STAFF ADVICE

APP203728 – Argento

August 2019
1. Executive Summary

1.1 Argento is a suspension concentrate containing flusulfamide at 50 g/L as the active ingredient, plus other components. It is intended for use as a fungicide for the control of club root in vegetable brassicas and of powdery scab in potatoes.

1.2 The hazard classifications of Argento determined by the EPA staff are: 6.1E (oral), 6.3B, 8.3A, 6.8B, 6.9B, 9.1B and 9.3C.

1.3 With the full suite of controls in place, the risks associated with the use of Argento can be adequately managed.

2. Application Context

Background

2.1 Argento is a suspension concentrate containing flusulfamide at 50 g/L as the active ingredient, plus other components. It is intended for use as a fungicide for the control of club root in vegetable brassicas and of powdery scab in potatoes.

2.2 The formulation of Argento is considered confidential by the applicant.

2.3 The active ingredient, flusulfamide, is already present in one other approved substance at the same concentration as in Argento. This substance (Nebijin 5S, HSR000626) is used to control club root in vegetable brassicas and powdery scab in potatoes.

2.4 Argento has previously been assessed via the s 26 Statutory Determination process with application number APP202937. This assessment determined the hazard classifications of Argento and that a new approval is required under the HSNO Act 1996.

2.5 A Category A assessment of Argento is appropriate because a similar substance (Nebijin 5S, HSR000626) with an identical use pattern is approved. Argento has a higher classification for skin irritancy and eye corrosivity than Nebijin 5S, but the difference in hazard classifications can be assessed qualitatively.

Active ingredient

2.6 To allow evaluation of Argento, key aspects of flusulfamide regulation have been summarised below.

Regulatory status

<table>
<thead>
<tr>
<th>Active ingredient name</th>
<th>Regulatory status and history in New Zealand</th>
<th>International regulatory status and history (Australia, Canada, Europe, Japan, USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flusulfamide</td>
<td>Approved (HSR000626)</td>
<td>Not approved in Australia, Canada, Europe and the USA. Approved in Japan.</td>
</tr>
</tbody>
</table>
2.7 Flusulfamide has previously been approved in New Zealand for use as a fungicide to control club root in vegetable brassicas and powdery scab in potatoes. It is only available for professional use. It is approved in Japan and not approved in other main jurisdictions.

2.8 No quantitative assessment of the risks that flusulfamide poses to human health and the environment has been undertaken, the current approval HSR000626 was approved via the transfer notice.

2.9 The formulation of Argento is considered confidential by the applicant.

Regulatory parameters of active ingredient(s)

Impurities and or restrictions on purity or composition

2.10 No impurity limits for flusulfamide have been identified by FAO / APVMA. The applicant provided a list of impurities that can be present in the technical grade active ingredient, however these impurities are not of toxicological or ecotoxicological concern.

Concentration and maximum application rate

2.11 The concentration of flusulfamide in Argento is the same as the other approved substance with a similar use pattern.

2.12 A maximum application rate has not previously been set for flusulfamide.

Physical form and use pattern

2.13 Argento is formulated as a suspension concentrate.

2.14 The intended use of Argento is as a fungicide for the control of club root in vegetable brassicas applied as a high volume broadcast spray and of powdery scab in potatoes applied as a tuber treatment. The use pattern is summarised in Table 2 and the full outline of intended uses, application methods and application rates are detailed in the GAP table, Table 3.

