benthiavalicarb-isopropyl

ADDITIONAL INFORMATION ON ENDOCRINE PROPERTIES

EVALUATION OF THE NECESSITY OF BENTHIAVALICARB-ISOPROPYL AS A FUNGICIDE TO CONTROL A SERIOUS DANGER TO PLANT HEALTH, WHICH CANNOT BE CONTAINED BY OTHER AVAILABLE MEANS INCLUDING NON-CHEMICAL METHODS

INTRODUCTION

On 18 January 2019, the notifying company K-I Chemical Europe SA/NV was informed that the European Food Safety Authority (EFSA) has concluded that the active substance benthiavalicarb-isopropyl satisfies the criteria of an endocrine disruptor in humans as laid down in Regulation (EU) No 2018/605. In accordance with Regulation (EU) No 2018/1659, further information is submitted to demonstrate that benthiavalicarb may be used such that exposure is negligible (Appendix B) and that benthiavalicarb is necessary to control a serious danger to plant health that cannot be contained by any other available means including non-chemical alternatives (Appendix C). The meeting minutes of the expert consultation were assessed and the comments on the assessment are also submitted (Appendix A).

This document contains information to demonstrate that benthiavalicarb can be approved under the provisions of Article 4(7) of Regulation (EC) No 1107/2009. The information is provided in line with a Technical Report (EFSA, 2017) outlining a protocol concerning the application of fungicide active substance to control a serious danger to plant health. The information provided considers the authorised uses of benthiavalicarb in seven Member States, *i.e.* Belgium, the Czech Republic, Germany, Spain, Ireland, the Netherlands and Poland. Uses against early and late blight in potatoes, downy mildew in onions and shallots and late blight in tomatoes were considered. The registered use against downy mildew in vines was not considered due to evolved resistance in field populations of *Plasmopara viticola.*

TABLE OF CONTENTS

BELGIUM (BE)

VALBON (17.5 g/kg benthiavalicarb-isopropyl + 700 g/kg mancozeb) is authorised for controlling *Phytophthora infestans* in potato and *Peronospora destructor* in onions and shallots. VERSILUS (150 g/kg benthiavalicarb-isopropyl) is authorised for controlling *Phytophthora infestans* in potato. The evaluation of the necessity for benthiavalicarb in Belgium focusses on the control of a) late blight in potato and b) downy mildew in onion.

1 List of authorised fungicide active substances on crop/pest combinations

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:

- ametoctradin
- amisulbrom
- azoxystrobin
- chlorothalonil
- copper compounds
- cyazofamid
- difenoconazole ([1])
- famoxadone
- fluazinam
- mancozeb
- pyraclostrobin
- zoxamide

Translaminar fungicides:

- benthiavalicarb
- cymoxanil
- dimethomorph
- fenamidone
- fluopicolide
- mandipropamid
- valifenalate

Systemic fungicides:

- benalaxyl-M
- metalaxyl-M
- oxathiapiprolin
- propamocarb

b) Onion, *Allium cep*a (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Contact fungicides:

- azoxystrobin
- chlorothalonil
- mancozeb
- pyraclostrobin

Systemic fungicides:

- benthiavalicarb
- dimethomorph
- fluopicolide
- fluoxastrobin
- metalaxyl-M
- propamocarb
- prothioconazole ([1])

2 Data on fungicide resistance risk

2.1 Step 1: Evaluation of fungicide alternatives with the same mode of action (MoA)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb, plant protection products containing dimethomorph and mandipropamid that have the same mode of action (cellulose synthase inhibition) are authorised for controlling late blight in potato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a “presumed reproductive toxicant (Cat 1B)”. As a result dimethomorph may be banned from the European market according to current legislation.

VERSILUS (150 g/kg benthiavalicarb-isopropyl) applied at 75 g as/ha is rated with a score of 4.2 for controlling leaf blight in the EuroBlight Fungicide Table (rev. 5-Feb-2019) and has a 0.2 points higher rating than REVUS (250 g/l mandipropamid) applied at 150 g as/ha. These results

([1]) DMI fungicides have no activity against oomycetes and are not further considered in the evaluation suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than mandipropamid.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Besides benthiavalicarb, plant protection products containing dimethomorph, which has the same mode of action (cellulose synthase inhibition) is authorised for controlling downy mildew in onions.

