

REGISTRATION REPORT

Part A

Risk Management

Product code: Difenoconazole 10.7 + Folpet 360 SC

Product name: DIFOL 360

Chemical active substances:

difenoconazole, 10.7 g/L

folpet, 360 g/L

Southern Zone

Zonal Rapporteur Member State: France

NATIONAL ASSESSMENT FRANCE

(authorisation)

Applicant: Globachem NV

Updated version : 02/06/2023

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PART A

RISK MANAGEMENT

1 Details of the application

The company Globachem NV has requested a marketing authorisation in France for the product DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) (formulation code: Difenoconazole 10.7 + Folpet 360 SC), containing 10.7 g/L difenoconazole and 360 g/L folpet, as a fungicide for professional uses.

The risk assessment conclusions provided in this document are based on the information, data and assessments provided in the Registration Report, Part B Sections 1-10 and Part C, and where appropriate the addenda for France. The information, data and assessments provided in the Registration Report, Part B include assessment of further data or information as required at national registration by EU regulations. It also includes assessment of data and information related to DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) where those data have not been considered in the EU peer review process. Otherwise assessments for the safe use of DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) have been made using endpoints agreed in the EU peer reviews of difenoconazole and folpet.

This document describes the specific conditions of use and labelling required for France for the registration of DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC).

Appendix 1 of this document provides a copy of the product authorisation.

Appendix 2 of this document contains a copy of the product label (draft as proposed by the applicant).

Appendix 3 of this document contains a copy of the Letter(s) of Access.

Appendix 4 of this document is the list of data considered for national authorisation.

1.1 Application background

The present registration report concerns the evaluation of Globachem NV's application to market DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) in France as a fungicide (product uses described under point 2.3). France acted as a zonal Rapporteur Member State (zRMS) for this request and assessed the application submitted for the first authorisation of this product in France and in other MSs of the Southern zone.

The present application (2016-2023) was evaluated in France by the French Agency for Food, Environmental and Occupational Health & Safety (Anses) in the context of the zonal procedure for all Member States of the Southern zone, taking into account the worst-case uses ("risk envelope approach")¹ – the highest application rates applied for in the Southern Zone. When risk mitigation measures were necessary, they are adapted to the situation in France.

The updated version concerns the evaluation of new data submitted by Globachem NV's on the 29/12/2020 for the Toxicology, Ecotoxicology and Efficacy sections (application 2021-0167).

The current document (RR) based on Anses's assessment of the application submitted for this product is in

¹ SANCO document "risk envelope approach", European Commission (14 March 2011). [Guidance document on the preparation and submission of dossiers for plant protection products according to the "risk envelope approach"; SANCO/11244/2011 rev. 5](#)

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compliance with Regulation (EC) no 1107/2009², implementing regulations, and French regulations.

The data taken into account are those deemed to be valid either at European Union level or at zonal/national level. This part A of the RR presents a summary of essential scientific points upon which recommendations are based and is not intended to show the assessment in detail.

The conclusions on the acceptability of risk are based on the criteria provided in Regulation (EU) No 546/2011³, and are expressed as “acceptable” or “not acceptable” in accordance with those criteria.

1.2 Letters of Access

The applicant has provided letters of access for active substance and PPP data.

1.3 Justification for submission of tests and studies

According to the applicant: “As *Difenoconazole 10.7 + Folpet 360 SC* is a mixture of two active substances and was not the lead formulation during the Annex I inclusion of *Difenoconazole* and *Folpet*, it is not possible to refer to the DAR and the EFSA conclusions on *Difenoconazole* and *Folpet* with regard to the formulation studies. Therefore, studies on the plant protection product *Difenoconazole 10.7 + Folpet 360 SC* had to be generated for authorisation purposes in the Southern zone.”

1.4 Data protection claims

Where protection for data is being claimed for information supporting registration of DIFOL 360, it is indicated in the reference lists in Appendix 1 of the Registration Report, Part B Sections 1-7.

2 Details of the authorisation decision

2.1 Product identity

| | |
|--|---|
| Product code | Difenoconazole 10.7 + Folpet 360 SC. |
| Product name in MS | DIFOL 360. |
| Authorisation number | N/A : no marketing authorisation granted |
| Low risk (article 47) | No. |
| Function | Fungicide. |
| Applicant | Globachem NV. |
| Active substance(s) (incl. content) | 10.7 g/L difenoconazole + 360 g/L folpet. |
| Formulation type | Suspension concentrate [code: SC]. |
| Packaging | N/A : no marketing authorisation granted |
| Coformulants of concern for national authorisations | None. |
| Restrictions related to identity | None. |
| Mandatory tank mixtures | None. |

² REGULATION (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC

³ COMMISSION REGULATION (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products

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| | |
|---------------------------|-------|
| Recommended tank mixtures | None. |
|---------------------------|-------|

2.2 Conclusion

The evaluation of the application for PRODUCT NAME resulted in the decision **to refuse** the authorisation.

2.3 Substances of concern for national monitoring

Refer to 5.1.1.

2.4 Classification and labelling

2.4.1 Classification and labelling under Regulation (EC) No 1272/2008

2.4.2 N/A : no marketing authorisation granted Standard phrases under Regulation (EU) No 547/2011

2.4.3 N/A : no marketing authorisation granted Other phrases (according to Article 65 (3) of the Regulation (EU) No 1107/2009)

None.

