Australian Government
Australian Pesticides and
Veterinary Medicines Authority

PROJECT TO ACHIEVE GREATER ALIGNMENT BETWEEN SUBSTANCES LISTED IN APPENDIX J OF THE STANDARD FOR THE UNIFORM SCHEDULING OF DRUGS AND POISONS AND PRODUCTS DECLARED AS RESTRICTED CHEMICAL PRODUCTS*

MAY 2008

* This report is Part 1 of a two-Part project. Information on the scope of Part 1 and Part 2 of the project is presented in the Preamble of this report.

CONTENTS

PREAMBLE

The objective of the project is to achieve greater alignment between substances in Appendix J of the Standard for the Uniform Scheduling of Drugs and Poisons and products declared as Restricted Chemical Products. The project consists of two Parts and this report describes the findings of Part 1.

Part 1 of the project considers only the application of the s. 93(3) criteria of the *Agricultural and Veterinary Chemicals Code Act 1994* (Cwlth) relating to Restricted Chemical Products. It does not comprehensively consider all public health interest factors for and against the declaration of a product as a Restricted Chemical Product. However, it does identify some public interest factors against restriction, e.g. alternative controls already in place to control the risk.

Part 2 of the project will consider the application of s. 93(2) criteria of the *Agricultural and Veterinary Chemicals Code Act 1994* (Cwlth) relating to Restricted Chemical Products. It will also address user training and accreditation applicable to Restricted Chemical Products, a task that will require the APVMA, in collaboration with the jurisdictions, to set nationally consistent competency standards for Restricted Chemical Products. There is a direct link between Part 2 of the project and the intention of the Product Safety and Integrity Committee (PSIC) to develop a proposal for national training and user accreditation for high-risk chemicals.

Finally, the APVMA expresses its gratitude to those groups which submitted comments during a public consultation period on a draft version of this report. All comments received were considered during the preparation of this final report.

SUSDP APPENDIX J/RCP PROJECT

Introduction

The National Drugs and Poisons Schedule Committee (NDPSC) classifies highly toxic substances in poisons schedule 7 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). An additional restriction on supply is placed on many of these substances through inclusion in Appendix J of the SUSDP. Recommendations in the SUSDP are given effect through State/Territory poisons legislation. However, many of the records concerning the origins of the entries in Appendix J are no longer available (Thirty-eighth Meeting of the National Drugs and Poisons Committee, hereafter referred to as NDPSC 38[1]) and the criteria for listing substances in Appendix J are not recorded.

Under the *Agricultural and Veterinary Chemicals Code Act 1994*, a chemical product may be declared as a restricted chemical product (RCP). The relevant extract from the *Act* is provided in Appendix 1 of this report. Declaration as a RCP enables control over access and conditions associated with use of the product as determined by and enforced under State/Territory control-of-use legislation. General criteria for designation of RCP status are provided in the legislation.

Thus, inclusion in Appendix J of the SUSDP and declaration as a RCP provide separate mechanisms for restricting the supply of highly toxic products. A discussion paper[2] produced by the Tasmanian Departments of Primary Industries, Water and Environment, and Health and Human Services has highlighted "inconsistencies" between the substances listed in Appendix J and products designated as RCPs. In particular, the paper identified the following agricultural and veterinary medicines listed in Appendix J.

Substances listed in Appendix J and present in registered products:

Acrolein
4-Aminopyridine
Arsenic
Chloropicrin
1,3-Dichloropropene
Epidermal growth factor
Ethylene dibromide

1 Anon. (2003) Appendix J—Background; Thirty-eighth Meeting of the National Drugs and Poisons Schedule Committee, Canberra.

2 Norman, M. and Galloway, J. (2004) Appendix J agricultural poisons and declaration as Restricted Chemical Products —A discussion paper; Fortieth Meeting of the National Drugs and Poisons Schedule Committee, Canberra.

Ethylene oxide
Fluoroacetic acid
Methoxyethylmercuric chloride
Methyl bromide
Mirex
Phosphides, metallic
Phosphine
Strychnine

Substances listed in Appendix J and with either no registered products or no products covered by the S7 entry:

Abamectin
Brodifacoum
Bromadiolone
Coumatetralyl
Halofuginone
Maduramicin
Mercury (substances other than methoxyethylmercuric chloride)

Acrolein, ethylene dibromide and fluoroacetic acid are currently declared as RCPs. However, the majority of the above substances (16) were included in Appendix J prior to the inception of the APVMA and thus have not been considered for RCP status.

Scope

Recently, priorities have been developed to address the apparent inconsistencies (NDPSC 40[2]). Accordingly, the current project has been instituted to evaluate the following 11 substances in order to determine whether retention in Appendix J is appropriate and to consider whether products containing the substances meet the criteria for declaration as a RCP:

4-Aminopyridine
Arsenic—arsenic as trioxide, arsenic as arsenic pentoxide, 3-nitro-4-hydroxyphenylarsonic acid (roxarsone)
Chloropicrin
1,3-Dichloropropene
Ethylene oxide
Methoxyethylmercuric chloride
Methyl bromide
Mirex
Phosphides, metallic—specifically aluminium and zinc phosphides
Phosphine gas
Strychnine

The remaining 11 substances were identified at the Twenty-ninth Meeting of the Registration Liaison Committee (hereafter referred to as RLC 29)[3] as having no basis to be reviewed under this process. This view was based on a number of different factors peculiar to each of the substances. For example, the existing control mechanisms were regarded as being adequate (epidermal growth factor); formulated products are S5 and S6 rather than S7 (abamectin, brodifacoum, bromadialone, coumatetralyl); presently there are no registered products (halofuginone, maduramicin, mercury compounds); and three substances (acrolein, ethylene dibromide, fluoroacetic acid) are already RCPs.

However, RLC 29 requested that advice be sought from NDPSC regarding the need to review these 11 substances. A paper was tabled at NDPSC 45[4] in October 2005 when the Committee agreed to the APVMA proposal not to proceed with a review of the remaining substances as these are either already controlled by the APVMA or there are no S7 products containing the substance.

Process

The poisons schedules list individual substances, with or without concentration cut-offs, under stated circumstances. Appendix J of the SUSDP applies to certain substances listed in S7, and all products which contain the substance at a concentration which would be covered by the S7 entry. On the other hand, declaration as a RCP relates to a formulated product or class of products. With this important difference in mind, the available toxicological assessment reports for each substance and relevant NDPSC minutes and other documents were examined to ascertain the toxicological profile. Published information, where possible, was also reviewed in summarising the available toxicological information. Independent assessment of data was not undertaken.

While listing in Appendix J is based on human health concerns, declaration as a RCP also takes account of the possibility of an unintended effect that is harmful to any animal, plant or thing or to the environment. Therefore, environmental issues pertinent to each substance were considered.

Before a product can be declared to be a RCP, the APVMA must have certified in writing that it is in the public interest for the product to be so declared. In deciding where the overall public interest lies, the APVMA must consider the factors set out in subsection 93(3) of the Agvet Codes but may have regard to other factors. Consideration is also given to factors against declaring a product to be a RCP. This report only considers the application of the s. 93(3) factors to the substances in question, which, throughout the remainder of this report, will be referred to as the "RCP criteria".

3 Reeves, P.T. (2005) Review of substances in Appendix J of the SUSDP for RCP status—an update; Twenty-ninth Meeting of the Registration Liaison Committee, Canberra.

4 Reeves, P.T. (2005) Appendix J; Forty-fifth Meeting of the National Drugs and Poisons Schedule Committee, Canberra.

The products and formulations considered in this report were based solely on information obtained from the APVMA's NCRIS database. Based on the ingredients present in individual formulations, the toxicological and environmental hazards of each product were estimated. These reviews are summarised in Appendix 2. The RCP criteria were then applied to the potential toxicological and environmental hazards of each product in order to identify public interest factors in favour of declaring the product as a RCP.

This report does not comprehensively consider all public interest factors for and against the declaration of a product as a RCP. However, it does identify some public interest factors against restriction, e.g. alternative controls already in place to control the risk.

Discussion

4-Aminopyridine is present in two products, Reverzine SA Injection and Scatterbird. The main active ingredient in Reverzine SA Injection is yohimbine which is in poisons schedule 4 and is more toxic than 4-aminopyridine. There is little concern from an environmental perspective arising from this use as a minor constituent in a veterinary product. Since prescription by a veterinarian is required, it may be considered that there is sufficient control of use and this product may not require declaration as a RCP.

