Environmental Protection Authority
Te Mana Rauhī Taiao

EPA STAFF REPORT

Application for approval to import or manufacture Xivana for release

APP204042

FEBRUARY 2022

Overview

Substance	Xivana
Application code	APP204042
Application type	To import or manufacture for release any hazardous substance under Section 28 of the Hazardous Substances and New Organisms Act 1996 (“the HSNO Act”)
Applicant	Bayer New Zealand Limited
Purpose of the application	To import or manufacture Xivana for release
Date application lodged	12 May 2020
Date application formally received	4 September 2020
Submission period	17 November 2021 – 26 January 2022
Submissions	Five submissions were received. Two submissions supported the application, three opposed the application. One submitter wishes to be heard
Information requests and time waivers	The timeframe for the opening of the public consultation was waived under section 59 of the Act

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1. Executive summary

Background

1.1. The applicant Bayer New Zealand Limited, submitted an application on 12 May 2020 to import or manufacture Xivana for release. Xivana is a fungicide for the control of downy mildew in onions and late blight in tomatoes and potatoes, in the form of a suspension concentrate containing 20 g/L fluoxapiprolin as the active ingredient. It was given application number APP204042 and was formally received on 4 September 2020 as a notified Category C application.

1.2. The active ingredient, fluoxapiprolin, has not previously been approved in New Zealand and no overseas jurisdictions have approved this active ingredient to date. At the time the application for Xivana was submitted (May 2020), an application for the approval of fluoxapiprolin was under evaluation in Europe (and is still under evaluation to this date).

1.3. Details on the hazard classifications and risk assessment can be found in the Science Memorandum.

Hazardous properties

Fluoxapiprolin

1.4. The classifications applicable to the active ingredient, fluoxapiprolin, are based on toxicological and ecotoxicological studies conducted using the technical grade active ingredient.

1.5. The following hazard classifications have been identified as applicable to fluoxapiprolin (Table 1).

Table 1: Hazard classifications of fluoxapiprolin

Hazard class	Hazard classification
Acute toxicity (inhalation)	Acute inhalation toxicity Category 4
Hazardous to the aquatic environment	Hazardous to the aquatic environment chronic Category 1

1.6. Fluoxapiprolin is considered persistent in the aquatic environment and in the soil environment. Fluoxapiprolin is considered to have a medium mobility in soil. Fluoxapiprolin is considered to have a low potential for bioaccumulation.

Xivana

1.7. The classifications applicable to Xivana were based on product data, the composition of the substance, and the properties of its components.

1.8. The following hazard classifications have been identified as applicable to Xivana (Table 2).

Table 2: Hazard classifications of Xivana

Hazard class	Hazard classification
Skin sensitisation	Skin sensitisation Category 1B
Hazardous to the aquatic environment	Hazardous to the aquatic environment chronic Category 3

Public consultation

1.9. The application was publicly notified because this substance contains a new active ingredient that has not been approved in New Zealand

1.10. The application was publicly notified, and five submissions were received. Of these, two submissions supported the application and three opposed the application.

Risk assessment

1.11. The EPA conducted quantitative human health and environmental risk assessments to determine if the amount of exposure that people and organisms may experience during use of the substance is likely to result in adverse effects.

Human health effects

1.12. The human health risk assessment results showed that the predicted exposure values to fluoxapiprolin for operators were below the Acceptable Operator Exposure Level (AOEL) without the use of Personal Protective Equipment (PPE). However, it was recommended that PPE is used to minimise risks to the health and safety of workers. The risk assessment results showed that exposure to re-entry workers and bystanders was below the AOEL without the need for an application of a Restricted Entry Interval (REI) control, or a need for a buffer zone to protect bystanders.

1.13. WorkSafe were notified of the application and have provided comments on whether the Health and Safety at Work (HSW) controls manage the risk to people from workplace activities. WorkSafe comments are provided in section 6.11 of this document and their full advice is available as a separate document.

Environmental effects

1.14. A full assessment of the risks for the active ingredient, fluoxapiprolin, in accordance with the Good Agricultural Practice (GAP) table for Xivana, was performed as this active ingredient is new to New Zealand.

1.15. The aquatic risk assessment indicated risks below the level of concern and no additional controls are necessary. Regarding the risk assessment to groundwater and sediment-dwelling organisms, no risks from the use of Xivana were identified.

1.16. Acute and chronic risks to soil organisms following the application of the formulated product Xivana are considered below the level of concern.

1.17. The non-target plant risk assessment indicated that there were no risks to non-target plants (including threatened non-target plants) from fluoxapiprolin when applied to tomatoes, potatoes and onions as the formulated product Xivana.

1.18. The birds risk assessment indicated risks below the level of concern for fluoxapiprolin when applied to tomatoes, potatoes, and onions as the formulated product Xivana.

