United States Environmental Protection Agency | Prevention, Pesticides And Toxic Substances (7508C) | EPA-738-F99-013 November, 1999

R.E.D. FACTS

Niclosamide

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 standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. To implement provisions of the Food Quality Protection Act of 1996, EPA considers the special sensitivity of infants and children to pesticides, as well as aggregate exposure of the public to pesticide residues from all sources, and the cumulative effects of pesticides and other compounds with common mechanisms of toxicity. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then reregisters pesticides that meet the safety standard of the FQPA and 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. The decisions for Niclosamide and TFM were combined into one publication because the use patterns are very similar and the compounds are often used together. This fact sheet summarizes the information in the RED document for reregistration case 2455, 2-amino ethanol salt of 2',5'-dichloro-4'-nitro salicylanilide (Niclosamide).

Use Profile

Niclosamide is used as (1) a lampricide to control sea lamprey larvae in tributaries to the Great Lakes, the Finger Lakes and Lake Champlain and (2) a molluscicide to control freshwater snails which carry the vectors for diseases which affect fish and humans. Less than 400 pounds of active ingredient niclosamide is used each year in lamprey and freshwater snail treatments. Niclosamide has been used as a human and veterinary drug for treatment of parasites.

Formulations include a 70% wettable powder (WP) and two granular formulations. The WP is applied by metered pump from the back of a boat or by backpack sprayer. The 3.2% granular product is applied with a backpack blower device that spreads the granules over a wide surface area.

Regulatory History

Niclosamide was first registered as a pesticide in the U.S. in 1964 by the U.S. Department of Agriculture (USDA), the Agency's predecessor for pesticide regulation under FIFRA. Currently, five niclosamide products are registered with EPA: a 70% WP for sea lamprey control, two Special Local Needs labels with the 70% WP, one 3.2% granular formulation, and one 5% granular formulation. The registrant has requested voluntary cancellation of the 5% granular product.

Human Health Assessment

Toxicity

Niclosamide has acute oral LD_{50} values of >1000 mg/kg (Toxicity Category III). The acute dermal toxicity is minimal, as indicated by a LD_{50} > 2000 mg/kg (Toxicity Category III). It produced slight skin irritation (Toxicity Category IV) and caused eye irritation (unclassified Toxicity Category based on short time interval of eye examination). It was a moderate skin sensitizer. The acute inhalation data are not available.

Niclosamide showed no evidence of causing developmental toxicity, mutagenicity or carcinogenicity.

Dietary Exposure

People are unlikely to be exposed to residues of niclosamide through the diet due to: the low amount of compound used, the United States Fish and Wildlife Service restrictions against removing irrigation and drinking water from streams during treatment, and the rapid dissipation of residues in fish and water. The Special Local Needs Labels for the use in ornamental fish ponds are also not likely to result in any dietary exposure. Tolerances have not have been established and are not required for niclosamide.

Occupational and Residential Exposure

Occupational and residential risk assessments were not conducted for niclosamide based on the low volume used. Protective measures currently on niclosamide labels were considered adequate for the products being reregistered. All products are Restricted Use Pesticides and all labels require double layers of clothing and respirators. Industrial hygiene and medical monitoring programs are required routinely for all handlers of products containing niclosamide.

Human Risk Assessment

Risk assessments were not conducted for niclosamide based on the extremely low volume and infrequency of use. Niclosamide use is closely regulated by the US Fish and Wildlife Service and by the states which issued Special Local Need labels.

Environmental Assessment

Niclosamide is applied to freshwater tributaries and is therefore expected to have little impact on terrestrial plants and animals. Applications are designed to have minimal effects on fish, but other aquatic animals are expected to be impacted.

Environmental Fate

- In addition to dilution and dispersion, sorption to sediments and suspended particulates and possibly photodegradation (in clear shallow waters), are the major routes of dissipation of niclosamide. Neither hydrolysis nor volatilization from soil or water surfaces should be major fate processes for this compound.
- In most aquatic environments, niclosamide will adsorb to suspended solids and sediment and this binding is reversible.
- It is unclear what role, if any, aerobic and anaerobic microbial degradation plays in the dissipation of niclosamide in the aquatic environment.
- Accumulation in fish is not expected.