As a result of a new proposal to classify the active substance dimethomorph as a “presumed reproductive toxicant (Cat 1B)”, dimethomorph may be banned from the European market according to current legislation.

2.2 Step 2: Evaluation of alternative non-fungicide programs

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Sustainable management strategies for late blight control in potato production were identified based on a literature review by Pacilly *et al*. (2016). Research on the biological control of potato late blight focusses on cultural practices and plant breeding for resistance.

Crop rotation

Infections originating from oospores are mainly found in regions with narrow rotation schemes and therefore a bigger rotation scheme should prevent such sources of infection. Producers of starch potatoes however have a rotation plan with fewer crops, which results in a larger risk on initial infection from surviving oospores in the soil.

Intercropping

Field experiments with intercropping systems often resulted in significant reductions of late blight in potato but were not able to eradicate the disease completely. Current potato production is however based on mono-cropping and the machinery used for planting and harvesting cannot be used in intercropping systems.

Harvesting dates

The time of harvesting can affect the spread of *Phytophthora infestans* because early harvesting results in lower crop densities later in the season slowing down a late blight epidemic. Compared to seed potatoes, starch and ware potatoes are harvested later in the season.

Crop density

High potato densities contribute to disease dispersal and corresponding late blight severity. A high density of potatoes is however the result of profit maximisation.

Fertilizers

In vitro studies have shown that nitrogen supply increased susceptibility of potato crops to *P. infestans*. However no effect was observed under field conditions.

Resistant plant genotypes

The use of resistant cultivars is an important aspect in sustainable management strategies. Breeding for resistance to late blight started a long time ago. The classical breeding process is time consuming and many resistant genes have already been overcome by the pathogen. Furthermore, recently introduced resistant cultivars were not attractive to the farmers because they lack some of the preferred market characteristics and are not as high yielding.

Variety mixtures

Mixing susceptible and resistant potato cultivars on small scales, *e.g*. in plant rows, was most effective in decreasing the spread of the disease. Applying cultivar mixtures is economically not interesting for farmers. A change in market demands for specific potato cultivars could limit these economic losses when moving towards cultivar mixtures.

Genetically engineered crops

Genetic engineering is faster than classical breeding. However, the production of genetically modified potatoes is strictly regulated and also under political and social debate. Besides the possible negative effects on the environment, one other issue is related to the intellectual property rights.

Biological control

Although some biological control agents, plant extracts and biopesticides have been proven to be effective, none of them work as well as chemical fungicides. Because many biological control strategies result in ineffective control, these can be combined with conventional use of chemical fungicides to improve disease management.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Biological control of downy mildew in onion focusses primarily on preventive measures; *i.e*. reducing primary infections sources, for example by warm water treatment of plant onions, to delay the onset of the epidemic allowing a longer growth period (Evenhuis & Spruijt, 2011). Fungicide treatments are however most effective in case of high disease pressure (Meier *et al*., 2005).

Crop burning

Burning of first-year plant onions can limit the transmission of downy mildew from the foliage into the bulbs but cannot be fully prevented. Burning contaminated areas can kill downy mildew spores and reduce their dispersion. For an optimal effect, the burner should be mounted at canopy level and trailed at a speed of 2 km/h. Under weather conditions that are favourable for downy mildew, sporulation can already take place soon after crop burning and it is therefore necessary to burn the crop several times per week (Evenhuis & Spruijt, 2011). Besides the costs, yield losses may occur when the crop foliage is burned early in the growing season.

Intercropping

Intercropping with coriander or mustard reduces the infestation of downy mildew in onions because of volatile compounds that may have an effect on the sporangia of downy mildew (Meier *et al*., 2005).

