Australian Government
Department of Health
Therapeutic Goods Administration

Notice of final decisions to amend (or not amend) the current Poisons Standard

7 May 2020

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

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

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1 Final decisions made pursuant to regulation 42ZCZR – proposals referred to the November 2019 Advisory Committee on Medicines Schedule (ACMS #28)

1.1. Final decision in relation to Sumatripan

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to vary the interim decision and amend the current Poisons Standard in relation to sumatriptan as follows:

Schedule 4 – Amend Entry

SUMATRIPTAN **except** when included in Schedule 3.

Schedule 3 – New Entry

SUMATRIPTAN when in divided oral preparations containing 50 milligrams or less per dosage unit and when sold in a pack containing not more than 2 dosage units for the acute relief of migraine in patients who have a stable, well-established pattern of symptoms.

Appendix H – New Entry

SUMATRIPTAN

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

I confirm the reasons for my final decision to create a Schedule 3 entry for sumatriptan are as detailed in my interim decision. Further to this, I have decided to vary my interim decision, to take into account dosage units and the specific indication for the acute relief of migraine in patients who have a stable, well-established pattern of symptoms. I consider the indication specific wording of the entry would support the quality use of sumatriptan under a Schedule 3 classification. I also affirm my interim decision to create an Appendix H entry for sumatriptan. In making my final decision, I have taken into account the material detailed in the interim decision and the two submissions received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

While I note the public submission expressing the view that if one triptan is suitable for down-scheduling then it is appropriate for all triptans to be down-scheduled at the same time, this consideration has not been material to my decision. The triptans are listed individually in the Poisons Standard and this current application is for sumatriptan only. As per the requirements of the SPF 2018, each individual substance must be assessed against the Scheduling Factors on their own merits.

Summary of public submissions on the interim decision

In response to the interim decision, two (2) submissions were received. Both submissions supported the interim decision.

The main points provided in support of the interim decision were:

- The submissions provided by industry stakeholders supported the proposed amendments and inclusion within Appendix H.
- One submission agreed the access controls in place for a Schedule 3 medicine are appropriate and sufficient to mitigate the risk of misuse of sumatriptan.
- Both submissions noted that the implementation date of February 2021 was decided by the delegate to allow the opportunity for sponsors to adhere to regulatory change and the opportunity to align labelling requirements to be developed and for the development of education and training material to be provided to pharmacists.
- One submission discussed that if one triptan is suitable for down-scheduling then it would be appropriate for all of the triptans to be down-scheduled at the same time in the absence of evidence that there is a particular reason why one particular triptan does not meet the scheduling criteria.

Date of effect of the decision

1 February 2021

1.2. Final decision in relation to Zolmitriptan

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to vary the interim decision and amend the current Poisons Standard in relation to zolmitriptan as follows:

Schedule 4 – Amend Entry

ZOLMITRIPTAN **except** when included in Schedule 3.

Schedule 3 – New Entry

ZOLMITRIPTAN when in divided oral preparations containing 2.5 milligrams or less per dosage unit and when sold in a pack containing not more than 2 dosage units for the acute relief of migraine in patients who have a stable, well-established pattern of symptoms.

Appendix H – New Entry

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

I confirm the reasons for my final decision to create a Schedule 3 entry for zolmitriptan are as detailed in my interim decision. I have decided to vary the interim decision to take into account dosage units and the specific indication for the acute relief of migraine in patients who have a stable, well-established pattern of symptoms. I consider the indication specific wording of the entry would support the quality use of zolmitriptan under a Schedule 3 classification. I also affirm my interim decision to create an Appendix H entry for zolmitriptan. In making my final decision, I have taken into account the material detailed in the interim decision and the two submissions received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

While I note the public submission expressing the view that if one triptan is suitable for down-scheduling then it is appropriate for all triptans to be down-scheduled at the same time, this consideration has not been material to my decision. The triptans are listed individually in the Poisons Standard and this current application is for sumatriptan only. As per the requirements SPF 2018, each individual substance must be assessed against the Scheduling Factors on their own merits.

Summary of public submissions on the interim decision

In response to the interim decision, two (2) submissions were received. Both submissions supported the interim decision.

The main points provided in support of the interim decision were:

- The submissions provided by industry stakeholders supported the proposed amendments and inclusion within Appendix H.
- One submission agreed the access controls in place for a Schedule 3 medicine are appropriate and sufficient to mitigate the risk of misuse of zolmitriptan.
- Both submissions noted that the implementation date of February 2021, was decided by the delegate to allow the opportunity for sponsors to adhere to regulatory change and the

opportunity to align labelling requirements to be developed and for the development of education and training material to be provided to pharmacists.

Additional comment:

- One submission expressed a view that if one triptan is suitable for down-scheduling then it would be appropriate for all of the triptans to be down-scheduled at the same time in the absence of evidence that there is a particular reason why one particular triptan does not meet the scheduling criteria.
- An implementation date of February 2021 was recommended to the Delegate to consider for any future triptan scheduling applications.

Date of effect of the decision

1 February 2021

1.3. Final decision in relation to Mometasone

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to vary the interim decision and amend the current Poisons Standard in relation to mometasone as follows:

Schedule 4 – Amend Entry

MOMETASONE **except** when included in Schedule 2 or 3.

Schedule 3 – New Entry

MOMETASONE as the only therapeutically active substance in preparations for dermal use containing 0.1 percent or less of mometasone in packs containing 15 g or less.

Schedule 2

MOMETASONE in aqueous nasal sprays delivering 50 micrograms or less of mometasone per actuation when the maximum recommended daily dose is no greater than 200 micrograms for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over.

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MOMETASONE

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

I have decided to vary the ACMS #26 interim decision not to down-schedule mometasone for dermal use from Schedule 4 to Schedule 3 and to introduce an actuation limit for mometasone. I find that mometasone for dermal use meets the Scheduling Factors for Schedule 3 without the requirement for an Appendix M entry; that the introduction of an actuation limit for intranasal mometasone in Schedule 2 is not required; and that in the interests of public safety, mometasone should not be included in Appendix H.

Material considered

In making my final decision, I have taken into account all available information including:

- The application to amend the current Poisons Standard with respect to mometasone;
- Advisory Committee on Medicines Scheduling's advice (ACMS #26 (March 2019) and ACMS #28 (November 2019));
- The public submissions received by the second closing date (ACMS #26);
- The public submissions received by the first closing date (ACMS #28);
- Section 52E 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 (f) any other matters that the Secretary considers necessary to protect public health.;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- Scheduling Handbook (V 1.1, July 2019).

Reasons for the final decision

The reasons for my decision are set out below.

In my view, the relevant parts of the SPF 2018 are the Scheduling Factors for Schedule 3 and the criteria for inclusion of a medicine in Appendix M and Appendix H.

Topical corticosteroids (TCS) are important in the treatment of active corticosteroid-responsive dermatoses, including atopic dermatitis and psoriasis, which may have a fluctuating clinical course requiring access to treatment during periods of increased disease activity. Poor symptom control can result in significant impacts on a person's quality of life.

An application to down-schedule mometasone from Schedule 4 to Schedule 3 in 15 g packs, create a new entry in Appendix M and revise the wording of the Schedule 2 entry for inhaled mometasone to include a limit of 200 actuations per pack was first considered by the ACMS in March 2019.[1] While the amendment to the Schedule 2 entry was supported by the Committee, down-scheduling to Schedule 3 and inclusion in Appendix M were not, in part because it was unclear what additional conditions or controls would be included in Appendix M. As a result, the Applicant was provided an opportunity to address the new Appendix M criteria published in the Scheduling Handbook[2] and provided additional information, including addressing how inclusion of mometasone in Appendix M would mitigate the risks identified to support down-scheduling for consideration at the November 2019 ACMS meeting.

Public submissions were received opposing the down-scheduling of dermal mometasone to Schedule 3. These submissions cited mometasone's high potency and potential for increase in adverse reactions including corticosteroid-induced rosacea (perioral dermatitis) leading to skin atrophy and the theoretical risk of hypothalamic pituitary adrenal (HPA) suppression. In considering TCS, it is important to recognise that potency does not equate to toxicity. The criteria for defining topical corticosteroid potency is based upon vasoconstrictor and skin blanching effects, which are somewhat removed from the systemic corticosteroid effects that constitute the systemic risk. As raised in the public submissions, the higher the corticosteroid potency, the more likely it is that side effects will occur. However, in the case of mometasone, even though it is a potent Class IIT TSC, it has lower systemic toxicity than other TSC and has longer lasting effects. Potential risks associated with dermal mometasone are predominantly related to its inappropriate application such as to the face or for conditions in which topical corticosteroids broadly are contraindicated, not specifically mometasone. While there is a risk of perioral dermatitis and steroid rosacea if mometasone is applied inappropriately to the face, it is my view that there is insufficient evidence to suggest that Schedule 3 availability will necessarily increase this risk. Furthermore, there is no evidence to suggest that the theoretical potential risk of HPA suppression has been observed with topical mometasone, consistent with its low systemic bioavailability. HPA suppression is dependent upon exposure to supra-physiologic glucocorticoid concentrations for a sufficient duration. In combination with the inherently low systemic bioavailability of mometasone, the proposed restricted quantity able to be supplied under Schedule 3 discourages its use on large areas of the body and for long durations, limiting the attainment of the critical factors required to induce HPA suppression. I consider that patient education and the proposed product labelling '*Do not use on the face, or for more than 4 weeks without advice from a medical professional*' are appropriate ways to mitigate these risks. In addition, the 15 g pack size limitation will also mean that patients with extensive disease requiring access to large quantities will continue to be appropriately managed by a general practitioner or dermatologist.

I have noted the concerns regarding the ability of pharmacists to perform a differential diagnosis in the supply of mometasone (e.g. fungal infections, herpes zoster infection etc.) as an impediment to down-scheduling. However, I am of the view that this consideration is not specific to mometasone and applies equally to the supply of other products that have been considered appropriate for down-scheduling from Schedule 4 to Schedule 2 or 3, including topical corticosteroids and anti-fungal products. Furthermore, pharmacists are already able to initiate treatment with Schedule 2 and Schedule 3 steroids based on their differential assessment of a patient's condition. There is no evidence to suggest that pharmacists are unable to recommend appropriate treatments and therefore, I do not consider this to present a barrier to down-scheduling.

In recognition that the use of mometasone at established therapeutic dosage levels may mask the symptoms or delay diagnosis of a serious condition, the proposal by the Applicant contains some caveats on use, and these are in the CMI – e.g. do not use around eyes, do not use on skin infections, check with a doctor etc. These label statements together with pharmacist oversight to monitor use and to provide education are consistent with and appropriate for a Schedule 3 entry and can effectively mitigate potential risks associated with down-scheduling.