Scatterbird is a bird repellent containing a low concentration of 4-aminopyridine. The toxicity of the product is expected to be moderate and it may not be harmful to humans. It is in line with the criteria for an S6 classification and the NDPSC may consider an appropriate amendment to the current S7 entry for 4-aminopyridine. The distribution of products containing 4-aminopyridine in the environment may, however, be hazardous for non-target birds. Therefore, Scatterbird is considered to meet one criterion for declaration as a RCP. Restriction of Scatterbird will ensure that persons authorised by the State/Territory authorities, including licensed pest control operators, have access to the chemical. Restricted access only to authorised people will prevent its use by untrained people who are unaware of the specific requirements for use of the product. This will protect the environment. There is no detriment to the public because even under current arrangements the public should not have access to Scatterbird.

Arsenic compounds are acutely toxic and likely to be carcinogenic, toxic to reproduction and neurotoxic in humans. Therefore, exposure should be avoided wherever possible. Some products used in preservation of timber require the use of special systems in pressure impregnation plants. Other products used in the treatment of termite infestations may be distributed around domestic buildings. In these situations, the operator would be expected to have the knowledge to distribute the product in a manner that ensures no exposure to the inhabitants of treated dwellings. The use pattern of these products may cause the disposal of large amounts of arsenic or a prolonged contamination with lower amounts of arsenic, which may lead to levels that are harmful in the

environment. Arsenic-containing feed additives may be harmful to human beings but are not likely to present environmental concerns in view of the relatively low dose rates and limited duration of use. All of the arsenic-containing products are considered to meet one or a number of the RCP criteria. Restriction of all arsenic-containing products will ensure that persons authorised by the State/Territory authorities, including licensed pest control operators, have access to the chemical. Restricted access only to authorised people will prevent its use by untrained people who are unaware of the specific requirements for use of the product. This will protect human health and the environment. There is no detriment to the public because even under current arrangements the public should not have access to arsenic-containing products.

Half of the substances considered are primarily used as fumigants. These substances are generally present in the gaseous phase or in a form that leads to the release of a gas. Often, the presence of the gas is difficult to detect because of a lack of colour or odour. Therefore, protection against exposure to such products which consist of high concentrations of toxic gases is relatively difficult. The prescribed safety directions for these products commonly specify the need for respiratory protection with appropriate cartridge or canister, and in a number of cases special application procedures are required. There are few environmental issues arising from the use of fumigant products and, in general, current controls are regarded as sufficient to avoid environmental hazards. All of the fumigant products containing chloropicrin, 1,3-dichloropropene, ethylene oxide, methyl bromide, metallic phosphides and/or phosphine are considered to meet one or more of the RCP criteria. In the case of metallic phosphides contained in tablets and blankets, the risk posed by their use may already be adequately addressed by the training requirements in some jurisdictions. More generally, restriction of fumigant products will ensure that persons authorised by the State/Territory authorities, including licensed pest control operators, have access to the chemical. Restricted access only to authorised people will prevent its use by untrained people who are unaware of the specific requirements for use of the product. This will protect human health. There is no detriment to the public because even under current arrangements the public should not have access to these fumigant products.

Methoxyethylmercuric chloride is present in one product used for dipping sugar cane setts. The acute toxicity of the product is expected to be high and developmental toxicity potential is an additional concern. There are significant environmental concerns regarding the use of mercury-containing pesticides**.** Shirtan Liquid Fungicide may have an effect that is harmful to human beings and the environment and is considered to meet two of the RCP criteria. Restriction of Shirtan Liquid Fungicide will ensure that persons authorised by the State/Territory authorities, including licensed pest control operators, have access to the chemical. Restricted access only to authorised people will prevent its use by untrained people who are unaware of the specific requirements for use of the product. This will protect human health and the environment. There is no detriment to the public because even under current arrangements the public should not have access to Shirtan Liquid Fungicide.

Strychnine is present in two products—a bait product which contains strychnine at a low concentration and a product approved for use with animal traps in Western Australia. The acute oral toxicity of the products is high and also contact with the eyes or open wounds could be dangerous. Dynamice Mouse Bait may be distributed around domestic buildings and the operator would be expected to have the knowledge to distribute the product in a manner that ensures no exposure to the inhabitants of treated dwellings. Special training for safe and effective use of this product is considered necessary in order to prevent an unintended effect that is harmful in the environment. Dynamice Mouse Bait is considered to meet a number of the RCP criteria. Restriction of Dynamice will ensure that persons authorised by the State/Territory authorities, including licensed pest control operators, have access to the chemical. Restricted access only to authorised people will prevent its use by untrained people who are unaware of the specific requirements for use of the product. This will protect human health and the environment. There is no detriment to the public because even under current arrangements the public should not have access to Dynamice. In relation to the use of Strychnine Alkaloid Crystals in Western Australia, adequate controls are already in place. These include listing in the Western Australia Poisons Act of those shires where its use is permitted; a Code of Practice for the use of the product; and restriction of use of the product to approved persons.

Zinc phosphide is present at a low concentration in a grain bait formulation for the control of mice in agricultural situations. The acute toxicity of the product is expected to be low. Phosphine would be released slowly and in small quantities which would reduce the hazards to the operator. The product is not for distribution around dwellings and therefore exposure of bystanders is unlikely. It is considered that Mouseoff Zinc Phosphide Bait does not meet the RCP criteria. The toxicity of the product is in line with the criteria for an S6 classification and the NDPSC may consider an appropriate amendment to the current S7 entry for zinc phosphide.

The available toxicological information on mirex is limited and was reviewed over 20 years ago. While the conclusions at the time were that the substance was associated with liver tumours and reproduction/developmental toxicity in rodents, very few details are recorded. Mirex is in a similar chemical class to other termiticides, such as chlordane, heptachlor, and dieldrin. The concern over the carcinogenic potential of these substances has lessened since the hepatic effects are thought to represent a rodent specific response. Mirex has been declared as a Persistent Organic Pollutant which requires a phase-out of use by 2009. The only registration of a product containing mirex (Mirant), which had a minor use in bait stations in the Northern Territory, has lapsed and product use has ceased. Consequently, there is no registered product containing mirex.

A wider issue concerns the enforcement mechanisms available to the States/Territories. The available regulatory system can be used to enforce the required restrictions in all jurisdictions, however this does not currently occur in a consistent manner. In Western Australia, the

adoption of Appendix J represents the only non-legislative mechanism to restrict supply and availability of a poison. Appendix J has an important role in South Australia. The inclusion of a chemical in Appendix J advises regulators of the degree of risk associated with use and provides the impetus for regulatory amendment to Schedule F of the Controlled Substances (Poisons) Regulations 1996. At the other end of the spectrum, a number of jurisdictions do not implement Appendix J at all. In Victoria, for example, Appendix J is not referenced in State drugs and poisons legislation. The Appendix J statement, which is applied to certain agricultural chemicals and veterinary medicines, is "Not to be available except to authorised or licensed persons". This statement is directed at suppliers and is concerned mainly with the hazards to the user of the product. There are concerns, however, that the risks to be managed are not identified and the measures required to effectively mitigate those risks are not enunciated. Furthermore, there is insufficient information and guidance on issues such as appropriate uses and methods of use. As a result, it is difficult for the health jurisdictions to impose appropriate conditions on approvals for use of many of the poisons included in Appendix J and to make decisions on whether or not an applicant should receive approval to be an "authorised or licensed person" as specified in Condition 1 of Appendix J.

Declaration of a product as a RCP is intended to limit availability as well as use of the product to authorised persons. While discussions have focussed on RCP status as a possible means of fostering user training and accreditation schemes, there is no mechanism in place that compels States/Territories to enforce the RCP provisions. Once again, while there is currently no mechanism that can deliver a consistent approach throughout the various jurisdictions, the Product Safety and Integrity Committee is working on a national training and accreditation scheme for high-risk chemicals.

Appendix J was introduced primarily to limit access to highly hazardous substances. Historically, State/Territory poisons legislation may have been the only means by which such controls could be enforced. In recent years, with the advent of legislation directed at hazardous substances in the workplace and control of use, a variety of mechanisms may now be available which could be employed in restricting access and exposure to toxic substances. However, it would appear that there is no current system which could ensure that the required restrictions are enforced in all jurisdictions. This is a critical consideration.