Change in planting dates

Late cultures (May-Aug) have a higher risk of infestation with downy mildew. Depending on the weather conditions, onions can be planted mid-March to avoid early infestations of downy mildew resulting in high yield losses. As regards sowing, there are however many cases in which late sowing prevented downy mildew infestations due to early growth stage resistance (Meier *et al*, 2005).

Plant density

A lower plant density is an important option to delay downy mildew infestations. Several observations have shown that in cases of lower plant densities, the crop growth period would be longer compensating the overall field production loss (Meier *et al*, 2005). Optimal plant density was determined to be 70-80 plants per m^2 sown in 5 rows per seedbed with a width of 1.5 m (van den Broek, 2008).

Fertilizers

Nutrient deficient soils can result in early infestations of downy mildew. Soil fertilization, including nitrogen fixation by preceding crops, can increase crop vigour and disease resistance. However, higher fertilizer application rates can result in a lush crop in which bulb production is delayed. (Meier *et al*, 2005). Nitrogen fertilization should be limited (van den Broek, 2008).

Raised beds

Some growers cultivate onions on raised beds. It is believed that the circulation of more air between the plants reduces the infestation risk (Meier *et al*, 2005); infestation risk is also believed to be reduced because the top soil remains drier. Cultivation on raised beds in field research had however no quantitative and qualitative effects on yield. Cultural control measures are not sufficient in case of high disease pressure (van den Broek, 2008).

Temperature and humidity management (micro-climate)

The presence of weeds in the crops causes a higher air humidity, which increases the infestation risk. Mechanical and thermal weed control may be advised in organic farming or chemical weed control in a conventional production system.

Organic matter

Literature data suggest that compost could strengthen onion plants because of the soil-improving activity and stimulation of soil functions. The potential effects of different compost types on plant growth and control of downy mildew infestations in onions have been assessed but no significant effects were observed (Zanen & Hospers-Brands, 2007).

Resistant plant genotypes

There are a few onion varieties available that are resistant to downy mildew. The resistance is based on one gene. Although the resistance is believed to be strong and durable, increased selection pressure on the resistance gene can lead to resistance breakdown.

Soil suppressiveness enhancement

Resistance against downy mildew in onions can be induced by treating seeds and bulbs with metabolites produced by *Fusarium solani*. These metabolites activate phytoalexins in onion plants.

Heat

Warm water treatment of first year plant onions prevents systemic infection. Plant onions should be treated for at least one hour at temperatures at or above 40°C. The water temperatures should not exceed 43°C because it can inhibit the germination capacity of more heat-sensitive plant onions (Evenhuis & Spruijt, 2011).

Water

Overhead irrigation during the night could prevent the dispersion of downy mildew. Field research showed that overhead irrigation during the early morning suppressed downy mildew epidemics. However, applying overhead irrigation every night could have adverse effects, such as the development of other fungal leaf diseases (Meier *et al*., 2009).

Radiation

Laboratory experiments have shown that downy mildew spores can be killed by UV-radiation (Lamers & van Rozen, 2009). Under field conditions, sporulation was inhibited by UV-irradiation between the rows. UV-irradiation above the crop canopy led to an infestation at the end of the season. Application frequency is important to achieve a high effectiveness. Further research is necessary into sporulation prediction models to determine the appropriate application timing.

Natural products and basic substances

It is suggested that some natural products and basic substances (sulphur, whey, seaweed extract, calcium chloride and potassium bicarbonate) can control downy mildew except in case of a high disease pressure. Based on further field investigations it was concluded that whey could control downy mildew infestations but not to an extent that is practically feasible (Termorshuizen & Volker, 2007). Algae extracts, lecithin and rape seed oil have no effect on downy mildew. Sodium hydrocarbonate, sulphur, calcium chloride and plant extracts have little effect on downy mildew infestations. Although garlic extract is used to disinfect onion seeds, the effect on downy mildew infestation has not been proven (Meier *et al*., 2005).

Natural inducers

Siberian fir extract induces the natural resistance and has been reported to be effective against downy mildew in onions. It is recommended spraying from the 4th true leaf stage and repeating the spray application 15 days later (Meier *et al*., 2005).

