NEW CHEMICAL FACT SHEET

1. DESCRIPTION OF THE CHEMICAL

Generic Name: (N{[[3,5-dichloro-2-fluoro-4-(1,1,2,3,3,3-hexafluoropropoxy) phenyl] amino] carbonyl}-2,6-difluorobenzamide))

Common Name: Noviflumuron
Trade Name: Recruit III
EPA Shaughnessy Code (OPP Chemical Code): 118204
Chemical Abstracts Service (CAS) Number: 121451-02-3
Year of Initial Registration:
Pesticide Type: Insecticide
Chemical Family: Fluorinated Benzophenyl Urea
Producer: Dow AgroSciences

2. USE PATTERNS AND FORMULATIONS

Application Sites:	In ground around structures and interior and exterior surfaces Buildings and crawl spaces, fences, utility poles, decking, landscape decorations, trees or other features that could be damaged by termite foraging and feeding activity.
Type and Methods of Application:	Above and below ground bait stations.
Types of Formulations:	96% a.i. Technical; 50% Manufacturing Concentrate; 0.5% In ground bait and 0.5% Above ground bait stations.
Target Pests:	Termites.

3. SCIENCE FINDINGS

SUMMARY STATEMENT

Technical grade Noviflumuron has very mild or no acute toxic effects. It is classified as Toxicity Category IV in all acute studies. Noviflumuron is a mild ocular and dermal irritant, but does not produce skin sensitization. Developmental NOAELs and LOAELs for both rats and

rabbits occurred at either the same dose levels or were above the NOAELs [≥1000 mg/kg/day-the limit dose] and LOAELs [not determined] for maternal toxicity. Noviflumuron was not shown to be mutagenic in a battery of tests.

The toxicology data base is complete and no additional studies are required.

Based on the use pattern as a termite bait, a soft malleable bait matrix contained in a rigid plastic housing, there is low concern for acute risks to non-endangered and endangered freshwater species. Acute risks to endangered and non-endangered birds are not expected based on the use pattern. General and widespread exposure to non-target insects, terrestrial plants and mammals are expected to be low based on the use pattern. Thus, this registration will have no effect on endangered species.

Noviflumuron for use as a termite bait is classified as a Reduced Risk Pesticide.

CHEMICAL CHARACTERISTICS

Technical Grade

Physical:	Powder
Color:	White
Odor:	None
Melting Point:	156.2°C
Molecular Formula:	$C_{17}H_7Cl_2F_9N_2O_3$
Molecular Weight:	529.15g/mole
Vapor Pressure:	7.19×10^{-10} Pa @ 25°C
Henry's Law Constant:	6.0×10^{-7} Pam^3/mole (20°C)
Log K_{ow}:	4.94 (86,000)
Solubility:	0.194 mg/L
Dissociation Constant:	Molecule does not contain reversibly ionizable Functional groups

HUMAN HEALTH ASSESSMENT

ACUTE TOXICITY

Technical Grade

* Acute Oral - Rat: LD_{50} >5000 mg/kg (Limit Test) in males and females.
  Toxicity Category IV

* Acute Dermal - Rabbit: LD_{50} >5000 mg/kg (Limit Test) in males and females.
  Toxicity Category IV

* Acute Inhalation - Rat: LC_{50} >5.24 mg/L.
  Toxicity Category IV

* Primary Eye Irritation - Rabbit: Mild irritant - irritation subsided in all animals within 24

hours.
Toxicity Category IV

* Primary Skin Irritation - Rabbit: Mild irritant - irritation subsided within 72 hours of removing patch.
Toxicity Category IV

* Dermal Sensitization - Guinea Pig: Not a dermal sensitizer.

Manufacturing Use Concentrate

* Acute Oral - Rat: LD_{50} >5000 mg/kg (Limit Test) in males and females.
Toxicity Category IV

* Acute Dermal - Rat: LD_{50} >5000 mg/kg (Limit Test) in males and females.
Toxicity Category IV

* Acute Inhalation - Rat: LC_{50} > 0.92 mg/L in males and females.
Toxicity Category III

* Primary Eye Irritation - Rabbit: No signs of ocular irritation.
Toxicity Category IV

* Primary Dermal Irritation - Rabbit: No signs of dermal irritation.
Toxicity Category IV

* Dermal Sensitization - Guinea Pig: Not a dermal sensitizer.