The NDPSC has previously considered the possibility of deleting Appendix J from the SUSDP (May 1996) and more recently has proposed a review of the substances in Appendix J (February 2005). At the May 1996 meeting it was determined that where control of availability was considered necessary through poisons legislation, it may be achieved through Part 3 of the SUSDP. Currently, Paragraph 41 recommends that possession or use of a number of schedule 7 poisons must be subject to appropriate authorisation. Arsenic, cyanides, fluoroacetic acid, fluoroacetamide, hydrocyanic acid, strychnine and thallium are listed in this section. However, the current situation is that Paragraph 41 of the SUSDP is not adopted by all health jurisdictions.

For example, the provisions of Part 3 of the SUSDP are mirrored in the Queensland regulations. Therefore, the transfer of poisons currently included in Appendix J to Paragraph 41 of the SUSDP will not facilitate the update of the intended control provisions for these poisons by the jurisdictions.

Recommendations

General

1. Because of the absences of uniformity in the applicability of Appendix J within the jurisdictions, it is suggested that more appropriate and practical control mechanisms should be considered. Controls through poisons legislation through recommendations in SUSDP Part 3 Paragraph 41 are not an option because these provisions are not adopted by all health jurisdictions. Declaration as a RCP may achieve the desired result through control-of-use measures. However, appropriate action and control at a national level would be required to achieve consistent enforcement across all jurisdictions.

RLC

2. The toxicological potential of Mirant, which contains mirex, could not be estimated. However, further action is unnecessary because the registration of Mirant has lapsed and its use has ceased.

3. The following product is covered by the provisions of S4 because of its constituents. Since the product must be prescribed by a veterinarian, there is sufficient control of use and it need not be considered further against the RCP criteria.

- Reverzine SA Injection

4. The following product has low human and environmental health hazards. Therefore, it does not meet the RCP criteria:

- Mouseoff Zinc Phosphide Bait

5. The following products may have an effect that is harmful to human beings. Therefore, they meet one RCP criterion:

- A.L. 3-Nitro 1000 Feed Additive Powder
- B&J 3-Nitro 1000 Feed Additive Powder
- CCD 3-Nitro (Growth Promotant Feed Additive Powder)
- Selectochem 3-Nitro Feed Additive Powder

6. The following product may have an effect that is harmful to human beings and may have an unintended effect that is harmful to any animal, plant or thing or to the environment.

Therefore, it meets two of the RCP criteria:

- Shirtan Liquid Fungicide

7. The following product may have an effect that is harmful to human beings and may have an unintended effect that is harmful to any animal, plant or thing or to the environment, and special knowledge is required in the application of the product. Therefore, it meets three of the RCP criteria:

- Dynamice Mouse Bait

The following product is approved only in Western Australia where it is adequately controlled under the Western Australia Poisons Act and its use is restricted to approved persons in accordance with a Code of Practice. Currently, there is sufficient control of use and it need not be considered further against the RCP criteria:

- Strychnine Alkaloid Crystals

8. The following products may have an effect that is harmful to human beings and may have an unintended effect that is harmful to any animal, plant or thing or to the environment, and special equipment is required to use the products safely. Therefore, they meet three of the RCP criteria:

- Sarmix 3 CCA Salts
- Tanalith CP Wood Preservative Paste

9. The following products may have an effect that is harmful to human beings and special knowledge is required in the application of the products. Therefore, they meet two of the RCP criteria:

- Aldi Arsenic Trioxide Termite Dust
- Garrard's Termite Powder Insecticide
- One Bite Arsenic Trioxide Termite Treatment

10. The following products may have an effect that is harmful to human beings and special equipment is required to use the products safely. Therefore, they meet two of the RCP criteria:

- Agrigas M Methyl Bromide Fumigant
- Agrigas MC Methyl Bromide Fumigant
- AIC Bromo-Chlor 700-300
- Chloropicrin Soil Fumigant
- Dibbs Brom-O-Gas 980 Fumigant
- Dibbs Brom-O-Gas 1000 Fumigant
- Fumigas 900 Fumigant

- Fumigas 1000 Fumigant
- Fumigas Non-Flammable Fumigant
- Nufarm Bromopic 700:300 Soil Fumigant
- Nufarm Fungafume Soil Fumigant
- Nufarm Methyl Bromide 980 Fumigant
- Nufarm Methyl Bromide 1000 Fumigant
- Nufarm Vertafume Soil Fumigant
- Rural Larvacide Rabbit Fumigant
- Rural Methyl Bromide 1000 Fumigant
- Rural Soil Fumigant 300-700
- Rural Soil Fumigant 500-500
- SA Rural Methyl Bromide 980 Fumigant
- Southern Cross Methyl Bromide 980 Fumigant
- Southern Cross Methyl Bromide 1000 Fumigant
- Southern Cross Soil Fumigant 500-500
- Southern Cross Soil Fumigant 700-300

11. The following products may have an effect that is harmful to human beings, special knowledge is required in the application of the products and special equipment is required to use the products safely. However, the current training requirements in some jurisdictions may already adequately address the risks posed by use of the products. Therefore, the products meet one or more of the RCP criteria:

- Celphide Fumigation Blanket
- Celphide Fumigation Pellets
- Celphide Fumigation Tablets
- Chemag Fostoxin Fumigation Tablets
- CM Alphos Fumigation Pellets
- CM Alphos Fumigation Tablets
- Eco2fume Phosphine Fumigant
- Farmoz Pestex Fumigation Tablets
- Fumaphos Fumigation Blanket
- Fumaphos Fumigation Tablets
- Fumitoxin Coated Insecticide Tablets
- Genfume AP Fumigation Pellets
- Phosfume Phosphine Fumigant
- Quickphos Fumigation Bags
- Quickphos Fumigation Bags-Chain
- Quickphos Fumigation Blanket
- Quickphos Fumigation Pellets
- Quickphos Fumigation Tablets

- Rentokil Gastion Phosphine Fumigation Belt
- Rentokil Gastion Phosphine Fumigation Tablets
- Rentokil Gastion Rabbit Fumigation Tablets
- Rural Telone C-35 Soil Fumigant
- Sanphos Fumigation Tablets
- Telone C-35 Soil Fumigant
- Telone Soil Fumigant
- Vaporphos Phosphine Fumigant

12. The following product may have an unintended effect that is harmful to any animal, plant or thing or to the environment, and special knowledge is required in handling the product. Therefore, it meets two of the RCP criteria:

- Scatterbird

NDPSC

13. The NDPSC may consider amendments which would include grain based products containing 10 g/kg or less of 4-aminopyridine in S6.

14. The NDPSC may consider amendments which would include grain based products containing 25 g/kg or less of zinc phosphide in S6.

APPENDIX 1

Restricted Chemical Products and APVMA legislation

Sections 93, 94 and 95 of the *Agricultural and Veterinary Chemicals Code Act 1994* (Cwlth) relate to RCPs and are given below:

Division 4—Restricted chemical products

93 Restricted chemical product

(1) Subject to subsection (2), the regulations may declare a chemical product to be a restricted chemical product.

(2) A chemical product may not be declared by the regulations to be a restricted chemical product unless the NRA has certified in writing that it is in the public interest for the product to be so declared.

(3) In deciding whether to give a certificate in relation to a chemical product under subsection (2), the NRA must have regard to the following:

(a) whether the product may have an effect that is harmful to human beings;

(b) whether the product may have any unintended effect that is harmful to any animal, plant or thing or to the environment;

(c) whether any special knowledge, skill or qualification is required in the preparation or handling of the product;

(d) whether any special equipment is required to use the product with safety.

94 Restricted chemical products may be supplied only to authorised persons

(1) A person must not supply a restricted chemical product, or cause or permit a restricted chemical product to be supplied, to a person who is not authorised to use the product under another law of this jurisdiction.

Penalty: 120 penalty units.

(2) Subsection (1) does not apply if the person has a reasonable excuse.

Note: The defendant bears an evidential burden in relation to the matter in subsection (2). See subsection 13.3(3) of the *Criminal Code*.

95 Labels for restricted chemical products

(1) A person must not supply a restricted chemical product, or cause or permit a restricted chemical product to be supplied, unless the label attached to the container for the product contains the words "RESTRICTED CHEMICAL PRODUCT—ONLY TO BE SUPPLIED TO OR USED BY AN AUTHORISED PERSON".

