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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

January 22, 1996

MEMORANDUM

SUBJECT: STRYCHNINE. HED Chapter of the Reregistration Eligibility Decision Document (RED), Case #3133.

FROM: Jane Smith, Chemist
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THRU: Debra Edwards, Ph.D., Branch Chief
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Health Effects Division 7509C
and
Stephanie Irene, Ph.D., Acting Director
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TO: Jay Ellenberger, Branch Chief
Accelerated Reregistration Branch
Special Review and Reregistration Division 7508W

The Human Health Assessment for the Reregistration Eligibility Document for Strychnine is attached. This chapter includes the hazard assessment by John Redden (RCAB), the product chemistry and dietary exposure by Sue Hummel (CBRS), and the occupational and residential exposure by John Leahy (OREB).

Overall, strychnine was found to be extremely toxic. Incident data indicates occupational and residential exposures are likely and there are risks associated with this chemical based on the current use patterns. The risk mitigation recommendations are explained in detail following the occupational and residential risk characterization.

A. Physical and Chemical Properties Assessment

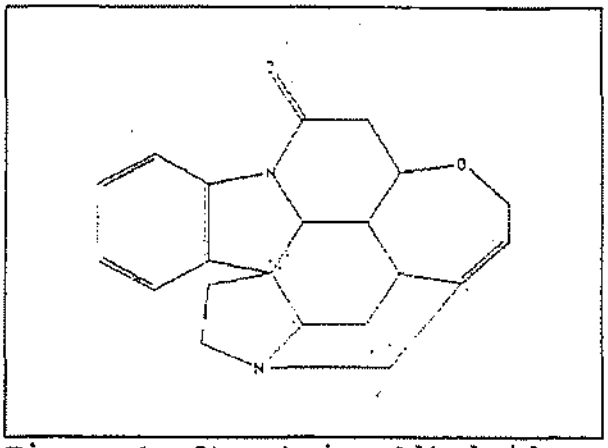

Figure 1 Strychnine Alkaloid

Strychnine is the principal alkaloid present in nux vomica, the seeds of a tree native to India. Strychnine is a white crystalline powder, melting at 270-280° Celsius, and is practically insoluble in cold ethanol and ether; and slightly soluble in chloroform and benzene. Strychnine sulfate is a white powder melting above 199° Celsius. Strychnine sulfate is moderately soluble in alcohol, and insoluble in ether.

B. Human Risk Assessment

1. Hazard Assessment

The toxicological database for strychnine is adequate and will support reregistration eligibility for current nonfood uses. Three studies are required as confirmatory data: (1) 81-3 Acute Inhalation LC50 Toxicity Study in rats; (2) 81-6 Dermal Sensitization Study in Guinea Pigs; and (3) 82-2 21-Day Dermal Toxicity Study in rats.

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a. Acute Toxicity

TABLE I. STRYCHNINE ACUTE TOXICITY

Guideline # Study	Results	Toxicity Category	MRID #s
81-1 Acute Oral LD50, rat	6.4 mg/kg males 2.2 mg/kg females Death occurred within 1 hr.	I	409089-01 412107-01
81-2 Acute Dermal LD50, rabbit	2000 mg/kg. No signs of toxicity observed.	III	409089-02 412107-02
81-3 Acute LC50 inhalation	DATA GAP	I*	
81-4 Primary eye irritation, rabbit	Irritation and mortality	I	409089-04 412107-04
81-5 Primary dermal irritation, rabbit	No irritation, mortality or signs of toxicity were observed.	IV	409089-03 410107-03

All studies performed with Strychnine Alkaloid Technical (Purity = 99.42%)
* Assigned Toxicity Category I until a 81-3 is submitted and reviewed by the Agency.

b. Subchronic Toxicity

A 21-day dermal Toxicity study (82-2) is required on the end-use product(s) because the bait is applied by hand baiting. This study is considered confirmatory.

c. Other Toxicological Considerations

i. Mechanism

Strychnine is a powerful convulsant. The convulsant action of strychnine is

due to interference with postsynaptic inhibition (mediated by glycine). Glycine is an important inhibitory transmitter to motorneurons and interneurons in the spinal cord, and strychnine acts as a selective competitive antagonist to block the inhibitory effects of glycine at all glycine receptors.

ii. Poisoning Incidents

Approximately 100 cases of accidental exposure to strychnine rodenticides are reported annually to U.S. Poison Control Centers. Typically, three of these 100 cases result in symptoms requiring serious medical attention and one of the three results in life-threatening effects or fatality. Incident surveys conducted 10 or more years in California and from the literature indicate pesticide fatalities were higher, given the use then, as compared with the reduced use of strychnine today. Based on ALL (U.S. Poison Control Center, CA, literature) of the incident data available on strychnine, the projection is 0.5 to 2 deaths annually in the United States are likely to occur from strychnine rodenticides.

Incident data for domestic pets indicate that of the 90 plus cases of strychnine rodenticide exposures, 19 percent were fatal (mostly dogs). Considering there is no more than a two fold difference between the weights of dogs and the weights of children, we can assume that children could be exposed to a lethal dose in a single swallow of strychnine as occurred with dogs.

Based on strychnine's high acute toxicity and the number and severity of poisoning incidents, HED recommends that strychnine for home use be discontinued unless formulated and packaged in a manner that would assure no access by young children, i.e. child-proof.

Relatively few occupational incidents of strychnine poisoning have been reported in California where its use is restricted. These restrictions require eye protection and gloves for those who are directly handling powdered or dusty strychnine and that workers be advised to wash off the skin immediately if accidentally exposed.

2. Dose Response Assessment

The HED Less Than Life Time Peer Review Committee, on 11/7/95, determined that due to the lack of identifiable endpoints no risk assessments are required at this time. However, if any food uses arise or the conditions as outlined in the *Dietary Exposure - Regulatory Background Section of this document* are not met, the entire food use database as outlined in Appendix C is required. In addition, an acute inhalation (81-3), a dermal sensitization study (81-6) and a 21-day dermal toxicity study (82-2) are requested for labeling purposes. These studies

are considered confirmatory. It should be noted that in the absence of the 81-3 acute inhalation the toxicity category for inhalation is I. This is consistent with HED's policy requiring 6 acute studies to support regulation of all chemicals.

Based on the severe oral toxicity of this chemical and the nonfood use status a reference dose and carcinogenicity classification has not been determined at this time.

Strychnine has not been reviewed by the Joint FAO/WHO pesticide committee.

3. Dietary Exposure and Risk Characterization

a. Dietary Exposure and Regulatory Background

The above ground uses of strychnine were "temporarily canceled" by EPA in 1988 ([OPP-3000/7E; PH-FRL 2451-2] Federal Register / Vol. 48, No. 203 / Wednesday, October 19, 1983). Above ground uses of strychnine are enjoined from being used by a court order, and cannot be reinstated without active participation from EPA (i.e. EPA has to request that the injunction be vacated and then has to rescind the "temporary cancellation" notices).

In a Chemistry Branch II Memorandum [No MRID No.; CB No. 11862; DPBarcode D190866; Susan V. Hummel; 1/27/94] the following was determined:

"In the Reregistration Phase 4 review, the strychnine registrants were advised that their labeling needed to be changed as follows, or all residue chemistry data provided.

1. Allow underground applications only.
2. Allow applications to agricultural buffer zones (perimeters of a field) only, with appropriate grazing restrictions.
3. Allow orchard uses with appropriate grazing restrictions.
4. Allow applications to bare ground around animal burrow entrances, dens, tunnels, and animal nests.
5. Allow spot baiting applications to ditch banks.
6. Allow applications to non-crop land and in non-agricultural areas where livestock are not present.
7. Allow bait box applications in V shaped above ground troughs.
8. Prohibit any aerial applications where food or feed crops or livestock are present.
9. Prohibit broadcast and above ground spot baiting on pasture or rangeland.
10. Prohibit broadcast applications to food or feed crops.
11. Prohibit broadcast applications to ditch banks.