1.19. The risks to pollinators are below the level of concern and risks are negligible.

1.20. The risks to arthropods are below the level of concern for both off-field and in-field exposure.

Summary of the Māori Impact Assessment

1.21. Kaupapa Kura Taiao (the EPA's Māori Policy and Operations team) has undertaken an assessment to consider potential impacts of Xivana on the economic, social, and cultural well-being of Māori, and the relationship of Māori with the environment, pursuant to sections 5(b), 6(d) and 8 of the HSNO Act.

1.22. Xivana is not likely to adversely affect the relationship of Māori and their culture and traditions with their environment and taonga, including culturally significant species, resources, and places, and the customary values, practices and uses associated with these taonga.

1.23. Xivana is not likely to adversely affect the ability and capacity of Māori to maintain their economic, social, and cultural well-being.

1.24. Ngā Mātāpono o Te Tiriti o Waitangi (the Principles of the Treaty of Waitangi) have been considered in relation to this application – no issues arise in this regard.

Benefit assessment

1.25. The applicant considers that the approval and subsequent availability of Xivana would give rise to benefits, such as; a high level of efficacy against downy mildews in onions, late blight in tomatoes and potatoes, a fungicide with a new mode of action, a fungicide which would be one of the least hazardous amongst the current fungicides registered for the same use pattern, and low levels of residues in treated crops (see the application form for full details about the benefits provided by the applicant).

1.26. The potential benefits of using Xivana have been assessed as significant.

Recommendation

1.27. It is considered that there is sufficient information available to assess the application to import or manufacture Xivana for release. With the proposed controls in place, the risks to human health and the environment from the importation, manufacture, and use of Xivana are negligible. It is considered that the use of Xivana will provide some benefits to onion, tomato, and potato growers.

1.28. With the proposed controls in place, it is therefore considered that benefits of the substance, based on the assessment of the information available, outweigh the risks of the substance.

1.29. It is therefore recommended that the Committee approves the application to import or manufacture Xivana for release.

2. Background

Use pattern

2.1. Xivana is a suspension concentrate (SC) containing 20 g/L fluoxapiprolin as the active ingredient, plus other components. It is intended for use as a fungicide for the control of downy mildew in onions and late blight in tomatoes and potatoes. The applicant seeks to have Xivana approved for ground-based and aerial application methods.

2.2. Application will be at the rate of 1 L of Xivana per hectare, which is equivalent to 20 g fluoxapiprolin per hectare, with a maximum frequency of three applications per season a minimum of seven days apart.

Regulatory status

2.3. Fluoxapiprolin is a new substance to New Zealand.

2.4. Fluoxapiprolin has not been approved in overseas jurisdictions to date. An application for the approval of fluoxapiprolin is currently under evaluation in Europe.

Life cycle of the substance

2.5. The applicant has described the lifecycle of Xivana as follows:

- Xivana will be manufactured overseas and imported by sea or air into New Zealand and packaged ready for sale.

- Xivana will be available in 1 L to 200 L HDPE[1] and co-extruded HDPE/EVOH[2]/HDPE bottles and drums.
- Upon arrival Xivana will be delivered into chemical warehouses in Auckland and Christchurch for bulk storage.
- Form these warehouses, the product will be transported to agricultural distributors who have dedicated pesticide storage facilities.
- In the event of accidental contamination, the applicant recommends that contaminated material should be disposed of at an appropriate chemical disposal facility.
- The applicant recommends that empty packaging should be triple-rinsed and taken to an Agrecovery collection site.

3. Process, consultation, and notification

3.1. The application was formally received on 4 September 2020.

3.2. It was considered that the application would be of significant public interest. This was because Xivana contains a new active ingredient that has not previously been assessed under the Act and it was considered there would be public interest in its intended use; as such, the application was publicly notified.

3.3. The Ministry for the Environment, the Ministry of Health, the Agricultural Compounds and Veterinary Medicines (ACVM) group of the Ministry for Primary Industries (MPI) and the Department of Conservation (DOC) were notified of the submission period. No comments were received.

3.4. WorkSafe New Zealand (WorkSafe) was also notified of this application in order to receive their assessment on aspects of this application related to the Health and Safety at Work Act 2015 (HSW Act) and Health and Safety at Work (Hazardous Substances) Regulations 2017 (HSW HS Regulations). The feedback from WorkSafe is provided in section 6.

3.5. The timeframe for the opening of the public consultation was waived under section 59 of the Act to allow preparation of the draft Science Memorandum, which contains the EPA risk assessment, in order to allow any potential submitter to have this document at their disposal for making an informed submission.

3.6. The application was open for submissions from 17 November 2021 to 26 January 2022.

[1] High density polyethylene

[2] Ethylene vinyl alcohol copolymer

3.7. In preparing this report, the following documents and information were taken into account:

- the application form
- confidential material submitted by the applicant with the application form, including toxicological, ecotoxicological and environmental fate studies on fluoxapiprolin and Xivana
- the submissions
- the Māori Impact Assessment
- information received from WorkSafe
- the science memorandum
- the cultural assessment
- other available information.