2.5 Risk management

According to the French law and procedures, specific conditions of use are set out in the Decision letter. The French Order of 4 May 2017⁴ provides that:

- unless otherwise stated in the product authorisation, the pre harvest interval (PHI) is at least 3 days;
- unless otherwise stated in the product authorisation, the minimum buffer zone alongside a water body is 5 metres;
- unless otherwise stated in the product authorisation, the minimum re-entry period is 6 hours for field uses and 8 hours for indoor uses.

Drift reduction measures such as low-drift nozzles are not considered within the decision-making process in France. However, non-spraying buffer zones may be reduced under some circumstances as explained in appendix 3 of the above-mentioned French Order.

Finally, the French Order of 12 April 2021⁵ provides that:

- an authorisation granted for a “reference” crop applies also for “linked” crops, unless formally stated in the Decision
- the “reference” and “linked” crops are defined in Appendix 1 of that French Order.

Thus, at French national level, possible extrapolation of submitted data and the corresponding assessment from “reference” crops to “related” ones are undertaken even if not clearly requested by the applicant in their dRR, and a conclusion is also reached on the acceptability of the intended uses on those “related”

⁴ Arrêté du 4 mai 2017 relatif à la mise sur le marché et à l'utilisation des produits phytopharmaceutiques et de leurs adjuvants visés à l'article L. 253-1 du code rural et de la pêche maritime <https://www.legifrance.gouv.fr/eli/arrete/2017/5/4/AGRG1632554A/jo/texte>

⁵ <http://www.legifrance.gouv.fr/eli/arrete/2014/3/26/AGRG1407093A/jo>

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crops. The aim of this Order, mainly based on the EU document on residue data extrapolation⁶ is to supply “minor” crops with registered plant protection products.

Therefore the GAP table (Section 2.3) and Decision may include uses on crops not originally requested by the applicant.

The Decision, as reproduced in Appendix 1, takes also into account national provisions, including national mitigation measures.

2.5.1 Restrictions linked to the PPP

N/A : no marketing authorisation granted

2.5.2 Specific restrictions linked to the intended uses

Some of the authorised uses are linked to the following conditions in addition to those listed under point 2.5.1 (mandatory labelling):

None.

⁶ SANCO document “guidance document:- Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs”: SANCO/ 7525/VI/95 - rev.9

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2.6 Intended uses (only NATIONAL GAP)

Please note: The GAP Table below reports the intended uses proposed by the applicant, and possible extrapolation according to French Order of 12 April 2021 (highlighted in green), evaluated and concluded as safe uses by France as zRMS. Those uses are then granted in France.

When the conclusion is “not acceptable”, the intended use is highlighted in grey and the main reason(s) reported in the remarks.

When a use is “acceptable” with GAP restrictions, the modifications of the GAP are in bold.

Use should be crossed out when the applicant no longer supports this use.

GAP rev. 1, **date: June-02-2023**

| | | | |
|--------------------------|---|-----------------------|-------------------------------------|
| PPP (product name/code): | DIFOL 360/Difenoconazole 10.7 + Folpet 360 SC | Formulation type: | Suspension concentrate (SC) |
| Active substance 1: | difenoconazole | Conc. of a.s. 1: | 10.7 g/L |
| Active substance 2: | folpet | Conc. of a.s. 2: | 360 g/L |
| Applicant: | Globachem NV | Professional use: | <input checked="" type="checkbox"/> |
| Zone(s): | Southern | Non-professional use: | <input type="checkbox"/> |
| Verified by MS: | yes | | |
| Field of use: | fungicide | | |

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
|----------------------------|--------------------|---|---|--|------------------|---|--|--|---|---|-----------------------------------|---------------|---|
| Use- No. ^(e) | Member state(s) | Crop and/ or situation (crop destina- tion / purpose of crop) | F, Fn, Fpn G, Gn, Gpn or I | Pests or Group of pests controlled (additionally: devel- opmental stages of the pest or pest group) | Application | | | | Application rate | | | PHI (days) | Remarks: e.g. g saf- ener/synergist per ha ^(f) |
| | | | | | Method / Kind | Timing / Growth stage of crop & season | Max. number a) per use b) per crop/ season | Min. interval between applications (days) | L product / ha a) max. rate per appl. b) max. total rate per crop/season | g a.s./ha a) max. rate per appl. b) max. total rate per crop/season | Water L/ha min / max | | |

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| Zonal uses (field or outdoor uses, certain types of protected crops) | | | | | | | | | | | | | |
|--|----|-------|---|--|---------------------------------|--------------------------------------|--------------|--------------------------|-----------------------------|---|------------|-----|------------------------------------|
| 1 | FR | Apple | F | Apple scab (<i>Venturia inaequalis</i>) | Broadcast air-assisted spraying | When first symptoms occur, up to PHI | a) 3 b) 3 | a) 10 days b) 10 days | a) 3.5 L/ha b) 10.5 L/ha | a) 37.5 g difenoconazole/ha + 1260 g folpet/ha b) 113 g difenoconazole/ha + 3780 g folpet/ha | 300 - 1000 | 120 | Not Acceptable (consumer exposure) |
| 2 | FR | Pear | F | Pear scab (<i>V. pyrina</i>) | Broadcast air-assisted spraying | When first symptoms occur, up to PHI | a) 3 b) 3 | a) 10 days b) 10 days | a) 3.5 L/ha b) 10.5 L/ha | a) 375 g difenoconazole/ha + 1260 g folpet/ha b) 113 g difenoconazole/ha + 3780 g folpet/ha | 300 - 1000 | 120 | Not Acceptable (consumer exposure) |

