Environmental Protection Authority
Te Mana Rauhī Taiao

# Rapid science memo

## REVYLUTION Fungicide

### May 2022

| Substance | REVYLUTION Fungicide |
|---|---|
| Application code | APP204273 |
| Application sub-type | Rapid - Similar |
| Applicant | BASF New Zealand Limited |
| Purpose of the application | To import or manufacture REVYLUTION Fungicide for release |
| Date application formally received | 5 May 2022 |

# 1. Key points

1.1 REVYLUTION Fungicide is an emulsifiable concentrate containing 100 g/L mefentrifluconazole as the active ingredient. It is intended to be imported and applied using ground-based and aerial application methods at rates of up to 150 g mefentrifluconazole/ha to control diseases in cereal and grass seed crops.

1.2 No major issues were identified with this substance.

# 2. Status Of Substance (SOS) or statutory determination history

2.1 No SOS or statutory determinations were issued for REVYLUTION Fungicide.

# 3. Identification of substance and reference

3.1 The reference proposed by the applicant and identified by the EPA are the same (see Table 1)

**Table 1: Identified references for the rapid assessment of REVYLUTION Fungicide**

| | Substance to be approved | Reference |
|---|---|---|
| Name | REVYLUTION Fungicide | Revystar® Fungicide |
| Substance database ID | 27f512bc-f0c4-4625-aaf6-c911c99ecd0f | CFB8E739-472A-44A5-8D26-3DADB23EE7ED |
| HSNO Approval number | - | HSR101415 |
| Substance physical form | Emulsifiable concentrate | Emulsifiable concentrate |
| Active ingredient(s) and concentration (g/L) | Mefentrifluconazole 100 g/L | Mefentrifluconazole 100 g/L and fluxapyroxad 50 g/L |

# 4. RAPID assessment criteria

## Active ingredient

4.1 This substance meets the active ingredients criteria. The concentration of the active ingredient in REVYLUTION Fungicide is the same as that of the reference substance, being mefentrifluconazole at 100 g/L.

## Physical form

4.2 REVYLUTION Fungicide is in the same physical form as the reference substance, namely as an emulsifiable concentrate.

## Use pattern

4.3 This substance meets the use pattern criteria. Both REVYLUTION Fungicide and the reference substance are fungicides used in a similar manner (see Table 2).

**Table 2: Use pattern of REVYLUTION Fungicide in comparison to its reference substance**

| | Substance to be approved | Reference |
|---|---|---|
| Target pest / condition | Various fungal diseases (leaf rust, speckled leaf blotch, stripe rust, brown rust, ramularia leaf spot) | Various fungal diseases (leaf rust, powdery mildew, speckled leaf blotch, stripe rust, brown rust, ramularia leaf and lawn spot, scald) |
| Target animal / crop | Cereals and grass seed (eg wheat, barley, oats, ryecorn triticale and ryegrass) | Wheat and barley |
| Application rate (kg a.i./ha) | 150 g ai/ha | 150 g ai/ha |
| Comment on any differences | NA | |
| Are the differences insignificant in terms of risk of adverse effects? | NA | |

## Major hazardous components

4.4 REVYLUTION Fungicide meets the major hazardous components criteria. The major hazardous components in REVYLUTION Fungicide constitute a lower proportion than in the reference substance.

## Adverse effects

4.5 REVYLUTION Fungicide meets the adverse effects criteria. This substance has an overall reduced hazard profile compared to the reference substance, however, REVYLUTION Fungicide triggers a specific target organ toxicity (single exposure) Category 3 classification. This is due to a solvent that is present in both substances but is at a higher concentration in REVYLUTION Fungicide, thereby triggering the classification (see Table 3).

4.6 This classification difference does not generate any additional controls under either Hazardous Substance and New Organisms (HSNO) or Health and Safety at Work (Hazardous Substances) Regulations 2017 (HSW (HS) Regulations) and any differences are expected to be minor in effect. Therefore, it is considered that REVYLUTION Fungicide meets the adverse effects criteria.