Subsequent to issuance of the Reregistration Phase 4 DCI (10/6/92), the Strychnine Consortium requested that the Residue chemistry data requirements be waived, stating that the above ground uses of strychnine were "temporarily canceled" by EPA in 1988, are enjoined from being used by a court order, and cannot be reinstated without active participation from EPA (EPA has to request that the injunction be vacated and then has to rescind the "temporary cancellation" notices). The Chemistry Branch II recommended that the data requirements be waived only for the underground use, which is considered to be a non-food use. Appropriate label restrictions or residue data will be required for above ground uses. We stated that the labels must be reviewed by the Chemistry Branches."

The labeling changes, as addressed in the above cited DCI, must be met or the Toxicology Requirements as listed in Appendix C are required. Also if any currently registered use for strychnine is determined to be a food use, the Toxicology Requirements in Appendix C are required.

b. Dietary Risk Characterization

Strychnine is extremely toxic by the oral route. This chemical has no food uses and for this reason, little risk is expected by the dietary route.

4. Occupational and Residential Exposure and Risk Characterization

a. Occupational and Residential Exposure

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain active ingredient toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete; or, if incidence data (acute poisonings) indicate use concerns.

Strychnine is classified as category I for acute oral toxicity, category III for acute dermal toxicity, category I for acute inhalation toxicity, category I for eye irritation potential, and category IV for primary dermal irritation. Based on the Dose Response (discussed previously) no short-term, intermediate-term, or chronic toxicological endpoints are identified for strychnine as appropriate for use to quantify an occupational or residential exposure assessments since dermal irritation studies showed no signs of irritation, toxicity, or mortality. However, due to the acute toxicity and the epidemiological incidence data, there are concerns for both occupational and residential users.

Occupational-use products and homeowner-use products

Strychnine alkaloid is a pesticide for non-food use only. Strychnine products are currently sold under the Strychnine Settlement Agreement (SSA) of 1989. As part of the SSA, all above-ground uses of strychnine are "temporarily canceled." as part of a Notice of Intent to Cancel. Therefore, only below-ground uses are currently being considered. Strychnine is used below-ground in rodent burrows, dens, tunnels and nests. It is formulated as a bait (0.39 to 1.89 percent active ingredient), powder (98.4 to 100 percent active ingredient), soft pellet (0.5 percent active ingredient), and as a paste (1.6 to 10 percent active ingredient).

At this time products containing strychnine are intended for both occupational use and homeowner use (i.e., to control rodents at a work site or residence).

Handler Exposures & Assumptions

Based on the use patterns and potential exposure scenarios described above, three major exposure scenarios were identified for strychnine: (1) mixing and applying bait, (2) mixing and applying paste, and (3) applying powder. EPA has concerns for both occupational and residential handlers of strychnine. This concern is based on the high acute toxicity of strychnine through the oral, inhalation, and ocular routes.

Post-Application Exposures & Assumptions

Strychnine is currently registered for use exclusively below-ground and as a result the potential for post-application dermal, inhalation, or ocular exposure is minimal when used according to label requirements.

Based on the incident data, the toxicity of the compound and the exposure potential, strychnine should be a restricted use compound for most uses. Minimum PPE including chemical-resistant gloves, dust/mist respirator, and protective eye wear for most formulations. See the Risk Mitigation Recommendations section below for details.

b. Occupational and Residential Risk Characterization

The *Minutes of the Less than Life Time Committee Meeting*, dated November 7, 1995, indicates that no short-term, intermediate-term, or chronic toxicological endpoints have been identified for strychnine as appropriate for use in the standard occupational or residential exposure/risk assessments. Dermal irritation studies showed no signs of irritation, toxicity, or mortality. However, for both occupational and residential users, HED has risk concerns. These concerns are

based on (1) the high acute toxicity of strychnine through the oral, inhalation, and ocular routes; (2) the data for domestic pets which suggest a very low margin of exposure for young children, as do calculations of potential dose based on a single swallow; (3) the number and severity of poisoning incidents reflected in epidemiological data; 14) the potential for exposure to both occupational and residential handlers of strychnine products; and (5) the absence of exposure data for all exposure scenarios considered.

HED has particular concerns about potential exposure to homeowners and others in residential settings. Based on the above concerns, HED recommends risk mitigation measures to reduce the potential for occupational and homeowner/residential exposures (see below).

c. Risk Mitigation Recommendations

One risk mitigation option would be to limit access to and use of strychnine end-use products to occupational handlers, as has been done in California. Limiting access to strychnine to professional pest control operators allows the Agency to require personal protective equipment, including respirators, for users. In addition, such users are more likely to have received training about the hazards of pesticides and safe use practices, such as washing thoroughly after use.

The powder formulations particularly (containing up to 100 percent strychnine) should not be sold to or used by homeowners. HED believes that powder formulations should not be stored at residences due to the risk of accidental poisonings, particularly to children and pets. This concern is supported by epidemiological evidence, the extremely low oral LD50, and potential for inhalation of powder and dust formulations.

Also, paste formulations of strychnine should be limited to use by professional pest control operators for similar reasons, and because pastes must be mixed with food to make a bait which increases the potential risk of accidental exposures in and around residential areas. (EPA notes that one paste formulation of strychnine, containing 10% active ingredient, is already classified as a restricted-use pesticide.)

As an exception to this recommendation, the Agency may allow strychnine end-use products formulated as ready-to-use baits or soft pellets (with concentrations of 0.039% to 1.89% active ingredient) to be sold to and used by homeowners, if such end-use products are contained in child-resistant packaging during sale and storage, and must be applied in tamper-resistant bait stations as defined by PR Notice 94-7, including when applied in rodent tunnels, burrows, or other below-ground habitats.

To mitigate potential risk for occupational uses, HED recommends that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers be taken for strychnine when formulated as a powder (unless contained in child-resistent packaging during sale, storage, and use) because of its high acute oral and inhalation toxicity and potential exposure concerns from open pouring such formulations. EPA should require the use of chemical-resistant gloves and a dust/mist respirator for all persons who handle powder formulations of strychnine. Also, because of the high acute toxicity strychnine via the ocular route, HED recommends that protective eyewear be required for occupational handlers.

HED also recommends the establishment of active-ingredient-based minimum PPE requirements for occupational handlers for strychnine when formulated as a paste due to its high acute toxicity when swallowed and through the ocular route. The Agency should require the use of chemical-resistant gloves and protective eyewear for all persons who handle such paste formulations.

HED does not recommend establishing minimum (baseline) handler PPE for strychnine end-use products that are intended primarily for homeowner use, because limiting the formulations available for homeowner use to ready-to-use baits and soft pellets contained in child-resistant packaging should adequately mitigate the concerns about the high acute toxicity.

APPENDIX A

(SECTION IV - REGULATORY POSITION AND LABELING RATIONALE)

Occupational and Residential Labeling Rationale for Recommended Risk Mitigation
[This section addresses labeling requirements for recommended risk mitigation as described in the OREB RED chapter for strychnine.]

The Worker Protection Standard (WPS)

Scope of the WPS

The 1992 Worker Protection Standard for Agricultural Pesticides (WPS) established certain worker-protection requirements (personal protective equipment, restricted-entry intervals, etc.) to be specified on the label of all products that contain uses within the scope of the WPS. Uses within the scope of the WPS include all commercial (non-homeowner) and research uses on farms, forests, nurseries, and greenhouses to produce agricultural plants (including food, feed, and fiber plants, trees, turf grass, flowers, shrubs, ornamentals, and seedlings). Uses within scope include not only uses on plants, but also uses on the soil or planting medium the plants are (or will be) grown in.