Penalty: 120 penalty units.

(2) Subsection (1) does not apply if the person has a reasonable excuse.

Note: The defendant bears an evidential burden in relation to the matter in subsection (2). See subsection 13.3(3) of the *Criminal Code*.

APPENDIX 2

Summary of Toxicological and Environmental Hazard Potential of Substances in Appendix J

and

Estimation of Product Hazards

4-AMINOPYRIDINE

S7, except when included in schedule 4.
S4, for therapeutic use.

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

A Department of Health assessment report was not available. One published paper[5] was obtained.

Acute:	Oral LD_{50} values were 20 mg/kg in rats and 4 mg/kg in dogs. In humans, poisoning with approximately 60 mg resulted in gastrointestinal, respiratory and neurological disturbances.
Repeat-dose:	No information.
Carcinogenicity/Genotoxicity:	No information.
Reproduction/Developmental:	No information.
Other:	Enhances transmission at neuromuscular junctions and other synapses. It is poorly absorbed through skin.
Conclusion:	Acute toxicity is very high.

Environmental issues:

The primary concern is the high toxicity of the substance. It is considered that distribution of products containing 4-aminopyridine in the environment may be hazardous for non-target birds. There is little concern from an environmental perspective arising from the use of the active ingredient as a minor constituent in veterinary products.

Products:

Two registered products.
Reverzine SA Injection (37698)
Scatterbird (39243)

5 Gosselin, R.E., Smith, R.P. and Hodge, H.C. (1984) Clinical toxicology of commercial products. 5th ed. Baltimore, MD: Williams and Wilkins, 11–345.

Assessment:

Reverzine SA Injection is an injectable formulation containing yohimbine as the active principle. Using a linear extrapolation for the toxicity of 4-aminopyridine alone, the approximate oral LD_{50} is likely to be 2000 mg/kg. The presence of yohimbine, which is in poisons schedule 4, would lead to greater toxicity. The product must be prescribed by a veterinarian, therefore it is considered that there is sufficient control of use. The product is unlikely to have an unintended effect that is harmful to any animal, plant, or thing or to the environment.

Scatterbird is a bird repellent. Using a linear extrapolation, the approximate oral LD_{50} is likely to be 800 mg/kg for the product and 400 mg/kg for a 10 g/kg strength formulation. Dermal contact would not result in significant exposure. The acute toxicity of the product is expected to be moderate and may not be harmful to human beings. However, special training for safe and effective use of this product is considered necessary in order to prevent an unintended effect on non-target birds. The product may have an unintended effect that is harmful to animals, plants, or things or to the environment.

Recommendations:

- Because Reverzine SA Injection is currently subject to sufficient control of use, the product need not be considered further against the RCP criteria.

- Because the product may have an unintended effect that is harmful to any animal, plant or thing or to the environment, and special knowledge is required in handling the product, Scatterbird meets two of the RCP criteria.

- The extrapolated acute toxicity of Scatterbird is commensurate with a S6 poisons schedule. The NDPSC may consider amendments which would include grain based products containing 10 g/kg or less of 4-aminopyridine in S6.

ARSENIC

Arsenic as trioxide, arsenic as arsenic pentoxide, 3-nitro-4-hydroxyphenylarsonic acid (roxarsone)

S7, except: when separately specified
when included in schedule 4 or 6
as selenium arsenide in photocopier drums
as 10,10'-oxydiphenoxarsine in silicone rubber mastic containing 120 mg/kg or less of arsenic
in animal feeds containing 75 g/tonne or less of arsenic
in paints containing 0.1 per cent or less of arsenic calculated on the non-volatile content of the paint

S6, in ant poisons containing 0.4 per cent or less of arsenic
in animal feed premixes containing 4 per cent or less of arsenic
in preparations for the treatment of animals except thiacetarsamide when included in schedule 4

S4, for human therapeutic use

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substances:

Arsenic trioxide and arsenic pentoxide.

A number of international reviews[6,7,8,9] and the Department of Health review of inorganic arsenic[10] were available.

6 Bahri, L.E. and Romdane, S.B. (1991) Arsenic poisoning in livestock. Vet. Hum. Toxicol. 33: 259–264.

7 Pearce, F. (1993) Arsenic in tapwater linked to skin cancer. New Scientist, 30 October: 5.

8 Anon (1988) EPA Final determination on canceling registrations of non-wood preservative uses of inorganic arsenicals. Chemical Regulation Report, 12(15); 559–568.

9 Anon (1991) Arsenic. IRPTC Bulletin, 10(2), 27–30.

10 Unpublished confidential report

Acute:	Oral LD_{50} values ranged from 15–293 mg/kg in rats. Humans exhibited signs of gastrointestinal irritation, general weakness, liver swelling and disturbances in heart function and sensory nerves.
Repeat-dose:	Liver lesions, anaemia and pathological skin changes were seen in animals. In humans, hyperkeratosis of skin, vascular disorders, anaemia and peripheral neuritis were observed.
Carcinogenicity/Genotoxicity:	Arsenic has been associated with tumours of the skin, liver, lung and urinary tract in humans, possibly by acting as a promoter through inhibition of DNA repair. Arsenic compounds have been associated with DNA damage and were genotoxic in a wide range of assays.
Reproduction/Developmental:	In animals and humans, neonatal mortality, retarded growth and neurological disturbances were produced in offspring.
Other:	Once absorbed, the toxicity of arsenical compounds is related to the systemic level of arsenic. Accumulation in humans is likely only at high exposure levels. Humans are more sensitive than animals to the toxicity of arsenical compounds.
Conclusion:	Acute toxicity is very high. Arsenic compounds are associated with the formation of tumours, reproductive abnormalities, neurological and vascular disorders, and skin lesions in humans.

Environmental issues:

Arsenic is known to accumulate in the environment. The disposal of large amounts or prolonged contamination with lower amounts may lead to levels that are harmful to natural organisms in the environment.

Products:

Five registered products.
Aldi Arsenic Trioxide Termite Dust (48410)
Garrard's Termite Powder Insecticide (48909)
One Bite Arsenic Trioxide Termite Treatment (51234)
Sarmix 3 CCA Salts (41680)
Tanalith CP Wood Preservative Paste (30691)

Assessment:

The Tanalith and Sarmix products are copper-chrome-arsenic formulations used in wood preservation. Sodium dichromate has high acute toxicity, it is mutagenic, a developmental toxin and is reported to be carcinogenic in occupational settings. Copper sulfate has high acute toxicity. Because of the presence of high concentrations of arsenic pentoxide, sodium dichromate and copper sulfate, the acute toxicity is estimated to be high and there is the possibility of formation of tumours, reproductive abnormalities, neurological and vascular disorders, and skin lesions. The products may be harmful to human beings and all forms of exposure should be avoided. Special systems are employed in the use of such products in pressure impregnation plants. The products are used in large quantities and therefore the possibility of contamination and an unintended effect that is harmful to animals, plants, or things or to the environment is high.

The remaining three products are dusts used for treatment of termite infestations containing at least 50 per cent arsenic trioxide. Because of the presence of high concentrations of arsenic trioxide, the acute toxicity is estimated to be high and there is the possibility of formation of tumours, reproductive abnormalities, neurological and vascular disorders, and skin lesions. The products may be harmful to human beings and all forms of exposure should be avoided. These products may be used to treat domestic buildings and should be restricted to trained personnel to ensure that applications are conducted in a manner which will ensure no direct exposure of the public. Usage according to label directions is unlikely to lead to unintended environmental effects; however, in the hands of untrained operators, misuse could occur resulting in accumulation to levels that may have an unintended effect that is harmful to animals, plants, or things or to the environment.

Toxicology of substance:

Roxarsone has been tested in the National Toxicology Program. The study results have been assessed by the Department of Health and are summarised below.

