Australian Government
Department of Health
Therapeutic Goods Administration

Notification of amendments to the Poisons Standard in relation to New Chemical Entities (NCEs) and Delegate-only decisions

24 January 2022

TGA Health Safety Regulation

Contents

1 Notice of Decisions to amend the current Poisons Standard

This web publication constitutes a notice for the purposes of regulation 42ZCZX of the *Therapeutic Goods Regulations 1990* (the Regulations). In accordance with regulations 42ZCZX, this notice publishes the:

- decisions made by a delegate of the Secretary pursuant to regulations 42ZCZU;
- reasons for those final decisions; and
- date of effect of those decisions.

2 Amendments to the Poison Standard in relation to New Chemical Entities (NCEs)

The NCEs listed below will be included in the new Poisons Standard that will come into effect on **1 February 2022**.

2.1 Infigratinib

Recommendation

Schedule 4 - New Entry

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INFIGRATINIB

Schedule 4

2.2 Ponesimod

Recommendation

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Appendix L − New Entry

PONESIMOD − Warning statement 76 (Do not become pregnant during use or within (Insert number of months as per approved Product Information) month(s) of stopping treatment.)

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2.3 Selumetinib

Recommendation

Schedule 4 - New Entry

SELUMETINIB

Appendix L – New Entry

SELUMETINIB – Warning statement 76 (Do not become pregnant during use or within (Insert number of months as per approved Product Information) month(s) of stopping treatment.)

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SELUMETINIB

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2.4 Sotorasib

Recommendation

Schedule 4 - New Entry

SOTORASIB

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SOTORASIB

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2.5 Molnupiravir

Recommendation

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2.6 Selinexor

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SELINEXOR

Appendix L – New Entry

SELINEXOR – Warning statements 62 (Do not use if pregnant.) and 77 (WARNING – May cause birth defects.)

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SELINEXOR

Schedule 4
Appendix L, Part 2

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Recommendation

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TEPOTINIB

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TEPOTINIB

Schedule 4

2.8 Nirmatrelvir

Recommendation

Schedule 4 - New Entry

NIRMATRELVIR

Index - New Entry

NIRMATRELVIR

Schedule 4

3 Amendments to the Poisons Standard made as delegate-only decisions

3.1 Final decision in relation to gliptins

Final decision

Pursuant to regulation 42ZCZU of the *Therapeutic Goods Regulations 1990* (Cth) (the **Regulations**) a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to gliptins as follows:

Schedule 4 – New entry

GLIPTINS **except** when separately specified in these Schedules.

Index – New entry

GLIPTINS

Schedule 4

Materials considered

In making this final decision, the Delegate considered the following material:

- Subsection 52E(1) of the *Therapeutic Goods Act 1989* (Cth) (the **Act**), in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (e) the potential for abuse of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.
- Pursuant to paragraph 52E(2)(a) of the Act, the Scheduling Policy Framework 2018 (**SPF**); and
- The Scheduling handbook: Guidance for amending the Poisons Standard (the **Handbook**).

Reasons for the final decision (including findings on material questions of fact)

This proposal to amend the Poisons Standard was made on my own initiative. In determining that this matter will be a Delegate-only decision I have taken into account the matters outlined under section 52E of the Act and the SPF. In particular, I note that:

- In relation to paragraphs 52E(1)(a), (b) and (c) of the Act, gliptins are a class of glucagon inhibitor used in medicines for the medical management of diabetes. Some substances from this class are individually included in Schedule 4 of the Poisons Standard including alogliptin, linogliptin, saxagliptin, sitagliptin and vildagliptin.
- In relation to paragraphs 52E(1)(a) and (c) of the Act, the substances in this class have similar toxicology profiles, yet some of the known substances in this class are yet to be placed in the Poisons Standard. Given the similarity in the toxicological profiles of medicines in this class, access to unscheduled gliptins through importation and other means poses an unacceptable risk to public health. I have therefore decided to create a new group entry in Schedule 4. The new group entry will include an exemption for gliptins that are specified

separately within the Poisons Standard, to avoid confusion and pre-empt any potential listing for a substance in this class outside Schedule 4.