Rescheduling of a substance into Schedule 3 may be facilitated by an entry in Appendix M of the Poisons Standard whereby additional controls or supply requirements are applied to enable substances to be provided by a pharmacist. However, the additional information provided by the Applicant addressing the new Schedule M criteria[3] and public submissions questioning the robustness of Applicant's proposals have not been material to my decision. After taking into account the matters stated above, I find that the Scheduling Factors under Schedule 3 are met and that additional controls under Appendix M for mometasone are not required.

While not proposed by the Applicant, I have given consideration to inclusion of mometasone in Appendix H. Since 2018 the SPF and the Guidelines for advertisements for medicines containing Schedule 3 substances[4] provide that in principle, all Schedule 3 substances are to be included in Appendix H unless it is determined that, in the interests of public health, it is not appropriate to allow a substance to be advertised directly to consumers. Given the potential for mometasone to be inappropriately used to treat conditions other than inflammatory conditions, I am of the view that there may only be limited additional benefit from the advertising of a more potent option and the choice of agent is best managed through consultation with the pharmacist. Consequently, I do not support an Appendix H entry for mometasone at this time.

In the matter of the introduction of an actuation limit for intranasal mometasone in Schedule 2, having had regard to the Committee's advice and the public submissions opposing the amendment, I am satisfied that an actuation limit is not required to ensure the medicine's continuing quality use. The introduction of an actuation limit for Schedule 2 mometasone is inconsistent with recent scheduling decisions from 2018[5] and 2019[6] that removed actuation limits from fluticasone and budesonide, aligning them to equivalent intranasal corticosteroids (including at that time, mometasone). In making these decisions, the Delegates determined that removal of the actuation limits to allow larger pack sizes to treat chronic conditions would be unlikely to impact the risk-benefit profiles of these substances.[7,8] Given there are no safety signals warranting an amendment to the Schedule 2 entry in order to protect public health, it is my view that the introduction of an actuation limit for mometasone is not required and would impose an unnecessary regulatory burden on industry.

Summary of public submissions on the interim decision

Interim decision public submissions (ACMS #26)

Two (2) public submissions were received in response to the notice published under regulation 42ZCZP advising of the interim decision and invitation for further comment on substances referred to the March 2019 ACMS/ACCS meeting.[9] Both public submissions were in opposition the interim decision.

[1] https://www.tga.gov.au/consultation-invitation/consultation-proposed-amendments-poisons-standard-accs-acms-and-joint-accsacms-meetings-march-2019
[2] https://www.tga.gov.au/publication/scheduling-handbook-guidance-amending-poisons-standard
[3] https://www.tga.gov.au/sites/default/files/scheduling-handbook-guidance-amending-poisons-standard.pdf
[4] https://www.tga.gov.au/sites/default/files/guidelines-advertisements-medicines-containing-schedule-3-substances.pdf
[5] https://www.tga.gov.au/book-page/13-fluticasone-0
[6] https://www.tga.gov.au/book-page/12-budesonide-0
[7] https://www.tga.gov.au/book-page/13-fluticasone
[8] https://www.tga.gov.au/book-page/12-budesonide-0
[9] https://www.tga.gov.au/scheduling-decision-interim/interim-decisions-and-invitation-further-comment-substances-referred-march-2019-acmsaccs-meetings

Main points provided in opposition were:

- Mometasone for dermal use containing 0.1 % or less mometasone, in packs containing 15 g or less, substantially meets the Scheduling Factors for inclusion in Schedule 3.
- Pharmacists currently intervene in the supply of lower potency dermal corticosteroids that have very similar precautions and contraindications to higher potency corticosteroids.
- The introduction of an actuation limit for the current Schedule 2 entry conflicts with recent decisions for budesonide (2019) and fluticasone (2018) to remove actuation limits from other intranasal corticosteroids so that they could align with the (then) Schedule 2 entry for mometasone.
- Concerns with the diagnosis, management and monitoring of mometasone under Schedule 3 can be managed with an Appendix M entry that requires patients to have a medical diagnosis of their condition and a prescription specifying mometasone and that this must be reviewed by their medical practitioner every 6 months.
- Label warning statements and advice in the CMI not to use mometasone on the face or for more than two weeks without advice from a medical professional can help mitigate risks, such as corticosteroid-induced rosacea and skin atrophy, from the inappropriate application of mometasone to the face.

Pre-meeting public submissions (ACMS #28)

In response to the notice published under regulation 42ZCZK advising of the proposed amendment, six (6) submissions were received. Two (2) submissions supported the amendment, one (1) with caveats and four (4) submissions opposed the amendment.

The main points provided in support of the proposed amendment were:

- The substance meets the scheduling criteria for Schedule 3 substances.
- Suggest that it is not necessary to include the phrase "*Specific pharmacist training on the provision of this medicine is required*" in the Appendix M wording. Pharmacists already know about corticosteroid dermal preparations and the treatment of corticosteroid responsive skin conditions. Further, pharmacists are trained to differentiate between varied skin conditions and they are well aware of the pharmacology of topical corticosteroids. Skin conditions and their treatment are a staple part of a community pharmacist's work as they are often the first health professional that a patient will speak to. A community pharmacy is where most consumers will have their prescriptions dispensed.
- The Delegate and ACMS members are reminded that pharmacists under current scheduling arrangements are already able to initiate hydrocortisone treatment from their own assessment of a patient's condition that would require a similar approach in differential diagnosis when considering whether mometasone is appropriate for a patient's condition.
- A patient provided with this substance under the Schedule 3 Appendix M mechanism would already have consulted a medical practitioner regarding their condition and have trialled mometasone. They would have been counselled by the medical practitioner and the pharmacist when they have their first prescription dispensed. Pharmacist can verify that a patient has previously been prescribed this substance either by interviewing the patient or by consulting the patient's My Health Record or the pharmacy dispense records.
- There are no additional risks associated with the dosage form that may impact on safe use that will be exacerbated by advertising. Only patients that have a formal diagnosis and have previously used this substance will be eligible for access. Advertising will act as a reminder that they can access treatment for their condition should they experience a flare-up of their condition and cannot consult with their medical practitioner in a timely fashion.
- The Appendix M wording ensures that a patient must have previously been diagnosed with a dermal condition suitable for treatment with mometasone within the last 6 months. This requirement will ensure that there is no potential for inappropriate use or diversion that would be exacerbated by advertising.

The main points provided in support of the proposed amendment with caveats were:

- The proposed Appendix M controls appear logical and appropriate and the overall rescheduling proposal for mometasone is appropriate from a patient safety perspective. However, the Scheduling handbook outlines the expectation that an applicant seeking to reschedule a Schedule 4 substance to Schedule 3 with Appendix M conditions will conduct preliminary discussions with the pharmacy profession. In the absence of any discussion with [redacted] regarding the rescheduling to Scheduling 3 through Appendix M controls and the apparent lack of preparatory work on a suitable pharmacist training package, [redacted] is unable to support this proposal in its current form.
- Agree with the interim decision that mometasone should not be included in Appendix H.
- While supportive of the inclusion of an upper limit to the supply of Schedule 2, the conditions in the Schedule 2 entry include "*… for the short term prophylaxis or treatment of allergic rhinitis for up to 6 months…*". However, the TGA recently communicated (albeit in the context of the Appendix M criteria consultation) advice from States and Territories that "*limits on frequency and duration of supply are not within their power to legislate*". Therefore, clarification is sought on whether the reference to "*for up to 6 months*" is still appropriate for inclusion in the Schedule 2 entry of the Poisons Standard for mometasone, and if so, how this condition is expected to be fulfilled in practice.

The main points provided in opposition to the proposed amendment were:

- The proposed addition to Appendix M is entirely insufficient to satisfy the concerns outlined in the ACMS' interim decision. The proposed entry lacks detail on:
  - the proposed pharmacist training and what this entails;
  - the validation of the patient questionnaire;
  - the required records of diagnosis and therapeutic recommendation from the medical practitioner;
  - the mechanisms for patient follow up and management of adverse events; and
  - the tracking of clinical outcomes. There is no evidence to support this approach and it does not reflect good clinical practice.
- The [redacted] oppose the scheduling amendment on the terms of patient safety and in health care costs. The [redacted] supports the [redacted] of [redacted] submission on the proposed amendments to mometasone[10] and refers the Delegate to its own submission to the ACMS in January 2019 that further outlines the issues with down-scheduling mometasone.[11]
- Mometasone is the most common cause of corticosteroid-induced rosacea (perioral dermatitis) and causes skin atrophy.[12] Pharmacists do not have the medical training or expertise to know when to appropriately recommend mometasone to a patient, and rectifying adverse reactions requires medical practitioner expertise.
- There are already existing, effective, over the counter, low-potency topical steroid options and expanding access to higher potency steroids is fraught with negative consequences. [redacted] members are concerned that the number of adverse reactions will increase with the proposed changes. Further, there is a cost to the patient if mometasone is used inappropriately and they must pay for further treatment or medication such as antibiotics.

[10] Australasian College of Dermatologists (2019): https://www.dermcoll.edu.au/wp-content/uploads/190121-ACD-submission-to-TGA-Proposed-mometasone-rescheduling-Jan-21-2019.pdf
[11] Australian Medical Association (2019): https://ama.com.au/system/tdf/documents/AMA%20submission%20-%20glyceryl%20trinitrate%20%26%20mometasone%20furoate%20scheduling%20proposals%20-%20Jan19.pdf?file=1&type=node&id=49973
[12] Australasian College of Dermatologists (2019) *https://www.dermcoll.edu.au/wp-content/uploads/190121-ACD-submission-to-TGA-Proposed-mometasone-rescheduling-Jan-21-2019.pdf*

- The proposed amendment to the Schedule 2 entry that seeks to introduce a pack size limit of 200 actuations for intranasal mometasone is not supported. There was no transparency of the rationale for its inclusion for in the agenda nor explanation for the basis upon which public comment was sought.
- An actuation limit for intranasal mometasone should not be introduced after it has already been decided that similar limits are not needed for other equivalent intranasal corticosteroids and after it was determined that making budesonide available in a larger pack size was unlikely to impact the risk-benefit profile significantly.
- In recent Scheduling decisions it has decided that similar limits were not needed for other equivalent intranasal corticosteroids. The 1 February 2019 Poisons Standard removed the actuation limit of 200 actuations or less from the entry for budesonide in aqueous nasal sprays (see the Final Decision), on the basis that there was no actuation limit for other intranasal corticosteroids, i.e. mometasone. Similarly, a decision was made to remove the actuation limit for fluticasone, and this was included in the 1 October 2018 update to the Poisons Standard, (see the Final Decision).
- When deciding to remove the actuation limit for fluticasone, the Delegate's interim decisions stated that '*There is no difference in the risks of the substance by allowing more doses per pack*".[13] Similarly, for budesonide, the Delegate stated that '*Removing the actuation limit will allow new larger pack sizes and provide a longer duration of treatment"; "This change to the scheduling of budesonide in the Poisons Standard will align the Schedule 2 entry with other intranasal corticosteroids" and "Making budesonide available in a larger pack size is unlikely to impact the risk-benefit profile significantly".*[14]
- Both decisions (for budesonide and fluticasone) and the corresponding updates to the Poisons Standard were made to align both of these intranasal corticosteroid entries with that of intranasal. It is concerning that the current proposal is contradictory and does not provide a level playing field or consistency in approach for intranasal corticosteroids.