At this time all registered uses of strychnine are outside the scope of the Worker Protection Standard for Agricultural Pesticides (WPS) since all uses to control vertebrate pests are outside the scope of the WPS.

Personal Protective Equipment/Engineering Controls for Handlers

For each end-use product, PPE requirements for pesticide handlers are set during reregistration in one of two ways:

1. If EPA determines that no regulatory action must be taken as the result of the acute effects or other adverse effects of an active ingredient, the PPE for pesticide handlers will be based on the acute toxicity of the end-use product. For occupational-use products, PPE must be established using the process described in PR Notice 93-7 or more recent EPA guidelines.

2. If EPA determines that REGULATORY ACTION ON AN ACTIVE INGREDIENT MUST BE TAKEN as the result of very high acute toxicity or to certain other adverse effects, such as allergic effects or delayed effects (cancer, developmental toxicity, reproductive effects, etc.):

- *In the RED for that active ingredient, EPA may establish minimum or "baseline" handler PPE requirements that pertain to all or most end-use products containing that active ingredient.*

- *These minimum PPE requirements must be compared with the PPE that would be designated on the basis of the acute toxicity of the end-use product.*
- *The more stringent choice for each type of PPE (i.e., bodywear, hand protection, footwear, eyewear, etc.) must be placed on the label of the end-use product.*

Personal protective equipment requirements usually are set by specifying one or more pre-established PPE units -- sets of items that are almost always required together. For example, if chemical-resistant gloves are required, then long-sleeve shirts, long pants, socks, and shoes are assumed and are also included in the required minimum attire. If the requirement is for two layers of body protection (coveralls over a long- or short-sleeve shirt and long or short pants), the minimum must also include (for all handlers) chemical-resistant footwear and chemical-resistant headgear for overhead exposures and (for mixers, loaders, and persons cleaning equipment) chemical-resistant aprons.

LANGUAGE FOR THE LABELING RATIONALE SECTION BASED ON PROPOSED RISK MITIGATION OPTIONS:

EPA has determined that certain strychnine end-use products should be limited to use by professional pest control operators and should not be available for sale or use by homeowners.

LANGUAGE BASED ON OREB RECOMMENDATION THAT READY-TO-USE BAIT AND SOFT-PELLET FORMULATIONS AVAILABLE FOR HOMEOWNER USE BE REQUIRED TO BE CONTAINED IN CHILD-RESISTANT PACKAGING -- EVEN AFTER APPLICATION:

EPA is allowing strychnine end-use products formulated as ready-to-use baits or soft pellets to be sold to and used by homeowners. However, such end-use products must be contained in child-resistant packaging during sale, storage, and application. The packaging must be designed to resist exposure to children even after placement in the tunnel, burrow, or other below-ground pest habitat.

<u>Occupational-Use Products</u>

EPA has determined that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers must be taken for strychnine when formulated as a powder (unless contained in child-resistent packaging during sale, storage, and use) because of its high acute oral, ocular, and inhalation toxicity and potential exposure concerns from open pouring such formulations. The Agency is requiring the use of chemical-resistant gloves,

protective eyewear, and a dust/mist respirator for all persons who handle such powder formulations of strychnine.

EPA has determined that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers must be taken for strychnine when formulated as a paste due to its high acute oral and ocular toxicity. The Agency is requiring the use of chemical-resistant gloves and protective eyewear for all persons who handle such paste formulations.

Homeowner-Use Products

EPA is not establishing minimum (baseline) handler PPE for strychnine end-use products that are intended primarily for homeowner use, because the Agency has determined that limiting the formulations available for homeowner use to ready-to-use baits and soft pellets contained in child-resistant packaging will adequately mitigate the concerns about the high acute toxicity.

Post-Application/Entry Restrictions

EPA is not establishing entry restrictions at this time for strychnine end-use products, since strychnine currently is registered for use only below-ground in rodent burrows, dens, tunnels and nests. Post-application exposures are unlikely following applications below-ground.

Other Labeling Requirements

The Agency is also requiring other use and safety information to be placed on the labeling of all end-use products containing strychnine. For the specific labeling statements, refer to Section V of this document.

APPENDIX B

(RED SECTION V - LABELING REQUIREMENTS)

LABELING REQUIREMENTS FOR END-USE PRODUCTS
[The following labeling requirements address the recommended risk mitigation options as described in the OREB RED chapter for strychnine.]

PPE/Engineering Control Requirements for Pesticide Handlers

For sole-active-ingredient end-use products that contain strychnine, the product labeling must be revised to adopt the handler personal protective equipment/engineering control requirements set forth in this section. Any conflicting PPE requirements on the current labeling must be removed.

For multiple-active-ingredient end-use products that contain strychnine, the handler personal protective equipment/engineering control requirements set forth in this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use

Minimum (Baseline) PPE/Engineering Control Requirements

EPA is limiting the use of some end-use products containing strychnine to occupational users (i.e., professional pest control operators). These include (1) all strychnine-containing end-use products formulated as a powder, (2) all strychnine-containing end-use products formulated as a paste, and (3) all strychnine-containing end-use products formulated as a bait or soft pellet, UNLESS these baits or soft pellets are contained in child-resistant packaging during sale, storage, and use. All occupational-use products must bear the following statement in a prominent location on the front panel of the end-use product labeling:

"For sale to and use by professional pest control operators only. Sale to or use by the general public is prohibited."

The minimum (baseline) PPE for strychnine end-use products formulated as a powder is:

"Applicators and other handlers must wear:

--long-sleeved shirt and long pants,
--chemical-resistant gloves*,
--shoes plus socks,
--protective eyewear**, and
--a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)."

* For the glove statement, use the statement established for strychnine through the instructions in Supplement Three of PR Notice 93-7.

** If a full face respirator is worn, eyewear may be waived.

The minimum (baseline) PPE for strychnine end-use products formulated as a paste is:

"Applicators and other handlers must wear:
--long-sleeved shirt and long pants,
--chemical-resistant gloves*,
--shoes plus socks, and
--protective eyewear.

* For the glove statement, use the statement established for strychnine through the instructions in Supplement Three of PR Notice 93-7.

Determining PPE Requirements for End-use Product Labels

The PPE that would be established on the basis of the acute toxicity category of the end-use product must be compared to the active-ingredient-based minimum (baseline) personal protective equipment specified above. The more protective PPE must be placed on the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Placement In Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7, and the format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

Products Intended Primarily for Homeowner Use

Minimum (baseline) PPE Requirements

EPA is not establishing active-ingredient-based minimum (baseline) handler PPE for strychnine end-use products that are intended primarily for homeowner use.

Determining PPE Requirements for End-Use Product Labels

Any necessary PPE for each strychnine end-use product intended primarily for homeowner use will be established on the basis of the end-use product's acute toxicity category.

Placement in Labeling

The personal protective equipment requirements, if any, must be placed on the end-use product labeling immediately following the precautionary statements in the labeling section "Hazards to Humans (and domestic animals)."

Entry Restrictions

For sole-active-ingredient end-use products that contain strychnine the product labeling must be revised to remove any entry restrictions on the current labeling.

For multiple-active-ingredient end-use products that contain strychnine the entry restrictions set forth in this section must be compared to the entry restrictions on the current labeling and the more protective must be retained. A specific time period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

Entry restrictions:

There are no entry restrictions for nonWPS uses.

Other Labeling Requirements

Products Intended Primarily for Occupational Use

The Agency is requiring the following labeling statements to be located on all end-use products containing strychnine that are intended primarily for occupational use.

Application Restrictions

"Do not apply this product in a way that will contact workers, other persons, pets, or domestic animals.