2.15 The intended application rates are the same as those already permitted under other approvals.

Table 2: Summary of use pattern for Argento

<table>
<thead>
<tr>
<th>Substance category</th>
<th>Wide dispersive use?</th>
<th>Home use?</th>
<th>Concentration</th>
<th>Application rate(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pesticide</td>
<td>✔️ No ☐</td>
<td>Yes ☐ No ✔️</td>
<td>50 g/L</td>
<td>See GAP table</td>
</tr>
</tbody>
</table>
### Table 3: GAP Table for Argento

<table>
<thead>
<tr>
<th>User (a)</th>
<th>Area of Use</th>
<th>Pest or group of pests controlled (c)</th>
<th>Formulation</th>
<th>Application</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetable brassicas (cabbage, cauliflower, broccoli)</td>
<td>F</td>
<td>Club root</td>
<td>SC</td>
<td>50 g/L</td>
<td>High volume broadcast spraying 1 NA 900 to 1800 g/ha</td>
</tr>
<tr>
<td>Potatoes</td>
<td>F</td>
<td>Powdery scab</td>
<td>SC</td>
<td>50 g/L</td>
<td>High volume broadcast spraying 1 NA 900 to 1800 g/ha</td>
</tr>
<tr>
<td>Potatoes</td>
<td>I/F</td>
<td>Powdery scab</td>
<td>SC</td>
<td>50 g/L</td>
<td>Tuber treatment 1 NA 1 to 2 g/tonne of potato tuber</td>
</tr>
</tbody>
</table>

**Remarks**
(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and sucking insects, soil-borne insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions
3. Hazard Assessment

Hazard classification of Argento

3.1 The hazard classifications of Argento determined by the EPA staff during the s26 determination are: 6.1E (oral), 6.3B, 8.3A, 6.8B, 6.9B, 9.1B and 9.3C. Table 4 shows the method used for classification and indicates the main component that contributes to each hazard classification.

Table 4: Hazard classification of Argento

<table>
<thead>
<tr>
<th>Hazard Class/Subclass</th>
<th>Mixture classification</th>
<th>Method of classification</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1 Explosiveness</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>Class 2, 3 &amp; 4 Flammability</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>Class 5 Oxidisers/Organic Peroxides</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>8.1 Metallic corrosiveness</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.1 Acute toxicity (oral)</td>
<td>6.1E</td>
<td>6.1E</td>
<td>☐ ☐ ☒ Flusulfamide</td>
</tr>
<tr>
<td>6.1 Acute toxicity (dermal)</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.1 Acute toxicity (inhalation)</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.1 Aspiration hazard</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.3/8.2 Skin irritancy/corrosion</td>
<td>6.3B</td>
<td>6.3B</td>
<td>☐ ☐ ☒ Component E</td>
</tr>
<tr>
<td>6.4/8.3 Eye irritancy/corrosion</td>
<td>8.3A</td>
<td>8.3A</td>
<td>☐ ☐ ☒ Flusulfamide</td>
</tr>
<tr>
<td>6.5A Respiratory sensitisation</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.5B Contact sensitisation</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.6 Mutagenicity</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.7 Carcinogenicity</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
<tr>
<td>6.8 Reproductive/developmental toxicity</td>
<td>6.8B</td>
<td>6.8B</td>
<td>☐ ☐ ☒ Flusulfamide</td>
</tr>
<tr>
<td>6.8 Reproductive/developmental toxicity (via lactation)</td>
<td>-</td>
<td>ND</td>
<td>☐ ☐ ☐</td>
</tr>
</tbody>
</table>
Staff advice on application for approval to import or manufacture Argento for release (APP203728)

<table>
<thead>
<tr>
<th>Hazard Class/Subclass</th>
<th>Mixture classification</th>
<th>Method of classification</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Applicant’s classification</td>
<td>EPA classification</td>
<td>Mixture data</td>
</tr>
<tr>
<td>6.9 Target organ systemic toxicity (oral)</td>
<td>-</td>
<td>6.9B</td>
<td>☒</td>
</tr>
<tr>
<td>9.1 Aquatic ecotoxicity</td>
<td>9.1B</td>
<td>9.1B</td>
<td>☐</td>
</tr>
<tr>
<td>9.2 Soil ecotoxicity</td>
<td>-</td>
<td>ND</td>
<td>☐</td>
</tr>
<tr>
<td>9.3 Terrestrial vertebrate ecotoxicity</td>
<td>9.3C</td>
<td>9.3C</td>
<td>☐</td>
</tr>
<tr>
<td>9.4 Terrestrial invertebrate ecotoxicity</td>
<td>-</td>
<td>ND</td>
<td>☐</td>
</tr>
</tbody>
</table>