ACMS #28 Advice for the delegate's consideration

The Advisory Committee on Medicines Scheduling recommended that that the current Schedule 4 entry for mometasone be amended and that a new Schedule 3 entry be created in the Poisons Standard as follows:

Schedule 4 – Amend Entry

MOMETASONE **except** when included in Schedule 2 or 3.

Schedule 3 – New Entry

MOMETASONE as the only therapeutically active substance in preparations for dermal use containing 0.1 percent or less of mometasone in packs containing 15 g or less.

Schedule 2

MOMETASONE in aqueous nasal sprays delivering 50 micrograms or less of mometasone per actuation when the maximum recommended daily dose is no greater than 200 micrograms for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over.

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[13] https://www.tga.gov.au/book-page/13-fluticasone
[14] https://www.tga.gov.au/book-page/12-budesonide

The Committee also recommended an implementation date of **1 June 2020**.

Members agreed that the relevant matters under Section 52E(1) of the *Therapeutic Goods Act 1989* included (a) the risks and benefits of the use of a substance; (b) the purpose for which a substance is to be used and the and extent of use of a substance; (c) the toxicity of a substance; (d) the dosage, formulation, labelling, packaging and presentation of a substance; and (f) any other matters that the Secretary considers necessary to protect public health.

The Advisory Committee on Medicines Scheduling stated its reasons for its advice and recommendations as follows:

(a) *risks and benefits of the use of a substance:*

- Poorly controlled skin conditions can result in significant impairment of quality of life.
- Easier access to limited amounts of a potent topical corticosteroid can assist suitable patients in managing these conditions.
- Contraindications apply to topical corticosteroids as a class and not mometasone specifically and as such apply to other topical corticosteroids available without prescription.
- Available evidence does not support a significant risk of skin atrophy.
- Theoretical risk of suppression of the HPA axis. Clinical trials and extensive clinical experience with product supplied on prescription do not indicate that this a significant concern.
- Risk of perioral dermatitis and rosacea if applied inappropriately to the face therefore pharmacist intervention is necessary.

(b) *the purpose for which a substance is to be used and the extent of use:*

- Used in the management of active corticosteroid-responsive dermatoses including atopic dermatitis.

(c) *the toxicity of the a substance:*

- The toxicity of mometasone meets the Schedule 3 factors

(d) *the dosage, formulation, labelling, packaging and presentation of a substance:*

- Limitation of Schedule 3 pack size to 15 g is a safety measure to limit the possibility of use on large areas of the body for prolonged durations.
- The addition of reference to the actuations is an unnecessary change to Schedule 2 given other recent scheduling decisions for other intranasal corticosteroids

(e) *the potential for abuse of a substance:*

- Nil.

(f) *any other matters that the Secretary considers necessary to protect public health:*

- Larger pack sizes of mometasone will still be available as a Schedule 4 medicine.

Date of effect of the decision

1 June 2020

1.4. Final decision in relation to calcifediol monohydrate

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and amend the current Poisons Standard in relation to calcifediol as follows:

Schedule 4 – New Entry

CALCIFEDIOL for human internal therapeutic use **except** in preparations containing 10 micrograms or less of calcifediol per recommended daily dose.

Index – New Entry

CALCIFEDIOL

Schedule 4

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

I confirm the reasons for my final decision to create a new Schedule 4 entry for calcifediol for human internal use with a concentration cut-off of 10 micrograms or less calcifediol per recommended daily dose, are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and the submission received before the second closing date in response for the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations. As the public submission reiterated a view consistent with a pre-meeting submission supporting access to calcifediol under Schedule 3, it has not be material to my decision.

Summary of public submissions on the interim decision

In response to the interim decision, one submission opposing the interim decision was received.

The main points opposing the proposed amendment were:

- Considering its use is consistent with the purpose of calciferol, but more useful in specific circumstances, it would be appropriate to enable sponsors to make applications for the S3 Pharmacist Only category that is equivalent in dose to the Vitamin D entry in Schedule 3:

  VITAMIN D for human internal therapeutic use in preparations containing 175 micrograms or less of vitamin D per recommended single weekly dose except in preparations containing 25 micrograms or less of vitamin D per recommended daily dose.

- For calcifediol, this could mean an equivalent dose of around 60-70 micrograms on a weekly basis could be considered for Schedule 3, pending appropriate evaluation through the registration process, to ensure that health professionals have the tools available to allow patients to access appropriate medicines without the need for managing prescriptions on an ongoing basis unless a higher dose was indicated.

- In summary, we propose that it would be appropriate to allow the gradation of access to calcifediol in an equivalent manner to colecalciferol.

Date of effect of the decision

1 June 2020

1.5. Final decision in relation to Paracetamol (liquid formulations)

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and amend the current Poisons Standard in relation to paracetamol (liquid formulations) as follows:

Schedule 3 – Amend Entry*

PARACETAMOL:

(a) when combined with ibuprofen in a primary pack containing 30 dosage units or less **except** when included in Schedule 2; or

(b) in modified release tablets or capsules containing 665 mg or less paracetamol; or

(c) in liquid preparations for oral use except when in Schedule 2.

*The proposed amended Schedule 3 entry for paracetamol as written includes the final decision[15] for modified paracetamol that will be implemented 1 June 2020.

Schedule 2 – Amend Entry

PARACETAMOL for therapeutic use:

(a) in liquid preparations for oral use containing a maximum of 10 g of paracetamol per container; or

(b) when combined with ibuprofen in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen in divided doses in a primary pack containing no more than 12 dosage units per pack; or

(c) in tablets or capsules enclosed in a primary pack containing not more than 100 tablets or capsules; or

(d) in tablets or capsules enclosed in a primary pack containing more than 100 tablets or capsules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

(e) in individually wrapped powders or sachets of granules enclosed in a primary pack containing not more than 50 wrapped powders or sachets of granules; or

(f) in individually wrapped powders or sachets of granules enclosed in a primary pack containing more than 50 wrapped powders or sachets of granules intended only as a bulk medicine pack and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'; or

(g) in other preparations **except**:

i) when included in Schedule 3 or 4; or

ii) in individually wrapped powders or sachets of granules each containing 1000 mg or less of paracetamol as the only therapeutically active constituent (other than caffeine, phenylephrine and/or guaifenesin or when combined with effervescent agents) when:

(A) enclosed in a primary pack that contains not more than 10 such powders or sachets of granules,

(B) compliant with the requirements of the Required Advisory Statements for Medicine Labels,

[15] https://www.tga.gov.au/book-page/14-final-decision-relation-paracetamol-modified-release

(C) not labelled for the treatment of children 6 years of age or less, and

(D) not labelled for the treatment of children under 12 years of age when combined with caffeine, phenylephrine and/or guaifenesin; or

iii) in tablets or capsules each containing 500 mg or less of paracetamol as the only therapeutically active constituent (other than caffeine, phenylephrine and/or guaifenesin or when combined with effervescent agents) when:

(A) packed in blister or strip packaging or in a container with a child-resistant closure,

(B) in a primary pack containing not more than 20 tablets or capsules,

(C) compliant with the requirements of the Required Advisory Statements for Medicine Labels,

(D) not labelled for the treatment of children 6 years of age or less, and

(E) not labelled for the treatment of children under 12 years of age when combined with caffeine, phenylephrine and/or guaifenesin.

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

I confirm the reasons for my final decision to schedule paracetamol in liquid preparations for oral use in Schedule 3 except when in Schedule 2 as liquid preparations for oral use containing a maximum of 10 g of paracetamol per container, are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and the two submissions received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations. Though not material to my decision, both submissions supported the interim decision and I acknowledge the concerns also expressed regarding the ambiguity of the initial scheduling proposal.

Summary of public submissions on the interim decision

In response to the interim decision, two (2) submissions were received. Both submissions supported the interim decision.

The main points provided in support of the interim decision were:

- The scheduling proposal in the Delegate's interim decision takes into consideration the appropriate balance between patient access to medicines and safety.
- The Delegate's interim decision on paracetamol (liquid formulations) is supported to the extent that current marketed products will not be affected by the decision.

Additional comment:

- One submission expressed their disappointment with the wording of the initial scheduling proposal due to ambiguity in the scheduling amendment as proposed which included both a concentration cut-off (50 mg/mL) and two different weight cut-offs (5 g and 50 g).

Date of effect of the decision

1 June 2020

1.6. Final decision in relation to Paracetamol + ibuprofen

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and not amend the current Poisons Standard in relation to paracetamol + ibuprofen.

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

I confirm the reasons for my final decision to retain the current Schedule 3, Schedule 3 and Schedule 4 entries in relation to paracetamol when in combination with ibuprofen, are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and have noted that no public submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the interim decision.

Date of effect of the decision

7 May 2020

1.7. Final decision in relation to Hyoscine butylbromide

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and amend the current Poisons Standard in relation to hyoscine butylbromide as follows:

Schedule 4 – New Entry

HYOSCINE BUTYLBROMIDE **except** when included in Schedule 2 or 3.

Schedule 3 – New Entry

HYOSCINE BUTYLBROMIDE in undivided preparations for oral use with a recommended single dose not exceeding 20 mg of hyoscine butylbromide in a pack containing 100 mg or less of hyoscine butylbromide when labelled for adults and children 6 years and over.

Schedule 2

HYOSCINE BUTYLBROMIDE as the only therapeutically active substance, in divided preparations for oral use, containing 20 mg or less of hyoscine butylbromide per dosage unit in a pack containing 200 mg or less of hyoscine butylbromide.