**Table 3: Comparison of the respective classifications of REVYLUTION Fungicide and its reference substance**

| | Classification comparison |
|---|---|
| Substance | acute inhalation toxicity Category 4 |
| | skin irritation Category 2 |
| | **specific target organ toxicity – single exposure Category 3** |
| | specific target organ toxicity – repeated exposure Category 2 |
| | hazardous to the aquatic environment chronic Category 1 |
| Reference | **acute oral toxicity Category 4** |
| | acute inhalation toxicity Category 4 |
| | skin irritation Category 2 |
| | **eye irritation Category 2** |
| | **skin sensitisation Category 1** |
| | specific target organ toxicity – repeated exposure Category 2 |
| | hazardous to the aquatic environment chronic Category 1 |
| | **hazardous to terrestrial vertebrates** |

# 5. Controls

## EPA Notice controls

5.1 The Labelling, Safety Data Sheet (SDS), Packaging, Disposal and Hazardous Property Controls (HPC) Part 1, Part 3, Part 4A, Part 4B and Part 4C Notices apply to REVYLUTION Fungicide.

5.2 No Tolerable Exposure Limit (TEL) values have been set previously for the active ingredient in REVYLUTION Fungicide because it is considered that exposure to this substance is not likely to result in an appreciable toxic effect to people, provided controls on use are followed.

5.3 No Environmental Exposure Limit (EEL) values are set at this time or have been set previously for the active ingredient in REVYLUTION Fungicide, as the level of risk of adverse effects to the environment has been qualitatively assessed as being negligible, with controls in place.

## Controls varied or added under section 77A and 77A

## Maximum application rate

5.4 The following maximum application, frequency rate and interval periods have been set for REVYLUTION Fungicide:

- The maximum application rate is 1.5 L of REVYLUTION Fungicide/ha (equivalent to 150 g mefentrifluconazole/ha), with a maximum of two applications per year and a minimum interval of 21 days between applications.

## Application method

5.5 When applied using ground-based methods, the nozzle must be set to a medium droplet quality spray, as defined by the American Society of Agricultural and Biological Engineers ASABE Standard (S572) or the British Crop Production Council guideline.

5.6 When applied using aerial methods, the nozzle must be set to a coarse droplet quality spray, as defined by the American Society of Agricultural and Biological Engineers ASABE Standard (S572) or the British Crop Production Council guideline.

5.7 The substance must not be applied when wind speeds are less than 3 km/h or more than 20 km/h as measured at the application site.

## Label

5.8 The information about the application method must be stated on the label.

## Impurity limit

5.9 The following maximum limits are set for the toxicologically relevant impurities in the active ingredient mefentrifluconazole used to manufacture REVYLUTION Fungicide, based on those identified by the European Union (EU):

- *N,N*-dimethylformamide (DMF; CAS 68-12-2): 0.5 g/kg
- Toluene (CAS 108-88-3): 1 g/kg
- 1,2,4-(1H)-triazole (CAS 288-88-0): 1 g/kg

# Appendix A: Study summaries

## Toxicity

### Table 4: Acute Oral Toxicity

| | |
|---|---|
| Type of study | Acute oral toxicity in rats |
| Flag | Key study |
| Test Substance | BAS 750 01 F |
| Endpoint | Acute lethality ($LD_{50}$), signs of toxicity |
| Value | $LD_{50}$: > 2000 mg/kg bw |
| Reference | [redacted] 2015. BAS 750 01 F - Acute oral toxicity study in rats. [redacted] |
| Klimisch Score | 1 |
| Amendments/Deviations | None of significance |
| GLP | Yes |
| Test Guidelines | OECD TG 423; Commission Regulation (EC) No 440/2008; US EPA OPPTS 870.1100; Japan MAFF. 8147 |
| Species | Rat |
| Strain | Wistar (Crl:WI (Han) SPF) |
| No/Sex/Group | Group 1: 2000 mg/kg bw in 3 F<br>Group 2: 2000 mg/kg bw in 3 F |
| Dose Levels | 2000 mg/kg bw |
| Exposure Type | Oral by gavage |
| Study Summary | Two test groups containing three female rats, each animal was given 2000 mg/kg bw of the test substance.<br>No mortality was observed in either test group.<br>Clinical signs of toxicity were detected in all animals from both groups, consisting of an impaired general state and piloerection. |

| | |
|---|---|
| | The body weight of the animals increased within the normal range throughout the study period.<br><br>No macroscopic pathologic abnormalities were observed in any animal at study termination. |
| Additional Comments | No additional comments |
| **Conclusion** | The $LD_{50}$ > 2000 mg/kg bw. Therefore, the substance does not classify as an acute oral toxicant. |