* The application is possible during the flowering period in line with the application of the French Order of November 20, 2021 (arrêté du 20 novembre 2021 relatif à la protection des abeilles et des autres insectes pollinisateurs et à la préservation des services de pollinisation lors de l'utilisation des produits phytopharmaceutiques).

| | | | | |
|-------------------------------|-----|--|-----|--|
| Remarks table heading: | (a) | e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR) | (d) | Select relevant |
| | (b) | Catalogue of pesticide formulation types and international coding system CropLife International Technical Monograph n°2, 6th Edition Revised May 2008 | (e) | Use number(s) in accordance with the list of all intended GAPS in Part B, Section 0 should be given in column 1 |
| | (c) | g/kg or g/L | (f) | No authorisation possible for uses where the line is highlighted in grey, Use should be crossed out when the notifier no longer supports this use. |
| Remarks columns: | 1 | Numeration necessary to allow references | 7 | Growth stage at first and 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 |
| | 2 | Use official codes/nomenclatures of EU Member States | 8 | The maximum number of application possible under practical conditions of use must be provided. |
| | 3 | For crops, the EU and Codex classifications (both) should be used; when relevant, the use situation should be described (e.g. fumigation of a structure) | 9 | Minimum interval (in days) between applications of the same product |
| | 4 | F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application | 10 | For specific uses other specifications might be possible, e.g.: g/m ³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products. |
| | 5 | Scientific names and EPPO-Codes of target pests/diseases/ weeds or, when relevant, the common names of the pest groups (e.g. biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named. | 11 | The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha). |
| | 6 | Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated. | 12 | If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under "application: method/kind". |
| | | | 13 | PHI - minimum pre-harvest interval |
| | | | 14 | Remarks may include: Extent of use/economic importance/restrictions |

3 Background of authorisation decision and risk management

3.1 Physical and chemical properties (Part B, Section 2)

DIFOL is a suspension concentrate (SC). All studies have been performed in accordance with the current requirements and the results are deemed acceptable. The appearance of the product is a uniform creamy white liquid, with a sweet odour. It is not explosive, has no oxidising properties, is not flammable and has no flash point below 100 °C. It has no self-ignition temperature below 400 °C. In 1 % aqueous solution, it has a pH value of 4.84 at 20 °C. There is no effect of low and high temperature on the stability of the formulation, since after seven days at 0 °C and eight weeks at 40 °C, neither the active substances' content nor the technical properties were changed. The stability data indicate a shelf life of at least two years at ambient temperature when stored in HDPE/PA and HDPE/EVOH. As the formulation is an SC, HDPE packaging can be considered acceptable. The technical characteristics are acceptable for an SC formulation.

The formulation is not classified for the physico-chemical aspect.

The product must be stored at a temperature below 40 °C.

3.2 Efficacy (Part B, Section 3)

DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) is a fungicide containing 10.7 g/L of difenoconazole and 360 g/L of folpet. It is formulated as a suspension concentrate (SC) and is intended to be used for the control of apple and pear scabs (respectively *Venturia inaequalis* and *Venturia pyrina*)

Registration of this product was firstly evaluated in 2019. The evaluation was not finalized because efficacy trials were not performed with the requested product.

This dossier is a re-submission dossier which provides new mediterranean data (8 valid trials + 1 non-GEP trial) with the requested product (DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC)).

Considering the data submitted:

The efficacy level of DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) is considered as satisfactory for all the claimed uses. It has to be noted that the number of trials against *Venturia pyrina* on Pear is limited (only 1 trial in Maritime zone). However, according to EPPO extrapolation table n°14/20152 (Extrapolation table for effectiveness of fungicides - diseases on pome fruit), efficacy data obtained against *Venturia inaequalis* on Apple can be extrapolated to *Venturia pyrina* on Pear. Therefore, zRMS considers that this extrapolation is acceptable. However, zRMS kindly asks each cMS to give their opinion on this extrapolation.

The phytotoxicity level of DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC), is considered as acceptable for all the claimed uses. However, this point needs to be confirmed by cMS for Pear. Indeed, it has to be noted that the number of trials on Pear is limited (only 1 trial in Maritime zone). If additional data on Pear are considered to be necessary, they may be required at MS level.

The risks of negative impact on yield, quality, propagation and adjacent crops are considered as negligible. As regards to cider-making, in the absence of specific data, a risk of negative impact cannot be excluded. Users should be warned about this risk on the label.

The risk of resistance development or appearance to folpet does not require a monitoring for the claimed uses. There is a risk of resistance development or appearance to difenoconazole for *Venturia* spp. in apple and pear requiring a monitoring. Management of the resistance risk has to be adapted at national level and a monitoring request can be validated at national level.