User Safety Requirements

"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry."

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing 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."

Products Intended Primarily for Home Use

Application Restrictions

"Do not apply this product in a way that will contact any person or pet. Keep people and pets out of the area during application."

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."

- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

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APPENDIX C

If any currently registered use for strychnine is determined to be a food use or product labels are not revised as required in the Phase IV DCI (10/6/92) the following studies are required:

TECHNICAL GRADE ALKALOID AND/OR SULFATE	GUIDELINE REF.
○ 90-Day Subchronic Feeding (2 species) Rodent (rat) Non-rodent (dog) [These studies may not be necessary if dose levels for the chronic bioassays can be properly selected without them.]	82-1
○ Chronic Feeding (2 species) Rodent (rat) Non-rodent (dog)	83-1
○ Oncogenicity (2 species) Rat Mouse (The rat oncogenicity study can be combined with the rat chronic feeding study to satisfy both requirements.]	83-2
○ Teratogenicity (2 species)	83-3
○ Reproduction (2-generation)	83-4
○ Mutagenicity Gene Mutation Chromosomal Aberration Other	84-2
○ General Metabolism (rat)	85-1
○ Domestic Animal Safety	85-2
○ Handler and Postapplication Studies Additional exposure studies are not required at this time.	
○ Residue chemistry Studies	171-4

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January 27, 1994

MEMORANDUM

SUBJECT: Strychnine (076901-037995) 90 day Response to Phase 4 DCI
Product and Residue Chemistry
[No MRID No.; CB No. 11862; DPBarcode D190866]

FROM: Susan V. Hummel, Chemist
Special Review Section II
Chemistry Branch II-Reregistration Support
Health Effects Division (7509C)

THRU: Francis B. Suhre, Section Head
Special Review Section II
Chemistry Branch II-Reregistration Support
Health Effects Division (7509C)

TO: Frank Rubis/Barbara Briscoe, PM#51
Accelerated Reregistration Branch
Special Review and Reregistration Division (7508W)

The Strychnine Consortium (H. Interdonati, Noris Chemical Corporation, and ORCO) has submitted a response to the Product Chemistry and Residue Chemistry Reregistration Data requirements, as outlined in the Phase 4 DCI for Strychnine dated 10/6/92. No new product or residue chemistry data were submitted.

Strychnine is on List C. The structure of strychnine alkaloid is shown in Figure 1 below. The Phase 4 Review for Residue Chemistry data pertaining to strychnine was completed 9/2/92 (B. Cropp-Kohlligian). Product Chemistry data for strychnine have apparently been reviewed by PCRS/RSB/RD. This review will include only residue chemistry issues. All product chemistry issues should continue to be addressed by PCRS/RSB/RD.

No tolerances for residues of strychnine alkaloid have been established.

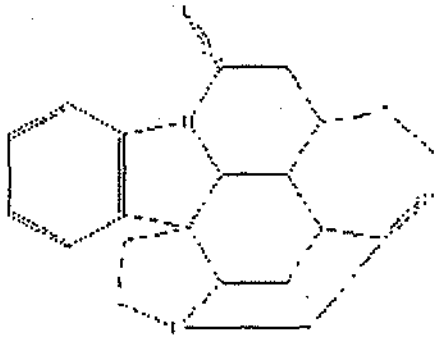

Figure 1 Strychnine Alkaloid

Background

In the Phase 4 review, the strychnine registrants were advised that their labeling needed to be changed as follows, or all residue chemistry data provided.

1. Allow underground applications only.
2. Allow applications to agricultural buffer zones (perimeters of a field) only, with appropriate grazing restrictions.
3. Allow orchard uses with appropriate grazing restrictions.
4. Allow applications to bare ground around animal burrow entrances, dens, tunnels, and animal nests.
5. Allow spot baiting applications to ditch banks.
6. Allow applications to non-crop land and in non-agricultural areas where livestock are not present.
7. Allow bait box applications in V shaped above ground troughs.
8. Prohibit any aerial applications where food or feed crops or livestock are present.
9. Prohibit broadcast and above ground spot baiting on pasture or rangeland.
10. Prohibit broadcast applications to food or feed crops.
11. Prohibit broadcast applications to ditch banks.

Guidelines 171-4(f) Magnitude of the Residue - Potable water, 171-4(g) Magnitude of the Residue - Fish, 171-4(h) Magnitude of the Residue - irrigated crop, 171-4(i) Magnitude of the Residue - Food Handling were all determined to be not applicable, based on current use directions for strychnine. The need for the above label restrictions or supporting Residue Chemistry data were also addressed in a previous Residue Chemistry Review (S. Hummel, 11/6/87).

The Phase 4 review did not specifically address 171-2 (Chemical Identity) and 171-3 (Directions for Use).

Subsequent to the Phase 4 review, the Strychnine Consortium requested that the Residue chemistry data requirements be waived, stating that the above ground uses of strychnine were "temporarily canceled" by EPA in 1988, are enjoined from being used by a court order, and cannot be reinstated without active participation from EPA (EPA has to request that the injunction be vacated and then has to rescind the "temporary cancellation" notices). The Chemistry Branch II recommended that the data requirements be waived only for the underground use, which is considered to be a non-food use. Appropriate label restrictions or residue data will be required for above ground uses. We stated that the labels must be reviewed by the Chemistry Branches.

This Submission

The Registrant response will be provided, followed by our comments

171-2 Chemical Identity: MRIDs 40894201 and 40937001 were referenced.

Comment: This Guideline requirement will be satisfied when all of the Product Chemistry data requirements are satisfied. Review will be completed by PCRS/RSB/RD.

171-3 Directions for Use: MRIDs 40894201 and 41900501 were referenced. Under later Residue Chemistry requirements, the Strychnine Consortium states that they will provide all product labels within 60 days (of 1/15/93) that will allow for:

1. Underground application only
2. application to field perimeters or orchards with appropriate grazing restrictions
3. application to bare ground around animal entrances, etc.
4. spot baiting to ditch banks
5. application to non-crop or non-agricultural land where livestock are prohibited.
6. allow application in bait boxes or V shaped troughs.

Product Labels will prohibit:

1. aerial application to food or feed crops or where livestock are present.
2. broadcast or spot baiting on pasture or rangeland where livestock are present
3. prohibit broadcast applications to food or feed crops and ditch banks.

Comment: This guideline requirement pertains to the registered labels for strychnine. MRIDs are not assigned to labels. Revised labels must be submitted and reviewed by the Chemistry Branches. The registrants should note that to waive residue chemistry data requirements, broadcast or spot baiting on pasture or rangeland are prohibited, regardless of whether livestock are present or not.

171-4 a - Nature of the Residue - Plants,
171-4 b - Nature of the Residue - Animals,

171-4 c - Residue Analytical Method - Plants.
171-4 d - Residue Analytical Method - Animals.
171-4 e - Storage Stability.
171-4 j - Magnitude of the Residue - Meat, Milk, Poultry, and Eggs.
171-4 k - Magnitude of the Residue - Crop Field Trials.
171-4 l - Magnitude of the Residue - Processed Food and Feed

The Strychnine Consortium requests that these data requirements be waived because they will provide label changes as outlined above under 171-3.

Comment: Revised labels must be submitted and reviewed by the Chemistry Branches. The registrants should note that to waive residue chemistry data requirements, broadcast or spot baiting on pasture or rangeland are prohibited, regardless of whether livestock are present or not. For more detail, refer to our review of 11/6/87 (S. Hummel) and the Residue Chemistry Guidelines.