4. Hazardous properties

Fluoxapiprolin

4.1. The hazard classifications of fluoxapiprolin determined by the EPA are shown in Table 3. Physico-chemical, mammalian toxicology and ecotoxicology studies were provided for the technical grade fluoxapiprolin. Information from these studies was used to classify the substance.

Table 3: Hazard classifications of fluoxapiprolin

Hazard class	Hazard classification
Acute toxicity (inhalation)	Acute inhalation toxicity Category 4
Hazardous to the aquatic environment	Hazardous to the aquatic environment chronic Category 1

4.2. Fluoxapiprolin is of relatively low acute toxicity in mammals by oral and dermal routes but should be classified Category 4 for acute inhalation toxicity. It is not a skin or eye irritant or a contact sensitiser. Fluoxapiprolin was found not to be genotoxic or carcinogenic and does not cause reproductive or developmental toxicity. Fluoxapiprolin was found not to be neurotoxic in acute or repeated dose oral toxicity studies in laboratory animals, nor display endocrine disrupting potential and should not be classified for target organ toxicity.

4.3. Fluoxapiprolin triggers a Category 1 classification for chronic aquatic ecotoxicicty based on study results available on *Daphnia magna*.

4.4. Fluoxapiprolin was shown to be not readily biodegradable and is considered persistent in the aquatic environment (water/sediment system; max DT_{50} = 42.4 days; criterion is 16 days < DT_{50} < 60 days). Fluoxapiprolin is also considered persistent in the soil environment (DT_{50} = 32.4 days; criterion is 30 days < DT_{50} < 6 months). Fluoxapiprolin is considered to have a medium mobility in soil (K_{oc} = 279 mL/g; criterion is 150 mL/g < K_{oc} < 500 mL/g). Fluoxapiprolin is considered to have a low potential for bioaccumulation (Log K_{ow} = 3.4; criterion is Log K_{ow}< 4).

Xivana

4.5. The hazard classifications of Xivana were determined based on the information provided by the applicant (including toxicity and ecotoxicity studies), information on the individual components of Xivana (mixture rules) and other available information on the active ingredient (Table 4).

Table 4: Hazard classifications of Xivana

Hazard class	Hazard classification
Skin sensitisation	Skin sensitisation Category 1B[3]
Hazardous to the aquatic environment	Hazardous to the aquatic environment chronic Category 3

4.6. Mammalian toxicity studies with Xivana indicate that the substance is of low acute toxicity and should not be classified for acute toxicity. The substance is not irritating to the skin or eyes but is a contact sensitiser (Category 1B).

4.7. No chronic toxicity data on aquatic organisms were available for Xivana. Since aquatic acute toxicity cannot be excluded based on the data available, Xivana is considered best described by chronic aquatic Category 3 due to the uncertainty.

[3] Sub-categories 1A and 1B form part of Category 1 and are used when data are sufficient to allow the allocation of sensitisers into these sub-categories. In the case of APP204042, information provided by the applicant allowed the allocation of Xivana in the sub-category 1B, which corresponds to substances showing a low to moderate frequency of occurrence in humans and/or a low to moderate potency in animals can be presumed to have the potential to produce skin sensitisation in humans (see Guide to classifying hazardous substances in New Zealand for more details).

5. Submissions

5.1. Five submissions were received for this application.

5.2. Two submissions supported the application and three opposed the application (see Table 5 for more details).

Table 5: List of submitters and submissions

Group/organisation	Position	Appearance at a hearing
Onions New Zealand	Support	No
Process Vegetables NZ	Support	No
Te Rūnanga o Ngāi Tahu	Oppose	Yes
Fonterra Cooperative Group Ltd	Oppose	No
Submitter elected to withhold their personal details	Oppose	No

5.3. Key issues raised in submissions are highlighted below. The views summarised below are the submitters views on the application and do not represent the EPA views.

Submissions in support of the application

5.4. Submissions from Onions New Zealand and Process Vegetables NZ highlighted the following benefits:

- The importance of having a new active ingredient / product that is efficacious and will provide more choice to growers, allowing rotation of different modes of action to prevent the development of resistance
- Xivana would be a less hazardous alternative compared with current fungicides registered on onions, tomatoes and potatoes
- The “good rainfastness” associated with Xivana would provide practical benefits for growers
- The low level of residues in treated crops, which is expected to be below the limit of quantification of analytical methods, and which is favourable to access export markets
- Xivana would be approved on several crops, which means that growers can stock less product

Submissions that opposed the application

5.5. Te Rūnanga o Ngāi Tahu expressed concerns that due to fluoxapiprolin's mobility in soil, persistence in the environment, bioaccumulative potential and non-biodegradability, it could affect taonga species. Te Rūnanga o Ngāi Tahu also highlighted that the contact sensitisation classification of Xivana could be removed by substituting the non-active ingredient component triggering this classification. Te Rūnanga o Ngāi Tahu also expressed concerns about the potential for fluoxapiprolin to cause fungicide resistance in the targeted Oomycete fungi.