Acute:	Oral LD_{50} values were 81 mg/kg in rats and 244 mg/kg in mice.
Repeat-dose:	In rats, mortality was increased at doses down to 40 mg/kg/day. Neurotoxicity, and renal toxicity at 20 mg/kg/day and minor hepatotoxicity were also noted. In mice, death occurred at doses down to 60 mg/kg/day.
Carcinogenicity/Genotoxicity:	There was a slight increase in adenomas of the exocrine pancreas in male rats. No neoplasia was found in female rats or in mice. Negative results were obtained in the Ames test and in Drosophila, but there was some evidence for genotoxicity at near cytotoxic doses in cultured mammalian cells.
Reproduction/Developmental:	No information.
Other:	There was evidence for accumulation of arsenic in liver and kidney following repeated administration of high doses in animals.
Conclusion:	Acute toxicity is very high. There was no clear evidence for carcinogenic activity. Because relatively little information is available for this specific compound, it will be treated similar to other arsenic compounds.

Environmental issues:

Arsenic is known to accumulate in the environment. The disposal of large amounts or prolonged contamination with lower amounts may lead to levels that are harmful to natural organisms. Dose rates and duration of administration to target animals are important factors in the assessment of environmental contamination.

Products:

Four registered products.
A.L. 3-Nitro 1000 Feed Additive Powder (51754)
B&J 3-Nitro 1000 Feed Additive Powder (50937)
CCD 3-Nitro (Growth Promotant Feed Additive Powder) (52016)
Selectochem 3-Nitro Feed Additive Powder (53128)

Assessment:

Each of the products contains 1000g/kg roxarsone as the only ingredient. Therefore, the acute toxicity is very high and there is the possibility of formation of tumours, reproductive abnormalities, neurological and vascular disorders, and skin lesions. The products may be harmful to human beings and all forms of exposure should be avoided. In view of the relatively low dose rates and limited duration of use, it is unlikely that there would be an unintended effect that is harmful to any animal, plant, or thing or to the environment.

Recommendations:

- Because the products may have an effect that is harmful to human beings and may have an unintended effect that is harmful to any animal, plant or thing or to the environment, and special equipment is required to use the products safely, Tanalith CP Wood Preservative Paste and Sarmix 3 CCA Salts meet three of the RCP criteria.

- Because the products may have an effect that is harmful to human beings and special knowledge is required in the application of the products, Aldi Arsenic Trioxide Termite Dust, Garrard's Termite Powder Insecticide and One Bite Arsenic Trioxide Termite Treatment meet two of the RCP criteria.

- Because the products may have an effect that is harmful to human beings, B&J 3-Nitro 1000 Feed Additive Powder, A.L. 3-Nitro 1000 Feed Additive Powder, CCD 3-Nitro (Growth Promotant Feed Additive Powder) and Selectochem 3-Nitro Feed Additive Powder meet one RCP criterion.

CHLOROPICRIN

S7, except when included in schedule 6
S6, in preparations containing 5 per cent or less of chloropicrin

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

A Department of Health assessment report was not available. A published review from the California EPA[11] was obtained.

Acute:	The oral LD_{50} was 250 mg/kg in rats. The inhalation LC^{50} was 79 mg/m^3 in rats and 800 mg/m^3 in dogs. Vapours caused intense irritation of mucous membranes leading to severe lacrymation, coughing and suffocation.
Repeat-dose:	Inhalation exposure produced signs of pulmonary irritation, decreased growth and resulting organ weight changes in rodents. The No Observable Effect Level (NOEL) was 1.9 mg/m$^{3.}$
Carcinogenicity/Genotoxicity:	There was no increase of tumours in inhalation studies in rodents. Mutagenic effects were seen in bacteria but not in cultured mammalian cells. Chromosome damage was observed in cultured mammalian cells, whereas unscheduled DNA synthesis (UDS) was not noted in rat hepatocytes and assays in Drosophila were negative.
Reproduction/Developmental:	No effects were observed on reproduction and development in inhalation studies.
Other:	Chloropicrin is highly reactive towards free thiol groups.
Conclusion:	Acute toxicity is very high. Carcinogenicity, genotoxicity and reproductive toxicity potential are low.

11 Anon (1987) Chloropicrin—Summary of toxicology data. California Environmental Protection Agency accessed at www.cdpr.ca.gov/docs/toxsums/toxsumlist.htm (Chemical Code 136).

Environmental issues:

Detailed assessment has not been undertaken; however, there are no strong reasons to suspect an impact on the environment. The requirement for special equipment and training in the use of such products to ensure human safety may also assist in protection of the environment.

Products:

Seventeen registered products.
Agrigas MC Methyl Bromide Fumigant (34060)
AIC Bromo-Chlor 700-300 (34059)
Chloropicrin Soil Fumigant (47431)
Dibbs Brom-O-Gas 980 Fumigant (41394)
Nufarm Bromopic 700:300 Soil Fumigant (41488)
Nufarm Fungafume Soil Fumigant (51125)
Nufarm Methyl Bromide 980 Fumigant (34066)
Nufarm Vertafume Soil Fumigant (51126)
Rural Larvacide Rabbit Fumigant (49792)
Rural Soil Fumigant 300-700 (51207)
Rural Soil Fumigant 500-500 (51208)
Rural Telone C-35 Soil Fumigant (54436)
SA Rural Methyl Bromide 980 Fumigant (41303)
Southern Cross Methyl Bromide 980 Fumigant (58001)
Southern Cross Soil Fumigant 500-500 (59240)
Southern Cross Soil Fumigant 700-300 (59241)
Telone C-35 Soil Fumigant (52476)

Assessment:

Two products contain chloropicrin as the sole ingredient. Therefore, the toxicity of these products is as above. Since the acute toxicity is very high, in particular after inhalation exposure, the products may be harmful to human beings. Special equipment such as a respirator and gas canister are prescribed in the safety directions and the operator is referred to State/Territory regulations for safe use. Under these conditions of use, an unintended effect that is harmful to any animal, plant, or thing or to the environment is unlikely.

Eight products contain a mixture of chloropicrin and methyl bromide in the ratios 7:3, 1:1, and 3:7. Since both ingredients have high or very high acute toxicity, the acute toxicity of the products is high to very high, particularly after inhalation exposure. The products may be harmful to human beings. Special equipment such as a respirator and gas canister are prescribed in the safety directions and the operator is referred to State/Territory regulations for safe use. Methyl bromide-containing products are restricted to quarantine uses and AQIS has control measures in place to limit environmental contamination.

Another five products contain predominantly methyl bromide with 2 per cent chloropicrin. These products are likely to mimic the toxicity of methyl bromide which has high acute toxicity, in particular after inhalation exposure. The products may be harmful to human beings. Special equipment such as a respirator and gas canister are prescribed in the safety directions. Methyl bromide-containing products are restricted to quarantine uses and AQIS has control measures in place to limit environmental contamination.

Acute studies on a formulation, similar to the C-35 products, have been evaluated in the Department of Health. In rats, LD_{50} values were 304 mg/kg by the oral route and <500 mg/kg by the dermal route, and the LC_{50} was 477 mg/m^3. Skin irritation was severe in rabbits. Since the acute toxicity is high, in particular after dermal and inhalation exposure, the product may be harmful to human beings. Special equipment such as a respirator and gas canister are prescribed in the safety directions and use is restricted to accredited fumigators. Under these conditions of use, an unintended effect that is harmful to any animal, plant, or thing or to the environment is unlikely.

Recommendations:

- Because the products may have an effect that is harmful to human beings, and special equipment is required to use the products safely, Chloropicrin Soil Fumigant, Rural Larvacide Rabbit Fumigant, Nufarm Fungafume Soil Fumigant, Rural Soil Fumigant 300-700, Nufarm Vertafume Soil Fumigant, Rural Soil Fumigant 500-500, Southern Cross Soil Fumigant 500-500, AIC Bromo-Chlor 700-300, Nufarm Bromopic 700:300 Soil Fumigant, Southern Cross Soil Fumigant 700-300, Agrigas MC Methyl Bromide Fumigant, Nufarm Methyl Bromide 980 Fumigant, SA Rural Methyl Bromide 980 Fumigant, Dibbs Brom-O-Gas 980 Fumigant and Southern Cross Methyl Bromide 980 Fumigant meet two of the RCP criteria.

- Because the products may have an effect that is harmful to human beings and special knowledge and equipment are required to use the products safely, Telone C-35 Soil Fumigant and Rural Telone C-35 Soil Fumigant meet three of the RCP criteria.

1,3-DICHLOROPROPENE

S7

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

A Department of Health assessment report[12] was available.