RECOMMENDATIONS

No residue chemistry data are required for underground uses of strychnine. The registrants may choose to submit revised labeling allowing only underground uses of strychnine. If any above ground uses are desired, the registrant should be advised to submit the required label changes or data as outlined in this review and our previous reviews. The registrants should note that to waive residue chemistry data requirements, broadcast or spot baiting on pasture or rangeland are prohibited, regardless of whether livestock are present or not.

cc: S. Hummel, Strychnine List C F.; R.F., circu, S.F.
RDI:FBS:01/27/94:MSM:01/27/94:EZ:01/27/94
H7509C:CBII:SVH:svh:RM:804:CM#2:01/27/94
STRY194

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

DEC - 4 1995

MEMORANDUM

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: The Toxicology Chapter of the Reregistration Eligibility Decision Document (RED) for Strychnine

Case: 3133
DP Barcode: N/A
Submission No.: N/A
PC Code: 076901
Caswell No.: 805

From: John C. Redden, M.S.
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

To: Arliene M. Aikens
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

Thru: James Rowe, Ph.D.
Toxicology Branch II, Section III
Health Effects Division (7509C)

and

Stephanie R. Irene, Ph.D., Acting-Chief
Toxicology Branch II
Health Effects Division (7509C)

Attached please find the Toxicology Chapter for the Reregistration Eligibility Decision document on strychnine. This chapter is be incorporated into the HED RED document for reregistration of strychnine for non-food uses.

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Human Health Assessment: Strychnine Case 3133

1. TOXICOLOGY ASSESSMENT

The toxicological database for strychnine is adequate and will support reregistration eligibility for current nonfood uses. Three studies are required as confirmatory data: (1) 81-3 Acute Inhalation LC50 Toxicity Study in rats; (2) 81-6 Dermal Sensitization Study in Guinea Pigs; and (3) 82-2 21 Day Dermal Toxicity Study in rats.

A. Physical/Chemical Properties

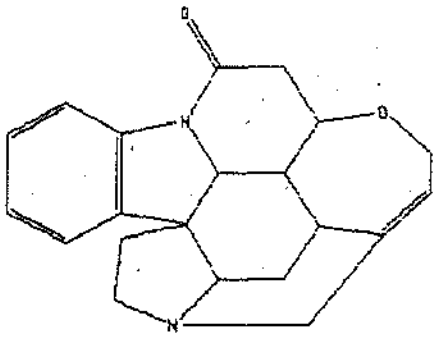

Figure 1 Strychnine Alkaloid

Strychnine is the principal alkaloid present in nux vomica, the seeds of a tree native to India. Strychnine is a white crystalline powder, melting at 270-280° Celsius, and is practically insoluble in cold ethanol and ether; slightly soluble in chloroform and benzene. Strychnine sulfate is a white powder melting above 199° Celsius. Strychnine sulfate is moderately soluble in alcohol, and insoluble in ether.

Strychnine is a powerful convulsant. The convulsant action of strychnine is due to interference with postsynaptic inhibition (mediated by glycine). Glycine is an important inhibitory transmitter to motorneurons and interneurons in the spinal cord, and strychnine acts as a selective competitive antagonist to block the inhibitory effects of glycine at all glycine receptors.

B. Regulatory Background

The above ground uses of strychnine were "temporarily canceled" by EPA in 1988 ([OPP-3000/7E; PH-FRL 2451-2] Federal

Register / Vol. 48, No. 203 / Wednesday, October 19, 1983). Above ground uses of strychnine are enjoined from being used by a court order, and cannot be reinstated without active participation from EPA (i.e. EPA has to request that the injunction be vacated and then has to rescind the "temporary cancellation" notices).

In a Chemistry Branch II Memorandum [No MRID No.; CB No. 11862; DPBarcode D190866; Susan V. Hummel; 1/27/94] the following was determined:

"In the Phase 4 review, the strychnine registrants were advised that their labeling needed to be changed as follows, or all residue chemistry data provided.

1. Allow underground applications only.
2. Allow applications to agricultural buffer zones (perimeters of a field) only, with appropriate grazing restrictions.
3. Allow orchard uses with appropriate grazing restrictions.
4. Allow applications to bare ground around animal burrow entrances, dens, tunnels, and animal nests.
5. Allow spot baiting applications to ditch banks.
6. Allow applications to non-crop land and in non-agricultural areas where livestock are not present.
7. Allow bait box applications in V shaped above ground troughs.
8. Prohibit any aerial applications where food or feed crops or livestock are present.
9. Prohibit broadcast and above ground spot baiting on pasture or rangeland.
10. Prohibit broadcast applications to food or feed crops.
11. Prohibit broadcast applications to ditch banks.

Subsequent to issuance of the Phase 4 DCI (10/6/92), the Strychnine Consortium requested that the Residue chemistry data requirements be waived, stating that the above ground uses of strychnine were "temporarily canceled" by EPA in 1988, are enjoined from being used by a court order, and cannot be reinstated without active participation from EPA (EPA has to request that the injunction be vacated and then has to rescind the "temporary cancellation" notices). The Chemistry Branch II recommended that the data requirements be waived only for the underground use, which is considered to be a non-food use. Appropriate label restrictions or residue data will be required for above ground uses. We stated that the labels must be reviewed by the Chemistry Branches."

The labeling changes, as addressed in the above cited DCI, must be met or the Toxicology Requirements as listed in Appendix I are required. Also if any currently registered use for strychnine is determined to be a food use, the Toxicology Requirements in Appendix I are required.

C. Acute Toxicity

81-1 Acute Oral LD50 Species: rat MB Res Lab for WY Dept Agric 88-9165A; 9/20/88	MRID 409089-01 & 412107-01; LD50 (M) = 6.4 (5.8-7.1) mg/kg, LD50 (F) = 2.2 (1.9-2.5) mg/kg. Death occurred within 1 hr. Signs of toxicity: piloerection, tremors, tachypnea, lethargy, dyspnea, and prostration wers observed within 1 hour.	Tox Cat 1 Supplementary 007035 Minimum 007615
81-2 Acute Dermal LD50 Species: rabbit MB Res Lab for WY Dept Agric 88-9165B; 10/21/88	MRID 409089-02 & 412107-02; LD50 2.0 g/kg. No signs of toxicity observed.	Tox Cat 3 Supplementary 007035 Guideline 007615
81-3 Acute LC50 inhalation	DATA GAP	Tox Cat 1*
81-4 Primary eye irritation Species: rabbit MB Res Lab for WY Dept Agric 88-9165D; 7/22/88	MRID 409089-04 & 412107-04; Mortality of 4/6 animals with slight irritation in 2 survivors clearing in one by 48 hrs and present at 72 hrs in the other survivor. (The average weight of ten, 0.1 mL equivalent doses, using the applicator, was determined to be 52 mg.)	Tox Cat 3 Supplementary 007035 Guideline 007615
81-5 Primary dermal irritation Species: rabbit MB Res Lab for WY Dept Agric 88-9165C; 9/2/88	MRID 409089-03 & 410107-03; No irritation, mortality or signs of toxicity were observed.	Tox Cat 4 Supplementary 007035 Guideline 007615

All studies performed with Strychnine Alkaloid Technical (Purity = 99.42%)
* Assigned Toxicity Category I until a 81-3 is submitted and reviewed by the Agency.

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The Less Than Life Time Peer Review Committee, on 11/7/95, requested an acute inhalation (81-3) and a dermal sensitization study (81-6) for labeling purposes. These studies are considered confirmatory. However, in the absence of the 81-3 acute inhalation the toxicity category for inhalation is I. This is consistent with HED's policy requiring 6 acute studies to support regulation of all chemicals.

D. Subchronic Toxicity

A 21 day dermal Toxicity study (82-2) is required on the use formulation because the bait is applied by hand baiting. This study is considered confirmatory.

