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EPA R.E.D. FACTS

Alachlor

Pesticide Reregistration

All pesticides sold or distributed in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered before November 1, 1984, be reregistered to ensure that they meet today's more stringent safety standards.

Under the Food Quality Protection Act of 1996, EPA must consider the increased susceptibility of infants and children to pesticide residues and determine the need for an additional safety factor for the protection of infants and children. When establishing or reassessing tolerances, the Agency must also consider aggregate exposures to a pesticide, that is, combining the exposures that result from consuming pesticide residues in food and water, or using pesticide products in and around the home. Additionally, the Agency must assess the cumulative effect of pesticides and other chemicals that demonstrate a common mechanism of toxicity. Mechanism of toxicity is defined as the steps leading to an adverse health effect following exposure to a chemical. A common mechanism of toxicity occurs when two or more chemicals produce the same adverse health effect by the same sequence of steps.

In evaluating pesticides for reregistration, the pesticide producers submit to EPA a complete set of studies describing the human health and environmental effects of each pesticide. Agency scientists review the submitted studies to determine if the studies are scientifically valid. These studies are the basis for the Agency's risk assessment. The Agency then develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks, and then reregisters those pesticides and/or uses that can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for reregistration case 0063, alachlor.

Use Profile

Alachlor is a herbicide used for weed control on corn, soybeans, sorghum, peanuts, and beans. There are liquid, dry flowable, microencapsulated, and granular formulations. The timing of applications is preplant, pre-emergent, at plant for corn and soybeans, post-transplant, post-emergent, and at ground crack for peanuts only. Alachlor is applied by ground, aerial, and chemigation equipment. It can also be mixed with dry bulk fertilizer.

Regulatory History

Alachlor was first registered in 1969 as a selective herbicide for control of broadleaf weeds and grasses. Alachlor is produced by the Monsanto Company in the US.

A Registration Standard was issued for alachlor on November 20, 1984. The Registration Standard involved a thorough review of the scientific data base underlying pesticide registrations and an identification of essential, but missing, studies. The Registration Standard (1) stated that alachlor was classified as an oncogen, (2) required additional data on the leaching and mobility of alachlor to examine the potential of alachlor to contaminate ground and surface water, (3) required a monitoring study of ground and surface water were required, and required additional data in the areas of toxicology, product chemistry, and residue chemistry.

On January 9, 1985, the Agency published a Notice of Initiation of Special Review of Registrations of Pesticide Products Containing Alachlor (Federal Register, Volume 50, No. 1115) and the Alachlor Position Document (PD-1) that detailed the basis for the Special Review. The Special Review was initiated under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) because pesticide products containing alachlor met or exceeded the Agency's oncogenicity criteria.

Following the review of public comments and additional information received in response to the Notice of Initiation of Special Review and the Alachlor PD-1, EPA issued a Notice of Preliminary Determination on October 8, 1986 (Federal Register, Volume 51, No. 36106). In this notice the Agency proposed to allow the continued use of alachlor products subject to modifications of the terms and conditions of registration .

Following review of comments and additional information received in response to the Preliminary Notice, EPA issued a notice entitled "Alachlor; Notice of Intent to Cancel Registrations, Conclusion of Special Review on December 31, 1987 (Federal Register, Volume 52, No. 49480). This notice is

also known as Alachlor Position Document 4 (PD-4). The PD-4 concluded the Special Review and stated that EPA would cancel the registrations and deny applications for registration of products containing alachlor that did not comply with the modified terms and conditions of registration set forth in this notice. The PD-4 stated that tolerances would be rewritten once all residue data required by the Registration Standard were received and evaluated. The PD-4 required the following label amendments: Restricted Use due to Oncogenicity, a tumor hazard warning, use of a mechanical transfer system to be used by mixer/loaders and/or applicators who treat 300 or more acres annually, and human flaggers were prohibited for aerial application. Additional ground water monitoring data were required. Labeling bearing required changes was submitted and accepted in early 1988.

Human Health Assessment

Toxicity

Data from acute toxicity studies serve as the basis for labeling and packaging requirements. In studies using laboratory animals, alachlor generally has been shown to be of low acute toxicity. All acute studies have been classified as either Category III or IV, the two lowest classifications.

