for enhanced sensitivity to infants and children. The chronic Population Adjusted Dose (cPAD) is a modification of the chronic RfD to accommodate the FQPA Safety Factor. The cPAD is equal to the chronic RfD divided by the FQPA Safety Factor. Hence for chronic exposures, the cPAD and chronic RfD are the same (0.0045 mg/kg/day).

Paraquat is classified as Group E (no evidence of carcinogenicity in humans).

Using the Dietary Exposure Evaluation Model (DEEM™) analysis at the 95th percentile exposure level, assuming 100 percent crop treated and tolerance level residues for all commodities, 13 percent of the aPAD was utilized for the U.S. Population and 23 percent of the aPAD was utilized for children (1-6 years old), the subgroup with the highest exposure; 31 percent of the cPAD was utilized for the U.S. Population and 69 percent of the cPAD was utilized for children (1-6 years old), the subgroup with the highest exposure. The results of this analysis indicate that the acute and chronic dietary risk associated with existing uses and the proposed use of paraquat is below the Agency's level of concern.

Paraquat dichloride binds strongly to soil clay particles and it did not leach from the surface in terrestrial field dissipation studies. There were, however, detections of paraquat in drinking water wells from two states cited in the Pesticides in Ground Water Database(1991). These detections are not considered to be representative of normal paraquat use. Therefore, paraquat is not expected to be a groundwater contaminant of concern based on normal use patterns. Due to its persistent nature, paraquat could potentially be found in surface water systems associated with soil particles carried by erosion, however, paraquat is immobile in most soils, and at very high application rates (50-1000X), there was no desorption of paraquat from soils. Therefore, based on paraquat's normal use patterns and unique environmental fate characteristics, exposures to paraquat in drinking water are not expected to be obtained from surface water sources.

Short- and intermediate-term aggregate exposure takes into account chronic dietary food and water (considered to be a background exposure level) plus indoor and outdoor residential exposure. Paraquat is not registered on any use sites which would result in non-dietary, non-occupational exposure. Therefore no short- and intermediate-term aggregate risk assessments are needed.

Acute and chronic aggregate risk to paraquat is assumed to be the same as estimated risk from food and feed uses: at the 95th percentile exposure level, assuming 100 percent crop treated and tolerance level residues for all commodities, 13 percent of the aPAD was utilized for the U.S. Population.

In a developmental study in rats, the maternal NOAEL is 8 mg/kg/day (HDT). No LOAEL was identified and there were no maternal or developmental effects observed in the study. In another developmental study in rats, the maternal NOAEL is 1 mg/kg/day based on thin and hunched appearance, decreased body weight gain, and histological changes in the lungs and kidneys of non-survivors at 5 mg/kg/day (LOAEL). The developmental NOAEL is 1 mg/kg/day based on delayed ossification in the fore- and hindlimb digits at 5 mg/kg/day (LOAEL). The overall maternal and developmental NOAEL for the rat is considered 3 mg/kg/day based on the results from two developmental studies.

In a developmental study in mice, the maternal NOAEL is 5 mg/kg/day based on statistically . significant decreases in body weight gain at 10 mg/kg/day (LOAEL). The developmental NOAEL is 5 mg/kg/day based on statistically significant decreases in body weight gain at 10 mg/kg/day (LOAEL). In

another developmental study in mice, the maternal NOAEL is 15 mg/kg/day based clinical signs, death, decreased body weight gain, decreased body weight, increased organ weight (lung w/ trachea, kidney), dark red lung lobes, and possible decrease in pregnancy rate at 25 mg/kg/day (LOAEL). The developmental NOAEL is 15 mg/kg/day based on decreased mean fetal weight, retarded ossification of occipital, increased number with extra 14th ribs, increased number with unossified astragalus in the hindlimb, and an increased number with $\leq$6 caudal centra.
In a 2-generation reproductive study in rats, the NOAEL for paternal toxicity is 1.25 mg/kg/day based on increased incidence of alveolar histiocytes, discolored lungs, fibrosis, edema at the LOAEL of 3.75 mg/kg/day. There were no reproductive effects seen in this study therefore, the reproductive NOAEL/LOAEL is 7.5 mg/kg/day (HDT).
The Agency has determined that there is no indication of additional sensitivity to young rats or mice following pre-and/or postnatal exposure to paraquat. There is a complete toxicity data base for paraquat and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. EPA concludes that reliable data support the use of the standard 100-fold uncertainty factor, and that an additional uncertainty factor is not needed to protect the safety of infants and children.

Non-target mammals, birds, and aquatic species are not expected to be adversely affected by this use. Based on comments by EFED in connection with similar uses of paraquat, the following recommendation is included in the attached authorization: If applications are made in counties containing any endangered plant species, then contact with appropriate authorities should be initiated before paraquat applications are made if the applicator is in doubt as to locations of these plants.

IV. RECOMMENDATION:

I recommend that the attached specific exemption for the use of paraquat dichloride on artichokes be granted. This recommendation is based on the following:

1. The situation is non-routine due to the loss of simazine. California artichoke growers may suffer significant economic losses if there are no effective or practical control alternatives.

2. Residues of paraquat are not expected to exceed 0.05 ppm in/on artichokes and a time-limited tolerance will publish in the *Federal Register* in the near future.

3. IR-4 submitted a petition in 1997 for a tolerance in connection with this use. Completion of Agency review is scheduled for first quarter 2000. Based on this, adequate progress toward registration of this use has been made.

4. Non-target mammals, birds, and aquatic species are not expected to be adversely affected by this use. The following recommendation is included in the attached authorization: If applications are made in counties containing any endangered plant species, then contact with appropriate authorities should be initiated before paraquat applications are made if the applicator is in doubt as to locations of these plants

Approve: Susan B. Hazen

Disapprove:_____

Date: 11/3/99