For France, the following management of the resistance risk is proposed:

Restrictions:

SPa 1: To avoid the development of resistance of *Venturia spp.* to difenoconazole, the number of applications is limited to 3 applications per crop cycle on apple and pear. To manage the risk of resistance with DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) it is recommended to follow the limitations of use by chemical group recommended by the national note on resistance management on apple scab.

Resistance monitoring data:

A monitoring of resistance to difenoconazole should be put in place on *Venturia spp.* (one monitoring for all products based on difenoconazole). A report on the results of the monitoring put in place should be provided at the time of the renewal of DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC).

3.3 Methods of analysis (Part B, Section 5)**3.3.1 Analytical method for the formulation**

Analytical methods for the determination of the active substances and the relevant impurities in the formulation are available and validated.

3.3.2 Analytical methods for residues

Analytical methods are available in the Draft Assessment Report (DAR) and in this dossier and validated for the determination of residues of difenoconazole and folpet in plants (high-water-content commodities), foodstuffs of animal origin, soil, water (surface and drinking) and air.

As the active substances are not toxic/very toxic, an analytical method for their determination in tissues and body fluids is not necessary.

3.4 Mammalian toxicology (Part B, Section 6)**Endpoints used in risk assessment**

| Active substance: difenoconazole | | | |
|----------------------------------|---|--|--|
| ADI | 0.01 mg kg bw/d | | EU (2009) |
| ARfD | 0.16 mg/kg bw | | |
| AOEL | 0.16 mg/kg bw/d | | |
| Dermal absorption | Based on default values according to guidance on dermal absorption (Efsa 2012): | | |
| | | Concentrate (used in formulation) 10.7 g/L | Spray dilution (used in formulation) 0.03745 g/L |
| | Dermal absorption endpoints % | 75 | 75 |

| Active substance: folpet | | |
|--------------------------|----------------|-----------|
| ADI | 0.1 mg/kg bw/d | EU (2008) |

| | | | |
|-------------------|--|--|--|
| ARfD | 0.2 mg/kg bw | | |
| AOEL | 0.1 mg/kg bw/d | | |
| Dermal absorption | Based on an <i>in vitro</i> human study performed on a similar formulation according to guidance on dermal absorption (Efsa 2012): | | |
| | | Concentrate (tested) 500 g/L | Diluted formulation (tested) 1.5 g/L |
| | <i>In vitro</i> (human) % | | |
| | | Concentrate (used in formulation) 360 g/L | Spray dilution (used in formulation) 1.57 g/L |
| | Dermal absorption endpoints % | 3 | 3 |

3.4.1 Acute toxicity

DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC), containing 360 g/L folpet and 10.7 g/L difenoconazole, has a low acute oral and dermal toxicity, is not irritating to the rabbit skin but is irritating to the rabbit eye and a skin sensitiser.

3.4.2 Operator exposure

Summary of critical use patterns (worst cases):

| Crop | F/G ⁷ | Equipment <i>Application method</i> | Maximum application rate L/ha (g a.s./ha) | Minimum volume water (L/ha) |
|----------------|------------------|---|---|--------------------------------|
| Apple and pear | F | Vehicle-mounted <i>Upward spraying</i> | 3.5 L product/ha (37.45 g difenoconazole/ha + 1260 g folpet/ha) | 300 |

Considering the proposed uses, operator systemic exposure was estimated using the EFSA model⁸:

| Crop | Equipment | PPE and/or working coverall | % AOEL difenoconazole | % AOEL folpet |
|----------------|-----------------|---|--------------------------|------------------|
| Apple and pear | Vehicle-mounted | Working coverall and gloves during mixing/loading and application | 4.61 | 13.35 |

⁷ Open field or glasshouse

⁸ AOEM – Agricultural Operator Exposure Model (EFSA Journal 2014:12 (10):3874)

According to the model calculations, it may be concluded that the risk for the operator using DIFOL 360 (DIFENOCONAZOLE 10.7 + FOLPET 360 SC) is acceptable with a working coverall and gloves during mixing/loading and application.

For details of personal protective equipment for operators, refer to the Decision in Appendix 1.

3.4.3 Worker exposure

EFSA model: Workers may have to enter treated areas after treatment for crop searching, reaching and picking activities. Therefore estimation of worker exposure was calculated according to the AOEM model.

| Model data | Level of PPE | Difenoconazole | | Folpel | | Cumulative risk workers (HI) |
|--|--|------------------------------------|--------------------|------------------------------------|--------------------|------------------------------|
| | | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL | Total absorbed dose (mg/kg bw/day) | % of systemic AOEL | |
| Searching, Reaching, picking Outdoor Work rate: 8 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 10 days Dermal absorption: 4.1% for both concentrate and dilution | | | | | | |
| Number of applications and application rate | | 3 x 0.03745 kg a.s./ha | | 3 x 1.26 kg a.s./ha | | |
| Body weight: 60 kg | Potential TC: 22500 cm ² /person/h | 0.04084 | 255.28 | 1.1268 | 1126.86 | 10.8 |
| | Work wear (arms, body and legs covered) TC: 4500 cm ² /person/h | 0.0817 | 51.06 | 0.2554 | 225.37 | 2.16 |
| | Work wear (arms, body and legs covered) and gloves TC: 2250 cm ² /person/h | 0.0408 | 25.53 | 0.1127 | 112.69 | 1.08 |
| | Work wear (arms, body and legs covered) and gloves TC: 2250 cm ² /person/h Rentry 15days | 0.0372 | 18.05 | 0.0751 | 79.68 | 0.98 |

For details of personal protective equipment for workers, refer to the Decision in Appendix 1.