E. Other Toxicological Considerations

1. Less Than Lifetime Peer Review

The Less Than Life Time Peer Review Committee, on 11/7/95, determined that due to the lack of identifiable endpoints no risk assessments are required at this time. However, if any food uses arise or the conditions as outline in Regulatory Background are not met the full database as outlined in Appendix I is required.

2. Incident Data

A search of the Reference Files revealed four incident packages:

(1) Package No.: I000783; Compilation of 127 domestic animal incidents: dogs, cats, horses, geese, and turkeys. certainty: unknown;

(2) Package No.: I000804; 36 environmental incidents in South Dakota: birds, fish, bees and dogs: some misuse. certainty: unknown;

(3) Package No.:I001566; a) death of 2 year old child, 6 people in hospital: phostoxin improperly stored, misused, b) misuse of strychnine vs. birds: 285 dead birds. Certainty: unknown; and

(4) Package No.: I002733; 49 brief listings of wildlife death incidents 1984-August 1995 in Wisconsin. Mostly birds, also beaver, deer, squirrel. Some not due to pesticides. Certainty: unknown.

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References
MRID:

40908901 Cerven, D. (1988) Strychnine Alkaloid Technical: Oral Toxicity in Albino Rats: Proj. ID MB 88-9165 A. Unpublished study prepared by MB Research Laboratories, Inc. 22 p.

40908902 Cerven, D. (1988) Strychnine Alkaloid Technical: Acute Dermal Toxicity in Albino Rabbits: Proj. ID MB 88-9165 B. Unpublished study prepared by MB Research Laboratories, Inc. 12 p.

40908903 Cerven, D. (1988) Strychnine Alkaloid Technical: Primary Dermal Irritation in Albino Rabbits: Proj. ID MB 88-9165 C. Unpublished study prepared by MB Research Laboratories, Inc. 8 p.

40908904 Cerven, D. (1988) Strychnine Alkaloid Technical: Eye Irritation in Albino Rabbits: Proj. ID MB 88-9165 D. Unpublished study prepared by MB Research Laboratories, Inc. 9 p.

41210701 Cerven, D. (1988) Strychnine Alkaloid Technical: Single Dose Oral Toxicity in Rats/LD 50 in Rats: Revised Final Report: Laboratory Project ID MB 88-9165 A. Unpublished study prepared by MB Research Laboratories, Inc. 24 p.

41210702 Cerven, D. (1988) Strychnine Alkaloid Technical: Acute Dermal Toxicity in Rabbits/LD 50 in Rabbits: Revised Final Report: Laboratory Project ID MB 88-9165 B. Unpublished study prepared by MB Research Laboratories, Inc. 14 p.

41210703 Cerven, D. (1988) Strychnine Alkaloid Technical: Primary Dermal Irritation in Albino Rabbits: Laboratory Project ID MB 88-9165 C. Unpublished study prepared by MB Research Laboratories, Inc. 10 p.

41210704 Cerven, D. (1988) Strychnine Alkaloid Technical: Primary Eye Irritation/Corrosion in Rabbits: Laboratory Project ID MB 88-9165 D. Unpublished study prepared by MB Research Laboratories, Inc. 13 p.

Non-MRID:

Strychnine (076901-037995) 90 day Response to Phase 4 DCI Product and Residue Chemistry [No MRID No.; CB No. 11862; DPBarcode D190866]; Susan V. Hummel; 1/27/94

Cassarett and Doull's TOXICOLOGY The Basic Science of Poisons 4th Edition

Goodman and Gilman's The Pharmacological Basis of Therapeutics 8th Edition; A.G. Gilman et al. © 1990 Pergamon Press Inc.

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APPENDIX I

If any currently registered use for strychnine is determined to be a food use or product labels are not revised as reguired in the Phase IV DCI (10/6/92) the following studies are required:

TECHNICAL GRADE ALKALOID AND/OR SULFATE	GUIDELINE REF.
○ 90-Day Subchronic Feeding (2 species) Rodent (rat) Non-rodent (dog) [These studies may not be necessary if dose levels for the chronic bioassays can be properly selected without them.]	82-1
○ Chronic Feeding (2 species) Rodent (rat) Non-rodent (dog)	83-1
○ Oncogenicity (2 species) Rat Mouse [The rat oncogenicity study can be combined with the rat chronic feeding study to satisfy both requirements.]	83-2
○ Teratogenicity (2 species)	83-3
○ Reproduction (2-generation)	83-4
○ Mutagenicity Gene Mutation Chromosomal Aberration Other	84-2
○ General Metabolism (rat)	85-1
○ Domestic Animal Safety	85-2

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

JAN 5 1996

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: OCCUPATIONAL AND RESIDENTIAL EXPOSURE ASSESSMENT AND RECOMMENDATIONS FOR THE REREGISTRATION ELIGIBILITY DECISION DOCUMENT FOR STRYCHNINE

TO: Debra Edwards, Chief
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

FROM: Tom Campbell

THRU: Alan P. Nielsen, Section Head
Reregistration Section II

Larry C. Dorsey, Chief
Occupational and Residential Exposure Branch
Health Effects Division (7509C)

Please find the OREB review of Strychnine.

DP Barcode:

Pesticide Chemical Codes: 076901

EPA Reg. Nos.: 299-213, 299-212, 322-6, 322-7, 641-1, 641-2, 52131-2, 9691-21, 4271-17, 5042-32, 8007-1, 9691-28, 9691-4, 9691-30, 9691-24, 10031-1, 10031-5, 10140-4, 10140-5, 10140-7, 10140-8, 27995-1, 35380-1, 35380-3, 36029-7, 56228-8, 56228-11, 56228-16, 56228-19, 56228-20, 07690-1, 07650-1, 07690-1, 07650-1, 37259-1, 10031-4, 10031-2, 959-2, 814-4, 4271-10, 322-7, 322-1, 322-6

EPA MRID Nos.: 407993-01, 408942-01, 409370-02, 414882-02, 414992-01, 419005-01, 407993-01

LUIS Report Date: 2/21/92

PHED: No

OCCUPATIONAL AND RESIDENTIAL EXPOSURE CHAPTER

In this document, which is for use in EPA's development of the strychnine Reregistration Eligibility Decision Document (RED), EPA presents the results of its review of the potential human health effects of occupational and residential exposure to strychnine.

(RED SECTION III - TOXICITY, EXPOSURE, AND RISK)

(EXPOSURE)

Occupational and Residential

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain active ingredient toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete; or, if incidence data (acute poisonings) indicate use concerns. For strychnine, there are incidence data that warrant a review of the use patterns.

Occupational-use products and homeowner-use products

Strychnine alkaloid is a pesticide for non-food use only.[1] Strychnine products are currently sold under the Strychnine Settlement Agreement (SSA) of 1989. As part of the SSA, all above-ground uses of strychnine are "temporarily canceled." as part of a Notice of Intent to Cancel.[2] Therefore, for this review, only below-ground uses are currently being considered. Strychnine is used below-ground in rodent burrows, dens, tunnels and nests. It is formulated as a bait (0.39 to 1.89 percent active ingredient), powder (98.4 to 100 percent active ingredient), soft pellet (0.5 percent active ingredient), and as a paste (1.6 to 10 percent active ingredient).[3]

At this time products containing strychnine are intended for both occupational use and homeowner use (i.e., to control rodents at a work site or residence).

Acute Toxicity

The toxicological data base for strychnine is adequate and will support reregistration. Guideline studies for acute toxicity indicate that strychnine (strychnine alkaloid technical 99.42 percent active ingredient) is classified as category I for acute oral toxicity, category III for acute dermal toxicity, category I for acute inhalation toxicity (according to LTL meeting decision--November 7, 1995), category I for eye irritation potential, and category IV for primary dermal irritation.[3]

Other Endpoints of Concern

The *Minutes of the Less than Life Time Committee Meeting*, dated November 7, 1995, indicates that no short-term, intermediate-term, or chronic toxicological endpoints are identified for strychnine as appropriate for use to quantify an occupational or residential exposure assessments.[3] Dermal irritation studies showed no signs of irritation, toxicity, or

mortality. However, for both occupational and residential users, there are concerns about the high acute toxicity of strychnine through the oral, inhalation, and ocular routes. Epidemiological incidence data are being evaluated to determine if strychnine is being used safely.