Alachlor has been evaluated for carcinogenic activity in rats and mice. In accordance with the 1996 EPA proposed Guidelines for Carcinogen Risk Assessment, alachlor was classified as "likely" to be a human carcinogen at high doses, but " not likely" at low doses. Based on numerous studies submitted by the registrant that were reviewed by Agency scientists, as well as an external peer review panel, it was agreed that a margin of exposure (MOE) approach (indicative of a non-linear dose response) should be used for the risk assessment.

The scientific validity of the MOE approach has been documented by various review panels, such as the FIFRA Scientific Advisory Panel, and the Cancer Review Committee. However, the policy implications, methodology, and appropriateness of using an MOE approach in regulatory decision making have not yet been fully developed by the Agency. Perhaps, the most critical of the decision criteria to develop are those for determining the appropriate regulatory level. While informed by the science, this determination is ultimately a risk management decision. Once this methodology has been developed, then the available chemical-specific data would be used to determine whether or not the MOEs identified in the risk assessment constitute acceptable risks.

For now, the regulatory decision for alachlor will be based on both the Q_1^* approach and the MOE approach for the evaluation of carcinogenic potential. These are not directly comparable approaches. The Q_1^* approach

is indicative of a linear approach and reflects the assumption that any exposure to alachlor could cause cancer. The MOE approach is indicative of a non-linear approach and reflects the assumption that there is an exposure dose below which tumor formation is not likely to occur. Thus, the risk numbers do not translate from one approach to the other. Each approach must be considered separately.

The alachlor database for pre-and post-natal effects is complete based on current requirements. The Agency has reviewed two developmental toxicity studies: one in rats, and one in rabbits. Developmental studies are designed to identify possible adverse effects on the developing organism during pre-natal development, which may result from the mother's exposure to the pesticide. For alachlor, there is also a multi-generation rat reproduction study. A reproduction study is designed to provide general information concerning the effects of a test substance on mating begavior, conception, parturition, lactation, weaning, and growth and development of the offspring.

Review by Agency scientists indicates no evidence of increased susceptibility of rats or rabbits to in utero and/or early postnatal exposure to alachlor. Based on this conclusion, as well as additional information on exposure to alachlor in food and water, the Agency has concluded that the additional safety factor, as required by FQPA for the protection of infants and children, can be removed. Therefore, this safety factor need not be applied to the alachlor risk assessment.

The toxicological effects of a pesticide can vary with different exposure durations and routes. For example, an individual may be exposed throughout their lifetime to pesticide residues in the food and water consumed, but a farm worker could also be exposed for several days or a month to pesticide formulations that can enter the body through the skin, or be inhaled. The Agency considers the entire toxicity database and, based on the effects seen for different durations and routes of exposure, determines which risk assessments are necessary to insure that the public is adequately protected from any pesticide exposure.

The alachlor reregistration eligibility review considered the following assessments to be appropriate:

Assessment	Exposure Route	NOEL[1] for Use in Estimating Risk
Acute	Dietary (food and water)	Not required - no evidence of significant toxicity from a one day or single event exposure by the oral route
Chronic (non-carcinogenic)	Dietary (food and water)	RfD[2,3] = 0.01 mg/kg/day
Short-Term Occupational	Dermal + Inhalation	NOEL = 150 mg/kg/day Use of dermal absorption factor (0.24) required.[4]
Intermediate-Term	Dermal + Inhalation	NOEL = 50 mg/kg/day Use of dermal absorption factor not required since NOEL is from a dermal study.[4]
MOE Approach[5] Carcinogenic	Dietary (food and water)	NOEL = 0.5 mg/kg/day (nasal) NOEL = 14 mg/kg/day (stomach)
MOE Approach Carcinogenic Occupational	Dermal + Inhalation	Not appropriate - Exposure assessment does not indicate that use is long-term and continuous.
Q_1^* Approach[6] Carcinogenic	Dietary (food and water)	$Q_1^* = 0.08$ $(mg/kg/day)^{-1}$
Residential	Dermal + Inhalation	Not appropriate - The Agency has not identified any alachlor products that are intended for home use, or uses in/around schools, parks or other public areas.

1 A NOEL (no observed effect level) is the dose at which no effects were observed in the test animals.

2 The chronic Reference Dose (RfD) is the traditionally selected endpoint for chronic dietary risk. The RfD represents the quantity of a substance which if absorbed on a daily basis over a lifetime, is not expected to pose significant risk of adverse health effects.