5.6. Fonterra Cooperative Group Ltd expressed concerns about New Zealand potentially being the first country to accept fluoxapiprolin, which has not been approved by any overseas jurisdiction, and which risks the acceptance of dairy products to the export markets if they contain unacceptable residues of fluoxapiprolin (noting that onions and potatoes can be used as feed supplements, which risks residues in milk). Fonterra Cooperative Group Ltd recommended that the EPA defers consideration of the application for Xivana until a major trading partner (EFSA for the EU) has approved this fungicide and the residue risk in food and dairy products is quantified.

5.7. A member of the public expressed concerns about Xivana not being approved elsewhere or demonstrated to be safe over a long period, bringing unknown risks to New Zealand.

EPA response to the submissions

Efficacy and resistance management

5.8. Onions New Zealand and Process Vegetables NZ highlighted the high level of efficacy with improved yield in trials conducted with Xivana and explained that the approval of Xivana would provide more choice to growers, with the potential to limit resistance. However, Te Rūnanga o Ngāi Tahu explained that *"studies have shown that in test subjects the active ingredient has produced stable Fluoxapiprolin-resistant mutants obtained by fungicide adaptations"* (study reference provided in Te Rūnanga o Ngāi Tahu's submission).

5.9. The EPA notes that efficacy is a matter addressed by ACVM, and therefore is unable to comment on this matter.

5.10. The EPA notes that fluoxapiprolin belongs to Group 49, oxysterol binding protein homologue inhibition (OSBPI). There are currently two fungicide active ingredients that belong to Group 49; oxathiapiprolin and fluoxapiprolin[4]. On the draft label provided by the applicant to the EPA in support of their application, the following information is provided:

[4] Fungicide Action Resistance Action Committee (FRAC) classification of fungicides (https://www.frac.info/)

> *"XIVANA contains fluoxapiprolin from the oxysterol binding protein homologue inhibition (OSBPI) mode of action (Group 49). Resistance to this fungicide and related products could develop in some pest situations from repeated use. To minimize this risk, use strictly in accordance with label instructions. XIVANA must exclusively offered in mixtures or co- packs with non-cross resistant oomyticides with different biochemical modes of action."*

5.11. The EPA notes that resistance management is a well-known challenge associated with the use of pesticides in agricultural situations. Resistance management strategies are developed by the industry[5] and guidelines are developed by various organisations and the industry, which encourage the promotion of risk management tactics with their customers. Whilst there is potential for resistance to develop after the use of Xivana, it is not considered to be significantly different than for other fungicides (especially triazoles and SDHI fungicides).

Hazard profile

5.12. Onions New Zealand and Process Vegetables NZ explained that *"Xivana will be one of the least hazardous of the current fungicides registered for use"*, and that *"the application rate is also significantly less than currently used control options"*.

5.13. The hazard classification determined by the EPA for fluoxapiprolin is: Acute inhalation toxicity Category 4, hazardous to the aquatic environment chronic Category 1.

5.14. Fluoxapiprolin has been determined to have a low potential for bioaccumulation.

5.15. The hazard classifications determined by the EPA for Xivana are skin sensitisation Category 1B, and hazardous to the aquatic environment chronic Category 3. It should be noted that the aquatic classification was determined in the absence of conclusive evidence based on the information available, as opposed to direct test results (see science memo Appendix E for more details).

5.16. The EPA notes that the applicant provided, in the application form, a list of alternative active ingredient fungicides currently approved for the same uses as those proposed for fluoxapiprolin / Xivana. The table below (Table 6) includes some HSNO-approved substances, which contain those active ingredients, alongside their classification. All these

[5] New Zealand Plant Protection Society (Inc) – Pesticide Resistance Strategies (NZPPS pesticide resistance management strategy)

Agcarm – Pesticide resistance (Pesticide resistance - Agcarm)

Ministry for Primary Industries – Labelling Agricultural Chemicals (Guidance Document), 10 September 2020 (Labelling Agricultural Chemicals (mpi.govt.nz))

approvals are currently used by ACVM-registered products with a use pattern similar to Xivana.

5.17. The EPA notes that, when compared on the basis of their respective classifications, Xivana has a more favourable profile than most other fungicides currently available on the market and that were investigated as part of this application (see Table 6 for more details).