Schedule 2 – Amend Entry

HYOSCINE ~~(excluding hyoscine butylbromide):~~

(a) for transdermal use in preparations containing 2 mg or less of total solanaceous alkaloids per dosage unit; or

(b) for oral use:

i) in undivided preparations containing 0.03 per cent or less of total solanaceous alkaloids, when labelled with a dose of 0.3 mg or less of total solanaceous alkaloids and a recommended daily dose of 1.2 mg or less of total solanaceous alkaloids; or

ii) in divided preparations containing 0.3 mg or less of total solanaceous alkaloids per dosage unit when labelled with a recommended daily dose of 1.2 mg or less of total solanaceous alkaloids.

Appendix H – New Entry

HYOSCINE BUTYLBROMIDE

Index – Amend Entry

HYOSCINE BUTYLBROMIDE

Schedule 4
Schedule 3
Schedule 2
Appendix H

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

I confirm the reasons for my final decision to amend the Poisons Standard in relation to hyoscine butylbromide by creating new Schedule 3, Schedule 4 and Appendix H entries and removing the reference to hyoscine butylbromide in the Schedule 2 entry for hyoscine, are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and have noted that no public submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the interim decision.

Date of effect of the decision

1 June 2020

1.8. Final decision in relation to Lidocaine

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and amend the current Poisons Standard in relation to lidocaine as follows:

Schedule 2 – Amend Entry

LIDOCAINE in preparations for topical use other than eye drops:

(a) containing 10 per cent or less of total local anaesthetic substances, **except**:

i) in dermal preparations containing 2 per cent or less of total local anaesthetic substances; or

ii) in aqueous sprays for oromucosal use containing 0.6 per cent or less of total local anaesthetic substances; or

(b) in divided preparations containing 200 mg or less of total local anaesthetic substances, **except** in lozenges containing 30 mg or less of total local anaesthetic substances per dosage unit.

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

I confirm the reasons for my final decision to amend the Poisons Standard in relation to the Schedule 2 entry for lidocaine are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and have noted that no public submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the interim decision.

Date of effect of the decision

1 June 2020

2 Final decisions made pursuant to regulation 42ZCZR – proposals referred to the November 2019 Joint Advisory Committee on Medicines and Chemicals Scheduling (ACCS-ACMS #23)

2.1. Final decision in relation to Caffeine

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and amend the current Poisons Standard in relation to caffeine as follows:

Schedule 6 – New Entry

CAFFEINE **except**:

(a) when included in Schedule 4; or

(b) in divided preparations for internal human therapeutic use when labelled with a maximum recommended daily dose of no greater than 600 milligrams of total caffeine; or

(c) in undivided preparations for internal human therapeutic use with a concentration of less than 5 per cent of total caffeine and when labelled with a maximum recommended daily dose of no greater than 600 milligrams of total caffeine; or

(d) in preparations for external use; or

(e) in other preparations with a concentration of less than 5 per cent of caffeine.

Schedule 4 – New Entry

CAFFEINE for internal human therapeutic use **except**:

(a) in divided preparations when labelled with a maximum recommended daily dose of no greater than 600 milligrams of total caffeine; or

(b) in undivided preparations with a concentration of less than 5 per cent of caffeine and when labelled with a maximum recommended daily dose of no greater than 600 milligrams of total caffeine.

Index – New Entry

CAFFEINE
cross reference: PARACETAMOL, ASPIRIN, SALICYLAMIDE

Schedule 6
Schedule 4

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

I confirm the reasons for my final decision to create new Schedule 4 and Schedule 6 entries for caffeine are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and the submission received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations. The public submission, however, has not been material to my decision. While supportive, the views expressed were not relevant as they related to matters outside the scope of scheduling.

Summary of public submissions on the interim decision

One public submission supporting were received in response to the second interim decision.

The main points in support with amendments of the proposed amendment were:

- The submission supported the schedule 4 entries in the Delegate's interim decision.
- The submission proposes increasing the current 1% limit in the listing for caffeine in the Permissible Ingredient Determination to align with the 5% limit set for food by FSANZ.

Date of effect of the decision

1 June 2020

2.2. Final decision in relation to N-methyl-2-pyrrolidone (NMP)

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and not amend the current Poisons Standard in relation to *N*-methyl-2-pyrrolidone (NMP).

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

I confirm that the reasons for my final decision not to amend the Poison Standard with respect to NMP are as detailed in my second interim decision. In making my final decision. I have taken into account the material detailed in the interim decision and have noted that no public submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the second interim decision.

Date of effect of the decision

7 May 2020

3 Final decisions made pursuant to regulation 42ZCZR – proposals referred to the November 2019 Advisory Committee on Chemicals Scheduling (ACCS #26)

3.1. Final decision in relation to Carbon monoxide

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and not amend the current Poisons Standard in relation to carbon monoxide.

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

I confirm the reasons for my final decision not to amend the Poisons Standard with respect to carbon monoxide are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and the public submission received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Statements made in the public submission that industry is currently implementing further controls aimed at preventing public access to carbon monoxide products have not been material to my decision as these reiterate views I have previously taken into consideration. I am satisfied that at this time, carbon monoxide does not meet the requirements for inclusion in the Poisons Standard. The risk profile of carbon monoxide is largely mitigated by other regulations in industry and on balance, as carbon monoxide containing-products are not supplied to the public in the domestic market, public risk exposure is low.

Summary of public submissions on the interim decision

In response to the interim decision, one submission was received. The submission supported the interim decision and no submissions were received that opposed the interim decision.

The main points provided in support of the interim decision were:

- The submission supported the interim decision as a sensible and pragmatic decision not to schedule carbon monoxide.
- Industry has developed, through a member based working group, product stewardship guidelines for carbon monoxide and these have been recommended to members for implementation. The guidelines include barriers to obtaining the product using end user declarations.
- Training and support to customer service staff within industry is being provided to identify when a sale may be suspicious and if the declared use is not legitimate

Date of effect of the decision

7 May 2020

3.2. Final decision in relation to Momfluorothrin

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and to amend the current Poisons Standard in relation to momfluorothrin as follows:

Schedule 6 – Amend Entry

MOMFLUOROTHRIN **except** in preparations containing 0.2 per cent or less of momfluorothrin.

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MOMFLUOROTHRIN

Schedule 6

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

I confirm the reasons for my final decision to amend the Schedule 6 entry for momfluorothrin to exclude from scheduling, momfluorothrin in concentrations of up to 0.2 per cent, are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and have noted that no public submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the interim decision.

Date of effect of the decision

1 June 2020

3.3. Final decision in relation to Tetraniliprole

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and to amend the current Poisons Standard in relation to tetraniliprole as follows:

Schedule 5 – New Entry

TETRANILIPROLE **except** in preparations containing 20 per cent or less tetraniliprole.

INDEX – New Entry

TETRANIPROLE

Schedule 5

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

I confirm the reasons for my final decision to include tetraniliprole at concentrations greater than 20 percent in Schedule 5 of the Poisons Standard are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and have noted that no public submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the interim decision.

Date of effect of the decision

1 June 2020

3.4. Final decision in relation to Methiozolin

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and to amend the current Poisons Standard in relation to methiozolin as follows:

Schedule 5 – New Entry

METHIOZOLIN.

Index – New Entry

METHIOZOLIN

Schedule 5

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

I confirm the reasons for my final decision to include methiozolin in Schedule 5 are as detailed in the interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and have noted that no submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the interim decision.

Date of effect of the decision

1 June 2020

3.5. Final decision in relation to Lambda-cyhalothrin

Final decision

Pursuant to regulation 42ZCZR of the Regulations, a Delegate of the Secretary has made a final decision to affirm the interim decision and to amend the current Poisons Standard in relation to lambda-cyhalothrin as follows:

Schedule 7

LAMBDA-CYHALOTHRIN **except** when included in Schedule 5 or 6.

Schedule 6

LAMBDA-CYHALOTHRIN:

(a) in aqueous preparations containing 25 per cent or less of microencapsulated lambda-cyhalothrin; or

(b) in emulsifiable granule formulations containing 25 per cent or less lambda-cyhalothrin; or

(c) in other preparations containing 1.6 per cent or less of lambda-cyhalothrin except when included in Schedule 5.

Schedule 5 – Amend Entry

LAMBDA-CYHALOTHRIN:

(a) in aqueous preparations containing 1 per cent or less of lambda-cyhalothrin; or

(b) in aqueous preparations containing ~~2.5~~10 per cent or less of microencapsulated lambda-cyhalothrin.

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LAMBDA-CYHALOTHRIN

Schedule 7
Schedule 6
Schedule 5

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

I confirm the reasons for my final decision to amend the Schedule 5 entry for lambda-cyhalothrin to exclude aqueous preparations containing 10 per cent or less of microencapsulated lambda-cyhalothrin from scheduling are as detailed in my interim decision. In making my final decision, I have taken into account the material detailed in the interim decision and have noted that no public submissions were received before the second closing date in response to the call for further submissions published on 6 February 2020 under regulation 42ZCZP of the Regulations.

Summary of public submissions on the interim decision

No public submissions were received in response to the interim decision.

Date of effect of the decision

1 June 2020

4 Final decision(s) (without interim decision) made pursuant to regulation 42ZCZU

4.1. Final decision in relation to Acequinocyl

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 acequinocyl as follows:

Schedule 5 – New Entry

ACEQUINOCYL

Index – New Entry

ACEQUINOCYL

Schedule 5

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

Materials considered

In making this final decision, I have considered the following:

- The Applicant's application to amend the current Poisons Standard with respect to acequinocyle;
- 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; (e) the potential for abuse of a substance; and (f) any other matters considered necessary to protect public health;
- The Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- Scheduling Handbook (V 1.0, January 2018).

Findings on material questions of fact

An application was submitted by the Australian Pesticides and Veterinary Medicines Authority (APVMA) to amend the Poisons Standard with respect to acequinocyl. The application proposes to create a new Schedule 5 entry for acequinocyl in the Poisons Standard.

The Applicant's proposed amendments to the Poisons Standard are:

Schedule 5 – New Entry

ACEQUINOCYL

Index – New Entry

ACEQUINOCYL

Schedule 5

The Applicant's reasons for the proposal are:

- The proposal is to consider a new substance, acequinocyl, which it is considered appropriate for inclusion in Schedule 5 of the Poisons Standard, based on sufficient toxicological data being available to recommend a scheduling decision.