- In relation to paragraphs 52E(1)(e) and (f) of the Act, this new group entry will aid customs and enforcement bodies in the assessment of the restrictions on imported products containing gliptins that are not specifically listed in the Poisons Standard.

Therefore, I have decided to amend the current Poisons Standard in the manner outlined above. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.2 Final decision in relation to isotianil

Final decision

Pursuant to regulation 42ZCZU of the Regulations a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to isotianil as follows:

Schedule 6 – New Entry

ISOTIANIL

Index – New Entry

ISOTIANIL

Schedule 6

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to isotianil;
- Subsection 52E(1) of the Act, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the applicant (Australian Pesticides and Veterinary Medicine Authority (APVMA)), and the matters outlined under section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a) of the Act, the proposed amendment to the Poisons Standard is to include a new entry for isotianil in Schedule 6, based upon benefits to the agricultural industry from the introduction of a novel fungicide. In its application the regulator (APVMA) provided a Human Health Risk Assessment (HHRA) which concluded that the risks to human health and safety posed by this substance are acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act (1994)*.
- In relation to paragraph 52E(1)(b) of the Act, isotianil is a fungicide of the thiadiazole-carboxyamide chemical class. No other active constituent in the same class has been approved or considered in Australia. The substance and the formulation for a product containing isotianil are registered in Japan, Korea, Taiwan, Vietnam, the Dominican Republic, Honduras and Guatemala for the control of rice blast and/or for use on banana crops.
- In relation to paragraph 52E(1)(c) of the Act, the application provided data for a product containing isotianil 200g/L, which indicated that the toxicity profile is consistent with a Schedule 6 entry based on its potential for causing skin sensitisation. The data indicate that isotianil is of low acute toxicity by the oral route (LD_{50} >5000 mg/kg bw in rats), dermal route (LD_{50} >2000 mg/kg bw in rats), and inhalation (LC_{50} >4600 mg/m^3 in rats). Isotianil is not an eye or skin irritant based on tests on rabbits, but was shown to be sensitising to the skin in guinea pigs and mice. An acceptable daily intake (ADI) for isotianil of 0.03 mg/kg bw/day has been established by the APVMA.
- In relation to paragraphs 52E(1)(c), (d) and (e) of the Act, an exposure assessment for users of the formulated product was conducted and was found to have acceptable margins of exposure for workers wearing a single layer of clothing. Consideration of potential exposure to bystanders during application indicated a low risk.
- I am satisfied that, for the purposes of paragraph 52E(1)(d) of the Act, the regulator (APVMA) will consider the dosage, formulation, labelling, packaging and presentation of any commercial products.
- In relation to paragraph 52E(1)(e) of the Act, the substance has no human therapeutic value that would indicate a risk for diversion, misuse or abuse.

On the basis of the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner set out in the application. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.3 Final decision in relation to chromium trichloride hexahydrate

Final decision

Pursuant to regulation 42ZCZU of the Regulations a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to chromium trichloride hexahydrate as follows:

Schedule 6 – New Entry

CHROMIUM TRICHLORIDE HEXAHYDRATE **except** in preparations containing 0.5 per cent or less chromium.

Index – New Entry

CHROMIUM TRICHLORIDE HEXAHYDRATE

Schedule 6

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to chromium trichloride hexahydrate;
- Subsection 52E(1) of the Act, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the applicant (Australian Pesticides and Veterinary Medicine Authority (APVMA)), and the matters outlined under Section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a) of the Act, the proposed amendment to the Poisons Standard is to include a new entry for chromium trichloride hexahydrate in Schedule 6, based upon benefits to the agricultural industry from the introduction of a parenteral nutritional supplement for use in cattle. In its application, the regulator (APVMA) provided a Human Health Risk Assessment (HHRA) which concluded that the risks to human health and safety posed by this substance are acceptable according to the criteria stipulated in section 5A of the *Agricultural and Veterinary Chemicals Code Act (1994)*.
- In relation to paragraph 52E(1)(b) of the Act, trivalent chromium (Cr (III)), as is found in chromium trichloride hexahydrate, is an essential element in both animal and human nutrition. Parenteral supplementation in animals for example, is used to optimise chromium trace element levels in cattle at critical growth and development stages such as calving, joining and drying off.