Acute:	The oral LD_{50} was 240 mg/kg in rats, the dermal LD_{50} was 333 mg/kg in rabbits, and the inhalation LC_{50} was 3882 mg/m^3 in rats. It was a severe eye irritation in rabbits and a skin sensitiser in guinea pigs.
Repeat-dose:	Signs of severe irritation were seen at the site of entry in inhalation and oral dose studies in animals. Food consumption and body weight gain were reduced with consequent organ weight changes. Anaemia was observed in dogs. The NOELs were 23 mg/m^3 by inhalation in rodents and 2.5 mg/kg/day in the diet of rodents and dogs.
Carcinogenicity/Genotoxicity:	Benign adenomas were observed in lungs of mice and liver of rats, and thought to be due to depletion of GSH following prolonged administration. Positive genotoxicity was observed in *in vitro* studies but was concluded to be related to conditions such as low GSH levels or the presence of a mutagenic impurity. Generally negative results were obtained *in vivo*.
Reproduction/Developmental:	No reproductive or developmental concerns. There was no effect on male fertility in occupationally exposed humans.
Other:	Following inhalation exposure in human volunteers, 1,3-dichloropropene disappeared from the blood within 20 minutes.
Conclusion:	Acute toxicity is high. The primary toxic effect is irritation at site of exposure. Carcinogenicity, genotoxicity and reproduction toxicity potential are low.

12 Unpublished confidential report

Environmental issues:

Soil fumigant products containing 1,3-dichloropropene have been assessed as a low hazard to the environment provided label directions, good agricultural practice and State and Territory requirements are followed. The conclusion was reached in the understanding that the products were to be restricted to professional and accredited fumigators using adequately designed equipment and procedures to minimise hazards.

Products/Formulations:

Three registered products.
Rural Telone C-35 Soil Fumigant (54436)
Telone C-35 Soil Fumigant (52476)
Telone Soil Fumigant (52475)

Assessment:

Telone Soil Fumigant contains 1,3-dichloropropene as the sole ingredient. Therefore, the toxicity of this product is as above. Since the acute toxicity is high, in particular after dermal exposure, the product may be harmful to human beings. Special equipment such as a respirator and gas cartridge are prescribed in the safety directions and use is restricted to accredited fumigators. Under these conditions of use, an unintended effect that is harmful to any animal, plant, or thing or to the environment is unlikely.

Acute studies on a formulation, similar to the C-35 products, have been evaluated in the Department of Health. In rats, LD_{50} values were 304 mg/kg by the oral route and <500 mg/kg by the dermal route, and the LC_{50} was 477 mg/m^3. Skin irritation was severe in rabbits. It would appear that the presence of chloropicrin increases the inhalation and irritation hazards. Since the acute toxicity is high, in particular after dermal and inhalation exposure, the product may be harmful to human beings. Special equipment such as a respirator and gas cartridge are prescribed in the safety directions and use is restricted to accredited fumigators. Under these conditions of use, an unintended effect that is harmful to any animal, plant, or thing or to the environment is unlikely.

Recommendations:

- Because the products may have an effect that is harmful to human beings and special knowledge and equipment are required to use the products safely, Telone Soil Fumigant, Telone C-35 Soil Fumigant and Rural Telone C-35 Soil Fumigant meet three of the RCP criteria.

ETHYLENE OXIDE

S7

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

Assessment reports from the Department of Health[13] were available as were a number of international reviews[14,15,16].

Acute:	The oral LD_{50} values were 72–383 mg/kg in rats and mice and the inhalation LC_{50} values were 1500–2630 mg/m^3 in rats, mice and dogs. Humans exhibited signs of neurological disturbances, respiratory distress and in some cases peripheral neuropathy.
Repeat-dose:	Marked signs of neurotoxicity and degeneration of nerve tissue have been observed in all exposed species including humans. Other effects in rodents included pulmonary inflammation, anaemia and adrenal hyperplasia after inhalation exposure. The NOEL by inhalation in animals was approximately 200 mg/m^3.
Carcinogenicity/Genotoxicity:	Ethylene oxide was carcinogenic at multiple sites in rodents and has been associated with neoplasia in humans. It has demonstrated alkylating properties and was genotoxic in animals and humans.
Reproduction/Developmental:	Fertility was impaired in rats but foetal development was unaffected. Increased spontaneous abortion has been associated with occupational exposures.
Other:	Ethylene oxide is extremely irritant, highly reactive and flammable.
Conclusion:	Acute toxicity is high. Ethylene oxide is genotoxic and carcinogenic in humans and is a reproductive toxin.

13 Unpublished confidential reports

14 Anon (1994) Ethylene oxide. International Agency for Research on Cancer Summary and Evaluation, Volume 60.

15 Liteplo, R.G., Meek, M.E. and Lewis, M. (2003) Ethylene oxide. Concise International Chemical Assessment Document 54.

16 Anon (1988) Ethylene oxide Health and Safety Guide 16, International Programme on Chemical Safety, World Health Organization, Geneva.

Environmental issues:

Detailed assessment has not been undertaken; however, there are no strong reasons to suspect an impact on the environment. The requirement for special equipment and training in the use of such products to ensure human safety may also assist in protection of the environment.

Products:

Three registered products.
Fumigas 900 Fumigant (41087)
Fumigas 1000 Fumigant (41088)
Fumigas Non-flammable Fumigant (53895)

Assessment:

Fumigas 1000, 900 and Non-flammable contain 100 per cent, 90 per cent and 9 per cent ethylene oxide, respectively. The remainder is carbon dioxide. The products are presented as compressed gases for use in fumigation. The 90 and 100 per cent formulations are expected to have high acute toxicity and there is the possibility of formation of tumours, reproductive abnormalities and neurological disorders. The 9 per cent formulation is expected to have moderate acute toxicity. However, there is the possibility of formation of tumours because there may be no threshold for a substance which is a genotoxic carcinogen in humans. All three products may be harmful to human beings and all forms of exposure should be avoided. Special equipment is employed in the use of these products and under these conditions, an unintended effect that is harmful to any animal, plant, or thing or to the environment is unlikely.

Recommendations:

- Because the products may have an effect that is harmful to human beings and special equipment is required to use the products safely, Fumigas 1000 Fumigant, Fumigas 900 Fumigant and Fumigas Non-flammable Fumigant meet two of the RCP criteria.

METHOXYETHYLMERCURIC CHLORIDE

S7

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

A brief assessment report from the Department of Health[17] was available.

Acute:	The oral LD_{50} values were 22mg/kg in rats and 47 mg/kg in mice.
Repeat-dose:	Following intraperitoneal injection in rats, behavioural and neurological signs and kidney damage were observed at doses as low as 0.17 mg/kg/day. In humans, mercury toxicity included muscular tremors and gingivitis.
Carcinogenicity/Genotoxicity:	There was no evidence for carcinogenicity of mercury in limited animal studies. No genotoxic activity was seen in Drosophila. Mercury compounds are thought to be able to disrupt the mitotic spindle apparatus.
Reproduction/Developmental:	Retarded development of learning and motor skills was observed in young offspring of treated rats at oral doses as low as 0.62 mg/kg/day.
Other:	Inorganic mercury compounds are rapidly absorbed in rodents and transformed to mercury which accumulates in the kidney and may enter the CNS and placenta.
Conclusion:	Acute toxicity is very high. Prolonged exposure to mercury compounds may lead to accumulation resulting in kidney damage and neurotoxicity. Developmental deficits may occur in offspring. Carcinogenicity and genotoxicity potential are low.

17 Unpublished confidential report

Environmental issues:

There are general environmental concerns regarding the use of mercury-containing substances as pesticides.

Products:

One registered product.
Shirtan Liquid Fungicide (49572)

Assessment:

Using a linear extrapolation, the approximate oral LD_{50} is likely to be 125 mg/kg, and the dose of product which may lead to developmental toxicity is 3.5 mg/kg. The acute toxicity is expected to be high, in particular after oral exposure. The product may be harmful to human beings. There are significant potential environmental hazards.

Recommendation:

- Because the product may have an effect that is harmful to human beings and may have an unintended effect that is harmful to any animal, plant or thing or to the environment, Shirtan Liquid Fungicide meets two of the RCP criteria.

METHYL BROMIDE

S7

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

Assessment reports from the Department of Health[18] and published reviews[19,20] were available.