-: No information provided by the applicant

NA: Not Applicable. For instance, testing for a specific endpoint may be omitted if it is technically not possible to conduct the study as a consequence of the properties of the substance e.g. highly volatile, highly reactive or unstable substances cannot be tested; mixing of the substance with water may cause danger of fire or explosion; or the radio-labelling of the substance required in certain studies may not be possible.

ND: Not Determined. Data were unavailable for one or more components.

No: Data are available for the formulation or for all components and classification is not triggered.

1 Use of mixture rules may not adequately take into account interactions between different components in some circumstances and must be considered of lower reliability than data on the mixture itself.


Identification of components of concern (CMRs, vPBTs etc)

3.2 The following component that is present in Argento was identified to be of concern as it is a suspected reproductive toxicant, this classification is also proposed in Japan (suspected of damaging fertility or the unborn child).

Flusulfamide

3.3 Flusulfamide is a suspected reproductive toxicant. Flusulfamide is the active ingredient in Argento, therefore other similar substances also have this hazard classification and the applicant was not asked to reformulate.

4. Risk Assessment

4.1 It is considered that there is potential for significant exposure to people and the environment during the use phase of the lifecycle. Therefore, a qualitative risk assessment was undertaken to understand the likely exposures to the substance under the use conditions proposed by the applicant.
4.2 During the importation, manufacture, transportation, storage and disposal of this substance it is considered that the proposed controls and other legislative requirements will sufficiently mitigate risks to a negligible level.

4.3 This assessment takes into account the existing EPA Notices controls around packaging, identification and disposal of hazardous substances. In addition, the Land Transport Rule 45001, Civil Aviation Act 1990, Maritime Transport Act 1994 and New Zealand’s Health and Safety at Work (Hazardous Substances) (HSW (HS)) requirements all have provisions for the safe management of hazardous substances.

Human health risk assessment

4.4 Argento is intended to be supplied to the professional market. Argento is proposed to be applied by broadcast spray on brassicas and potatoes and then incorporated into the soil, or by band spraying at planting through spray nozzles mounted on the planter and sprayed into the covering discs on potatoes. Argento can also be applied through a misting spray nozzle as the tubers pass over a roller table, prior to planting. It is likely that users will be exposed to the substance during mixing, loading, applying the substance and manipulating potato tubers treated with the substance. Risks during other phases of the lifecycle are mitigated by the prescribed controls.

Acute toxicity via the oral route (6.1E)

4.5 It is very unlikely that people could be exposed to Argento through ingestion under normal operating circumstances during mixing, loading and spraying activities. In the event of exposure, the effect is expected to be minor.

4.6 It is unlikely that treated potatoes could be used for human consumption but contact with treated tubers and subsequent hand-to-mouth contact is likely, and any exposure may result in moderate effects. As such the risk is assessed as being low. It is therefore necessary to set an additional control to label the packages containing tubers treated with this substance to warn users of the hazards. With the prescribed and additional controls in place, the risks from the acute toxicity hazard is considered negligible.

Skin irritancy (6.3B)

4.7 It is unlikely that skin exposure to the undiluted substance may occur during the use of this substance, but any effect is expected to be moderate and reversible. As such the risk from the skin irritancy hazard is assessed as low.

4.8 For professional users, there are prescribed requirements under the Health and Safety at Work (Hazardous Substances) Regulations 2017 [HSW (HS) Regulations] for the use of Personal Protective Equipment (PPE) when working with class 6 or 8 substances to limit exposure to the substance. As such the risk from the skin irritancy hazard is assessed to be negligible.
Eye corrosivity (8.3A)
4.9 It is very unlikely that eye exposure with the undiluted substance will occur during the use of this substance. The most likely route is through getting the substance on the hands and then rubbing the eyes. Any effect is expected to be major and irreversible. As such the risk from the eye corrosivity hazard is assessed as low.