Poisoning Incidents

Approximately 100 cases of accidental exposure to strychnine rodenticides are reported annually to U.S. Poison Control Centers. Typically, three of these 100 cases result in symptoms requiring serious medical attention and one of the three results in life-threatening effects or fatality. Based on the earlier surveys of pesticide fatalities and reduced use in strychnine over time, it appears likely that strychnine rodenticides may be responsible for 0.5 to 2 deaths annually in the United States. The data for domestic pets suggest a very low margin of exposure for young children, as do calculations of potential dose based on a single swallow. Based on strychnine's high acute toxicity and the number and severity of poisoning incidents, HED does not recommend that strychnine for home use be continued (unless formulated and packaged to minimize potential exposure).

Relatively few incidents of strychnine poisoning have been reported in California where its use is restricted. However, these incidents indicate a requirement for eye protection and gloves among those who are directly handling powdered or dusty strychnine and that workers be advised to wash off the skin immediately if accidentally exposed.

Handler Exposures & Assumptions

Based on the use patterns and potential exposure scenarios described above, three major exposure scenarios were identified for strychnine: (1) mixing and applying bait, (2) mixing and applying paste, and (3) applying powder. EPA has concerns for both occupational and residential handlers of strychnine. This concern is based on the high acute toxicity of strychnine through the oral, inhalation, and ocular routes.

Post-Application Exposures & Assumptions

Strychnine is currently registered for use exclusively below-ground and as a result the potential for post-application dermal, inhalation, or ocular exposure is minimal when used according to label requirements.

(RISK)

The *Minutes of the Less than Life Time Committee Meeting*, dated November 7, 1995, indicates that no short-term, intermediate-term, or chronic toxicological endpoints have been identified for strychnine as appropriate for use in the standard occupational or residential exposure/risk assessments.[3] Dermal irritation studies showed no signs of irritation, toxicity, or mortality. However, for both occupational and residential users, HED has risk concerns. These concerns are based on (1) the high acute toxicity of strychnine through the oral, inhalation, and ocular routes; (2) the data for domestic pets which suggest a very low margin of exposure for young children, as do calculations of potential dose based on a single swallow; (3) epidemiological data which suggest that relatively small oral doses can be fatal

to small children; (4) the number and severity of poisoning incidents reflected in epidemiological data; (5) the potential for exposure to both occupational and residential handlers of strychnine products; and (6) the absence of exposure date for all exposure scenarios considered.

HED has particular concerns about potential exposure to homeowners and others in residential settings. **Based on the above concerns, HED recommends risk mitigation measures to reduce the potential for occupational and homeowner/residential exposures.**

One risk mitigation option would be to limit access to and use of strychnine end-use products to occupational handlers, as has been done in California. Limiting access to strychnine to professional pest control operators allows the Agency to require personal protective equipment, including respirators, for users. In addition, such users are more likely to have received training about the hazards of pesticides and safe use practices, such as washing thoroughly after use.

The powder formulations particularly (containing up to 100 percent strychnine) should not be sold to or used by homeowners. HED believes that powder formulations should not be stored at residences due to the risk of accidental poisonings, particularly to children and pets. This concern is supported by epidemiological evidence, the extremely low oral LD50, and potential for inhalation of powder and dust formulations.

~~Also,~~ Paste formulations of strychnine should be limited to use by professional pest control operators for similar reasons, and because pastes must be mixed with food to make a bait which increases the potential risk of accidental exposures in and around residential areas. (EPA notes that one paste formulation of strychnine, containing 10% active ingredient, is already classified as a restricted-use pesticide.)

As an exception to this recommendation, the Agency may allow strychnine end-use products formulated as ready-to-use baits or soft pellets (with concentrations of 0.039% to 1.89% active ingredient) to be sold to and used by homeowners, if such end-use products are contained in child-resistant packaging during sale and storage, and must be applied in tamper-resistant bait stations as defined by PR Notice 94-7, including when applied in rodent tunnels, burrows, or other below-ground habitats.

To mitigate potential risk for occupational uses, HED recommends that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers be taken for strychnine when formulated as a powder (unless contained in child-resistent packaging during sale, storage, and use) because of its high acute oral and inhalation toxicity and potential exposure concerns from open pouring such formulations. EPA should require the use of chemical-resistant gloves and a dust/mist respirator for all persons who handle powder formulations of strychnine. Also, because of strychnine's high acute toxicity through the ocular route, HED recommends that protective eyewear be required for occupational handlers. ~ all formulations

HED also recommends the establishment of active-ingredient-based minimum PPE requirements for occupational handlers for strychnine when formulated as a paste due to its high acute toxicity when swallowed and through the ocular route. The Agency should require

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the use of chemical-resistant gloves and protective eyewear for all persons who handle such paste formulations.

HED does not recommend establishing minimum (baseline) handler PPE for strychnine end-use products that are intended primarily for homeowner use, because limiting the formulations available for homeowner use to ready-to-use baits and soft pellets contained in child-resistant packaging should adequately mitigate the concerns about the high acute toxicity.

Additional Occupational/Residential Exposure Studies

Handler Studies:

Additional exposure studies are not required at this time.

Postapplication Studies:

Additional exposure studies are not required at this time.

APPENDIX A

(SECTION IV - REGULATORY POSITION AND LABELING RATIONALE)

Occupational and Residential Labeling Rationale for Recommended Risk Mitigation
[This section addresses labeling requirements for recommended risk mitigation as described in the OREB RED chapter for strychnine.]

The Worker Protection Standard (WPS)

Scope of the WPS

The 1992 Worker Protection Standard for Agricultural Pesticides (WPS) established certain worker-protection requirements (personal protective equipment, restricted-entry intervals, etc.) to be specified on the label of all products that contain uses within the scope of the WPS. Uses within the scope of the WPS include all commercial (non-homeowner) and research uses on farms, forests, nurseries, and greenhouses to produce agricultural plants (including food, feed, and fiber plants, trees, turf grass, flowers, shrubs, ornamentals, and seedlings). Uses within scope include not only uses on plants, but also uses on the soil or planting medium the plants are (or will be) grown in.

At this time all registered uses of strychnine are outside the scope of the Worker Protection Standard for Agricultural Pesticides (WPS) since all uses to control vertebrate pests are outside the scope of the WPS.

Personal Protective Equipment/Engineering Controls for Handlers

For each end-use product, PPE requirements for pesticide handlers are set during reregistration in one of two ways:

1. If EPA determines that no regulatory action must be taken as the result of the acute effects or other adverse effects of an active ingredient, the PPE for pesticide handlers will be based on the acute toxicity of the end-use product. For occupational-use products, PPE must be established using the process described in PR Notice 93-7 or more recent EPA guidelines.