Ecological Effects

- Avian acute- **moderately toxic** (LD_{50} 60 mg/kg)
- Avian subacute dietary- practically **nontoxic** (LC_{50} > 5,419 mg/kg diet()
- Mammalian acute- practically **nontoxic** (LD_{50} >1,000 mg/kg)
- Fish (freshwater acute)- highly toxic to **very highly toxic** (LC_{50} 0.03 - 0.23 mg/L)
- Invertebrates acute- slightly to **very highly toxic** (EC_{50} 0.034-50 mg/L)
- Invertebrates chronic- (NOAEC 0.03 mg/L; LOEC 0.05 mg/L)
- Aquatic plants- toxic (0.04 to > 1,450 mg/L)

Environmental Risk Characterization

The effects of niclosamide at the treatment site are likely to be mitigated by photodegradation and the flushing action of the stream/river.

At the predicted treatment levels, acute high risk, acute restricted use, and endangered species levels of concern are exceeded for aquatic animals. Although niclosamide is likely to have an immediate effect on the aquatic community, the data suggest that most organisms recover quickly and the treatment area community structure returns to pre-treatment conditions within weeks or months. This recovery is site specific and may take much longer in certain environments. Certain species

may be significantly impacted, most notably the indigenous lamprey species. In general, however, native lamprey species have tended to populate the upper reaches of tributary streams, whereas the sea lamprey is more likely to inhabit lower reaches of the stream. Thus, nontarget species that may have been affected in the treatment area are repopulated through downstream migration from untreated areas. Furthermore, retreatment of the stream will not occur for at least 3 to 5 years. Additionally, a genuine effort is made to document where sensitive populations reside, and steps are undertaken to avoid treatments at concentrations known to be toxic to these organisms. The long-term effects remain uncertain to more sensitive species, such as indigenous lampreys, and to aquatic communities downstream from the treatment sites where chronic effects may be more likely.

Risk Mitigation

The use practices of niclosamide have been refined over the past several years in order to lower the impacts of these applications on non-target organisms and to lower occupational and non-occupational exposure to people. Niclosamide is a Restricted Use Pesticide and the labels refer users to the US Fish and Wildlife Service's Manual for Pesticide Applications. Additional mitigation required by the Agency includes minor clarifications of label language. Aerial applications were prohibited on some of the current labels and will be prohibited on all new labels in order to lessen chances of nontarget human and other terrestrial animal exposures to these restricted use compounds.

Additional Data Required

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

Photodegradation in Water	Guideline # 835-2240 (161-2)
Aerobic Aquatic Metabolism	Guideline # 835-4300 (162-4)
Anaerobic Aquatic Metabolism	Guideline #835-4400 (162-3)

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 Changes Required

All niclosamide end-use products must comply with EPA's current pesticide product labeling requirements. For a comprehensive list of labeling requirements, please see attached labeling table from the Niclosamide RED document.

Regulatory Conclusion

The use of currently registered products containing niclosamide in accordance with approved labeling for sea lamprey control or in ornamental fish aquaculture will not pose unreasonable risks or adverse effects to humans or the environment. Therefore, uses of several niclosamide products are eligible for reregistration.

The registrant has requested cancellation of the 5% granular product used to kill snails which carry the vector for Swimmer's Itch.

The use of the 70% WP as a molluscicide in Puerto Rico against snails which carry the vector for Schistosomiasis is considered to be ineligible pending additional use information and exposure data.

Niclosamide products will be reregistered for all other uses 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 niclosamide during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. The document is entitled Reregistration Eligibility Decision: 3-Trifluoro-Methyl-4-Nitro-Phenol CASE 3082 and Niclosamide CASE 2455. To obtain a copy of this 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 Service Center for Environmental Publications (EPA/NSCEP), PO Box 42419, Cincinnati, OH 45242-2419, telephone 1-800-490-9198; fax 513-489-8695.

Following the comment period, the niclosamide RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 1-800-553-6847, or 703-605-6000.

For more information about EPA's pesticide reregistration program, the niclosamide RED, or reregistration of individual products containing niclosamide, 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 internet address is ace.orst.edu/info/nptn.