Table 6: Comparison between currently approved fungicides for use on potatoes and/or tomatoes (late blight) and/or onions (downy mildew) and Xivana

Fungicide active ingredients	HSNO approved substance	Health hazards (GHS)	Environmental hazards (GHS)
Fluoxapiprolin	Xivana (under evaluation)	Skin Sensitisation Category 1B	Aquatic Chronic 3
Oxathiapiprolin	DuPont Zorvec Enicade fungicide (HSR101125)	Skin Irritation Category 2 Skin Sensitisation Category 1	Designed for biocidal action
Dimethomorph and **Mancozeb**	Granular or powder material containing 75 - 90 g/kg dimethomorph and 600 - 667 g/kg mancozeb (HSR000531)	Skin Irritation Category 2 Eye Irritation Category 2 Skin Sensitisation Category 1 STOT RE 2	Aquatic Acute 1 Aquatic Chronic 1
Azoxystrobin	Azoxystrobin 250 (HSR100559) Note: The EPA has identified 14 ACVM registered products containing azoxystrobin with a similar use pattern (most of these products have a higher classification than HSR100559)	Acute Inhalation Toxicity Category 4 STOT RE 2	Aquatic Chronic 2
Mandipropamid	Revus (HSR007779)	STOT RE 2	Designed for biocidal action

Fungicide active ingredients	HSNO approved substance	Health hazards (GHS)	Environmental hazards (GHS)
Ametoctradin and **Dimethomorph**	Zampro (HSR100709)	Acute Oral Toxicity Category 4 STOT RE 2	Hazardous to terrestrial vertebrates Aquatic Chronic 3
Dimethomorph	Sovrin Flo (HSR007636) Note: The EPA has identified 5 ACVM registered products containing dimethomorph with a similar use pattern	STOT RE 2	Aquatic Chronic 2
Fenamidone	Reason (HSR001758)	STOT RE 2	Hazardous to soil organisms Aquatic Acute 1 Aquatic Chronic 1
Metalaxyl-M and **Mancozeb**	Water dispersible granule containing 640 g/kg mancozeb and 40 g/kg metalaxyl-m (HSR000470)	Skin Sensitisation Category 1 STOT RE 2	Aquatic Acute 1 Aquatic Chronic 1
Mancozeb	Water dispersible granule containing 750 g/kg mancozeb (HSR000808) Note: The EPA has identified 17 ACVM registered products containing mancozeb with a similar use pattern	Eye Irritation Category 2 Skin Sensitisation Category 1 STOT RE 2	Aquatic Acute 1 Aquatic Chronic 1
Copper (in the form of copper hydroxide)	Water dispersible granule or wettable powder containing 350 - 500 g/kg copper as copper hydroxide (HSR000739)	Acute Oral Toxicity Category 4 Serious Eye Damage Category 1 Skin Sensitisation Category 1	Hazardous to terrestrial vertebrates Aquatic Acute 1 Aquatic Chronic 1

Fungicide active ingredients	HSNO approved substance	Health hazards (GHS)	Environmental hazards (GHS)
	Note: The EPA has identified 10 ACVM registered products containing copper (in the form of copper hydroxide) with a similar use pattern	STOT RE 2	
Copper (in the form of copper hydroxide) and **Mancozeb**	Water dispersible granule containing 300 g/kg copper as copper hydroxide and 150 g/kg mancozeb (HSR000614)	Acute Oral Toxicity Category 4 Eye Irritation Category 2 Skin Sensitisation Category 1 STOT RE 2	Hazardous to terrestrial vertebrates Aquatic Acute 1 Aquatic Chronic 1

Rainfastness

5.18. The EPA is unable to comment on the technical properties of a product, such as rainfastness, which is linked to efficacy considerations.

Residues in crops

5.19. The EPA notes that residues in treated commodities is a matter addressed by ACVM, and therefore is unable to comment on this matter.

6. Risk assessment

6.1. During the importation, manufacture, transportation, storage, and disposal of this substance, it is expected that exposure is unlikely to occur and that the proposed controls and other legislative requirements will sufficiently mitigate the risks associated with these stages of the substance lifecycle to a negligible level. These include the existing Hazardous Substances Notices around packaging, identification, emergency management and disposal of hazardous substances, the Land Transport Rule 45001, Civil Aviation Act 1990, Maritime Transport Act 1994 and New Zealand's health and safety at work requirements.

6.2. In contrast, it is considered that there is the potential for exposure to humans and the environment to occur during the use phase of the substance. Therefore, a human health and environmental risk assessment was carried out. In this assessment, the above controls and legislative requirements were taken into account when identifying controls to mitigate risks associated with use of the substance.

Use pattern

6.3. Xivana is a suspension concentrate (SC) containing 20 g/L fluoxapiprolin as the active ingredient, intended for use as a fungicide for the control of downy mildew in onions and late blight in tomatoes and potatoes. Xivana is intended for ground-based and aerial application.

6.4. The proposed application rate is 1 L of Xivana per hectare, which is equivalent to 20 g fluoxapiprolin per hectare, with a maximum frequency of three applications per season a minimum of seven days apart.

Human health effects

6.5. Xivana is intended to be supplied to the professional markets. Users are expected to apply the substance by ground-based and aerial methods. It is likely that users will be exposed to the substance during the application stages of the substance.

6.6. The potential risks posed by Xivana to human health were assessed by estimating the exposure of operators, re-entry workers and bystanders to the active ingredient, fluoxapiprolin.