3 Acceptable risk is less than 100% of the RfD.

4 Acceptable risk results in a MOE that is greater than 100.

5 Acceptable risk has not been determined.

6 Acceptable risk is 1 x 10^{-6}, or lower.

Dietary Risk (Food Only)

People may be exposed to small amounts of alachlor through the consumption of food containing residues of alachlor. Tolerances are pesticide residue levels that should not be exceeded in or on a raw agricultural commodity in the channels of interstate commerce when the pesticide is applied according to label directions. Tolerances have been established (see 40 CFR 180.249) for residues of alachlor in/on a variety of food and feed commodities:

- beans, which includes dry beans, lima beans, forage and fodder;
- corn, fresh sweet, and forage, fodder, and grain;
- eggs;
- milk;
- peanuts, forage, hay, and hulls;
- sorghum, fodder, forage, and grain;
- soybeans, forage, and hay;
- meat and meat byproducts of cattle, goats, hogs, poultry and horses.

Sufficient data are available to determine the adequacy of most established tolerances. Based on this data, some tolerances need to be revoked, and some need to be increased. The reassessed tolerances for alachlor will range from 0.02 to 10 ppm.

EPA has also assessed the chronic (non-carcinogenic) dietary risk posed by alachlor. Using refinements to the dietary assessment process and considering all food uses recommended through reregistration, the Anticipated Residue Concentration (ARC) for the overall U.S. population represents less than 1% of the chronic Reference Dose (RfD), the amount believed not to cause adverse effects if consumed daily over a 70-year lifetime. The most highly exposed subgroup, non-nursing infants less than one year old, has an ARC which also represents less than 1% of the chronic RfD. This low fraction of the allowable RfD is considered to be an acceptable dietary risk.

EPA has assessed the total carcinogenic dietary risk posed by alachlor by both the Q_1^* approach and the MOE approach. Both approaches are discussed below in the Aggregate Dietary Discussion.

Dietary Risk (Drinking Water Only)

People may be exposed to small amounts of alachlor through the consumption of water containing residues of alachlor. Alachlor residues in drinking water are regulated under the SDWA (Safe Drinking Water Act). The MCL (Maximum Contaminant Level), set by the Agency, for alachlor is 2 ppb. An MCL is the maximum permissible level of a contaminant in drinking water that is delivered to any user of a public water supply system. For alachlor, there is extensive monitoring data for both ground and surface water sources.

EPA has assessed the chronic (non-carcinogenic) drinking water risk posed by alachlor. Using the monitoring data for alachlor only and Agency assumptions on the amount of water consumed, the estimated exposure represents less than 1% of the chronic Reference Dose (RfD), for adult males, adult females, and children (1 - 6 years) sub-population groups. This is considered to be an acceptable drinking water risk.

EPA has assessed the carcinogenic drinking water risk posed by alachlor, using water monitoring data and Agency assumptions on the amount of water consumed, for both the Q_1^* approach and the MOE approach. Both approaches are discussed below in the Aggregate Dietary Discussion.

Aggregate Dietary Risk (Food and Drinking Water)

FQPA requires that the Agency consider aggregate risk, that is, exposure from all food, water, and residential (non-occupational, non-dietary) exposures when making a safety determination. Since there are no residential uses of alachlor, the aggregate exposure is for food and water only. The highest chronic risk is 4% of the chronic RfD which represents the sub-population children (1 - 6 years). This was calculated considering both food and water containing residues of alachlor as well as consumption of water containing residues of the alachlor ESA degradate. The Agency considers this to be an acceptable risk.

The aggregate carcinogenic risk using the Q_1^* approach considers exposures from both food and water. For adult males and adult females carcinogenic risks range from 7.8×10^{-7} to 1.4×10^{-6}. These risks are consistent with the carcinogenic level (1×10^{-6}) that the Agency considers to be negligible.

The aggregate carcinogenic MOEs (food and drinking water) for adult males and adult females vary from 29,000 to 1,400,000. At this time, the Agency is not making any conclusions regarding the adequacy of these calculated MOEs for carcinogenic dietary risk. This is due to the fact that the Agency has not yet made a final decision as to the appropriate uncertainty

factors which would be adequately protective of a carcinogenic endpoint regulated using a non-linear approach. However, given that the cancer risk using the Q_1^* approach is acceptable and that the magnitude of the calculated MOEs is quite large, the Agency believes that the dietary cancer risk from the use of alachlor is not of concern.