3.4.4 Bystander and resident exposure

EFSA model (without AAOEL): Consideration of acute exposure should only be made where an AAOEL has been established during an approval, review or renewal evaluation of an active substance, i.e. no acute operator or bystander exposure assessments can be performed with the AOEM model where no AAOEL has been set⁹.

⁹ Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (SANTE-10832-2015 rev. 1.7, 2017)

Only resident exposure is provided since, according to EFSA Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (EFSA Journal 2014;12(10):3874): “No bystander risk assessment is required for PPPs that do not have significant acute toxicity or the potential to exert toxic effects after a single exposure. Exposure in this case will be determined by average exposure over a longer duration, and higher exposures on one day will tend to be offset by lower exposures on other days. Therefore, exposure assessment for residents also covers bystander exposure.”

EFSA model: Residential exposure was assessed according to the EFSA model. An acceptable risk was determined for residents (adult and/or child) without drift reduction technology but with 10 metres buffer zone mitigation measures :

| Model (AOEM) - All pathways (mean) | % AOEL difenoconazole | % AOEL folpet |
|---|----------------------------------|--------------------------|
| Resident (children) | 8.54 | 45.38 |
| Resident (adults) | 4.44 | 22.90 |

3.4.5 Combined exposure

Currently no EU-harmonised guidance is available on the risk assessment of combined exposure to multiple active substances. Most assessment approaches employed up to now make use of the Hazard Index (HI) concept. It is therefore suggested to use this as a first tier assessment.

A cumulative assessment for operators, bystanders/residents and workers has been performed. At the first tier, combined exposure is calculated as the sum of the component exposures without regard to the mode of action or mechanism/target of toxicity.

Hazard quotients (HQ) for each active substance and the HI (sum of hazard quotients) are:

⁹ Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products (SANTE-10832-2015 rev. 1.7, 2017)

| Application scenario | Active ingredient | Estimated exposure / AOEL (HQ) |
|---|--|--------------------------------|
| Operators – (PPE: work wear (arms, body and legs covered) M/L and A + gloves) | Difenoconazole | 0.0321 |
| | Folpet | 0.1871 |
| | Cumulative risk operators (HI) | 0.2192 |
| Workers (PPE: Work wear (arms, body and legs covered)) Rentry 4 days | Difenoconazole | 0.1805 |
| | Folpet | 0.7968 |
| | Cumulative risk workers (HI) | 0.9773 |
| Resident - child | Difenoconazole | 0.0854 |
| | Folpet | 0.4538 |
| | Cumulative risk resident – child (HI) | 0.5392 |
| Resident - adult | Difenoconazole | 0.0444 |
| | Folpet | 0.229 |
| | Cumulative risk resident – adult (HI) | 0.2734 |

For operators, bystanders/residents and workers, the Hazard Index is < 1.

Thus combined exposure to all active substances in DIFOL 360 (Difenoconazole 10.7 + Folpet 360 SC) is not expected to present a risk for operators, residents and bystanders. No further refinement of the assessment is required.

3.5 Residues and consumer exposure (Part B, Section 7)

The section on residues and consumer risk assessment is not covered by the previous assessment and would need to be updated to take into account new elements available following the European assessment and the current methodology (PRIMo rev 3).

3.6 Environmental fate and behaviour (Part B, Section 8)

The fate and behaviour in the environment have been evaluated according to the requirements of Regulation (EC) No 1107/2009. Appropriate endpoints from the EU conclusions were used to calculate PEC values for the active substances and their metabolites for the intended use patterns. In cases where deviations from the EU agreed endpoints were considered appropriate (for example when additional studies are provided), such deviations were highlighted and justified accordingly.

The PEC of difenoconazole, folpet and their metabolites in soil, surface water and groundwater have been assessed according to FOCUS guidance documents, with standard FOCUS scenarios to obtain outputs from the FOCUS models, and the endpoints established in the EU conclusions or agreed in the assessment based on new data provided.

PEC soil and PEC_{sw} derived for the active substances and their metabolites are used for the ecotoxicological risk assessment, and mitigation measures are proposed.

PEC_{gw} for both actives substances and their metabolites do not occur at levels exceeding those mentioned in regulation EC 1107/2009 and guidance document SANCO 221/2000¹⁰.

Therefore, no unacceptable risk of groundwater contamination is expected for the intended uses.

¹⁰ Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council directive 91/414/EEC. Sanco/221/2000-rev10-final, 25 February 2003.

As several azole active substances can be applied on a same field. Considering that 1,2,4-triazole can be formed from most of these azole active substances, an exceedance of the regulatory limit of 0.1 µg/L cannot be excluded. ~~In order to ensure that the regulatory limit in groundwater is not exceeded for 1,2,4 triazole,~~ all applicants of azole-based products are requested to set up a groundwater monitoring dedicated to this metabolite within two years.