6.7. To assess the risks posed by the substance to human health, the estimated exposure to fluoxapiprolin for each application scenario was compared to an Acceptable Operator Exposure Limit (AOEL) value for this active ingredient and a Risk Quotient (RQ) was calculated. RQ values below one indicate that predicted exposures are less than the AOEL and are not expected to result in adverse effects. The AOEL used for fluoxapiprolin is 1.7 mg/kg bw/day. This AOEL was based on a 90 days toxicity study on mice.

Risks to operators

6.8. The estimated exposures of the operator to fluoxapiprolin when mixing, loading and applying Xivana by ground-based or aerial application methods are below the AOEL, even without use of personal protective equipment (PPE). Although the quantitative risk assessment indicates that PPE is not required to ensure that exposures are below the AOEL, the requirements under the Health and Safety at Work (Hazardous Substances) Regulations, and in particular Regulations 13.7 and 13.8, state that PPE is to be used to minimise risks to the health and safety of workers.

Risks to workers

6.9. The estimated exposures to fluoxapiprolin for the workers re-entering and working in areas where Xivana has been applied are below the AOEL. Therefore, no restricted entry intervals are necessary to mitigate the risks to human health.

Risks to bystanders

6.10. To assess potential risks to the general population or bystanders from use of Xivana, predicted exposures to fluoxapiprolin for toddlers from different exposure scenarios of spray drift after application of Xivana are compared to an acceptable threshold level. Toddlers are regarded as the most sensitive sub-population and regarded as having the greatest exposures. The estimated risks to bystanders from spray drift are below the level of concern and no buffer zones are proposed to mitigate risks to human health.

WorkSafe's assessment

6.11. WorkSafe were notified of the application on 4 September 2020 and have provided the following comment on whether the HSW controls manage the risk to people from workplace activities:

"WorkSafe has assessed the available information for APP204042 and considers that compliance with the HSW HS Regulations and HSW GRWM Regulations will be adequate to reduce the risks associated with the use of this substance in the workplace. While the regulations cover standard risk mitigation measures, occupational exposure in the workplace needs to be assessed at each site and appropriate controls put in place to mitigate the identified risks."

"When using substances that have human health risks the PCBU must minimise the risks so far as is reasonably practicable by applying the hierarchy of controls set out in Regulation 6 GRWM Regulations."

"Regulation 13.8 of the HSW HS Regulations requires that PPE must be worn when working with this substance to minimise the risks to the health and safety of workers."

"However, PPE should only be used as a control measure for risk when other control measures (higher up the hierarchy of controls) do not mitigate the risk so far as is reasonably practicable. PPE should not be the first or only control considered, WorkSafe expects PCBUs to give preference to other controls that protect multiple at-risk workers at once."

"Under Sections 39 - 42 of HSWA manufacturers/importers/suppliers have a duty to ensure substances manufactured, imported or supplied are without risk so far as is reasonably practicable. Applicants should be mindful of their duties under the Health and Safety at Work Act 2015 when they apply for approval of new substances, where possible new active ingredients that pose no human health risks should be developed."

"In reviewing this application WorkSafe has noted that the EPA has not assigned any human health classifications to the active fluoxapiprolin. This is an good example of an upstream PCBU meeting their duties under section 39-42 of HSWA."

"However, Xivana contains non active ingredient components that may not be required for the efficacy of the product and result in a contact sensitizing classification (6.5B) for the product."

"Without further information from the applicant as to whether it is reasonably practicable to substitute the sensitizing components for non-hazardous components, WorkSafe is concerned that the duties under sections 39-42 may not have been met."

Environmental effects

6.12. It is noted that the applicant provided studies regarding the environmental fate and ecotoxicity of fluoxapiprolin (and metabolites), as well as a number of studies on the formulated substance. The risks to a range of environmental receptors, including plant, invertebrate and vertebrate species living in aquatic environments, groundwater, sediment and terrestrial environments from the use of fluoxapiprolin are considered as a proxy for the risks from Xivana. Full details can be found in the science memorandum.

Risks to aquatic organisms

6.13. Users are expected to apply Xivana by ground-based and aerial application methods. Therefore, it is likely that aquatic species may be exposed to Xivana through spray drift or runoff.

6.14. Predicted concentrations of fluoxapiprolin, applied as the formulated product Xivana, resulted in calculated risks below the level of concern for the aquatic environment. In this case, no additional controls are necessary.

6.15. Regarding the risk assessment to groundwater and sediment-dwelling organisms, risks were calculated as being below the level of concern.

Risks to soil organisms

6.16. Users are expected to apply Xivana by ground-based and aerial application methods on tomatoes, potatoes, and onions. Therefore, it is likely that soil organisms will be exposed to the substance through the substance reaching the soil.

Soil macro-organisms

6.17. No acute risks above the level of concern to threatened and non-threatened species of earthworms in-field were identified, consequently risks for off-field situations are also below the level of concern for earthworms.

6.18. No chronic risks above the level of concern to threatened and non-threatened species of earthworms, springtail and soil mites in-field were identified after application with Xivana, consequently risks for off-field situations are also below the level of concern for earthworms, springtail, and soil mites.