Acute:	The oral LD_{50} in rats was 214 mg/kg and the inhalation LC_{50} in rats was 3026 mg/m^3. It was highly irritating to mucous membranes. In human poisoning cases, symptoms included respiratory distress, intestinal disturbances, neurological disorders and skin irritation. The lowest toxic dose in humans was 140 mg/m^3.
Repeat-dose	Cellular damage to neurones, heart, adrenal cortex and testes and neurological signs were seen following inhalation exposure in animals. The NOEL was 130 mg/m^3 in monkeys. Oral dosing of rats resulted in atrophy and ulceration of stomach mucosa.
Carcinogenicity/Genotoxicity:	No tumour induction was seen in rodents. Positive genotoxicity results were obtained in *in vitro* assays but not in *in vivo* studies.
Reproduction/Developmental:	No reproduction or developmental effects were observed in animals.
Other:	Fumigators have exhibited a variety of neurological deficits following long-term exposure to low levels.
Conclusion:	Acute toxicity is high. The potential for carcinogenic, genotoxic and reproduction toxicity is low.

18 Unpublished confidential reports

19 Anon (1995) Methyl bromide. Environmental Health Criteria 166, International Programme on Chemical Safety, World Health Organization, Geneva.

20 Anon (2002) Methyl bromide. OECD Screening Information Data Set accessed at http://www.inchem.org/documents/sids/sids/methbrom.pdf

Environmental issues:

Under the Montreal Protocol on Substances that Deplete the Ozone layer, Australia has obligations to limit and phase out the use of methyl bromide**.** Therefore, the labels of methyl bromide-containing products are currently being revised to retain only quarantine uses. While control of use of methyl bromide products under general registration is considered necessary from an environmental perspective, limitation of its use to AQIS only is considered to represent sufficient restriction.

Products:

Eighteen registered products.
Agrigas M Methyl Bromide Fumigant (32106)
Agrigas MC Methyl Bromide Fumigant (34060)
AIC Bromo-Chlor 700-300 (34059)
Dibbs Brom-O-Gas 980 Fumigant (41394)
Dibbs Brom-O-Gas 1000 Fumigant (41390)
Nufarm Bromopic 700:300 Soil Fumigant (41488)
Nufarm Fungafume Soil Fumigant (51125)
Nufarm Methyl Bromide 980 Fumigant (34066)
Nufarm Methyl Bromide 1000 Fumigant (34067)
Nufarm Vertafume Soil Fumigant (51126)
Rural Methyl Bromide 1000 Fumigant (53267)
Rural Soil Fumigant 300-700 (51207)
Rural Soil Fumigant 500-500 (51208)
SA Rural Methyl Bromide 980 Fumigant (41303)
Southern Cross Methyl Bromide 980 Fumigant (58001)
Southern Cross Methyl Bromide 1000 Fumigant (52781)
Southern Cross Soil Fumigant 500-500 (59240)
Southern Cross Soil Fumigant 700-300 (59241)

Assessment:

Ten products contain predominantly methyl bromide with up to 2 per cent chloropicrin. These products are likely to mimic the toxicity of methyl bromide which has high acute toxicity, in particular after inhalation exposure. The products may be harmful to human beings. Special equipment such as a respirator and gas canister are prescribed in the safety directions. Methyl bromide-containing products are restricted to quarantine uses and AQIS has control measures in place to limit environmental contamination.

Eight products contain a mixture of chloropicrin and methyl bromide in the ratios 7:3, 1:1, and 3:7. Since both ingredients have high or very high acute toxicity, the acute toxicity of the products is high to very high, particularly after inhalation exposure. The products may be

harmful to human beings. Special equipment such as a respirator and gas canister are prescribed in the safety directions and the operator is referred to State/Territory regulations for safe use. Methyl bromide-containing products are restricted to quarantine uses and AQIS has control measures in place to limit environmental contamination.

Recommendations:

- Because the products may have an effect that is harmful to human beings, and special equipment is required to use the products safely, Agrigas M Methyl Bromide Fumigant, Nufarm Methyl Bromide 1000 Fumigant, Dibbs Brom-O-Gas 1000 Fumigant, Southern Cross Methyl Bromide 1000 Fumigant, Rural Methyl Bromide 1000 Fumigant, Agrigas MC Methyl Bromide Fumigant, Nufarm Methyl Bromide 980 Fumigant, SA Rural Methyl Bromide 980 Fumigant, Dibbs Brom-O-Gas 980 Fumigant, Southern Cross Methyl Bromide 980 Fumigant, AIC Bromo-Chlor 700-300, Nufarm Bromopic 700:300 Soil Fumigant, Southern Cross Soil Fumigant 700-300, Nufarm Fungafume Soil Fumigant, Rural Soil Fumigant 300-700, Nufarm Vertafume Soil Fumigant, Rural Soil Fumigant 500-500 and Southern Cross Soil Fumigant 500-500 meet two of the RCP criteria.

MIREX

S7

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

A Department of Health assessment report was not available. The information below was obtained from minutes of the August 1980 NDPSC and a review by the International Agency for Research on Cancer (IARC)[21].

Acute:	The oral LD_{50} was 300–600 mg/kg in rats, and 2.5 mg/kg bw in the diet was lethal to dogs.
Repeat-dose:	Marked cumulative toxicity was seen in rodents, especially in the liver at doses down to 25 ppm.
Carcinogenicity/Genotoxicity:	Mirex was hepatocarcinogenic in rats and mice, and negative for dominant lethal effects in mice.
Reproduction/Developmental:	Fertility was reduced in reproduction studies. Foetal development was affected in treated rats.
Other:	In one study, chronic dietary consumption resulted in tissue accumulation of up to 120 times the intake level.
Conclusion:	Although the NDPSC concluded that mirex is carcinogenic, teratogenic and accumulative, the minutes contained no details of these studies. Mirex was last considered by NDPSC in May 1984. Since that time, further data may have become available on the toxicology of mirex.

Environmental issues:

Mirex is extremely persistent in the environment. It has been declared as a Persistent Organic Pollutant which requires a phase-out of use by 2009. The only registration of a product containing mirex (Mirant), which had a minor use in bait stations in the Northern Territory, has lapsed and its use has ceased.

Products:

No registered product.

21 Anon (1979) Mirex. Monographs on the evaluation of the carcinogenic risk of chemicals to humans. 20: 283–301. International Agency for Research on Cancer, World Health Organization, Lyon, France.

PHOSPHIDES, METALLIC

S7

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

Assessment reports from the Department of Health[22] were available.

Acute:	Oral LD_{50} values were 20–70 mg/kg in rats for zinc phosphide and 8.9 mg/kg for aluminium phosphide. Dermal LD_{50} values were 2000–5000 mg/kg in rabbits for zinc phosphide. The average fatal dose in human poisoning incidents was 51 g zinc phosphide. Toxic signs included shock and respiratory distress. Numbness and paraesthesia may be experienced after touching tablets.
Repeat-dose:	Reduced growth rate, signs of neurotoxicity, liver damage and anaemia were observed in rats after oral exposure to zinc phosphide at doses down to 5 mg/kg bw.
Carcinogenicity/Genotoxicity:	There were equivocal findings for cytogenetic effects in mice.
Reproduction/Developmental:	No information.
Other:	Metal phosphides are partially absorbed intact and then hydrolysed to phosphine which is released in expired air. Zinc phosphide does not release phosphine as readily as aluminium phosphide.
Conclusion:	Acute toxicity is very high for both metal phosphides.

Environmental issues:

In the case of metallic phosphides, there are insufficient environmental concerns to warrant additional controls.