2. If EPA determines that REGULATORY ACTION ON AN ACTIVE INGREDIENT MUST BE TAKEN as the result of very high acute toxicity or to certain other adverse effects, such as allergic effects or delayed effects (cancer, developmental toxicity, reproductive effects, etc.):

- *In the RED for that active ingredient, EPA may establish minimum or "baseline" handler PPE requirements that pertain to all or most end-use products containing that active ingredient.*
- *These minimum PPE requirements must be compared with the PPE that would be designated on the basis of the acute toxicity of the end-use product.*
- *The more stringent choice for each type of PPE (i.e., bodywear, hand protection, footwear, eyewear, etc.) must be placed on the label of the end-use product.*

Personal protective equipment requirements usually are set by specifying one or more pre-established PPE units -- sets of items that are almost always required together. For

example, if chemical-resistant gloves are required, then long-sleeve shirts, long pants, socks, and shoes are assumed and are also included in the required minimum attire. If the requirement is for two layers of body protection (coveralls over a long- or short-sleeve shirt and long or short pants), the minimum must also include (for all handlers) chemical-resistant footwear and chemical-resistant headgear for overhead exposures and (for mixers, loaders, and persons cleaning equipment) chemical-resistant aprons.

LANGUAGE FOR THE LABELING RATIONALE SECTION BASED ON PROPOSED RISK MITIGATION OPTIONS:

EPA has determined that certain strychnine end-use products should be limited to use by professional pest control operators and should not be available for sale or use by homeowners.

LANGUAGE BASED ON OREB RECOMMENDATION THAT READY-TO-USE BAIT AND SOFT-PELLET FORMULATIONS AVAILABLE FOR HOMEOWNER USE BE REQUIRED TO BE CONTAINED IN CHILD-RESISTANT PACKAGING -- EVEN AFTER APPLICATION:

EPA is allowing strychnine end-use products formulated as ready-to-use baits or soft pellets to be sold to and used by homeowners. However, such end-use products must be contained in child-resistant packaging during sale, storage, and application. The packaging must be designed to resist exposure to children even after placement in the tunnel, burrow, or other below-ground pest habitat.

Occupational-Use Products

EPA has determined that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers must be taken for strychnine when formulated as a powder (unless contained in child-resistent packaging during sale, storage, and use) because of its high acute oral, ocular, and inhalation toxicity and potential exposure concerns from open pouring such formulations. The Agency is requiring the use of chemical-resistant gloves, protective eyewear, and a dust/mist respirator for all persons who handle such powder formulations of strychnine.

EPA has determined that regulatory action regarding the establishment of active-ingredient-based minimum PPE requirements for occupational handlers must be taken for strychnine when formulated as a paste due to its high acute oral and ocular toxicity. The Agency is requiring the use of chemical-resistant gloves and protective eyewear for all persons who handle such paste formulations.

Homeowner-Use Products

EPA is not establishing minimum (baseline) handler PPE for strychnine end-use products that are intended primarily for homeowner use, because the Agency has determined that limiting the formulations available for homeowner use to ready-to-use baits and soft

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pellets contained in child-resistant packaging will adequately mitigate the concerns about the high acute toxicity.

Post-Application/Entry Restrictions

EPA is not establishing entry restrictions at this time for strychnine end-use products, since strychnine currently is registered for use only below-ground in rodent burrows, dens, tunnels and nests. All above-ground uses of strychnine are temporarily canceled. Post-application exposures are unlikely following applications below-ground.

Other Labeling Requirements

The Agency is also requiring other use and safety information to be placed on the labeling of all end-use products containing strychnine. For the specific labeling statements, refer to Section V of this document.

APPENDIX B

(RED SECTION V - LABELING REQUIREMENTS)

LABELING REQUIREMENTS FOR END-USE PRODUCTS
[The following labeling requirements address the recommended risk mitigation options as described in the OREB RED chapter for strychnine.]

PPE/Engineering Control Requirements for Pesticide Handlers

For **sole-active-ingredient** end-use products that contain strychnine, the product labeling must be revised to adopt the handler personal protective equipment/engineering control requirements set forth in this section. Any conflicting PPE requirements on the current labeling must be removed.

For **multiple-active-ingredient** end-use products that contain strychnine, the handler personal protective equipment/engineering control requirements set forth in this section must be compared to the requirements on the current labeling and the more protective must be retained. For guidance on which requirements are considered more protective, see PR Notice 93-7.

Products Intended Primarily for Occupational Use

Minimum (Baseline) PPE/Engineering Control Requirements

EPA is limiting the use of some end-use products containing strychnine to occupational users (i.e., professional pest control operators). These include (1) all strychnine-containing end-use products formulated as a powder, (2) all strychnine-containing end-use products formulated as a paste, and (3) all strychnine-containing end-use products formulated as a bait or soft pellet, UNLESS these baits or soft pellets are contained in child-resistant packaging during sale, storage, and use. All occupational-use products must bear the following statement in a prominent location on the front panel of the end-use product labeling:

"For sale to and use by professional pest control operators only. Sale to or use by the general public is prohibited."

The minimum (baseline) PPE for strychnine end-use products formulated as a powder is:

"Applicators and other handlers must wear:
--long-sleeved shirt and long pants,
--chemical-resistant gloves*,
--shoes plus socks,
--protective eyewear**, and
--a dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C)."

* For the glove statement, use the statement established for strychnine through the instructions in Supplement Three of PR Notice 93-7.

** If a full face respirator is worn, eyewear may be waived.

The minimum (baseline) PPE for strychnine end-use products formulated as a paste is:

"Applicators and other handlers must wear:
--long-sleeved shirt and long pants,
--chemical-resistant gloves*,
--shoes plus socks, and
--protective eyewear.

* For the glove statement, use the statement established for strychnine through the instructions in Supplement Three of PR Notice 93-7.

Determining PPE Requirements for End-use Product Labels

The PPE that would be established on the basis of the acute toxicity category of the end-use product must be compared to the active-ingredient-based minimum (baseline) personal protective equipment specified above. The more protective PPE must be placed on the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Placement in Labeling

The personal protective equipment requirements must be placed on the end-use product labeling in the location specified in PR Notice 93-7, and the format and language of the PPE requirements must be the same as is specified in PR Notice 93-7.

Products Intended Primarily for Homeowner Use

Minimum (baseline) PPE Requirements

EPA is not establishing active-ingredient-based minimum (baseline) handler PPE for strychnine end-use products that are intended primarily for homeowner use.

Determining PPE Requirements for End-Use Product Labels

Any necessary PPE for each strychnine end-use product intended primarily for homeowner use will be established on the basis of the end-use product's acute toxicity category.

Placement in Labeling

The personal protective equipment requirements, if any, must be placed on the end-use product labeling immediately following the precautionary statements in the labeling section "Hazards to Humans (and domestic animals)."

Entry Restrictions

For **sole-active-ingredient** end-use products that contain strychnine the product labeling must be revised to remove any entry restrictions on the current labeling.

For **multiple-active-ingredient** end-use products that contain strychnine the entry restrictions set forth in this section must be compared to the entry restrictions on the current labeling and the more protective must be retained. A specific time period in hours or days is considered more protective than "sprays have dried" or "dusts have settled."

Entry restrictions:

There are no entry restrictions for nonWPS uses.

Other Labeling Requirements

Products Intended Primarily for Occupational Use

The Agency is requiring the following labeling statements to be located on all end-use products containing strychnine that are intended primarily for occupational use.

Application Restrictions

"Do not apply this product in a way that will contact workers, other persons. pets, or domestic animals.

User Safety Requirements

"Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry."

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing 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."

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Products Intended Primarily for Home Use

Application Restrictions

"Do not apply this product in a way that will contact any person or pet. Keep people and pets out of the area during application."

User Safety Recommendations

- "Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."
- "Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing."

References:

1) Strychnine labels

2) U.S. EPA 1995. Minutes of the Less than Life Time Committee Meeting, Dated 11/7/95. {Notice of Intent to Cancel Above Ground Uses Dated 10/19/83.} {Per conversation with J. Redden/HED 12/27/95, the Toxicology Chapter for strychnine will be revised to reflect an eye irritation toxicity category of I based on the lethality to the animals through the ocular route.}

3) U.S. EPA 1992. LUIS Report for Strychnine. Dated 2/21/92.

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