- In relation to paragraph 52E(1)(c) of the Act, the application provided data which indicate that the toxicity profile is consistent with a Schedule 6 entry, based on its potential for causing skin and eye sensitisation. The data indicate that chromium (III) is of low to moderate acute oral toxicity (LD_{50} 440 – 1970 mg/kg bw in rats), low acute dermal toxicity (LD_{50} >2000 mg/kg bw in rats) and low acute inhalational toxicity. It is likely to be a moderate to severe eye irritant, a slight skin irritant and may cause allergic skin reactions, based on tests on rabbits.
- The application also provided information that indicated that based on the use of chromium (III) as chromium trichloride hexahydrate in various unscheduled oral and parenteral preparations for therapeutic use in humans, and the overall low toxicity of an animal nutritional preparation containing 0.5% w/v chromium (III) as chromium trichloride hexahydrate, a concentration cut-off to unscheduled at 0.5% w/v could be supported.
- In relation to paragraph 52E(1)(c) of the Act, chromium (VI) is highly toxic, but there is no evidence that chromium (III) is transformed to chromium (VI) in biological systems. There are no reports of adverse reproductive outcomes in humans associated with chromium (III), although there is limited evidence of *in vitro* genotoxicity (but not *in vivo*). There are a few cases of chromium (III) toxicity in humans that have been reported in the literature. Those that were reported, resulted from overconsumption of nutritional supplements, with full recovery achieved in each case after treatment.
- I am satisfied that, for the purposes of paragraph 52E(1)(d) of the Act, the regulator (APVMA) will consider the dosage, formulation, labelling, packaging and presentation of any commercial products (52E(1)(d)).
- In relation to paragraph 52E(1)(e) of the Act, the substance has no human therapeutic value that would indicate a risk for diversion, misuse or abuse.

On the basis of the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner set out in the application. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.4 Final decision in relation to metobromuron

Final decision

Pursuant to regulation 42ZCZU of the Regulations a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to metobromuron as follows:

Schedule 5 – New Entry

METOBROMURON **except** in preparations containing 50 per cent or less of metobromuron.

Index – New Entry

METOBROMURON

Schedule 5

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to metobromuron;
- Subsection 52E(1) of the Act, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the applicant (Australian Pesticides and Veterinary Medicine Authority (APVMA)), and the matters outlined under Section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a) of the Act, the proposed amendment to the Poisons Standard is to include a new entry for metobromuron in Schedule 5, based upon benefits to the agricultural industry from the introduction of a new herbicide. In its application the regulator (APVMA) provided a Human Health Risk Assessment (HHRA) which concluded that the risks to human health and safety posed by this substance are acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act (1994)*.
- In relation to paragraph 52E(1)(b)(c) and (d) of the Act, metobromuron inhibits photosynthesis and is used commercially for control of weeds on potato crops. Metobromuron is chemically related to several herbicides which are approved for agricultural use in Australia and already listed in the Poisons Standard, including diuron, fluometuron and linuron in Appendix B, and siduron in Schedule 5.
- In relation to paragraph 52E(1)(c) of the Act, the application provided data for a product containing metobromuron 500g/L (i.e. 50 per cent), which indicated that the toxicity profile is consistent with a Schedule 5 entry. Metobromuron has low acute toxicity via the oral (LD_{50} 2603 mg/kg bw), dermal (LD_{50} >3000 mg/kg bw) and inhalation (LC_{50} >1597 mg/m^3) routes in rats. It is not an eye or skin irritant but was found to be a skin sensitiser in the guinea pig maximisation test. Metobromuron is not a developmental or reproductive toxin and was not found to be genotoxic in a battery of *in vivo* and *in vitro* assays. The substance was not found to be carcinogenic in long-term studies in mice and rats. The toxicity data associated with a formulated product indicate that a scheduling cut-off for products containing 50 per cent or less of metobromuron is appropriate.
- I am satisfied that, for the purposes of paragraph 52E(1)(d) of the Act, the regulator (APVMA) will consider the dosage, formulation, labelling, packaging and presentation of any commercial products.
- In relation to paragraph 52E(1)(e) of the Act, the substance has no human therapeutic value that would indicate a risk for diversion, misuse or abuse.