- Acequinocyl belongs to the quinoline class of miticides and the mode of action is binding to the Qo centre of Complex III in the mitochondria of the mite cells and inhibiting electron transfer. Acequinocyl is a known Vitamin K antagonist and thereby is thought to disrupt blood coagulation.
- Acequinocyl has low acute toxicity by oral, dermal and inhalational routes, although it resulted in evidence of significant respiratory irritation. It is a slight skin and eye irritant and although it was a skin sensitiser in the guinea pig via the Guinea Pig Maximisation Test (GPMT), it was not under the Buehler method, a method considered more relevant for occupational exposure.
- The active is not a developmental or reproductive toxicant, is not genotoxic in a battery of *in vivo* and *in vitro* assays and was not carcinogenic in life time studies in mice and rats. In repeat-dose studies in laboratory animals, the primary target was the coagulation system, characterised by increased prothrombin time (PT), increased activated partial thromboplastin time (APTT) and internal haemorrhage.
- Such effects were seen across the database which was largely administered by the oral route, but also following repeat dermal application in rats. Mechanistic studies showed prolonged PT and APTT in rats following a single dose, and the reversibility of these effects.
- The product, [redacted] [redacted] containing 156 g/L of acequinocyl has low acute toxicity by the oral, dermal and inhalational routes, is not a skin irritant, is slightly irritating to the eyes and is not a skin sensitiser in guinea pigs (Buehler method).
- The management of acequinocyl toxicological risks would be adequately achieved through a listing in Schedule 5 of the Poisons Standard with no cut-off or exemptions.

Current scheduling status and scheduling history

Acequinocyl is not specifically scheduled in the current Poisons Standard and has not been previously considered for scheduling. Therefore, a scheduling history is not available.

Australian regulations

- Acequinocyl is not available for use as an active ingredient in human therapeutic products as it is not listed in the TGA Ingredient Database.[16]
- There are currently no medicines active on the Australian Register of Therapeutic Goods (ARTG)[17] that contain acequinocyl as an active ingredient.
- Acequinocyl is not permitted to be included in listed medicines as it is not included in the Therapeutic Goods (Permissible Ingredients) Determination[18] No.1 of 2020.
- Acequinocyl is not listed on the TGA prescribing medicines in pregnancy database.[19]
- The Therapeutic Goods (Medicines Advisory Statements) Specification 2019[20] does not contain warning statements pertaining to acequinocyl.
- There are no adverse events reported for acequinocyl on the Database of Adverse Event Notifications (DAEN).[21]
- There are no products containing acequinocyl as an active ingredient that are listed on the Public Chemical Registration Information System Search (PubCRIS).[22]

[16] TGA Ingredient Database https://www.ebs.tga.gov.au/
[17] Australian Register of Therapeutic Goods (ARTG) https://www.tga.gov.au/artg
[18] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[19] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[20] Therapeutic Goods (Medicines Advisory Statements) Specification 2019 https://www.legislation.gov.au/Details/F2019L00213
[21] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[22] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris

International regulations

- Acequinocyl is classified as Group 20B Miticide[23] (Insecticide Resistance Action Committee, 2005).
- As of September 2003, acequinocyl is registered as an active ingredient for use in pesticides in the United States according to the United States (U.S) Environmental Protection Agency[24].
- Acequinocyl is currently registered to [redacted] as a 15% soluble-concentrate (SC) formulation.
- The European Chemicals Agency (ECHA)[25] hazard classification and labelling for acequinocyl identifies it as '*Danger! According to the harmonised classification and labelling (ATP03) approved by the European Union, this substance causes damage to organs, is very toxic to aquatic life, is very toxic to aquatic life with long lasting effects and may cause an allergic skin reaction*'.
- In New Zealand, there are no registered products containing acequinocyl according to the New Zealand Medicines and Medical Devices Safety Authority (MedSafe)[26] and the New Zealand Inventory of Chemicals (NZIoC).[27]
- In Canada, acequinocyl is registered as an active ingredient in 3 registered products on Canada's Pest Management Regulation Agency.[28] There are no registered medicines containing acequinocyl according to the Canadian (Health Canada) Drug Product Database.[29]

Substance summary

Acequinocyl is a new active constituent which is not currently scheduled in the Poisons Standard. Acequinocyl is in the quinoline class of miticides and is for the control of certain mites in pome and stone fruits. Toxicity studies on acequinocyl and its product have been submitted to the APVMA in support of the active approval and product registration.

Table 1: Chemical information for acequinocyl

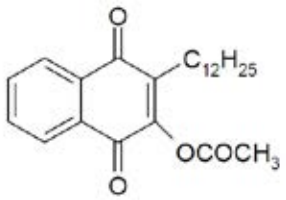
Property	Acequinocyl
Chemical structure	
Molecular formula	$C_{24}H_{32}O_4$
Molecular weight	384.5 g/mol
CAS numbers	57960-19-7
IUPAC and/or common and/or other names	IUPAC: 3-dodecyl-1,4-dihydro-1,4-dioxo-2-naphthyl acetate Common name: Acequinocyl Other names: 3-dodecyl-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetat

Table 2: Acute toxicity end-points for acequinocyl

Toxicity	Species	Endpoint	SPF (2018) Classification for acequinocyl	[redacted]	SPF (2018) Classification fo[redacted]
Acute oral toxicity	Mice	LD_{50} >5000 mg/kg bw[1]	-	LD_{50} >5000 mg/kg bw	-
	Rat	LD_{50} >5000 mg/kg bw[1]	-	LD_{50} >5000 mg/kg bw	-
Acute dermal toxicity	Rat	LD_{50} >2000 mg/kg bw	Schedule 5[2]	LD_{50} >2000 mg/kg bw	Schedule 5[2]
Acute inhalational toxicity	Rat	LC_{50} >840 mg/m^3 (whole body; 4-h)	Schedule 5[3]	LC_{50} >4560 mg/m^3(whole body; 4-h)	Schedule 5[4]
Skin irritation	Rabbit	Slightly irritating	Schedule 5	Non-irritating	-
Eye irritation	Rabbit	Slightly irritating	Schedule 5	Slightly irritating	Schedule 5
Skin sensitisation (Buehler)	Guinea pig	Non-sensitiser[5]	-	Non-sensitiser	-

1. Note that this was the only dose tested, with no deaths and no clinical signs of toxicity (other than watery faeces up to 2 h after administration) for either acequinocyl or the product tested.
2. Note that this was the only dose tested, with no deaths and no clinical signs of toxicity for either acequinocyl or the product tested.
3. 1/10 deaths at 840 mg/m^3 and 1/10 deaths at 690 mg/m^3. This was reported to be the maximal attainable concentration achievable under the test conditions, and particle size was of adequate respirability. There was clinical signs and histopathology indicative of severe pulmonary inflammatory reactions.
4. There were no deaths and clinical signs during exposure were considered consistent with exposure to a high concentration of aerosol and not specific toxicity.
5. Skin sensitisation via GPMT was positive, but Buehler is considered more representative of occupational exposure.

Reasons for final decision

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 *Therapeutic Goods* Act *1989* and the Scheduling Policy Framework (SPF, 2018). In particular, I note that:

- The proposed change to the Poisons Standard to include a new entry for acequinocyl, indicates that there are benefits to the agricultural industry from the introduction of this new pesticide (miticide), to control for the two-spotted mite (*Tetranychus urticae*) in pome and stone fruit. The product containing the new substance (acequinocyl) is intended for professional use in orchards, with limited potential for exposure to the general public. The risks associated with

[23] https://www.irac-online.org/modes-of-action/
[24] United States (U.S) Environmental Protection Agency https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-006329_26-Sep-03.pdf
[25] European Chemicals Agency (ECHA) https://echa.europa.eu/search-for-chemicals
[26] New Zealand Medicines and Medical Devices Safety Authority (MedSafe) https://www.medsafe.govt.nz/profs/class/classintro.asp
[27] New Zealand Inventory of Chemicals (NZIoC) https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=acequinocyl&DatabaseType=NZIOC
[28] Canada's Pest Management Regulation Agency https://pesticide-registry.canada.ca/en/active-ingredient-search.html
[29] Canadian (Health Canada) Drug Product Database https://health-products.canada.ca/dpd-bdpp/index-eng.jsp

human exposure to the substance have been adequately addressed by the pesticide regulator (APVMA) in its application (52E(1)(a)).

- The purpose and extent for which the substance is to be used has been adequately outlined by the Applicant. I have also noted the current registration of similar products for use in a range of fruit and vegetable crops, and ornamental plants in the USA, Canada and Europe (52E(1)(b)).
- The data indicate that acequinocyl has a low acute toxicity by the oral, dermal and inhalational routes of administration, although the undiluted substance is expected to be a respiratory irritant. It is slightly irritating to the eyes and skin, but is not expected to be a skin sensitiser. Acequinocyl was not genotoxic in a battery of *in vitro* and *in vivo* assays and was not considered carcinogenic in chronic/lifetimes studies in mice and rats. Acequinocyl was not a reproductive toxicant in rats or a developmental toxicant in rats and rabbits. There was no evidence of teratogenicity in either species, and any embryotoxicity occurred at maternotoxic doses. The potential for inhalational toxicity/irritation due to acequinocyl was considered on the whole to be a limited driver to place the substance in Schedule 6, according to the criteria set out in the SPF (2018). Moreover, the inhalation toxicity of a product containing 15.6% acequinocyl was shown to be low (LC_{50} >4560 mg/m^3(whole body; 4-h)), lending further support to the classification of the substance into Schedule 5 (52E(1)(c)).
- The Applicant has demonstrated that appropriate risk mitigation measures will be put in place for the proposed product containing the substance that may be registered for use in Australia, and that account for the dosage (application rate), formulation, labelling, packaging and presentation of the substance. As a result, no additional measures are required in the Poisons Standard. Further use of the substance in other pesticide products will be addressed by the pesticide regulator (APVMA) in any future applications to the regulator (52E(1)(d)).
- There is no information to indicate that products containing the substance could pose a risk to humans from abuse of the substance (52E(1)(e)).
- National and International Health Based Guidance Values have been or will be established for the substance that will protect consumers from residues of the substance in food (52E(1)(f)).

Therefore, 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 of the decision

1 June 2020

4.2. Final decision in relation to Agrobacterium radiobacter (Rhizobium rhizogenes)

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 *Agrobacterium radiobacter* (*Rhizobium rhizogenes*) as follows:

Appendix B, Part 3 – Amend Entry

Substance	Date of entry	Reason for listing	Area of use
~~*AGROBACTERIUM RADIOBACTER*~~ *RHIZOBIUM RHIZOGENES*	Nov 1989	b	1
b= Use pattern restricts hazard 1= Agriculture			

INDEX – Amend Entry

~~**AGROBACTERIUM RADIOBACTER**~~ **RHIZOBIUM RHIZOGENES**

Appendix B, Part 3

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

Materials considered

In making this final decision, I have considered the following:

- The Applicant's application to amend the current Poisons Standard with respect to *Agrobacterium radiobacter* (*Rhizobium rhizogenes*);
- 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 Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- Scheduling Handbook (V 1.0, January 2018).