Based on vapour pressure, information on volatilisation from plants and soil, and DT₅₀ calculation, no significant contamination of the air compartment is expected for the intended uses.

3.7 Ecotoxicology (Part B, Section 9)

The ecotoxicological risk assessment of the formulation was performed according to the requirements of Regulation (EC) No 1107/2009. Appropriate endpoints from the EU conclusions for the active substances and their metabolites were used for the intended use patterns. In cases where deviations from the EU agreed endpoints were considered appropriate (for example when additional studies are provided), such deviations were highlighted and justified accordingly.

Based on the guidance documents, the risks for birds, aquatic organisms, mammals, bees and other non-target arthropods, earthworms, other soil macro-organisms and micro-organisms and terrestrial plants are acceptable for the intended uses. Risk mitigations are required for aquatic organisms.

3.8 Relevance of metabolites (Part B, Section 10)

The difenoconazole metabolites CGA71019 and CGA205375, and the folpet metabolites phthalimide, phthalamic acid and phthalic acid are predicted to occur in groundwater at concentrations below 0.1 µg/L (see dRR Part B Section 8). Assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.10 is therefore not required.

4 Conclusion of the national comparative assessment (Art. 50 of Regulation (EC) No 1107/2009)

Difenoconazole is an identified candidate for substitution.

Step 2 (French guidance document 27 July 2015):

The identification of alternatives was carried out on the uses for which the substitution was not excluded at the end of step 1 of this French guidance document.

In accordance with Article 50(1) (b) of Regulation (EC) No 1107/2009:

- Taking into account the agronomic usefulness of other solutions:

In the absence of any other available solution showing a similar agronomic interest [i.e., usefulness] (product formulated with a similar mixture of a.s.s) and not presenting any major practical or economic inconvenience for the user, **substitution will not be considered for the use in question on pome fruits against scab(s).**

5 Further information to permit a decision to be made or to support a review of the conditions and restrictions associated with the authorisation

When the conclusions of the assessment is “Not acceptable”, please refer to relevant summary under point 3 “Background of authorisation decision and risk management”.

Appendix 1 Copy of the product authorisation

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Décision relative à une demande d'autorisation de mise sur le marché d'un produit phytopharmaceutique

Vu les dispositions du règlement (CE) N° 1107/2009 du 21 octobre 2009 et de ses textes d'application,

Vu le code rural et de la pêche maritime, notamment le chapitre III du titre V du livre II des parties législative et réglementaire,

Vu la demande d'autorisation de mise sur le marché du produit phytopharmaceutique DIFOL 360

de la société GLOBACHEM NV
enregistrée sous le n° 2021-0167

Vu les conclusions de l'évaluation de l'Anses du 21 février 2023,

Considérant qu'un risque d'effet nocif pour le consommateur, lié à l'utilisation du produit, ne peut être exclu,

Considérant qu'il ne peut pas être établi que les exigences mentionnées à l'article 29 du règlement (CE) n°1107/2009 sont respectées,

La mise sur le marché du produit phytopharmaceutique désigné ci-après n'est pas autorisée en France.

DIFOL 360
AMM n°-

Page 1 sur 3

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| Informations générales sur le produit | |
|---------------------------------------|--|
| Nom du produit | DIFOL 360 |
| Type de produit | Produit de référence |
| Titulaire | GLOBACHEM NV Lichtenberglaan 2019 Brustem Industriepark 3800 SINT-TRUIDEN Belgique |
| Formulation | Suspension concentrée (SC) |
| Contenant | 360 g/L - folpel 10,7 g/L - difénoconazole |
| Numéro d'intrant | 9978-2021.01 |
| Numéro d'AMM | - |
| Fonction | Fongicide |
| Gamme d'usage | Professionnel |

A Maisons-Alfort, le 02/06/2023

DocuSigned by:
Charlotte Grassilleur

AC281A9955A42454
Directrice générale déléguée
en charge du pôle produits réglementés
Agence nationale de sécurité sanitaire
de l'alimentation, de l'environnement et du travail (ANSES)

DIFOL 360
AMM n°-

Page 2 sur 3

ANNEXE : Conditions de mise sur le marché demandées

| Liste des usages refusés | | | |
|--|---------------|-------------------------------|-----------------------------|
| Usages | Dose d'emploi | Nombre maximum d'applications | Délai avant récolte (jours) |
| 12603203 Fruits à pépins*Trt Part.Aer.*Tavelure(s) | 3,5 L/ha | 3/an | 120 |
| Motivation du refus : L'usage est refusé car les données disponibles ne permettent pas d'exclure un risque d'effet nocif pour le consommateur. | | | |

The draft product label as proposed by the applicant is reported below. The draft label may be corrected ~~with consideration of any new element. The label shall reflect the detailed conditions stipulated in the~~ Decision.