On the basis of the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner set out in the application. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.5 Final decision in relation to kinetin

Final decision

Pursuant to regulation 42ZCZU of the Regulations a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to kinetin as follows:

Appendix B – New Entry

Substance	Date of entry	Reason for listing	Area of use
KINETIN	February 2022	a	1.6

Index – New Entry

KINETIN

Appendix B, Part 3

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to kinetin;
- Subsection 52E(1) of the *Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the applicant (Australian Pesticides and Veterinary Medicine Authority (APVMA)), and the matters outlined under Section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a) of the Act, the proposed amendment to the Poisons Standard is to include a new entry for kinetin in Appendix B, thereby exempting the substance from any requirements that are imposed by scheduling, based upon benefits to the agricultural industry from the introduction of a new plant growth regulator. In its application the regulator (APVMA) provided a Human Health Risk Assessment (HHRA)

which concluded that the risks to human health and safety posed by this substance are acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act (1994)*.

- In relation to paragraph 52E(1)(b) of the Act, kinetin is a synthetic form of cytokinin and is classified in Australia as a plant growth regulator. The substance has not previously been considered for inclusion in the Poisons Standard.
- In relation to paragraph 52E(1)(c) of the Act, the application provided data for kinetin which indicated that the toxicity profile is not consistent with inclusion into the Schedules, based on its very low acute oral toxicity (LD_{50} > 5000 mg/kg bw), low dermal toxicity (LD_{50} > 5000 mg/kg bw), and low inhalational toxicity (LC_{50} > 2.09 mg/L/3h). While kinetin is a slight eye irritant, it is not a skin irritant or sensitiser.
- I am satisfied that, for the purposes of paragraph 52E(1)(d) of the Act, the regulator (APVMA) will consider the dosage, formulation, labelling, packaging and presentation of any commercial products.
- In relation to paragraph 52E(1)(e) of the Act, the substance has no human therapeutic value that would indicate a risk for diversion, misuse or abuse.

On the basis of the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner set out in the application. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.6 Final decision in relation to iron compounds

Final decision

Pursuant to regulation 42ZCZU of the Regulations a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to iron compounds as follows:

Schedule 5 – Amend entry

IRON COMPOUNDS:

a) for the treatment of animals (excluding up to 1 per cent of iron oxides when present as an excipient):

   i) in preparations for injection containing 20 per cent or less of iron **except** in preparations containing 0.1 per cent or less of iron; or

   ii) in other preparations containing 4 per cent or less of iron **except**:

      A. in liquid or gel preparations containing 0.1 per cent or less of iron; or

      B. in animal feeds or feed premixes; or

b) ~~in~~ for use as agricultural chemicals ~~garden preparations~~ **except** in preparations containing 4 per cent or less of iron.

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to iron compounds;
- Subsection 52E(1) of the *Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the Applicant (Australian Pesticides and Veterinary Medicine Authority (APVMA)), and the matters outlined under Section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a)and (b) of the Act, the proposed amendment to the Poisons Standard is to expand the existing Schedule 5 entry for iron compounds to capture 'professional agricultural products' such as snail baits that may not currently be considered subject to scheduling control. In its application the regulator (APVMA) stated that the current Schedule 5 entry was created to capture available products at that time, and that a recent review identified a new product which is not currently subject to scheduling controls but which contains between 5-20% elemental iron.
- In relation to paragraph 52E(1)(c) of the Act, the application provided data for iron compounds which indicated that the toxicity profile is consistent with inclusion into Schedule 5 when the concentration of iron is greater than 4 per cent. Of particular concern is the accidental consumption of products containing iron compounds by young children. The acute toxic dose of iron in infants is considered to be approximately 20 mg/kg bw associated with gastrointestinal irritation, whilst systemic effects do not generally occur at doses < 60 mg/kg bw. The lethal dose in children is approximately 200-300 mg/kg bw.
- I am satisfied that, for the purposes of paragraph 52E(1)(d) of the Act, the regulator (APVMA) will consider the dosage, formulation, labelling, packaging and presentation of any commercial products.
- In relation to paragraph 52E(1)(e) of the Act, the potential for misuse or abuse of the substance is unchanged from previous considerations.

