United States Environmental Protection Agency

Office of Prevention, Pesticides and Toxic Substances (7501C)

Pesticide Fact Sheet

Name of Chemical: **Amicarbazone**
Reason for Issuance: **Conditional Registration**
Date Issued: **October 4, 2005**

DESCRIPTION OF CHEMICAL

Generic Name: **4-amino-4,5-dihydro-N-(1,1-dimethylethyl)-3-(1-methylethyl)-5-oxo-1H-1,2,4-triazole-1-carboxamide**

Common Name: **Amicarbazone**

Trade Names: Amicarbazone Technical
Amicarbazone DF

EPA Chemical Code: 114004

Chemical Abstracts Service (CAS) Number: 129909-90-6

Year of Initial Registration: 2005

Pesticide Type: Herbicide

U.S. Producers: Arvesta Corporation
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San Francisco, California 94105

USE PATTERNS AND FORMULATIONS

Amicarbazone is intended for use in field corn, in either conventional, conservation or no-tillage crop management systems and will be applied preplant, preemergence, and early postemergence through ground application only.

Amicarbazone has herbicidal activity against annual broadleaf weeds. It selectively inhibits acetolactase synthase, and enzyme involved in photosystem II of plants

SCIENCE FINDINGS

Hazard and risk assessments were conducted in relation to this registration application and tolerance petition for amicarbazone on corn that suggest that its use, consistent with the proposed labeling measures, will be protective of the public health and the environment.

Amicarbazone exhibits low acute toxicity. The major effects observed across species in multiple dose studies were body weight changes and liver effects. Amicarabazone is not mutagenic and has been classified as "not likely to be a human carcinogen". Although the acute neurotoxicity study in rats showed signs of neurotoxicity, no such effects were seen in the subchronic and developmental neurotoxicity studies. The database is complete with respect to pre- and post-natal toxicity and shows no evidence of increased qualitative or quantitative susceptibility. There are no residual uncertainties. HED recommends that the special FQPA safety factor be reduced to 1X and that no database uncertainty factor is needed.

Health Effects Division's Review - Hazard Identification

The acute reference dose (RfD) and population adjusted dose (PAD) have been selected at 0.10 mg/kg/day for all populations based on neurotoxic effects in the acute rat neurotoxicity study. The chronic RfD and PAD have been selected at 0.023 mg/kg/day based on body weight effects in the chronic rat study and liver effects in the chronic dog study. No dermal endpoint was selected for occupational risk assessment based on the lack of systemic toxicity in a dermal rat study. The inhalation endpoint was based on a 90-day oral dog study in which assorted effects were observed in the thyroid, liver, gall bladder, and blood.

Although there are some residue chemistry data deficiencies, the database is adequate for conditional registration, provided the enforcement methods are adequate. The residues of concern in plants and livestock for tolerances and risk assessment consist of the parent, a desamino metabolite, and a hydroxylated derivative of the latter. The desamino metabolite is also included in the drinking water assessment along with its N-methyl derivative.

The acute and chronic dietary assessments were conducted using DEEM-FCID and are very conservative in that 100% crop treated and tolerance level residues were used in all commodities. Modeled drinking water levels provided by EFED were also included in the assessments. The risks for all populations are well below HED's level of concern. Since no residential uses are proposed for amicarbazone, these dietary risk estimates also represent the aggregate risks. Occupational risks are also below HED's level of concern.

FQPA Decision

The toxicology database is complete for FQPA purposes and there are no residual uncertainties for pre-/post-natal toxicity. Based on the quality of the exposure data, EPA determined that the special FQPA safety factor be reduced to 1X and that no database uncertainty factor is needed. There are no residential uses of amicarbazone.

Consideration of Risks to Pesticide Applicators and Handlers

There are two handler scenarios that are expected to result in the highest exposure for the proposes uses: mixing/loading dry flowable for ground applications and applying sprays with groundboom equipment. The maximum application rate listed on the proposed labels was used for all exposure assessments. The maximum rate is 0l45 lb ai/A. Based on HED's Exposure Science Advisory Council Policy Number 9.1, 200 acres per day treated was assumed for application on corn using groundboom equipment. The average body weight for general population (70 k g) was used for all exposure scenarios covered in this risk assessment. No data on the number of exposure days per year was provided. For this risk assessment, it was assumed that handlers would be exposed for less than 6 months per year (i.e., short-/intermediate-term in duration). Risks to agricultural workers were also considered. Occupational risks are below HED's level of concern.