Globachem nv
Brustem Industriepark • Lichtenberglaan 2019
BE-3800 Sint-Truiden • Belgium
Tel. +32 (0)11 78 57 17 • Fax +32 (0)11 68 15 65
E-mail: globachem@globachem.com • Website: www.globachem.com
BTW: BE 0473.590.226 • H.R. Hasselt: 105.213 • BIC: KREDBEBB
Bank: KBC 735-0020421-39 • IBAN: BE13 7350 0204 2139

Projet d'étiquette

DIFOL 360

Fongicide foliaire en pommier, poirier.
Contient 10.7 g/L (0.9 % p/p) de difenoconazole et 360 g/L (30.32%) de folpet sous forme de suspension concentrée (SC)



DANGER

H317: Nocif en cas d'ingestion

H318: Provoque des lésions oculaires graves

H332: Nocif par inhalation

H351: Susceptible de provoquer le cancer

H410: Très toxique pour les organismes aquatiques, entraîne des effets néfastes à long terme

P201: Se procurer les instructions avant utilisation

P280: Porter des gants de protection, des vêtements de protection, un équipement de protection des yeux, un équipement de protection du visage

P305+P351+P338: EN CAS DE CONTACT AVEC LES YEUX: rincer avec précaution à l'eau pendant plusieurs minutes. Enlever les lentilles de contact si la victime en porte et si elles peuvent être facilement enlevées. Continuer à rincer

P308+P313: En cas d'exposition prouvée ou suspectée : consulter un médecin

P333+P313 : En cas d'irritation ou d'éruption cutanée : consulter un médecin

P310 : Appeler immédiatement un centre antipoison ou un médecin

P501: Éliminer le contenu/récipient selon les Directives nationales

EUH401: Respectez les instructions d'utilisation pour éviter les risques pour la santé humaine et l'environnement.

SP1 : Ne pas polluer l'eau avec le produit ou son emballage

SPe3 : Pour protéger les organismes aquatiques, respecter une zone non traitée de 50 m avec dispositif végétalisé de 20 m par rapport aux points d'eau

SPe3 : Pour protéger les arthropodes non-cibles, respecter une zone non traitée de 5 m par rapport à la zone non cultivée adjacente.

Délai de rentrée dans la culture : 24 heures en application de l'arrêté du 12 septembre 2006.

En cas d'urgence appelez le 15 ou le centre antipoison puis signalez vos symptômes au réseau Phyt'attitude, numéro vert 0800 887 887 (appel gratuit depuis un poste fixe).

Conserver le produit dans l'emballage original et fermé dans un endroit sec, frais et sombre, à l'abri du gel. Bien agiter avant l'emploi

N° du lot et date de fabrication : voir sur le bidon

Contenu: 5 litres



Détenteur d'AMM:
 Globachem NV
 Brustem Industriepark, Lichtenberglaan 2019, 3800 Sint-Truiden
 Belgique
 Tel. +32 (0)11 78 57 17
 Fax. +32 (0)11 68 15 65

Fiche de données de sécurité disponible sur simple appel au 04 78 83 40 66 ou sur le site www.quickfds.com,
 24h/24 Numéro d'appel d'urgence : 0032 14 58 45 45

CHAMP D'ACTIVITE

DIFOL 360 est un fongicide composé de difenoconazole, matière active appartenant à la famille chimique des triazoles (code FRAC 3) et de folpet, matière active appartenant à la famille chimique des phthalimides (code FRAC M4).

USAGES, DOSES D'EMPLOI ET CONDITIONS D'APPLICATION

| Usage | Cultures cibles recommandées | Cibles | Dose autorisée (L/ha) | Nombre d'applications max/an | Délai avant récolte (DAR) |
|---------------------------------------|------------------------------|--|-----------------------|------------------------------|---------------------------|
| Pommier* Trt Part.Aer.*Tavelure(s) | Pommier, Poirier, | Tavelures (<i>Venturia inaequalis</i> et <i>Venturia pyrina</i>) | 3.5 | 3 | 95 jours |

L'utilisation du DIFOL 360 sur ces usages autorisés n'est recommandée que sur les cultures mentionnées dans le tableau ci-dessus. Globachem N.V. décline en conséquence toute responsabilité en cas d'utilisation du produit sur des cultures ou pour des cibles non recommandées.

Traiter en fonction des avertissements et selon les recommandations de votre distributeur et au plus tard lors de l'apparition des premiers symptômes.

Volume d'eau : 300 à 1000 L/ha

Les limites maximales de résidus sont consultables à l'adresse suivante :
http://ec.europa.eu/food/plant/protection/pesticides/index_fr.htm

MODE D'EMPLOI PAR CULTURE

Pommier, poirier : selon les avertissements agricoles.

PREPARATION DE LA BOUILLIE

Verser DIFOL 360 dans la cuve du pulvérisateur à moitié remplie d'eau. Compléter le volume d'eau par la suite. Pulvériser immédiatement après la préparation de la bouillie. Maintenir une bonne agitation durant le remplissage et le temps du traitement.

COMPATIBILITE

Les mélanges doivent être mis en œuvre conformément à la réglementation en vigueur et aux recommandations des guides de bonnes pratiques officiels. En cas d'utilisation en mélange avec un autre produit, il est obligatoire de réaliser un test préalable pour vérifier la compatibilité physique et biologique selon les conditions particulières de l'exploitation. Notre société décline toute responsabilité sur les conséquences résultant du mélange de différents produits.