Therefore, based on the information provided in the application I have decided to address the inconsistency in the current scheduling for iron compounds by including professional agricultural preparations containing greater than 4 per cent of iron in the existing Schedule 5 entry. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 June 2022

3.7 Final decision in relation to rescalure

Final decision

Pursuant to regulation 42ZCZU of the Regulations a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to rescalure as follows:

Schedule 6 – New entry

RESCALURE for agricultural use **except** when enclosed in a vapour releasing device which in normal use prevents access to its contents.

Index – New entry

RESCALURE
cross reference: (3S,6R)-(3S,6S)-6-isopropenyl-3-methyldec-9-en-1-yl acetate

Schedule 6

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to rescalure;
- Subsection 52E(1) of the *Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;
- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the applicant (Australian Pesticides and Veterinary Medicine Authority (APVMA)), and the matters outlined under Section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a) of the Act, the proposed amendment to the Poisons Standard is to include a new entry for rescalure in Schedule 6, based upon benefits to the agricultural industry from the introduction of a new pesticide. In its application the regulator (APVMA) provided a Human Health Risk Assessment (HHRA) which concluded that the risks to human health and safety posed by this substance are acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act (1994)*.
- In relation to paragraph 52E(1)(b) of the Act, rescalure is a synthetic arthropod pheromone commercialised as a control for the California Red Scale pest in citrus and other crops. Rescalure is authorised for use in the USA, EU and Uruguay.
- In relation to paragraph 52E(1)(e) of the Act, the application provided data for rescalure which indicated that the toxicity profile is consistent with inclusion into Schedule 6, based

on its low acute oral (LD_{50} > 5000 mg/kg bw), dermal (LD_{50} > 5000 mg/kg bw) and inhalational toxicity[1]. Rescalure is an eye irritant, a weak skin sensitiser and does not appear to cause skin irritation. The risk of genotoxicity appears to be negligible.

- I am satisfied that, for the purposes of paragraph 52E(1)(d) of the Act, the regulator (APVMA) will consider the dosage, formulation, labelling, packaging and presentation of any commercial products. The product whose details are included in the application consists of a small reservoir containing the active constituent within a plastic dispenser, which are suspended from tree branches.
- The substance has no human therapeutic value that would indicate a risk for diversion, misuse or abuse.

Therefore, based on the information provided in the application, I have decided to amend the current Poisons Standard in the manner set out in the application. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.8 Final decision in relation to fluoxapiprolin

Final decision

Pursuant to regulation 42ZCZU of the Regulations a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to fluoxapiprolin as follows:

Appendix B – New entry

Substance	Date of entry	Reason for listing	Area of use
FLUOXAPIPROLIN	February 2022	a	1.3

Index – New entry

FLUOXAPIPROLIN

Appendix B, Part 3

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to fluoxapiprolin;
- Subsection 52E(1) of the *Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance;

[1] The applicant reported an LC_{50} >5000 mg/m^3 from a QSAR (*in silico*) extrapolation. Although this extrapolation was not in the submitted data, it was reported in EFSA (2015).

- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the Applicant (Australian Pesticides and Veterinary Medicine Authority (APVMA)), and the matters outlined under Section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a) of the Act, the proposed amendment to the Poisons Standard is to include a new entry for fluoxapiprolin in Appendix B, thereby exempting the substance from any requirements that are imposed by scheduling, based upon benefits to the agricultural industry from the introduction of a novel fungicide. In its application the regulator (APVMA) provided a Human Health Risk Assessment (HHRA) which concluded that the risks to human health and safety posed by this substance are acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act (1994)*.
- In relation to paragraph 52E(1)(b) of the Act, fluoxapiprolin is a fungicide closely related to oxathiapiprolin, which is currently included in Appendix B of the Poisons Standard as a substance considered not to require control through scheduling.
- In relation to paragraph 52E(1)(c) of the Act, the application provided data for a product containing fluoxapiprolin 20 g/L which indicated that the toxicity profile is not consistent with inclusion into the Schedules, based on its very low acute oral, dermal and inhalational toxicity. Fluoxapiprolin is a slight eye irritant, but not a skin irritant or sensitiser, and the applicant concluded that irritation caused was due to excipients in the commercial formulation assessed in the application. Fluoxapiprolin has not demonstrated developmental or reproductive toxicity, is not neurotoxic, and is not a human-relevant carcinogen at expected exposure levels.
- In relation to paragraph 52E(1)(d) of the Act, the substance is the active constituent of a new product that is proposed for the control of downy mildew on grapes, intended for application by airblast or hand-held spray equipment. Use of the substance, and therefore potential exposure, is considered to be discontinuous, seasonal and of short duration.
- In relation to paragraph 52E(1)(e) of the Act, the substance has no human therapeutic value that would indicate a risk for diversion, misuse or abuse.