22 Unpublished confidential reports

Products:

Twenty-one registered products.
Celphide Fumigation Blanket (45391)
Celphide Fumigation Pellets (46118)
Celphide Fumigation Tablets (45876)
Chemag Fostoxin Fumigation Tablets (49398)
CM Alphos Fumigation Pellets (48803)
CM Alphos Fumigation Tablets (46849)
Farmoz Pestex Fumigation Tablets (49230)
Fumaphos Fumigation Blanket (52019)
Fumaphos Fumigation Tablets (52020)
Fumitoxin Coated Insecticide Tablets (32069)
Genfume AP Fumigation Pellets (58620)
Mouseoff Zinc Phosphide Bait (50532)
Quickphos Fumigation Bags (47323)
Quickphos Fumigation Bags-Chain (49743)
Quickphos Fumigation Blanket (47322)
Quickphos Fumigation Pellets (47152)
Quickphos Fumigation Tablets (46948)
Rentokil Gastion Phosphine Fumigation Belt (46212)
Rentokil Gastion Phosphine Fumigation Tablets (32071)
Rentokil Gastion Rabbit Fumigation Tablets (33879)
Sanphos Fumigation Tablets (51900)

Assessment:

There are 20 products containing aluminium phosphide, the lowest concentration being 560 mg/kg, which generates 330 g/kg of phosphine. Using a linear extrapolation, the approximate oral LD_{50} is likely to be 16 mg/kg for the lowest strength product. All of the products are expected to have very high acute toxicity, in particular after oral and inhalation exposure. They may be harmful to human beings. The method of application includes placement through probes below the surface or under sheeting, and on the surface in gastight enclosures. Great care must be exercised because phosphine gas is released on exposure to moisture. The use of a respirator is specified in the safety directions. Special knowledge is required in the handling of these products and special equipment is necessary to use the products safely. By comparison, the application and/or use of some products are associated with lower risk and as a consequence, no additional chemical-specific training may be justified. Examples include the application of tablets to silos and the use of blankets containing metallic phosphides. An unintended effect of the metallic phosphides that is harmful to any animal, plant, or thing or to the environment is unlikely.

The single zinc phosphide product is used for the control of mice in agricultural situations. Using

a linear extrapolation, the approximate oral LD_{50} is likely to be 800–2800 mg/kg and dermal toxicity would be low. Because of the low levels of zinc phosphide present, phosphine would be released slowly and in low quantities. The acute toxicity of the product is expected to be low to moderate and may not be harmful to human beings. There is low potential for an unintended effect that is harmful to any animal, plant, or thing or to the environment.

Recommendations:

- Because the products may have an effect that is harmful to human beings, special knowledge is required in the application of the products and special equipment is required, Fumitoxin Coated Insecticide Tablets, CM Alphos Fumigation Tablets, CM Alphos Fumigation Pellets, Farmoz Pestex Fumigation Tablets, Rentokil Gastion Phosphine Fumigation Tablets, Rentokil Gastion Rabbit Fumigation Tablets, Rentokil Gastion Phosphine Fumigation Belt, Chemag Fostoxin Fumigation Tablets, Celphide Fumigation Blanket, Celphide Fumigation Tablets, Celphide Fumigation Pellets, Sanphos Fumigation Tablets, Fumaphos Fumigation Blanket, Fumaphos Fumigation Tablets, Genfume AP Fumigation Pellets, Quickphos Fumigation Tablets, Quickphos Fumigation Pellets, Quickphos Fumigation Blanket, Quickphos Fumigation Bags and Quickphos Fumigation Bags (Chain) meet three of the RCP criteria. However, the training requirements in the use of these products that is mandatory in some jurisdictions may be sufficient and additional chemical-specific training may not be justified.

- Because of the low human and environmental health concerns, Mouseoff Zinc Phosphide Bait does not meet any of the RCP criteria.

- The extrapolated acute toxicity of Mouseoff Zinc Phosphide Bait is commensurate with a S6 poisons schedule. The NDPSC may consider amendments which would include grain based products containing 25 g/kg or less of zinc phosphide in S6.

PHOSPHINE

S7

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

Assessment reports from the Department of Health[23] were available.

Acute:	Inhalation LC_{50} values were 11–55 mg/m^3 in rats and 37.5 mg/m^3 in mice. In humans, exposure to 1400 mg/m^3 for 30 minutes has been fatal. Toxic signs included respiratory irritation, neurological and intestinal disturbances.
Repeat-dose:	Reduced growth, anaemia, CNS depression and kidney lesions were observed in rats following inhalation exposure. The NOEL was approximately 1 mg/m^3.
Carcinogenicity/Genotoxicity:	There were no increases in tumours in an inhalation study in rats. No effect was seen in an Ames test but equivocal findings were obtained for cytogenetic damage in human lymphocytes *in vitro* and *in vivo*.
Reproduction/Developmental:	There were no developmental effects in rats in an inhalation study.
Other:	Humans are considered to be more sensitive to phosphine than animals.
Conclusion:	Acute toxicity is very high. Carcinogenicity, genotoxicity and teratology potential are low.

Environmental issues:

There are insufficient environmental concerns to warrant additional controls over the use of phosphine-containing products.

23 Unpublished confidential reports

Products:

Three registered products.
Eco2fume Phosphine Fumigant (50177)
Phosfume Phosphine Fumigant (45730)
Vaporphos Phosphine Fumigant (51209)

Assessment:

The Vaporphos product consists of phosphine as the only ingredient. Therefore, the product has very high acute toxicity, in particular after inhalation exposure. It may be harmful to human beings. The product is supplied in the form of a liquefied compressed gas in high pressure cylinders and is highly flammable. Special knowledge would be necessary to control the rate of treatment during the fumigation process, and the use of a respirator is prescribed in the safety directions. An unintended effect that is harmful to any animal, plant, or thing or to the environment is unlikely.

Phosfume and Eco2fume contain only 2 per cent phosphine. Using a linear extrapolation the approximate inhalation LC_{50} values are likely to be 550–2750 mg/m^3. The products are expected to have high acute toxicity, in particular after inhalation exposure. They may be harmful to human beings. The products are supplied in the form of a liquefied compressed gas in high pressure cylinders and are designed to be distributed via a gastight system. Therefore, special knowledge and special equipment are necessary in the application of the products. An unintended effect that is harmful to any animal, plant, or thing or to the environment is unlikely.

Recommendations:

- Because the products may have an effect that is harmful to human beings, special knowledge is required in the application of the products and special equipment is required, Vaporphos Phosphine Fumigant, Phosfume Phosphine Fumigant and Eco2fume Phosphine Fumigant meet three of the RCP criteria.

STRYCHNINE

S7, except when included in schedule 4

S4, in preparations containing 1.5 per cent or less of strychnine for the treatment of animals

Appendix J statement:

Not to be available except to authorised or licensed persons.

Toxicology of substance:

Brief assessment reports from the Department of Health[24] and an US EPA assessment[25] were available.

Acute:	Oral LD_{50} values were 2.2 mg/kg in rats, 0.93 mg/kg in mice and 0.5 mg/kg in dogs. The dermal LD_{50} was >2000 mg/kg in rabbits. Ocular exposure has caused death in rabbits. A potentially lethal oral dose was 5–10 mg for a small child and 30–120 mg for an adult.
Repeat-dose:	No information.
Carcinogenicity/Genotoxicity:	No information.
Reproduction/Developmental:	No information.
Other:	No information.
Conclusion:	Acute toxicity is extremely high.

Environmental issues:

Because of high toxicity, non-target animals are at risk particularly after misuse of strychnine-containing products. Supply should be restricted to trained operators.

Products:

Two registered products.
Dynamice Mouse Bait (46647)
Strychnine Alkaloid Crystals (42515)

24 Unpublished confidential reports

25 Anon (1988) Strychnine (CASRN 57-24-9), US Environmental Protection Agency; accessed at www.epa.gov/iris/subst/index.html (Chemical Code 0103)

Assessment:

Using a linear extrapolation, the approximate oral LD_{50} is likely to be 125 mg/kg. Dermal exposure should not pose a significant hazard but contact with the eye or open wounds could be dangerous. The products are expected to have high acute toxicity, in particular after oral exposure. The products may be harmful to human beings. Dynamice Mouse Bait may be used around domestic buildings and should be restricted to trained personnel to ensure that applications are conducted in a manner which will ensure no public contact with the baits. Special training for safe and effective use of this product is considered necessary in order to prevent an unintended effect that is harmful to any animal, plant, or thing or to the environment. The use of Strychnine Alkaloid Crystals is restricted to Western Australia where it is applied to animal traps. Adequate controls on its use are already in place; these include listing in the Western Australia Poisons Act of those shires where its use is permitted; a Code of Practice for use of the product; and restriction of use of the product to approved persons.

Recommendation:

- Because the product may have an effect that is harmful to human beings and may have an unintended effect that is harmful to any animal, plant or thing or to the environment, and special knowledge is required in the application of the product, Dynamice Mouse Bait meets three of the RCP criteria.

- The use of Strychnine Alkaloid Crystals is restricted to Western Australia and the existing controls on such use are sufficient. Therefore, the product may not require declaration as a RCP.