GESTION DU RISQUE DE RÉSISTANCE

L'utilisation répétée, sur une même parcelle, de préparations à base de substances actives de la même famille chimique ou ayant le même mode d'action, peut conduire à l'apparition d'organismes résistants.

Pour réduire ce risque, il est conseillé d'alterner ou d'associer, sur une même parcelle, des préparations à base de substances actives de familles chimiques différentes ou à modes d'action différents, tant au cours d'une saison culturale que dans la rotation. En l'occurrence, il convient de limiter le nombre d'application d'IDM à trois par saison dans le cadre de la lutte contre la tavelure du pommier.

En dépit du respect de ces règles, on ne peut pas exclure une altération de l'efficacité de cette préparation liée à ces phénomènes de résistance. De ce fait, Globachem NV décline toute responsabilité quant à d'éventuelles conséquences qui pourraient être dues à de telles résistances.

Consultez votre distributeur pour connaître les cas avérés de résistance au niveau de votre région.

PRECAUTIONS D'EMPLOI

Pendant le stockage :

- Conserver le produit uniquement dans l'emballage d'origine, à l'abri de l'humidité, du gel, dans un endroit frais, aéré et ventilé, à l'écart des aliments et boissons y compris ceux pour animaux. Conserver hors de la portée des enfants.

Pendant la préparation de la bouillie et en cours d'application :

- Ne pas manger, boire, fumer.
- Porter un vêtement de protection approprié, des gants et un appareil de protection des yeux et du visage, selon la réglementation en vigueur.
- Vérifier régulièrement et maintenir le bon état et le réglage du matériel d'application, en conformité avec la législation.
- Surveiller le remplissage de la cuve du pulvérisateur et ajuster le volume de bouillie (clapet anti-retour, dispositif de surverse).
- Ne pas souffler dans les buses pour tenter de les déboucher.
- En cas de contact avec la peau et les yeux, laver immédiatement et abondamment avec de l'eau et consulter un spécialiste.
- En cas d'ingestion consulter immédiatement un CENTRE ANTIPOISON ou un médecin et lui montrer l'emballage ou l'étiquette.
- Ne pas respirer les vapeurs, ni le brouillard de pulvérisation.
- Ne pas pulvériser à proximité des points d'eau (mares, cours d'eau, fossés...).
- Ne pas traiter en présence de vent afin de respecter les cultures voisines.
- En présence d'un léger vent (3/4 m/s) préférer les buses à limitation de dérive

Après application :

- Éliminer les fonds de cuve et les eaux de rinçage conformément à la réglementation en vigueur.
- Ne pas conserver la bouillie de pulvérisation dans la cuve plus de 48 heures.
- Nettoyer très soigneusement avec un produit adapté (type Phytnet) et rincer le pulvérisateur aussitôt après le traitement conformément à la réglementation en vigueur.
- Immédiatement après l'application, nettoyer les équipements de protection, se laver les mains à l'eau savonneuse, prendre une douche et changer de vêtements.

PROTECTION DE L'OPERATEUR ET DU TRAVAILLEUR

A ajouter sur base de la décision

ELIMINATION DU PRODUIT ET DES EMBALLAGES

Lors de l'utilisation du produit, rincer le bidon 3 fois en veillant à verser l'eau de rinçage dans la cuve du pulvérisateur. Pour l'élimination des produits non utilisables, faire appel à une entreprise habilitée pour la collecte et l'élimination des produits dangereux. Réutilisation de l'emballage interdite. Éliminer les emballages vides via une collecte organisée par un service de collecte spécifique.





IMPORTANT

Respectez les usages, doses, conditions et précautions d'emploi mentionnées sur l'emballage, qui ont été déterminées en fonction des caractéristiques du produit et des applications pour lesquelles il est autorisé. Conduisez sur ces bases, la culture et les traitements selon la bonne pratique agricole, en tenant compte, sous votre responsabilité, de tous les facteurs particuliers concernant votre exploitation, tels que la nature du sol, les conditions météorologiques, les méthodes culturales, les variétés végétales, la résistance des espèces, ...

Compte tenu de la diversité des législations existantes, il est recommandé, dans le cas où les denrées protégées avec cette spécialité sont destinées à l'exportation, de vérifier la réglementation en vigueur dans le pays importateur. Le fabricant garantit la qualité de ses produits vendus dans leur emballage d'origine ainsi que leur conformité à l'autorisation de vente du Ministère de l'Agriculture. Globachem NV ne saurait être tenu en aucun cas responsable des conséquences inhérentes à toute copie de cette étiquette et la diffusion ou à l'

GARANTIE

Le fabricant ne donne aucune garantie, explicite ou implicite, relative à l'utilisation du produit d'une autre manière que celle indiquée sur l'étiquette. L'utilisateur sera responsable des risques liés à l'utilisation et/ou la manipulation et/ou l'entreposage de ce produit en cas de non-respect des recommandations de l'étiquette.

RESPONSABILITES

En cas de non-respect de la garantie ou de négligence, le recours de l'utilisateur sera limité au remboursement de dommages et intérêts, à concurrence du prix d'achat, à l'exclusion de tout autre dommage.

Toute reproduction du présent texte est interdite.