On the basis of the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner set out in the application. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.9 Final decision in relation to disodium manganese EDTA

Final decision

Pursuant to regulation 42ZCZU of the Regulations, a Delegate of the Secretary has made a final decision to amend the current Poisons Standard in relation to disodium manganese EDTA as follows:

Appendix B – New Entry

Substance	Date of entry	Reason for listing	Area of use
DISODIUM MANGANESE EDTA	February 2022	a	2.1

Index – New Entry

DISODIUM MANGANESE EDTA

Appendix B, Part 3

Materials considered

In making this final decision, the Delegate considered the following material:

- The application to amend the current Poisons Standard with respect to disodium manganese EDTA;
- Subsection 52E(1) of the *Therapeutic Goods Act 1989*, in particular (a) the risks and benefits of the use of a substance; (b) the purposes for which a substance is to be used and the extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (e) the potential for abuse of a substance.
- The SPF, pursuant to paragraph 52E(2)(a) of the Act; and
- The Handbook.

Reasons for the final decision (including findings on material questions of fact)

In determining that this matter will be a delegate-only decision I have taken into account the information provided in the application from the Applicant (APVMA), and the matters outlined under Section 52E of the Act and the SPF. In particular I note that:

- In relation to paragraph 52E(1)(a) and (b) of the Act, the proposed amendment to the Poisons Standard is to include a new entry for disodium manganese EDTA in Appendix B, thereby exempting the substance from any requirements that are imposed by scheduling. The risks to human health and safety from disodium manganese EDTA have been addressed by the regulator (APVMA) in its application that concluded that the human health risk posed by the product is acceptable according to the criteria stipulated in Section 5A of the *Agricultural and Veterinary Chemicals Code Act* (1994).
- In relation to paragraph 52E(1)(c) and (d) of the Act, the applicant provided toxicity data indicating that a product containing 10 mg/mL disodium manganese EDTA for use as a nutritional supplement for injection in cattle to have low acute oral (LD_{50} >2000 mg/kg bw),

dermal (LD_{50} >2000 mg/kg bw) and inhalational (LC_{50} >5000 mg/m^3) toxicity, is a slight to moderate irritant to the eye and skin, and is unlikely to cause allergic skin reactions. It is non-genotoxic and not carcinogenic in studies in mice, rats and dogs. There is no reported evidence of adverse reproductive outcomes in humans.

- In relation to paragraph 52E(1)(e) of the Act, products containing disodium manganese EDTA have negligible potential for abuse. The substance has an established therapeutic value in humans as a nutritional supplement, and there is no associated risk of dependency, abuse, misuse or diversion into illicit use. Products containing manganese for human consumption are available over-the-counter. An equivalent formulation to that outlined in the application is registered for use in cattle in South Africa and New Zealand.

On the basis of the above considerations and the information provided in the application, I have decided to amend the current Poisons Standard in the manner set out in the application. The proposed amendment was not referred to an expert advisory committee.

Date of effect

1 February 2022

3.10 Final decision in relation to deutetrabenazine

Note that final decision on deutetrabenazine inadvertently misspelled the substance name as deutetrabenzine. A delegate-only decision has been made to correct this as follows:

Schedule 4 – Amend Entry

DEUTETRABENAZINE.

Appendix K – Amend Entry

DEUTETRABENAZINE.

Index – Amend Entry

DEUTETRABENAZINE

Schedule 4
Appendix K

Date of effect

1 February 2022