Table 15: Summary of Required Labeling Changes for Niclosamide		
Description	**Required Labeling**	**Placement on Label**
Manufacturing Use Products		
Formulation Instructions required on all MUPs	"Only for formulation into a lampricide for use in tributaries to the Great Lakes,Lake Champlain or the Finger Lakes or into a mollusicide for use against fresh water snails.	Directions for Use
Environmental Hazards Statements Required by the RED and Agency Label Policies	"This chemical is toxic to fish and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your state Water Board or Regional Office of the EPA."	
End Use Products Intended for Occupational Use (Non-WPS)		
Restricted Use Pesticide is Triggered by Active Ingredient	"RESTRICTED USE PESTICIDE due to:" *For Bayluscide 70% WP insert:* "acute inhalation toxicity, aquatic organism toxicity and to the need for highly specialized applicator training." *For Bayluscide 3.2% Granular:* "to acute hazards to the eye, nontarget aquatic organisms, and to the need for highly specialized applicator training."	Top of Front Panel and enclosed in a box.
	"RESTRICTED USE PESTICIDE"	Immediately under the heading Directions for Use.

Table 15: Summary of Required Labeling Changes for Niclosamide		
Description	**Required Labeling**	**Placement on Label**
PPE Requirements Established by the RED Based on the Active Ingredient.[1]	"Personal Protective Equipment (PPE) Some materials that are chemical-resistant to this product are listed below. If you want more options, follow the instructions for category [insert A,B,C,D,E,F,G,or H] on an EPA chemical-resistance category selection chart." "Mixers, loaders, applicators and other handlers must wear: Long sleeved shirt and long pants Rubber boots & socks Chemical resistant gloves such as (registrant inserts correct glove type) Chemical resistant aprons or coveralls Face shield NIOSH approved respirator with: - an organic-vapor removing cartridge with a prefilter approved for pesticides (MSHA/NIOSH approval number prefix TC-23C), or - a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or a NIOSH approved respirator with an (OV) cartridge, or - a canister with any N,R,P or HE prefilter NIOSH approved organic vapor resistant respirator."	Precautionary Statements: Hazards to Humans and Domestic Animals
User Safety Requirements	"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washable exist, use detergent and hot water. Keep and wash PPE separately from other laundry."	Precautionary Statements: Hazards to Humans and Domestic Animals immediately following the PPE requirements

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Description	**Required Labeling**	**Placement on Label**
User Safety Recommendations	"User Safety Recommendations" "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet." "Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing." "Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing."	Precautionary Statements under: Hazards to Humans and Domestic Animals immediately following Engineering Controls (Must be placed in a box.)
Environmental Hazards	"Environmental Hazards" "This chemical is toxic to fish and aquatic invertebrates. Nontarget aquatic organisms may be killed at rates recommended on this label." "Directions for use must be strictly followed to minimize hazards to non-target organisms. Do not contaminate water when cleaning equipment or disposing of equipment washwaters." "Local, State, and Provincial Fish and Game Agencies must be contacted before product is applied. Municipalities that use streams requiring treatment as potable water sources must be notified of the impending treatment at least 24 hours prior to application. Agricultural irrigators that use streams requiring treatment as a source of irrigation water must be notified of the impending treatment at least 24 hours prior to application. Agricultural irrigators must turn off their irrigation systems for a 24-hour period during and after treatment." "May not be used by unauthorized personnel."	Precautionary Statements under Environmental Hazards
Application Restrictions	"Do not apply this product in a way that will contact workers or other persons, either directly or through drift"	Directions for Use

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Description	**Required Labeling**	**Placement on Label**
Other Use/Application Restrictions	"Applicators must follow the instructions provided in the "Manual for Application of Lampricides in the U.S. Fish and Wildlife Service Sea Lamprey (*Petromyzon marinus*) Control Program" for correct rates of application. Prior to and during the application of this chemical, take all appropriate actions to notify public water users including notification actions specified in this manual."	Directions for Use under Application Instructions and/or General Precautions and Restrictions
Other Use/Application Restrictions	"Aerial applications of this product are prohibited."	Directions for Use under Application Instructions and/or General Precautions and Restrictions

[1] PPE that is established on the basis of Acute Toxicity of the end-use product must be compared to the active ingredient PPE in this document. The more protective PPE must be placed in the product labeling. For guidence on which PPE is considered more protective, see PR Notice 93-7.