MUTAGENICITY

Technical

* Salmonella typhimurium & Escherichia coli/Mammalian Microsome Reverse Mutation Assay
Not mutagenic

* In Vivo Mouse Micronucleus Assay
Not mutagenic

* Forward Gene Mutation Assay in Chinese Hamster Ovary (CHO) Cells
Not mutagenic

* In Vitro Mammalian Chromosome Abberations in Primary Rat Lymphocytes
Not mutagenic

* In Vitro Mammalian Chromosome Aberrations in Primary Rat Lymphocyte Cultures

Not mutagenic

SUBACUTE TOXICITY

Technical Grade

* 4 Week Dietary Study in Rats

In a subchronic toxicity study, Noviflumuron (99.6% a.i.; Lot/Batch no. DECO-615-112) was administered to 5 Fischer-344 rats/sex/dose in the diet at dose levels of 0, 1, 10, 100, 500 or 1000 mg/kg bw/day (0, 1.0 10.4, 101.4, 512.6, 1029.1 mg/kg/day for males and 0, 1.1, 10.9, 105.1, 520.6, 1055.6 mg/kg/day for females) for 4 weeks. There were no compound-related effects on mortality, clinical signs, body weights, body weight gains, gross pathology, hematology, clinical chemistry or urinalysis parameters.

There appeared to be a treatment related effect on food consumption in males in the 1000 mg/kg/day group during the latter part of the study (days 23-28). All males in the 1000 mg/kg/day group consumed less diet than any of the controls (13.1-15.0 g/animal/day), and 2 of 5 males in the 1000 mg/kg/day group consumed less than half that amount (5.1 and 5.5 g/animal/day). Absolute liver weights were significantly increased at 500 and 1000 mg/kg/day in both sexes (males:118 and 128% of controls, respectively; females:124 and 125% of controls, respectively). Relative liver weights were also increased in males at 500 and 1000 mg/kg/day (116 and 125% of controls, respectively), and in females in the 500 and 1000 mg/kg/day groups (118 and 120% of controls, respectively). Microscopic examination of the liver revealed very slight centrilobular hepatocellular hypertrophy in all 5 male and 5 female rats in the 1000 mg/kg/day and in all 5 females in the 500 mg/kg/day group. The changes in liver weight correlate fairly well with the increased incidence of centrilobular hepatocellular hypertrophy in animals in the 500 and 1000 mg/kg/day groups, and are considered to be treatment related. However, the liver changes are considered to be an adaptive response, rather than an adverse response. **The LOAEL is 1029 mg/kg/day based on decreased food consumption in males. The NOAEL is 513 mg/kg/day.**

* 28 Day Dietary Toxicity Study in Mice

In a subchronic toxicity study, Noviflumuron (98.4% a.i.; Lot/Batch no. F0031-148; TSN102332) was administered to 5 CD-1 mice/sex/dose in the diet at dose levels of 0, 10, 100, 500 or 1000 mg/kg/day (0, 10.8, 110, 538, 1060 mg/kg/day for males and 0, 11.2, 113, 504, 1140 mg/kg/day for females) for 28 days. There were no compound-related effects on mortality, clinical signs, body weights, body weight gains, food consumption, ophthalmology, hematology, clinical chemistry or gross pathology.

Absolute liver weights were significantly increased in males and females in the 100 (127and 112% of controls, respectively), 500 (122 and 124% of controls, respectively), and 1000 (130 and 126% of controls, respectively) mg/kg/day. Similarly, relative liver weights were significantly increased in males at 100, 500 and 100 mg/kg/day (120, 122 and 133% of controls,

respectively), and in females at 500 and 1000 mg/kg/day (123 and 118% of controls, respectively). Treatment related liver lesions were observed in males at 500 and 1000 mg/kg/day and females at 1000 mg/kg/day. Microscopic examination revealed hepatocellular hypertrophy with altered tinctorial properties (centrilobular/midzonal to panlobular) in males at 500 and 1000 mg/kg/day and very slight vacuolization (consistent with fatty change) of the periportal hepatocytes in males at 500 and 1000 mg/kg/day and in females at 1000 mg/kg/day. **The LOAEL is 110 mg/kg/day based on increased liver weights in both sexes, progressing to liver toxicity at higher dose levels. The NOAEL for this study is 10.8 mg/kg/day.**