Findings on material questions of fact

An application was submitted by the Australian Pesticides and Veterinary Medicines Authority (APVMA) to amend the Poisons Standard with respect to the Appendix B entry for *Agrobacterium radiobacter*. The application proposes to amend the Appendix B entry for *Agrobacterium radiobacter* and rename it to *Rhizobia rhizogenes* to reflect the reclassification in the scientific nomenclature of this organism.

The Applicant's proposed amendments to the Poisons Standard are:

Appendix B, Part 3 – Amend Entry

Substance	Date of entry	Reason for listing	Area of use
~~*AGROBACTERIUM RADIOBACTER*~~ *RHIZOBIA RHIZOGENES*	Nov 1989	b	1
b= Use pattern restricts hazard 1= Agriculture			

INDEX – Amend Entry

~~**AGROBACTERIUM RADIOBACTER**~~ **RHIZOBIA RHIZOGENES**

Appendix B, Part 3

The Applicant's reasons for the proposal are:

- The proposed change is purely an amendment to the entry in Appendix B to reflect the correct phylogenetic identification of this species.
- No public health impact is anticipated from this change, as it will not result in any change of the quantity of the substance available in the market, and will not change the current use pattern.
- *Agrobacterium* was originally included in Appendix B in 1989 based on very low oral toxicity, no skin or eye irritation and no evidence of sensitisation.

Current scheduling status

Agrobacterium radiobacter is currently included in Appendix B, Part 3 of the Poisons Standard as follows:

Appendix B, Part 3 – Amend Entry

Substance	Date of entry	Reason for listing	Area of use
AGROBACTERIUM RADIOBACTER	Nov 1989	b	1
b= Use pattern restricts hazard 1= Agriculture			

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AGROBACTERIUM RADIOBACTER

Appendix B, Part 3

Scheduling history

In November 1989, the Drugs and Poisons Schedule Committee considered a proposal to exempt *Agrobacterium radiobacter* (var. Radiobacter strain K1026) from scheduling. The bacterium was noted to be developed by genetic manipulation and had been cleared for use by the Genetic Manipulation Advisory Committee. The Committee noted that no toxicological studies were available for strain K1026 but accepted that the toxicological profile of the related K84 strain which

had demonstrated low toxicology. The Committee recommended an exemption from scheduling through the inclusion of *Agrobacterium radiobacter* in Appendix B of the Poisons Standard.

Australian regulations

- There is one (1) registered fungicide product containing *Agrobacterium radiobacter* listed on the Public Chemical Registration Information System Search (PubCRIS).[30] *Agrobacterium radiobacter* is also listed as an approved active constituent on PubCRIS. In both listings, *Agrobacterium radiobacter* var *radiobacter* strain K1026, is specifically named as the active.
- There have been no adverse experiences reported between 2009-2019 for *Agrobacterium radiobacter* in the APVMA Adverse Experience Reporting Program database (AERP).[31]
- *Agrobacterium radiobacter* is not identified in the following databases:
  - TGA Ingredient Database[32]
  - Australian Register of Therapeutic Goods (ARTG)[33]
  - Therapeutic Goods (Permissible Ingredients) Determination[34] No.1 of 2020
  - TGA prescribing medicines in pregnancy database[35]
  - Therapeutic Goods (Medicines Advisory Statements) Specification 2019[36]
  - Database of Adverse Event Notifications (DAEN)[37]
  - NICNAS Australian Inventory of Chemical Substances (AICS).[38]

International regulations

- In the USA, *Agrobacterium radiobacter* strain K1026 is registered[39] as an active ingredient in pesticide products registered with the United States Environmental Protection Agency's (US EPA) Office of Pesticides Programs.[40]
- It is not listed on the United States Food and Drug Administration Approved Drug Products Database (Drugs@FDA).[41]
- *Agrobacterium radiobacter* was not identified in the European Chemicals Agency (ECHA)[42] or the European Commission database for information on cosmetic substances and ingredients database.[43]
- While *Agrobacterium radiobacter* strain K1026 is not specifically listed in the European Union Pesticides Database,[44] the related strain K84, is identified in this database although it is currently not approved.

[30] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris
[31] APVMA Adverse Experience Reporting Program database (AERP) https://apvma.gov.au/node/10946
[32] TGA Ingredient Database https://www.ebs.tga.gov.au/
[33] ARTG database https://www.tga.gov.au/artg
[34] Therapeutic Goods (Permissible Ingredients) Determination
https://www.legislation.gov.au/Search/Therapeutic%20Goods%20LBPermissible%20IngredientsRB%20Determination
[35] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[36] Therapeutic Goods (Medicines Advisory Statements) Specification 2019 https://www.legislation.gov.au/Details/F2019L00213
[37] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[38] Australian Inventory of Chemical Substances (AICS) https://www.nicnas.gov.au/chemical-inventory
[39] Agrobacterium radiobacter strain K1026
(006474) Fact Sheet https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-006474_25-Nov-09.pdf
[40] United States Environmental Protection Agency's (US EPA) Office of Pesticides Programs
https://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:1
[41] FDA Approved Drug Products Database https://www.accessdata.fda.gov/scripts/cder/daf/
[42] European Chemicals Agency (ECHA) https://echa.europa.eu/search-for-chemicals
[43] European Commission database for information on cosmetic substances and ingredients database
https://ec.europa.eu/growth/tools-databases/cosing/
[44] European Union Pesticides Database https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

- In New Zealand, *Agrobacterium radiobacter* is not registered for use as a pesticide or as an active in medicines according the New Zealand Inventory of Chemicals (NZIoC)[45] and New Zealand Medicines and Medical Devices Safety Authority (MedSafe),[46] respectively.

- In Canada, *Agrobacterium radiobacter* is not registered for use as a pesticide or as an active medicines according to Canada's Pest Management Regulation Agency[47] and the Canadian (Health Canada) Drug Product Database,[48] respectively.

Substance summary

Agrobacterium radiobacter strain K1026 is a microbial pesticide that can be used to treat germinating seeds or roots and stems of certain stone fruit and nut trees and ornamentals to protect them from crown gall disease.[49] Products are intended for use in the greenhouse or in nurseries.

Agrobacterium radiobacter strain K1026 is a derivative (deletion of specific genetic material) of *Agrobacterium radiobacter* strain K84. Removal of this genetic material prevents the transfer of resistance from strain K1026 to other strains. Except for the deletion of a small portion of DNA removed in K84, the two strains are essentially identical and have the same characteristics. The naturally occurring bacterium *Agrobacterium radiobacter* strain K84 is widespread in soil and found near plant roots. A toxic compound produced by both K1026 and K84 controls certain other *Agrobacterium spp*. that cause crown gall disease.

An EPA assessment[50] found *Agrobacterium radiobacter* strain K1026 microbe is not likely to produce adverse effects in humans. The very similar organism, *Agrobacterium radiobacter* strain K84, has been used for decades without any reports of adverse effects or reactions. *Agrobacterium radiobacter* strains K1026 and K84 are not known to cause any infectious diseases in humans. This microbial pesticide is not intended for use on food crops. Consequently, it is not likely to pose a hazard to human adults, infants, children, or other sensitive subpopulations via the dietary route of exposure. The potential aggregate exposure, derived from non-dietary and non-occupational exposure, should be minimal or non-existent. Tier 1 ecotoxicology studies were waived based on the derivation of *Agrobacterium radiobacter* strain K1026 from strain K84, minimal exposure to non-target organisms, and no evidence of any unintended effects on non-target species by strain K84. Based upon this evaluation, the EPA determined that *Agrobacterium radiobacter* strain K1026 is likely to pose only a minimal risk to the environment or non-target organisms.

Reasons for final decision

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 *Therapeutic Goods Act 1989* and the Scheduling Policy Framework (SPF, 2018). In particular, I note that:

- The proposed change to the Poisons Standard to update the scientific name of the organism will not affect the risk or benefits from the use of products containing this substance (organism). *Agrobacterium radiobacter* var *radiobacter* has been used in Australia for more than 40 years for the control of crown gall in a range of crops. It has been included in Appendix B of the SUSMP since November 1989, based on its low toxicity via the oral route, and no evidence of skin or eye irritation or skin sensitisation. No additional risks are anticipated with the change in name to the substance (organism) to read *Rhizobium rhizogenes* (52E(1)(a)).
- The pattern and extent of use is not expected to change following the change in the name of the substance (organism) to reflect current scientific nomenclature (52E(1)(b)).

[45] New Zealand Inventory of Chemicals (NZIoC) https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=acequinocyl&DatabaseType=NZIOC
[46] New Zealand Medicines and Medical Devices Safety Authority (MedSafe) https://www.medsafe.govt.nz/profs/class/classintro.asp
[47] Canada's Pest Management Regulation Agency https://pesticide-registry.canada.ca/en/active-ingredient-search.html
[48] Canadian (Health Canada) Drug Product Database https://health-products.canada.ca/dpd-bdpp/index-eng.jsp
[49] *Agrobacterium radiobacter* strain K1026(006474) Fact Sheet https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-006474_25-Nov-09.pdf
[50] *Agrobacterium radiobacter* strain K1026 (006474) Fact Sheet https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-006474_25-Nov-09.pdf

- There has been no substantive change in the information available regarding the toxicity of the substance (organism) since it was last considered for Scheduling, which would warrant a change to its current exemption (Appendix B) in the Poisons Standard based on the criteria set out in SPF (2018) (52E(1)(c).
- The dosage (application rate), formulation, labelling, packaging and presentation of the substance (organism) will not change as a result of the name change, other than to provide a correction to the name of the active constituent on products containing the substance (organism) (52E(1)(d)).
- There is no information to indicate that products containing the substance (organism) could pose a risk to humans from abuse of the substance (organism). Furthermore, the change in name of the substance (organism) will not affect the potential for abuse (52E(1)(e).
- There were no other matters that were considered necessary to protect human health (52E(1)(f)).

Therefore, I have decided to amend the current Poisons Standard in the manner set out in the application with the minor change to the name of the genus. The name of the substance (organism) will be changed to *Rhizobium rhizogenes*. The proposed amendment was not referred to an expert advisory committee.

Date of effect of the decision

1 June 2020

4.3. Final decision in relation to Nonanoic acid

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 nonanoic acid as follows:

Schedule 5 – Amend Entry

NONANOIC ACID:

(a) when used as a pesticide; or

(b) in other preparations, **except** in preparations containing 10 per cent or less of nonanoic acid.

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NONANOIC ACID

Schedule 5

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

Materials considered

In making this final decision, I have considered the following:

- The Applicant's application to amend the current Poisons Standard with respect to nonanoic acid;
- 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 Australian Health Ministers' Advisory Council's Scheduling Policy Framework (SPF 2018); and
- Scheduling Handbook (V 1.0, January 2018).