Occupational Exposure

Based on current use patterns, handlers (mixers, loaders, and applicators) may be exposed to alachlor during normal use of granular, liquid, and dry flowable formulations. No protective equipment is required for the granular formulations. For worker protection, the Agency will require the use of additional protective equipment (chemical resistant gloves, apron, and chemical resistant shoes) when handling liquid and dry flowable formulations for workers supporting groundboom applications. For workers supporting aerial applications, closed (mechanical transfer) systems will be required for liquid formulations. Monsanto will be required to develop water soluble packaging for dry flowable formulations for aerial applications. Closed (mechanical transfer)systems will be required for the dry bulk fertilizer impregnation process.

The levels of protection required were based on the intermediate-term exposure (one week to several months) scenario. As previously stated, the exposure assessment indicated that use of alachlor is an intermittent exposure (not long-term and continuous.) The carcinogenic MOE approach is not appropriate for an occupational risk assessment for alachlor, because the exposure is not of sufficient duration (i.e., chronic) to produce tumors.

Unlike the MOE approach to carcinogenic risk assessment, the Q_1^* approach assumes that any exposure could result in tumor formation. Thus, this type of assessment could be performed for an intermittent exposure. However, the scientific validity of the MOE approach for carcinogenic risk assessment of alachlor has been documented. Alachlor was classified as "likely" to be a carcinogen at high doses, but "not likely" at low doses. It is only the policy on determining an appropriate regulatory level that has not been fully developed by the Agency. Since, performing a carcinogenic MOE risk assessment for the occupational scenario is not appropriate, a Q_1^* carcinogenic occupational assessment for comparison purposes is not necessary.

The potential for post-application worker exposure is negligible, provided the Restricted Entry Interval of 12 hours is observed. This is due to the timing of applications. Alachlor is applied to the soil and/or soil incorporated preplant, and pre-emergent. Thus the application of alachlor to

emerging plants, well before the plants are mature, mitigates the potential for post-application exposure.

Environmental Assessment

Environmental Fate

The Environmental Fate Assessment shows that:

- Alachlor has a low affinity to adsorb to soils and is expected to be highly mobile.
- Alachlor is moderately persistent and dissipates primarily by aerobic soil metabolism processes with a half-life of 2-3 weeks.
- The major acid degradates of alachlor are very mobile and appear to be persistent.
- Field dissipation studies confirm this fate profile (half-life of 6-11 days; leaching through 42-48 inches in one of the studies).

Water Resources Assessment

The Water Resources Assessment concludes that:

- Alachlor is highly mobile and moderately persistent. These two characteristics are generally observed in chemicals that reach ground water and surface water.
- Alachlor presents a clear hazard to groundwater quality. Reliable monitoring studies have demonstrated that alachlor, even when used according to label directions, results in significant groundwater contamination. Alachlor use also results in groundwater in the use areas being contaminated with degradation products, which are also very mobile and persistent.
- Monitoring studies show that alachlor levels in surface water result in effects on aquatic plants and indirectly on aquatic animals.
- Available information indicates that (surface) drinking water supply systems will usually comply with the SDWA.

Ecological Effects

The available toxicity data for alachlor indicate that alachlor is:

- Slightly to practically non-toxic to birds on an acute oral basis (LD_{50} of 1500 mg/kg).
- Slightly toxic to mammals, based on a rat study (LD_{50} of 930 mg/kg).
- Slightly toxic to honey bees (LD_{50} >36 ug/bee).
- Slightly to moderately toxic on an acute basis to freshwater fish (LC_{50} 1-33 ppm).
- Highly to moderately toxic to freshwater fish on a chronic basis ($NOEC \geq 0.1$ ppm, $LOEC \geq 0.2$ ppm).

- Moderately toxic to saltwater fish (3.9 ppm), moderately toxic to saltwater mysid (2.4 ppm) and moderately toxic to shellfish (1.6 ppm).
- Highly toxic to aquatic plants (based on a single species tested: NOEL=0.35 ppb, LOEL=0.69 ppb, EC_{50}=1.64ppb).