Soil micro-organisms

6.19. No effects on the nitrogen and carbon transformation were observed following application of Xivana. The risks are considered below the level of concern to soil micro-organisms.

Risks to non-target plants

6.20. No risks were identified for fluoxapiprolin to non-target plants (including threatened non-target plants) when applied to tomatoes, potatoes and onions as the formulated product Xivana.

Risks to birds

6.21. The bird screening risk assessment identified acute and chronic risks below the level of concern for threatened and non-threatened species of birds. As no risks were above the level of concern a Tier 1 risk assessment was not performed.

6.22. Fluoxapiprolin is not considered bioaccumulative and therefore no risk assessment via secondary poisoning was performed.

Risks to pollinators

6.23. The risks to pollinators are considered below the level of concern and risks are considered negligible.

Risks to non-target arthropods

6.24. The risks to non-target arthropods are considered below the level of concern for both in-field and off-field exposure.

Assessment of impacts on cultural receptors (Māori Impact Assessment)

Impact on Papatūānuku (Land and soils)

6.25. Xivana is not likely to have a significant impact on Papatūānuku (land and soils) including Te Aitanga a Punga (soil dwelling organisms). See section 3 in Appendix A of the Māori Impact Assessment for more information regarding Papatūānuku.

Impact on Ngā otaota (Plants)

6.26. Xivana is not likely to have a significant impact on culturally important species of otaota (plants). See section 4 in Appendix A of the Māori Impact Assessment for more information regarding ngā otaota.

Impact on Ngā manu, me ngā ngārara (Birds and reptiles)

6.27. Xivana is not likely to have a significant impact on culturally important species of manu (birds) or ngārara (reptiles). See section 5 in Appendix A of the Māori Impact Assessment for more information regarding manu and ngārara.

Impact on Te Aitanga Pepeke (Arthropods)

6.28. Xivana is not likely to have a significant impact on culturally important species of pepeke (arthropods). See section 6 in Appendix A of the Māori Impact Assessment for more information regarding Te Aitanga Pepeke.

Impact on Ngā wai koiora (Aquatic habitats)

6.29. Xivana has been assigned a low-level default classification of being potentially harmful to ngā wai koiora (aquatic habitats) in accordance with international guidelines due to some information gaps regarding toxicity. However, our general assessment based on the available information is that Xivana is not likely to have a significant impact on ngā wai koiora. The controls proposed to be assigned to Xivana should be sufficient for any managing potential adverse effects on these receptors. See section 7 in Appendix A of the Māori Impact Assessment for more information regarding ngā wai koiora.

Impact on Taha hauora (Human health and well-being)

6.30. Although Xivana has a classification indicating potential skin sensitisation, it is not likely to have a significant impact on taha hauora (human health and well-being) even if personal protective equipment (PPE) is not used. However, health and safety at work requirements stipulating use PPE will apply in this case. Therefore, it is anticipated that all four dimensions

of taha hauora would be protected for users, these being: Taha tinana (physical well-being); taha wairua (spiritual well-being); taha hinengaro (mental and emotional well-being); and taha whanaunga (family and social well-being). The controls proposed to be assigned to Xivana should be sufficient for managing any potential adverse effects on taha hauora. See section 8 in Appendix A of the Māori Impact Assessment for more information regarding taha hauora.

Impact on kaitiakitanga and manaakitanga (environmental guardianship and due care)

6.31. Xivana is not likely to have a significant impact on the ability of Māori to exercise kaitiakitanga and manaakitanga (environmental guardianship and due care). See section 9 in Appendix A of the Māori Impact Assessment for more information regarding kaitiakitanga and manaakitanga, as well as section 2 (Ngā taonga tuku iho / Cultural legacies) for further context.

7. Assessment of risks to society, the community, and the market economy

7.1. No risks to society, communities or the market economy from the approval of Xivana have been identified.

8. New Zealand's international obligations

8.1. No international obligations that may be impacted by the approval of Xivana have been identified.

9. Assessment of benefits

High level of efficacy

9.1. The applicant explained that *"a new fungicide like Xivana will be a vital additional tool to assist in safeguarding and promoting the productivity of New Zealand horticulture. It has shown a very high level of efficacy against downy mildews in onions, late blight in tomatoes and potatoes with improved yield in field trials conducted by Bayer".*

9.2. The EPA considers that an efficacious product would be a significant benefit, however, it is noted that efficacy data is assessed by ACVM. Therefore, the level of this benefit is undetermined.

Resistance management strategy

9.3. The applicant noted that *"approval for a new fungicide with a new mode of action for tomatoes and potatoes is useful in resistance management"*.

9.4. The EPA notes that fluoxapiprolin belongs to Group 49, oxysterol binding protein homologue inhibition (OSBPI). There are currently two fungicide active ingredients that belong to Group 49; oxathiapiprolin and fluoxapiprolin.

9.5. The EPA notes that Xivana contains a new active ingredient, which could provide for an additional tool for tomato, potato, and onion growers, therefore this is considered a significant benefit.