Findings on material questions of fact

An application was submitted by the Australian Pesticides and Veterinary Medicines Authority (APVMA) to amend the Poisons Standard with respect to nonanoic acid. The application proposes to amend the current Schedule 5 entry for nonanoic acid to include all pesticide uses of nonanoic acid in Schedule 5, with the previous cut off being limited to other preparations containing 10% or less of nonanoic acid.

The applicant's proposed amendments to the Poisons Standard are:

Schedule 5 – Amend Entry

NONANOIC ACID:

(a) when used as a pesticide; or

(b) in other preparations, **except** in preparations containing 10 per cent or less of nonanoic acid.

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NONANOIC ACID

Schedule 5

The applicant's reasons for the proposal are:

- Nonanoic acid (NNA) is a medium chain fatty acid, and is a naturally occurring carboxylic acid with a carbon chain length of nine. It is used in agricultural and veterinary (AgVet) chemical products as an herbicide, and may have other uses in therapeutic goods or fragrances.
- NNA has previously been considered for inclusion in the Poisons Standard. During the initial consideration, a range of cut-offs were considered, with the original APVMA proposal being for a 3% cut-off, a public submission cut-off of 4% being proposed, and an exemption for the use of the substance as an excipient in therapeutic goods being proposed. The Committee recommended inclusion of NNA in Schedule 6 rather than Schedule 5, with a cut-off to unscheduled of 10%. The delegate's final decision was to include NNA in Schedule 5 with a cut-off to unscheduled for preparations containing 10% or less of NNA.
- NNA has been used in a range of agricultural chemicals as an herbicide, both in combination with other actives (particularly glyphosate), but also as a stand-alone active constituent. Commercial products are available with high concentrations of NNA. It is available as products for use in the home garden, both in ready to use formulations and also as concentrated formulations which require dilution prior to use.
- A recent evaluation has indicated moderate eye irritancy resulting from exposure to a 1.8% formulation. Effects included reversible corneal opacity. The potential for eye irritation with these products is recognised, and can be mitigated with a combination of label warnings and personal protective equipment. However, the additional control of inclusion in Schedule 5 with the requirement for the appropriate signal heading would increase the level of protection.
- Noting the previous consideration for scheduling of NNA, and reflecting that there are other uses of NNA (for example it is included in the Australian Register of Therapeutic Goods (ARTG) ingredient list and may have uses as an excipient in fragrances), the proposed entry includes separate consideration for the pesticide use of NNA and other uses.

Current scheduling status

Nonanoic acid is currently listed in Schedules 5 of the Poisons Standard as follows:

Schedule 5

NONANOIC ACID **except** in preparations containing 10 per cent or less of nonanoic acid.

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NONANOIC ACID

Schedule 5

Scheduling history

In March 2016, the Advisory Committee on Chemicals Scheduling (ACCS #16) considered a proposal to create a new Schedule 5 entry for the use of nonanoic acid in agricultural preparations with a proposed exemption concentration cut-off at 3%. The ACCS recommended a Schedule 6 listing for NNA, noting the broad use pattern of NNA and given its irritancy, the schedule entry should not be restricted to agricultural uses only to capture other areas of potential public exposure.

The Committee advised that a 10% cut off for the substance was appropriate, below which the substance would not be scheduled. This cut off concentration was considered appropriate to avoid capturing its use in food additives and cosmetics.

The Delegate noted the advice from the ACCS that a new Schedule 6 entry be created for nonanoic acid with a cut-off to exempt in preparations containing 10% or less. The advice for a primary listing in Schedule 6 was based primarily on the potential for severe eye damage associated with exposure to this fatty acid, while most of the other toxicological criteria are consistent with SPF criteria for listing in Schedule 5. The Delegate noted comments made by the ACCS that the evaluation of the eye irritancy studies presented lacked rigour and that there is some uncertainty about the severity and reversibility of the lesions associated with concentrated solutions of the acid.

The Delegate decided to create a primary listing for NNA in Schedule 5, with an exemption for products containing 10% or less and was satisfied that there was sufficient evidence at the time that concentrations below 10% should cover most uses and natural occurrences of nonanoic acid in products available to the public, the risks of eye damage are sufficiently ameliorated to warrant scheduling controls unnecessary.

Australian regulations

- According to the TGA Ingredient Database,[51] nonanoic acid is:
  - Available for use as an active ingredient in biologicals and prescription medicines;
  - Available for use as an excipient ingredient in biologicals, devices, listed medicines and prescription medicines; and
  - Not available as an equivalent ingredient in any application.
- The related substance, cetearyl nonanoate (also known as nonanoic acid cetearyl ester nonanoic acid cetyl/stearyl ester) is not available as an active ingredient in any application. However, it is available for use as excipient ingredient in export only, listed medicines, over the counter and prescription medicines.
- There are 27 products currently active on the Australian Register of Therapeutic Goods (ARTG)[52] that contain nonanoic acid as an active ingredient. These include; 14 prescription medicines, 4 non-prescription medicines, 6 listed medicines, 1 medical device and 2 other therapeutic good (OTG) devices.
- According to the Therapeutic Goods (Permissible Ingredients) Determination[53] No.1 of 2020, nonanoic acid is permitted to be included in listed medicines as follows:

Item	Ingredient name	Purpose	Specific requirements
3465	NONANOIC ACID	E	Permitted for use only in combination with other permitted ingredients as a flavour or a fragrance. If used in a flavour the total flavour concentration in a medicine must be no more than 5%. If used in a fragrance the total fragrance concentration in a medicine must be no more 1%.
E = excipient for a medicine meaning an ingredient that is not an active ingredient or a homoeopathic preparation ingredient			

- Nonanoic acid is not listed on the TGA prescribing medicines in pregnancy database.[54]
- There are no warning statements pertaining to nonanoic acid in the Therapeutic Goods (Medicines Advisory Statements) Specification 2019.[55]
- There have been no reported adverse event for nonanoic acid recorded on the Database of Adverse Event Notifications (DAEN).[56]
- There are 20 registered herbicide products with nonanoic acid listed as an active ingredient on the Public Chemical Registration Information System Search (PubCRIS).[57]

[51] TGA Ingredient Database https://www.ebs.tga.gov.au/
[52] ARTG database https://www.tga.gov.au/artg
[53] Therapeutic Goods (Permissible Ingredients) Determination https://www.legislation.gov.au/Details/F2019L01472/Html/Volume_4
[54] TGA prescribing medicines in pregnancy database https://www.tga.gov.au/prescribing-medicines-pregnancy-database
[55] Therapeutic Goods (Medicines Advisory Statements) Specification 2019 https://www.legislation.gov.au/Details/F2019L00213
[56] Database of Adverse Event Notifications (DAEN) https://apps.tga.gov.au/Prod/daen/daen-entry.aspx
[57] Public Chemical Registration Information System Search (PubCRIS) https://portal.apvma.gov.au/pubcris

- Between 2009-2019 the following adverse experiences were recorded for nonanoic acid in the APVMA Adverse Experience Reporting Program database (AERP):[58]
  - 1 report of a serious incident classified as related to human health reported occurring in 2017-2018.
- Nonanoic acid is included in the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) Australian Inventory of Chemical Substances (AICS).[59] However, there have been no assessments conducted by NICNAS on nonanoic acid that are publically available.

International regulations

- On 30 September 1974 nonanoic acid was registered with the United States Environmental Protection Agency's (US EPA) Office of Pesticides Programs.[60] It is registered for use as a antimicrobial, biochemical use and conventional chemical. Through the Pesticide Registration Review program,[61] the EPA reviews all registered pesticides at least every 15 years, as mandated by the *Federal Insecticide, Fungicide, and Rodenticide Act*. The registration status of nonanoic acid currently being reviewed under this mandated review process.
- Nonanoic acid is not an approved drug product in the United States according to the United States Food and Drug Administration Approved Drug Products Database (Drugs@FDA).[62]
- The European Chemicals Agency (ECHA)[63] hazard classification & labelling for nonanoic acid identifies it as '*Warning! According to the harmonised classification and labelling (ATP07) approved by the European Union, this substance causes serious eye irritation, is harmful to aquatic life with long lasting effects and causes skin irritation*.' It is approved for use as a biocide in the European Economic Area (EEA) and/or Switzerland, for: disinfection, repelling or attracting pests. It was granted approval for use in plant protection products in 2009 according to the European Union Pesticides Database.[64]
- According to the European Commission database for information on cosmetic substances and ingredients database[65] nonanoic acid is used in cosmetics in Europe, specifically it is used in cleansing, emulsifying, masking and perfume products.
- In New Zealand, nonanoic acid is classified as an approved hazardous substance according to the New Zealand Inventory of Chemicals (NZIoC).[66] There are no approved medicines containing nonanoic acid that are registered with the New Zealand Medicines and Medical Devices Safety Authority (MedSafe).[67]
- In Canada, there are currently 3 herbicide products containing nonanoic acid under review according to Canada's Pest Management Regulation Agency.[68] Nonanoic acid is not registered as an active ingredient for use in medicines according to the Canadian (Health Canada) Drug Product Database.[69]

Substance summary

Nonanoic acid (frequently referred to as pelargonic acid) is a naturally occurring carboxylic acid with a carbon chain-length of nine, belonging to the chemical class of saturated fatty acids commonly referred to as medium chain fatty acids (C8 to C12). It is a clear, colourless liquid with a

[58] APVMA Adverse Experience Reporting Program database (AERP) https://apvma.gov.au/node/10946
[59] Australian Inventory of Chemical Substances (AICS) https://www.nicnas.gov.au/chemical-inventory
[60] United States Environmental Protection Agency's (US EPA) Office of Pesticides Programs https://iaspub.epa.gov/apex/pesticides/f?p=CHEMICALSEARCH:1
[61] EPA Registration Review Schedules https://www.epa.gov/pesticide-reevaluation/registration-review-schedules
[62] FDA Approved Drug Products Database https://www.accessdata.fda.gov/scripts/cder/daf/
[63] European Chemicals Agency (ECHA) https://echa.europa.eu/search-for-chemicals
[64] European Union Pesticides Database https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN
[65] European Commission database for information on cosmetic substances and ingredients database https://ec.europa.eu/growth/tools-databases/cosing/
[66] New Zealand Inventory of Chemicals (NZIoC) https://www.epa.govt.nz/database-search/new-zealand-inventory-of-chemicals-nzioc/DatabaseSearchForm/?SiteDatabaseSearchFilters=36&Keyword=acequinocyl&DatabaseType=NZIOC
[67] New Zealand Medicines and Medical Devices Safety Authority (MedSafe) https://www.medsafe.govt.nz/profs/class/classintro.asp
[68] Canada's Pest Management Regulation Agency https://pesticide-registry.canada.ca/en/active-ingredient-search.html
[69] Canadian (Health Canada) Drug Product Database https://health-products.canada.ca/dpd-bdpp/index-eng.jsp

weak odour. Nonanoic acid is soluble in aqueous solutions however it can readily form esters and partially dissociate into the pelargonate anion ($CH_3(CH_2)_7COO^-$) and the hydronium cation (H_3O^+) in an aqueous solution. The molecular weight (158.24 g/mol) and octanol-water partition coefficient (3.4 logPow) of nonanoic acid suggest that dermal penetration is possible. The structure of nonanoic acid is shown in **Table 1**.