4.10 The prescribed controls include requirements for PPE and as such the risk from the eye corrosivity hazard is assessed to be negligible.

Reproductive toxicity (6.8B)

4.11 Given the use pattern, any long term effects will require multiple exposures to this product over a time period which is improbable. Any effect is expected to be major. As such the risk from the reproductive toxicity hazard is assessed as negligible.

Target organ toxicity via the oral route (6.9B)

4.12 It is considered very unlikely that the substance could be ingested during the use of this substance. The most likely route is through getting the substance on the hands and then putting the hands in the mouth. Any effect is expected to be moderate. As such the risk from the target organ toxicity hazard is assessed as negligible.

Conclusion on human health risk assessment
4.13 For professional users, there are prescribed requirements under the Health and Safety at Work (Hazardous Substances) Regulations 2017 [HSW (HS) Regulations] for the use of PPE when working with class 6 or 8 substances to limit exposure to the substance.

4.14 Taking into account the proposed controls, and the intended use profile and lifecycle of the substance, it is considered that the overall risk to human health from Argento is negligible.

Environmental risk assessment

4.15 Argento is a fungicide that is ecotoxic to the aquatic environment and harmful to terrestrial vertebrates and that will be applied to vegetable brassicas and potatoes; therefore, it has the potential to affect aquatic organisms and terrestrial vertebrates if significant exposure occurs.

4.16 Argento is proposed to be applied by broadcast spray on brassicas and potatoes and then incorporated into the soil, or by band spraying at planting through spray nozzles mounted on the planter and sprayed into the covering discs on potatoes. Argento can also be applied through a misting spray nozzle as the tubers pass over a roller table, prior to planting.

Aquatic ecotoxicity (9.1B)

4.17 It is likely that aquatic organisms will be exposed to Argento, as application may result in spray drift or runoff that results in the substance entering waterways.
4.18 Argento is classified as ecotoxic to aquatic organisms and as such, it is expected that exposure may result in moderate effects to aquatic organisms. The prescribed controls include a requirement not to apply the substance into or into water and not to cause adverse effects beyond the application area.

4.19 Additional controls to restrict the application method to ground-based only and to restrict the application rate to that proposed by the applicant are proposed to minimize environmental exposure.

4.20 With the prescribed and additional controls in place, the risks to aquatic organisms are considered to be negligible.

Toxicity to terrestrial vertebrates (9.3C)

4.21 It is very unlikely that terrestrial vertebrates could be exposed to Argento. Argento is classified as harmful to terrestrial vertebrates and as such, it is expected that any exposure may result in moderate effects to organisms.

4.22 Argento is proposed to be used as a tuber treatment on potatoes and present a risks to terrestrial vertebrates consuming the treated tubers. This risk is considered very unlikely because the treated potatoes are quickly covered by soil and therefore not accessible, and birds are not reported to feed on raw potatoes. As such the risk from the toxicity to terrestrial vertebrate (bird) hazard is assessed as being negligible.

4.23 It is unlikely that treated potatoes could be used for animal consumption, but any exposure may result in moderate effects. As such the risk is assessed as being low. The EPA Labelling Notice requires class 9.3 pesticides coated on seed to be labelled to mitigate this risk. With the prescribed controls in place, the risks to terrestrial vertebrates is considered negligible.

Conclusions on environmental risk assessment

4.24 Additional controls to set application restrictions including a maximum application rate and application method are proposed for Argento in order to limit exposure of this substance to the environment.

4.25 Taking into account the proposed controls, and the intended use profile and lifecycle of the substance, it is considered that the overall risk to the environment from Argento is negligible.