* 90 Day Oral(feeding) Toxicity Study in Dogs

In a 90-day oral (feeding) toxicity study, Noviflumuron (98.4% a.i., batch/lot# F0031-148) was administered to 4 beagle dogs/sex/dose in the diet at dose levels of 0, 0.003, 0.3 or 3% (equivalent to 0, 0.931, 115, or 1040 mg/kg/day for males and 0, 1.06, 113, or 1150 mg/kg/day for females).

There were no treatment-related changes with respect to mortality, clinical signs of toxicity, body weights, body weight gains, food consumption, ophthalmology, clinical chemistry or urinalysis. The erythrocyte count was decreased in males and females in the 0.3 and 3.0% feeding groups at 6- (82-89% of controls) and 13-weeks (82-96% of controls). The erythrocyte count was decreased in males and females in the 3% dietary (recovery) group at 13 weeks (91% of controls). Males in the 0.3 and 3% dietary groups had treatment related decreases in mean hemoglobin concentration (87-91% of controls) and hematocrit (89-94% of controls) at 6 and 13 weeks. Males and females in the 0.3 and 3.0% dietary groups had an increase in MCV (107-110% of controls at 6- and 13 weeks. [Analysis of the changes in red blood cell parameters was conservative, but considered appropriate, based on the absence of long-term studies, or another 90-day study.] Males receiving 3.0% in the diet had a shift from lymphocytes to neutrophils in analysis of the WBC differential count at 6- and 13 weeks. At the end of the 28-day recovery period, the erythrocyte counts, hemoglobin and hematocrit returned to normal levels. The MCV was still elevated at the end of the 28-day recovery period in the 3.0% dietary group. A very slight increase in polychromasia was observed in one female in the 0.3% dietary group, and in three males and one female in the 3.0% dietary group. Very slight bone marrow hyperplasia was observed in 4 males and 4 females in the 0.3% dietary group, and in 1 male and 1 female in the 3.0% dietary group. In addition, slight bone marrow hyperplasia was observed in 3 males and 3 females in the 3.0% dietary group. In the recovery phase group, 3 males and 2 females in the 3.0% dietary group exhibited "very slight" bone marrow hyperplasia, and 1 female exhibited slight bone marrow hyperplasia. The observance of bone marrow hyperplasia in the 2 highest dose groups was indicative of a regenerative response to the decrease in erythrocytic parameters. **The LOAEL is 0.3% Noviflumuron in the diet (corresponding to 115 mg/kg/day in males and 113 mg/kg/day in females), based on changes in red blood cell parameters (hematocrit, hemoglobin, RBC and MCV) and compensatory bone marrow hyperplasia. The NOAEL is 0.003% Noviflumuron in the diet (corresponding to 1 mg/kg/day in males and females).**

* Oral Gavage Developmental Toxicity Study in Rabbits

In a developmental toxicity study, Noviflumuron (98% a.i., lot/reference number: F0031-

68/TSN101708) was administered to 25 time-mated female New Zealand rabbits/dose in by gavage at dose levels of 0, 250, 500 or 1000 mg/kg bw/day from days 7-27 of gestation.

There were no treatment-related maternal effects noted at the highest dose tested of 1000 mg/kg bw/day. **The maternal LOAEL was not determined. The maternal NOAEL is greater than or equal to 1000 mg/kg bw/day (HDT).**

There were no treatment-related developmental effects noted at the highest dose tested of 1000 mg/kg bw/day. **The developmental LOAEL was not determined. The developmental NOAEL is greater than or equal to 1000 mg/kg bw/day (HDT).**

* Oral Gavage Developmental Toxicity Study in Rats

In a developmental toxicity study, Noviflumuron (98% a.i., lot/reference number: F0031-68/TSN101708) was administered to 25 time-mated female CD rats/dose by gavage at dose levels of 0, 250, 500 or 1000 mg/kg bw/day from days 6-20 of gestation.