Previous consideration of nonanoic acid by the ACCS in March 2016[70] considered that nonanoic acid has low systemic toxicity and is not corrosive. The acute oral and dermal toxicity in the rat is greater than 2000 mg/kg bw. It was noted that human clinical data indicates reversible moderate irritation, and eye irritation was considered to be slight to moderate. The evaluation considered at the time whether the eye irritation observed and the uncertainty in the data available was sufficient to classify nonanoic acid as an irreversible eye irritant (Schedule 6). Recent studies for octanoic acid and decanoic acid (*in vivo* eye irritation Good Laboratory Practice (GLP) test according to OECD TG 403[71] and a Bovine Corneal Opacity and Permeability (BCOP) test respectively) showed evidence for reversible eye irritation. On this basis Schedule 5 was recommended.

Nonanoic acid is now used relatively extensively as an herbicide in the home garden. A recent evaluation of an acute eye irritation study indicated moderate eye irritation following exposure to a product formulation containing 1.8% nonanoic acid.

Table 1: Chemical information for nonanoic acid

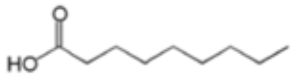
Property	Nonanoic acid
Chemical structure	
Molecular formula	$C_9H_{18}O_2$
CAS numbers	112-05-0
IUPAC and/or common and/or other names	Pelargonic acid (INCI) Nonoic acid

Table 2: Acute toxicity end-points for nonanoic acid

Toxicity	Species	Previous Endpoint conclusions for nonanoic acid	[redacted] Herbicide	SPF (2018) Classification for [redacted] Herbicide
Acute oral toxicity	Rat	LD50 >2000 mg/kg bw	LD50 >2000 mg/kg bw (estimated)	-
Acute dermal toxicity	Rat	LD50 >2000 mg/kg bw	LD50 >2000 mg/kg bw (estimated)	Schedule 5

[70] Nonanoic acid Final Decision, June 2016 https://www.tga.gov.au/book-page/111-nonanoic-acid-0
[71] Test No. 403: Acute Inhalation Toxicity https://www.oecd.org/env/test-no-403-acute-inhalation-toxicity-9789264070608-en.htm

Acute inhalational toxicity	Rat	LC50 >5300 mg/m3 (whole body; 4-h)	LC50 >5000 mg/m3(whole body; 4-h) (estimated)	-
Skin irritation	Rabbit	Irritating	Slight (estimated)	-
Eye irritation	Rabbit	Irritating	Moderately irritating	Schedule 6
Skin sensitisation (Buehler)	Guinea pig	Non-sensitiser5	Non-sensitiser (estimated)	-

Reasons for final decision

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 *Therapeutic Goods Act 1989* and the Scheduling Policy Framework (SPF, 2018). In particular, I note that:

- The proposed change to the Poisons Standard for the Schedule 5 entry for nonanoic acid is in response to new toxicity data. These data indicate that there is a risk to human health and safety from the use of this substance in pesticides (herbicides) that is not adequately mitigated by the current exemption in Schedule 5. The new information demonstrates that even low concentrations (ca 1.8%) of nonanoic acid are irritating to the eye and therefore, together with the overall toxicity profile of nonanoic acid, meets the criteria laid out in the SPF (2018) for a Schedule 5 entry without a concentration cut-off. The Applicant (APVMA) has indicated that various agricultural (pesticide) products containing nonanoic acid are currently available for use both commercially and in the home garden, thus highlighting its continued benefit for the agricultural industry. The proposed change is not expected to affect the benefits obtained from the use of agricultural products containing nonanoic acid or in other preparations that contain nonanoic acid (52E(1)(a)).
- The purpose and extent for which the substance is to be used has been adequately outlined by the Applicant. It has a demonstrable use as a herbicide both alone and in combination with other active constituents (ingredients) in commercial settings and in the home garden. The proposed change to the Schedule 5 entry for nonanoic acid is not expected to significantly alter the registered uses of the substance (52E(1)(b)).
- The toxicity of nonanoic acid has been previously considered by a Delegate of the Secretary of the Department of Health (Final decision published in June 2016) in response to an application prepared by the APVMA. Overall, nonanoic acid was found to be of low acute oral, dermal and inhalational toxicity and not a skin sensitiser, but was considered irritating to the eyes and skin. In addition, nonanoic acid was not genotoxic, did not show evidence for carcinogenicity, and was not a reproductive or developmental toxicant. Nonanoic acid has also be found to be irritating to epithelial and mucosal membranes. The current application by the APVMA, provides new information about the potential eye irritation of the substance, via the extrapolation from an eye irritation toxicity study in which a product containing a low concentration of nonanoic acid (ca 1.8%), was shown to be 'moderately' irritating to the eyes. The new data supports the Applicant's contention that the existing Schedule 5 exemption of 10%, does not adequately protect users of products that produce aerosols. This is particularly important for agricultural products that are routinely applied by spraying. Moreover, the data do not provide an alternative concentration cut-off that could see a lower exemption from Scheduling for agricultural products (52E(1)(c)).
- The dosage (application rate), formulation, labelling, packaging and presentation of the substance in agricultural products will largely be unaffected by the proposed change. The only exception would be for products that currently contain 10% or less of nonanoic acid and that do not have any other scheduled substance (active or non-active ingredient/constituent), that

would now require an applicable Schedule 5 signal heading on its label. The proposed change to the Schedule 5 entry in the Poisons Standard will not affect nonanoic acid-containing products listed under the ARTG (52E(1)(d)).

- There is no information to indicate that the substance could pose a risk to human from abuse of the substance (52E(1)(e)).
- There were no other matters that were considered necessary to protect human health (52E(1)(f)).

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

Date of effect of the decision

1 June 2020

5 Notice of an amendment to the current Poisons Standard in relation to Modified-release (MR) paracetamol

5.1. Decision in relation to modified-release (MR) paracetamol

A decision has been made to amend the Schedule 3 and Schedule 4 entries for paracetamol in regards to bulk packs of modified release dosage forms. These changes will come into effect at the same time as the final decision on paracetamol (modified release) published in August 2019.

Schedule 4 –Amend Entry*

PARACETAMOL:

(a) when combined with aspirin or salicylamide or any derivative of these substances **except** when separately specified in these Schedules;

(b) when combined with ibuprofen in a primary pack containing more than 30 dosage units;

(c) in modified release tablets or capsules containing more than 665 mg paracetamol;

(d) in non modified release tablets or capsules containing more than 500 mg paracetamol;

(e) in individually wrapped powders or sachets of granules each containing more than 1000 mg paracetamol;

(f) in tablets or capsules enclosed in a primary pack containing more than 100 tablets or capsules **except** in Schedule 2 or 3;

(g) in individually wrapped powders or sachets of granules enclosed in a primary pack containing more than 50 wrapped powders or sachets of granules **except** when included in Schedule 2;

(h) for injection;

(i) for the treatment of animals.

Schedule 3 –Amend Entry*

PARACETAMOL:

(a) when combined with ibuprofen in a primary pack containing 30 dosage units or less **except** when included in Schedule 2; or

(b) in modified release tablets or capsules containing 665 mg or less paracetamol enclosed in a primary pack containing not more than 100 tablets or capsules; or

(c) in modified release tablets or capsules containing 665 mg or less paracetamol enclosed in a primary pack containing more than 100 tablets or capsules intended only as a bulk medicine and labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'.

*The proposed amended Schedule 4 and Schedule 3 entries for paracetamol as written includes the final decision[72] for modified paracetamol that will be implemented 1 June 2020.

Reasons for the decision

- Paracetamol, both in immediate and modified released forms, in a primary pack containing more than 100 tablets or capsules is currently captured under Schedule 2 of the Poisons Standard and are required to be labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'.

[72] https://www.tga.gov.au/book-page/14-final-decision-relation-paracetamol-modified-release

- Paracetamol, both in immediate and modified released forms, in primary pack containing more than 100 tablets or capsules are used in pharmacies for packing medicine packs and are not directly supplied to patients.
- In August 2019, a final decision was published that made MR paracetamol a Schedule 3 medicine with an implementation date of 1 June 2020. As written, the final decision makes MR paracetamol in a primary pack containing more than 100 tablets or capsules a Schedule 4 medicine. It was not the intention of the final decision to make bulk packs of MR paracetamol a Schedule 4 medicine.
- This decision to make the above technical amendments would appear, in accordance with the Scheduling Policy Framework (SPF), to be sufficiently straightforward as to not require consultation;
- The amendment provides further clarity on different pack sizes of MR paracetamol in Schedule 3 and the requirements for primary packs containing more than 100 tablets or capsules to be labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'.
- In making this decision 52E(1)(a)-(f) has been taken into account as follows:

  (a) *the risks and benefits of the use of a substance*

  – N/A

  (b) *the purposes for which a substance is to be used and the extent of use of a substance*

  – Paracetamol, both in immediate and modified released forms, in bulk packs are used in pharmacies for packing medicine packs and are not directly supplied to patients.

  (c) *the toxicity of a substance*

  – N/A

  (d) *the dosage, formulation, labelling, packaging and presentation of a substance*

  – Paracetamol, both in immediate and modified released forms, in bulk packs are used in pharmacies for packing medicine packs and are not directly supplied to patients.

  – Paracetamol, both in immediate and modified released forms, in bulk packs is currently captured under Schedule 2 of the Poisons Standard and are required to be labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'.

  – The final decision for MR paracetamol published on the TGA website in August 2019 inadvertently made MR paracetamol in bulk packs a Schedule 4 medicine. This recommended amendment will make bulk packs of MR paracetamol a Schedule 3 medicines and will prevent them from being captured as a Schedule 4 medicine. Further, bulk packs of MR paracetamol will be required to be labelled 'For dispensing only' and 'This pack is not to be supplied to a patient'.

  (e) *the potential for abuse of a substance*

  – N/A

  (f) *any other matters that the Secretary considers necessary to protect public health*

  – N/A

Date of effect of the decision

1 June 2020