Good rainfastness

9.6. The applicant highlighted that Xivana has good rainfastness which would give growers practical benefits.

9.7. The EPA is unable to comment on the technical properties of a product, such as rainfastness, and therefore the level of this benefit is undetermined.

9.8. However, the EPA notes that products, which have low susceptibility to wash-off from precipitation, and which are therefore less likely to lose their efficacy following an event of rain, represent a practical benefit for farmers.

Residues on harvested crops

9.9. The applicant explained that the *"level of residues in treated crops are expected to be below limit of quantification (LoQ). New Zealand produce can continue to enjoy access to overseas markets".*

9.10. The EPA notes that residues in treated commodities is a matter assessed by ACVM, and therefore, the level of this benefit is undetermined.

Hazardous profile and application rate

9.11. The applicant explained that *"Xivana will be one of the least hazardous of the current standard fungicides registered for use in onions, tomatoes and potatoes*" and that *"the application rate of Xivana is significantly less than currently used alternatives"* (resulting in less active ingredient loading to the environment).

9.12. The EPA notes that, when compared on the basis of their respective classifications, Xivana has a more favourable profile than most other fungicides currently available on the market that were investigated as part of this application (more details provided in section 5 and Table 6 of this document).

10. Controls

10.1. The hazard classifications of Xivana determine a set of prescribed controls specified by the EPA Notices. There are also requirements in the Health and Safety at Work (Hazardous Substance, HSW (HS)) Regulations under the HSW Act.

10.2. 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.

10.3. The Hazardous Substances Labelling, Safety Data Sheet (SDS), Packaging, Disposal and Hazardous Property Controls (HPC) Notices Part 1, Part 3, Part 4A and Part 4B 2017 apply to Xivana.

Exposure limits

10.4. The EPA has not set a Tolerable Exposure Limit (TEL) for Xivana, or any element or compound in the substance. This is because it is not considered that exposure is likely to result in an appreciable toxic effect based on the quantitative risk assessment. However, the Acceptable Daily Exposure (ADE) and Potential Daily Exposure (PDE) shown below are proposed by the EPA as health-based exposure guidance values that can be used to inform risk assessments as well as the setting of controls, such as Maximum Residue Levels (MRLs) under the Agricultural Compounds and Veterinary Medicines Act 1997.

10.5. The following values have been provided for fluoxapiprolin:

- ADE = 0.55 mg/kg bw/day
- PDE (food) = 0.385 mg/kg bw/day
- PDE (drinking water) = 0.11 mg/kg bw/day
- PDE (other) = 0.05 mg/kg bw/day

10.6. No Environmental Exposure Limit (EEL) values are proposed for fluoxapiprolin at this time. This is because it is not considered that, with controls in place, environmental exposure is likely to result in an appreciable ecotoxic effect based on the quantitative risk assessment.

Addition and variation of controls to manage risk

10.7. The following variation to clause 50 of the Hazardous Property Controls (HPC) Notice (Part 4B) is proposed under section 77A of the Act to manage the risks of use of Xivana.

Maximum application rate

10.8. The environmental risk assessment was based on the application rates proposed by the applicant. Therefore, it is considered necessary to propose a maximum application rate, number of applications and frequency.

10.9. The maximum application rate for Xivana is 1 L/ha (equivalent to 20 g fluoxapiprolin/ha), with a maximum frequency of three applications per year, and an interval of seven days between applications.

11. Overall evaluation and recommendation

11.1. The proposed use of Xivana results in negligible risks to human health and the environment.

11.2. The potential benefits of using Xivana have been assessed as significant.

11.3. Therefore, it is considered that benefits of the substance, based on the assessment of the information available, outweigh the risks of the substance.

11.4. It is recommended that the Committee approves the application to import or manufacture Xivana for release.

Appendix A: Proposed controls for Xivana

EPA Controls

Control code	Regulation	Control description
LAB	EPA Labelling Notice 2017	Requirements for labelling of hazardous substances
PKG	EPA Packaging Notice 2017	Requirements for packaging of hazardous substances
SDS	EPA Safety Data Sheet Notice 2017	Requirements for safety data sheets for hazardous substances
DIS	EPA Disposal Notice 2017	Requirements for disposal of hazardous substances
HPC-1	EPA Hazardous Property Controls Notice 2017 Part 1	Hazardous Property Controls preliminary provisions
HPC-3	EPA Hazardous Property Controls Notice 2017 Part 3	Hazardous substances in a place other than a workplace
HPC-4A	EPA Hazardous Property Controls Notice 2017 Part 4A	Site and storage controls for substances that are hazardous to the environment
HPC-4B	EPA Hazardous Property Controls Notice 2017 Part 4B	Use of substances that are hazardous to the environment

HSNO Additional Controls and Modifications to Controls

Code	HSNO Act	Control
Application rate	Section 77A	The maximum application rate of this substance is 20 g fluoxapiprolin/ha, maximum 3 application/year, 7 days between applications