Acute and Chronic Dietary Exposure

An acute and chronic dietary exposure analysis was conducted using Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™), which incorporates food consumption data as reported by respondents in the USDA 1994-1996 and 1998 Nationwide Continuing Surveys of Food Intake by Individuals (CSFII), and accumulated exposure to the chemical for each commodity. The following assumptions were made for the acute and chronic exposure assessments: tolerance-level residues were assumed for all food commodities with proposed amicarbazone tolerances, and it was assumed that all of the crops included in the analysis were treated. Percent Crop Treated (PCT) and/or anticipated residues were not used in the acute and chronic risk assessments.

Drinking Water

The Agency lacks sufficient monitoring exposure data to complete a comprehensive dietary exposure analysis and risk assessment for amicarbazone in drinking water. Because the Agency does not have comprehensive monitoring data, drinking water concentration estimates are made by reliance on simulation or modeling taking into account data on the physical characteristics of amicarbazone. Based on the FIRST and SCI-GROW models, the EECs of amicarbazone for acute exposures are estimated to be 21.4 parts per billion (ppb) for surface water and 102.9 ppb for ground water. The EECs for chronic exposures are estimated to be 13.4 ppb for surface water and 102.9 ppb for ground water.

The acute dietary exposure from food and drinking water to amicarbazone will occupy 6 % of the aPAD for females 13 years and older. The chronic exposure to amicarbazone from food and drinking water will utilize 14 % of the cPAD for the U.S. population, 39 % of the cPAD for all infants (< 1 year old), and 24 % of the cPAD for children 3-5 years old. .

Amicarbazone is not registered for use on any sites that would result in residential exposure. Therefore, the aggregate risk is the sum of the risk from food and water, which do not exceed the Agency's level of concern.

Environmental Fate and Effects Division's Review

Amicarbazone is moderately persistent in the environment as it eventually transforms by biotic mechanisms ($t_{1/2}$= 87 days). Under acidic and neutral environments, amicarbazone is stable to hydrolysis, but transforms slowly under alkaline conditions. Photolysis also occurs slowly for amicarbazone in water and on soil with half-lives on the order of about two months, estimated for outdoor environmental conditions. The primary transformation products of amicarbazone are **Des-amino:** N-(1,1-dimethylethyl)-4,5-dihydro-3-(1-methylethyl)-5- oxo-1H-1,2,4-triazole-1-carboxamide; **N-methyl Des-amino:** N-(1,1-dimethylethyl)-4,5-dihydro-4-methyl-3-(1-methylethyl)-5-oxo-1H-1,2,4-triazole-carboxamide; and **Decarboxamide:** 4-amino-2,4-dihydro-5-(1-methylethyl)-3H-1,2,4-triazol-3-one.

Amicarbazone has a low vapor pressure and Henry's Law constant. Therefore, volatilization, from water and soil surfaces, is not expected to be an important environmental fate process. The moderate persistence and high mobility of amicarbazone in soil make leaching of this compound to lower soil horizons and groundwater possible. Likewise, leaching and possible ground water contamination with amicarbazone's major three transformation products are possible due to their apparent long persistence and high mobility. Amicarbazone is not to be applied on calcareous soils with pH values substantially higher than 7.4. Therefore, the fate of the chemical under neutral and acidic conditions only is considered in this assessment. In such environments, two major amicarbazone transformation products (Des-amino and N-methyl Des-amino) are expected to be formed. Given the moderate persistence/high mobility and solubility of the parent compound and the apparent high persistence/high mobility of the two transformation products, both amicarbazone and its first two transformation products are expected to dissipate slowly and at the same time be vulnerable to leaching/run-off. If amicarbazone is transported into alkaline ground water, surface water bodies and/or soils, the third transformation product (Decarboxamide) may be formed since this was the only major metabolite identified in the base-catalyzed hydrolytic transformation of amicarbazone.