## Table 5: Acute Dermal Toxicity

| | |
|---|---|
| Type of study | Acute dermal toxicity study in rats |
| Flag | Key study |
| Test Substance | BAS 750 01 F |
| Endpoint | $LD_{50}$ |
| Value | $LD_{50}$: > 5000 mg/kg bw |
| Reference | [redacted] 2015. BAS 750 01 F - Acute dermal toxicity study in rats. [redacted] |
| Klimisch Score | 1 |
| Amendments/Deviations | None of significance |
| GLP | Yes |
| Test Guidelines | OECD TG 402; Commission Regulation (EC) No 440/2008; US EPA OPPTS 870.1200; Japan MAFF 8147 |
| Species | Rat |
| Strain | Wistar (Crl:WI (Han) SPF) |
| No/Sex/Group | 5/sex/group |
| Dose Levels | 5000 mg/kg bw |
| Exposure Type | Dermal under a semi-occlusive dressing |
| Study Summary | No mortality or signs of toxicity were detected or observed.<br><br>One female animal showed very slight to well-defined erythema, incrustations and scaling within the first three days after receiving the test substance. |

| | |
|---|---|
| | The body weight of the animals increased within the normal range throughout the study period.<br>No macroscopic pathologic abnormalities were observed in any animal at study termination. |
| Additional Comments | No additional comments |
| **Conclusion** | The $LD_{50}$ was > 5000 mg/kg bw. Therefore, the substance does not classify as an acute dermal toxicant. |

**Table 6: Acute** Inhalation Toxicity

| | |
|---|---|
| Type of study | Acute inhalation toxicity study in rats |
| Flag | Key study |
| Test Substance | BAS 750 01 F |
| Endpoint | $LC_{50}$ |
| Value | 2.4 mg/L < $LC_{50}$ < 5.4 mg/L |
| Reference | [redacted] 2014. BAS 750 01 F: 4-Hour Acute Inhalation Toxicity Study in the Rat. [redacted] |
| Klimisch Score | 1 |
| Amendments/Deviations | None of significance |
| GLP | Yes |
| Test Guidelines | OECD 403; Commission Regulation (EC) No 1907/2006 and 440/2008; US EPA OPPTS 870.1300; Japan MAFF. 8147 |
| Species | Rat |
| Strain | RccHan: WIST(SPF) |
| No/Sex/Group | 5/sex/group |
| Dose Levels | Group 1: 5.4 mg/L air; MMAD / GSD (mean): between 1.89 µm and 1.97 µm / 2.34<br>Group 2: 2.4 mg/L air; MMAD / GSD* (mean): between 2.35 µm and 2.41 µm / 2.35<br>*Mass Median Aerodynamic Diameter (MMAD) and Geometric Standard Deviation (GSD) |

| | |
|---|---|
| Exposure Type | Nose only (4-hour exposure) |
| Study Summary | Two test groups containing five male and five female rats were exposed to 2.4 mg/L and 5.4 mg/L air.<br><br>In group 1, three males and four females died after being exposed to 5.4 mg/L air, while all remaining animals in this group survived the scheduled observation period.<br><br>In group 2, one female animal died after being exposed to 2.4 mg/L air, while all remaining animals in this group survived the scheduled observation period.<br><br>Signs of toxicity were observed after exposure to 5.4 mg/L air. These were: decreased activity, hunched posture, ruffled fur, laboured breathing, breathing noises and salivation. The observed ruffled fur and breathing noises in the two surviving males persisted until the end of the test period, while ruffled fur, hunched posture, laboured breathing and breathing noises persisted until the end of the observation period in the surviving female animal.<br><br>Signs of toxicity were also observed after exposure to 2.4 mg/L air. These were: ruffled fur, laboured breathing, breathing noises and salivation. These generally receded within the first week after exposure. However, breathing noises were observed during the first and second week after exposure (in females), with slight breathing noises in one male and two females persisting until the end of the observation period.<br><br>Body weight loss or stagnation of body weight gain was observed after exposure in both groups. The surviving animals exposed to 5.4 mg/L air continued to lose weight in the second week after exposure, while surviving animals exposed to 2.4 mg/L air regained body weight in the second week, with the exception of one female animal.<br><br>Macroscopic pathologic abnormalities were observed at necropsy. In animals that died or were sacrificed *in extremis* during the observation period following the exposure to 5.4 mg/L air, reddish discoloration of the lungs, dark red discoloration of the lungs and mandibular lymph nodes, sore skin and beginning autolysis were observed. However, these were not considered a result of exposure to the test substance but rather a result of decaying processes.<br><br>Intestines distended in three females exposed to 5.4 mg/L air and one female exposed to 2.4 mg/L air.<br><br>No macroscopic findings were present at necropsy in the male animals that survived exposure to 5.4 mg/L and 2.4 mg/L. The one surviving female exposed to 5.4 mg/L and three surviving females exposed to 2.4 mg/L air showed no macroscopic abnormalities. |
| Additional Comments | No additional comments |

| | |
|---|---|
| **Conclusion** | The $LC_{50}$ is greater than 2.4 mg/L but less than 5.4 mg/L. Therefore, the substance classifies as acute inhalation toxicity Category 4. |