There were no treatment-related maternal effects noted at the highest dose tested of 1000 mg/kg bw/day. **The maternal LOAEL was not determined. The maternal NOAEL is greater than or equal to 1000 mg/kg bw/day (HDT).**

There were no treatment-related developmental effects noted at the highest dose tested of 1000 mg/kg bw/day. **The developmental LOAEL was not determined. The developmental NOAEL is greater than or equal to 1000 mg/kg bw/day (HDT).**

OCCUPATIONAL AND RESIDENTIAL EXPOSURE

Occupational:

Only a qualitative exposure assessment was performed for the following reasons:

* The end-use product is enclosed in a plastic station except when the PCO adds water for moisture and looks for termites;
* The end-use product contains impregnated material with 0.5% ai;
* The vapor pressure is very low (5.4×10^{-12} mm Hg at 25°C);
* The acute toxicity categories for all routes were low;
* There is little or no anticipated exposure for handlers; and
* This is a reduced exposure method of termite control, preferable to more toxic spray applications.

The target MOEs are 100 for short-/intermediate-term exposure and 1,000 for long-term exposure. No exposure data were available that reflect the use/installation of this specific type of termite control system. However, for characterization purposes, a preliminary and conservative

estimation of exposure was made using data from a proprietary study of dermal and inhalation exposure during production of a termiticide barrier product (i.e., an impregnated polymer film sheet that is placed beneath the foundation of buildings during construction). When the exposure data were adjusted for percent active ingredient and duration of exposure (i.e, the study lasted 2 hours, while it was conservatively assumed that the PCOs install/monitor stations for 8 hrs/day), and compared to the NOAEL of 10.8 mg/kg/day, a total MOE of 8,000 is obtained. Based on these conclusions, the target MOEs are 100 for short-/intermediate-term exposure, and 1,000 for long-term exposure. The conservatively estimated MOE is well above the targets; this confirms the qualitative assessment indicating that this use pattern for Noviflumuron is not of concern.

Residential:

No residential exposure exposure is anticipated. While this product may be used in residential settings, it is only sold to trained pest control operators for installation and monitoring. When installed, the Noviflumuron-impregnated matrix is enclosed within the devices, which prevents post application dermal exposure. Because the vapor pressure is very low (5.4×10^{-12} mm Hg @ 25°C), inhalation post application exposure is also not expected.

ECOLOGICAL EFFECTS CHARACTERISTICS

* Avian Acute Oral: Practically Non-toxic
  Bobwhite quail: LD_{50} = >2000 mg ai/kg-bw

* Avian Dietary: Slightly Toxic
  Bobwhite quail: LC_{50} = 4100mg ai/kg-diet

* Avian Dietary: Practically Non-toxic
  Mallard duck: LC_{50} = > 5300 mg ai/kg-diet

* Freshwater Fish: Moderately Toxic
  Bluegill: 96-hr LC_{50} = 1.63
  Rainbow trout: 96-hr LC_{50} = 1.77

* Freshwater Invertebrates: Very Highly Toxic
  Daphnia Magna: 48-hr EC_{50} = 308 (294,374)

ENVIRONMENTAL FATE

* Hydrolysis:
  Noviflumuron is stable in sterile aqueous buffered solutions at pH 5 and 7.
  Noviflumuron has a calculated half-life of 19 days in a pH 9 solution.

* Aerobic Soil Metabolism:

Noviflumuron degraded with half-lives ranging from 202 to 399 days in three different U.S. soils.

* Batch Equilbrium:

  Noviflumuron was immobile in four U.S. soils. Adsorption K_d values ranged from 1,614-1,994 for the Indiana loam soil, 859-1,437 for the Indiana sand soil, 4,013-7,828 for the North Dakota loam soil, and 3,008-3,755 for the North Dakota clay soil indicating high adsorption potential. Corresponding K_{oc} values ranged from 159,776-197,432 for the Indiana loam soil, 53,673-89,783 for the Indiana sand soil, 211,237-412,004 for the North Dakota loam soil, and 376,061-469,335 for the North Dakota clay soil.

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For more information about EPA's pesticide registration program, please contact the Registration Division (7505C), OPP, US EPA, Washington, DC 20460, telephone 703-305-5446.

For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, from 6:30 a.m. to 4:30 p.m. Pacific Time, or 9:30 a.m. to 7:30 p.m. Eastern Standard Time, seven days a week.