Results of acute toxicity studies indicate that technical grade amicarbazone (amicarbazone TGAI) is practically non-toxic to honey bees, slightly toxic to mammals, and slightly toxic to practically non-toxic to birds. However, results of chronic toxicity studies show that longer-term exposure to amicarbazone TGAI results in adverse effects on growth and reproductive parameters in birds and toxicity to parents and offspring in mammals. Chronic exposure of bobwhite quail and mallard ducks resulted in exposure-related reproductive effects, including decreased number of viable embryos per eggs set, number of hatchlings per egg set, and eggshell thickness as the most sensitive endpoints. In mammals, chronic exposure of rats resulted in decreased body weight and body weight gain in parents and offspring, but no adverse effects on reproductive outcome. No data are available to characterize the effects of amicarbazone metabolites in mammals, birds, or insects.

Results of Tier 2 seedling emergence and vegetative vigor terrestrial plant studies with the amicarbazone formulated product MKH 3586 70 WG show that both monocots and dicots are sensitive to exposure, with dicots appearing more sensitive. Tier 2 seedling emergence and vegetative vigor studies with the amicarbazone metabolite MKH 3594 (Des-amino) indicate that the metabolite is less toxic than the parent compound for the four species tested, except for onion. Based on the results of the seedling emergence test, Des-amino appears to be more toxic to onion than the parent.

Toxicity studies demonstrate that amicarbazone is practically non-toxic on an acute basis to freshwater and estuarine/marine fish, slightly toxic to freshwater invertebrates, and slightly toxic to practically non-toxic to estuarine/marine invertebrates. Longer-term exposure of aquatic animals to amicarbazone produces adverse effects on growth parameters in freshwater fish and on growth and reproductive parameters in freshwater and estuarine/marine invertebrates. Data are not available to characterize the effects of longer-term exposure of estuarine/marine fish to amicarbazone. No data are available to characterize the effects of amicarbazone metabolites in aquatic animals.

In the aquatic environment, amicarbazone appears to be particularly toxic to algae, but produces adverse effects on survival and growth in both algae and vascular plants. The results of a single study assessing the toxicity of the amicarbazone metabolite Des-amino in *Selenastrum capricornutum* (a freshwater green algae), indicate that Des-amino is less toxic than the parent compound.

OUTSTANDING DATA

The following details the data gaps and/or additional information required from the registrant:

1. **Submission of an independent laboratory validation and radio-validation data using Method 200258 is needed, so this alternate plant enforcement method can be used.**

- **Method validation data are needed for cattle liver.**
- **A poultry feeding study is needed.**
- **Information pertaining to weather conditions is needed for the corn field trials and on the rotational crop studies.**
- **Analytical reference standards on amicarbazone and metabolites should be sent to the EPA National Pesticide Standards Repository.**

PUBLIC INTEREST FINDING:

According to Arvesta's Public Interest Statement, amicarbazone will compete against atrazine (in all markets), and alachlor, acetochlor and metolachlor where grasses are not the significant weed. The registrant expects that the use of amicarbazone will primarily impact the use of atrazine and will also have some impact on the use of alachlor, acetochlor and metolachlor since these four active ingredients have major market shares and are effective against a comparable weed spectrum.

Amicarbazone is not mutagenic, oncogenic or a reproductive toxicant. Amicarbazone has no known common mechanism of toxicity with other pesticide compounds. Alachlor, acetochlor and butachlor share a common mechanism of toxicity. Metolachlor does not share a common mechanism of toxicity with these two chemicals. Alachlor is classified as a likely human carcinogen at high doses. Acetochlor is classified as a probable human carcinogen, regulated with a q*. Metolachlor is a possible human

carcinogen.

GOVERNMENT PERFORMANCE AND RESULTS ACT (GPRA)

Registering amicarbazone will meet the objectives of GPRA title 3.1.1 by assuring new pesticides that enter the market are safe for humans and the environment and title 4.1.2 by reducing environmental exposure to herbicides.

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