**Table 7: Skin** Corrosion/Irritation

| | |
|---|---|
| Type of study | Acute dermal irritation/corrosion in rabbits |
| Flag | Key study |
| Test Substance | BAS 750 01 F |
| Endpoint | Mean Draize Score |
| Value | The Mean Draize Scores (24, 48, 72 hours) is 2.0 for erythema and 0.8 for oedema |
| Reference | [redacted] 2015. BAS 750 01 F - Acute dermal irritation / corrosion in rabbits. [redacted] |
| Klimisch Score | 1 |
| Amendments/Deviations | None of significance |
| GLP | Yes |
| Test Guidelines | OECD 404; Commission Regulation (EC) No 1907/2006 and 440/2008; US EPA OPPTS 870.2500; Japan MAFF 8147 |
| Species | Rabbit |
| Strain | New Zealand White: Crl:KBL(NZW) – Charles River (SPF) |
| No/Sex/Group | 3 F |
| Dose Levels | 0.5 mL |
| Exposure Type | Dermal under semi-occlusive dressing |
| Study Summary | Cutaneous reactions were observed approximately 1, 24, 48 and 72 hours after application of the test substance, and weekly until day 14 of the study period.<br><br>The following clinical observations were observed during the study period: very slight to moderate erythema (grade 1 to 3); very slight to slight oedema (grade 1 to 2); scaling; findings of erythema and oedema beyond the application site. |

Irreversible cutaneous reactions were observed within the 14-day study period.

The Mean Draize Scores (24, 48, 72 hours) for erythema and oedema are:

Erythema:

| **Animal No.** | **0 hr** | **1 hr** | **24 hr** | **48 hr** | **72 hr** | **7 d** | **14 d** |
|---|---|---|---|---|---|---|---|
| **1** | 1 | 2 | 2 | 2 | 2 | 3 | 3 |
| | | | Mean score: 6 / 3 = 2 | | | | |
| **2** | 2 | 2 | 2 | 2 | 3 | 3 | 3 |
| | | | Mean score: 7 / 3 = 2.3 | | | | |
| **3** | 1 | 3 | 2 | 2 | 3 | 3 | 2 |
| | | | Mean score: 7 / 3 = 2.3 | | | | |

Oedema:

| **Animal No.** | **0 hr** | **1 hr** | **24 hr** | **48 hr** | **72 hr** | **7 d** | **14 d** |
|---|---|---|---|---|---|---|---|
| **1** | 0 | 1 | 0 | 1 | 1 | 2 | 2 |
| | | | Mean score: 2 / 3 = 0.67 | | | | |
| **2** | 0 | 1 | 1 | 1 | 2 | 2 | 2 |
| | | | Mean score: 4 / 3 = 1.3 | | | | |
| **3** | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | | | Mean score: 1 / 3 = 0.33 | | | | |

| | |
|---|---|
| Additional Comments | No additional comments |
| **Conclusion** | The mean scores over 24, 48 and 72 hours were 2.2 for erythema and 0.8 for oedema. Cutaneous reactions were observed as being irreversible, therefore, the substance is classified as a skin irritant Category 2. |