Risk assessment conclusion

4.26 Risks during other phases of the lifecycle are also mitigated by the prescribed controls.

4.27 With the proposed controls in place, the residual risks of the use of Argento are negligible.

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1 Risk assessment provided by the rapporteur Member State the United Kingdom for the new active substance penflufen prepared in the context of the possible inclusion of penflufen in Annex I of the Council Directive 91/414/EEC
5. Controls

Prescribed controls (EPA Notice controls)

5.1 The hazard classifications of Argento determine a set of prescribed controls specified by the EPA Notices. There are also requirements in the HSW (HS) Regulations under the HSW Act.

5.2 The prescribed controls set the baseline for how the substance should be managed and include specifications on how the substance is to be packaged, labelled, stored, disposed of, transported, handled and used. The prescribed controls also set information requirements (e.g., Safety Data Sheets), signage and emergency management.

Labelling and identification

5.3 The name and concentration of the following components need to be specified on the label and SDS:

<table>
<thead>
<tr>
<th>Table 6: List of components requiring identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Label</td>
</tr>
<tr>
<td>Flusulfamide (6.1E, 8.3A, 6.8B)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Variations to prescribed controls

5.4 For the purpose of the prescribed controls under the EPA Hazardous Property Controls Notices, it is considered that potato “seeds” (tubers) are not considered as seeds, and therefore Clause 54 of the Hazardous Property Controls does not apply to Argento.

5.5 This does not apply to the EPA labelling Notice, therefore Clause 21 of the Labelling Notice applies to Argento.

Exposure limits

5.6 No Tolerable Exposure Limit (TEL) has been set previously for the active ingredient in Argento because it is considered that exposure to this substance is not likely to result in an appreciable toxic effect to people, provided conditions of use are followed.

5.7 No Environmental Exposure Limit (EEL) values are set at this time, or have been set previously for flusulfamide, as the level of risk of adverse effects to the environment has been qualitatively assessed as being negligible, with controls in place.
Staff advice on application for approval to import or manufacture Argento for release (APP203728)

Maximum application rate

5.8 Argento has been assessed based on the use pattern described by the applicant. Additional adverse environmental effects (which are not addressed by the prescribed controls) could occur if this product was used outside of its intended use pattern, for example, if it was applied at higher application rate. Therefore, it is considered necessary to set a maximum application rate of 36 L/ha (equivalent to 1800 g flusulfamide/ha) at a frequency of one application per year.

Application method

5.9 Argento has been assessed based on the use pattern described by the applicant. Additional adverse environmental effects (which are not addressed by the prescribed controls) could occur if this product was used outside of its intended use pattern, for example, if it was applied by aerial application methods. Therefore, it is considered necessary to restrict the use of Argento to ground-based application methods.

Additional information

5.10 Information must be provided with tubers coated with this substance that indicates the substance that the tubers have been treated with, its hazardous properties and precautions to be taken in handling the tubers.

Disposal

5.11 The controls specified under the Hazardous Substances (Disposal) Notice 2017 for this substance are applied to tubers treated with this substance as though the tubers have the same hazard classification as this substance.

Labelling

5.12 The substance label and the label of packages containing tubers treated with this substance must specify the personal protective equipment that users must wear when handling the substance, tubers treated with the substance, and equipment that has been used with the substance or tubers treated with the substance.

5.13 The following statement (or words to this effect) must be included on the substance label, and information provided with tubers treated with this substance: “Tubers treated with this substance must be disposed of in accordance with the disposal requirements for toxic and ecotoxic substances as specified under the Hazardous Substances (Disposal) Notice 2017.”

5.14 The label of packages containing tubers treated with this substance must include the following statement (or words to this effect): “Tubers must be completely covered with soil once sown.”
6. Conclusion

6.1 After taking into account the prescribed controls and any proposed variations and additions to these controls, it was concluded that the residual level of risk of any potentially significant adverse effects is negligible.
Confidential appendix: substance composition

The composition of Argento is confidential.