Therefore, a potential risk to nontarget terrestrial and aquatic plants, and endangered plant species exists. The available information on the major alachlor degradates indicates that the degradates appear to be less toxic to aquatic organisms than the parent.

Ecological Risk Assessment

An evaluation of the risk to nontarget organisms from the use of alachlor products, combining toxicity data with potential exposure, indicates that:

- Alachlor poses a potential risk to terrestrial animals on a chronic basis. Additional information are required to confirm this assessment.
- The granular formulations and high use rate pose the greatest risk to nontarget organisms.
- Alachlor levels observed in surface water monitoring studies could result in extensive adverse effects on aquatic plants.
- Aquatic animals are not at acute risk due to exposure to alachlor, but chronic effects may be observed under certain circumstances.

Risk Mitigation

To lessen the human health, ecological, water and food quality risk posed by alachlor, the registrant has voluntarily agreed to reduce the maximum single application rate from 6 lb to 4 lb ai/acre, and to classify alachlor as a restricted use pesticide (RUP) for groundwater concerns. EPA is requiring additional mitigation measures that will: protect non-target species, control surface water and ground water contamination, and protect workers.

Additional Data Required

EPA is requiring the following additional generic studies for alachlor to confirm its regulatory assessments and conclusions:

- avian reproduction
- aquatic plant studies
- analytical methodologies
- handler exposure studies

The Agency also is requiring product-specific data including product chemistry and acute toxicity studies, revised Confidential Statements of Formula (CSFs), and revised labeling for reregistration.

Product Labeling

All alachlor end-use products must comply with EPA's current pesticide product labeling requirements. The following label changes are required: (For

Changes Required

a comprehensive list of labeling requirements, please see the Alachlor RED Document, Table 78.)

- Classify alachlor as a Restricted Use Pesticide (RUP) for ground water concerns.
- Label language regarding mixing/loading setbacks must appear in Precautionary Statements in the Environmental Hazards Section.
- Groundwater advisory language.
- Surface water advisory language.
- Advisory statement in the Environmental Hazards Section of toxicity to terrestrial and aquatic plants, fish, and aquatic invertebrates.
- Advisory statement for granular products.
- Spray Drift Labeling Language.
- For liquid (emulsifiable concentrate) formulations or dry flowable formulations require that mixers, loaders, and persons cleaning equipment must wear long-sleeved shirt, long pants, chemical-resistant gloves, chemical-resistant footwear, and chemical-resistant apron for those workers supporting groundboom application.
- For workers supporting aerial applications and chemigation, for liquid (emulsifiable concentrate) formulations require that mixers, and loaders, must wear long-sleeved shirt, long pants, and chemical-resistant gloves, and the use of closed (mechanical transfer) systems.
- For workers supporting aerial applications and chemigation, for dry flowable formulations require that Monsanto develop water soluble packaging.
- For impregnating dry bulk fertilizer with alachlor require the use of closed mixing systems.
- A 12 hour restricted entry interval (REI) is required for uses within the scope of the WPS. The PPE required for early entry is coveralls, chemical-resistant gloves, and shoes plus socks.

Regulatory Conclusion

EPA has determined that the reassessed tolerances for alachlor meet the safety standard under the FQPA, and that there is a reasonable certainty that no harm will result to infants and children or to the general population from aggregate exposure to alachlor residues. The use of currently registered products containing alachlor in accordance with approved labeling will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, all uses of these products are eligible for reregistration. Alachlor products will be reregistered once the required product-specific data, revised Confidential Statements of Formula, and revised labeling are received and accepted by EPA.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for alachlor during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED document or to submit written comments, please contact the Pesticide Docket, Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Electronic copies of the RED and this fact sheet are available on the Internet. See http://www.epa.gov/REDs.

Printed copies of the RED and fact sheet can be obtained from EPA's National Center for Environmental Publications and Information (EPA/NCEPI), PO Box 42419, Cincinnati, OH 45242-2419, telephone 1-800-490-9198; fax 513-489-8695.

Following the comment period, the Alachlor RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-605-6000.

For more information about EPA's pesticide reregistration program, the Alachlor RED, or reregistration of individual products containing alachlor please contact the Special Review and Reregistration Division (7508C), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticide Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, from 6:30 am to 4:30 pm Pacific Time, or 9:30 am to 7:30 pm Eastern Standard Time, seven days a week. Their website address is ace.orst.edu/info/nptn/.