**Table 8: Serious eye damage/eye irritation**

| | |
|---|---|
| Type of study | Acute eye irritation/corrosion in rabbits |
| Flag | Key study |
| Test Substance | BAS 750 01 F |
| Endpoint | Mean Draize Score corneal opacity, conjunctiva (redness and chemosis) and iris lesions |
| Value | Mean Draize Score -<br>Cornea opacity: 1.4<br>Conjunctiva:<br>- Redness: 1.0<br>- Chemosis: 1.0<br>Iris: 0.9 |
| Reference | [redacted]2015. BAS 750 01 F - Acute eye irritation in rabbits. [redacted] |
| Klimisch Score | 1 |
| Amendments/Deviations | None of significance |
| GLP | Yes |
| Test Guidelines | OECD 405; Commission Regulation (EC) No 1907/2006 and 440/2008; US EPA OPPTS 870.2400; Japan MAFF. 8147 |
| Species | Rabbit |
| Strain | New Zealand White; Hsdlf: NZW – Harlan (SPF) |
| No/Sex/Group | 3 F |
| Dose Levels | 0.1 mL |
| Exposure Type | Ocular application to conjunctival sac (right eye) |
| Study Summary | Ocular reactions were assessed approximately 1, 24, 48 and 72 hours after application of the test substance.<br><br>The following clinical observations were observed during the study period: very slight to moderate corneal opacity (grade 1 to 2); moderate iritis (grade 1); slight conjunctival redness (grade 1); slight conjunctival chemosis (grade 1); slight to severe discharge (grade 1 to 3). |

Additionally, contracted pupil, desquamation of corneal epithelium, corneal lesions detected with the aid of fluorescein (grade 2 to 4) and injected scleral vessels in a circumscribed or circular area were noted in the animals within 72 hours after application.

Reversible ocular reactions were observed within 7-day study period.

The Mean Draize Scores (24, 48, 72 hours) for corneal opacity, conjunctiva (redness and chemosis) and iris lesions are:

Corneal opacity

| **Animal No.** | **1 hr** | **24 hr** | **48 hr** | **72 hr** | **7 d** |
|---|---|---|---|---|---|
| **1** | 1 | 2 | 2 | 2 | 0 |
| | | Mean score: 6 / 3 = 2 | | | |
| **2** | 1 | 1 | 1 | 2 | 0 |
| | | Mean score: 4 / 3 = 1.33 | | | |
| **3** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |

Conjunctiva redness

| **Animal No.** | **1 hr** | **24 hr** | **48 hr** | **72 hr** | **7 d** |
|---|---|---|---|---|---|
| **1** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |
| **2** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |
| **3** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |

Conjunctiva chemosis:

| **Animal No.** | **1 hr** | **24 hr** | **48 hr** | **72 hr** | **7 d** |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| **1** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |
| **2** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |
| **3** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |

Iris:

| **Animal No.** | **1 hr** | **24 hr** | **48 hr** | **72 hr** | **7 d** |
|---|---|---|---|---|---|
| **1** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |
| **2** | 1 | 1 | 1 | 1 | 0 |
| | | Mean score: 3 / 3 = 1 | | | |
| **3** | 1 | 1 | 1 | 0 | 0 |
| | | Mean score: 2 / 3 = 0.67 | | | |

| | |
|---|---|
| Additional Comments | No additional comments |
| **Conclusion** | The mean scores over 24, 48 and 72 hours for all three animals were 1.4 for Cornea opacity, 1.0 for conjunctiva redness and chemosis, respectively, and 0.9 for iritis. Therefore, the substance is not classified for eye irritation/corrosion. |

**Table 9: Skin Sensitisation**

| | |
|---|---|
| Type of study | Skin Sensitisation – Local Lymph Node Assay (LLNA) |
| Flag | Key study |
| Test Substance | BAS 750 01 F |
| Endpoint | Stimulation Index (SI) |
| Value | SI < 3 |
| Reference | [redacted]2015. BAS 750 01 F: Skin Sensitisation: Local Lymph Node Assay. [redacted] |
| Klimisch Score | 1 |
| Amendments/Deviations | None of significance |
| GLP | Yes |
| Test Guidelines | OECD 429; Commission Regulation (EC) No. 440/2008, B.42; US EPA OPPTS 870.2600 |
| Species | Mouse |
| Strain | CBA/CaOlaHsd |
| No/Sex/Group | 5 F/ group |
| Dose Levels | 1, 2 and 5% (w/w) |
| Exposure Type | Topical application (25 µL/ear dorsum) |
| Study Summary | Animals treated with 1 and 2% test substance concentration did not show any signs of skin irritation, while erythema was observed in animals treated with the 5% (score 1).<br><br>No significant increase in ear weights was observed in any of the test groups when compared to the vehicle control group.<br><br>Stimulation Indices (SI) of 0.89, 0.80 and 0.94 were determined with the test substance at concentrations of 1, 2 and 5% (w/w) in acetone/olive oil (4+1, v/v), respectively.<br><br>As no SI greater than 3 were observed, the EC3 value could not be calculated. |
| Additional Comments | No additional comments |

| | |
|---|---|
| **Conclusion** | SI < 3, therefore, the test substance is not considered a skin sensitiser. |