2.3 Step 3: Evaluation of alternative modes of action

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fenamidone, fluopicolide and mandipropamid.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Besides benthiavalicarb, other systemic fungicides are dimethomorph, fluopicolide, propamocarb, fluoxastrobin and metalaxyl. Prothioconazole has no activity against downy mildew and is not further considered in the evaluation.

2.4 Step 4: Evaluation of fungicide risk of resistance, pathogen risk of resistance and evaluation of non-fungicide alternatives

2.4.1 Evaluation of fungicide risk of resistance (*X*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

In case of high disease pressure during the main growth phase it is recommended to use translaminar or systemic fungicides containing active substances such as benthiavalicarb, cymoxanil, dimethomorph, fenamidone, fluopicolide, propamocarb, mandipropamid, oxathiapiproline and valifenalate. Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Due to frequent resistance against metalaxyl-M and benalaxyl-M, these fungicides should be applied only once at the early growth stages to seize the upward growth of the fungus through the stem and are not taken into account. Active substances with contact activity (amisulbrom, mancozeb, cyazofamid, fluazinam and zoxamide) are also not considered in the calculation.

Table 2.4.1-1 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in potatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benelaxyl-M metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	fenamidone	C3 - Respiration complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b gene*)	QoI fungicides (Quinone outside Inhibitors)	11	high
3	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
4	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
5	fluopicolide	B5 - Cytoskeleton and motor proteins delocalisation of spectrin-like proteins	benzamides	43	medium *
6	benthiavalicarb dimethomorph mandipropamid valifenalate	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
7	oxathiapiprolin	F9 - Lipid synthesis or membrane integrity lipid homeostasis and transfer/storage	OSBPI oxysterol binding protein homologue inhibition	49	high

* not counted

Four alternative modes of action were identified. Two modes of action are classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be 2 × 0.50 + 2 × 0.75 = 2.50.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Fungicide active substances with a systemic or local systemic activity are considered in the calculation. There are two modes of action with a high risk for resistance and one mode of action with a low risk for resistance. Accordingly, the risk of resistance for fungicides (*X*) with (local) systemic activity is calculated to be 2 × 0.50 + 1 × 0.75 = 1.75.

Table 2.4.1-2 Mode of action and resistance risk for (local) systemic fungicides used in combatting downy mildew in onions

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high
2	fluoxastrobin	C3 - Respiration complex III: cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b* gene)	QoI fungicides (Quinone outside Inhibitors)	11	high
3	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
4	fluopicolide	B5 - Cytoskeleton and motor protein delocalisation of spectrin-like proteins	benzamides	43	medium *
5	benthiavalicarb dimethomorph	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *

* not counted

2.4.2 Evaluation of fungal pathogen risk (*Z*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Phytophthora infestans developed resistance quite rapidly to the phenylamide fungicides (metalaxyl and benalaxyl) but not to the CAA fungicides, QoI fungicides, cymoxanil and carbamates. Therefore, the Fungicide Resistance Action Committee classified *P. infestans* as a medium risk pathogen (*Z* = 2) for all modes of action.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Downy mildew (*Peronospora* spp.) is regarded as posing a medium risk of development of resistance to fungicides (*Z* = 2).

2.4.3 Evaluation of non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in potato is provided under point 2.2.

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	1 - available	1 - moderate	3 - applied (≥ 50%)	1 - feasible with restrictions
	intercropping	1 - available	1 - moderate	-	0 - not feasible
	harvesting date	1 - available	1 - moderate	-	1 - feasible with restrictions
	crop density	1 - available	1 - moderate	-	0 - not feasible
	fertilizers	1 - available	0 - none	-	0 - not feasible
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	-	1 - feasible with restrictions
	variety mixtures	1 - available	1 - moderate	-	0 - not feasible
	multiline cultivar	-	-	-	-
	genetic engineering	0 - not available	-	0 - not applied	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	1 - moderate	0 - not applied	-
	predation	-	-	-	-
	soil management	1 - available	1 - moderate	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	1 - available	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	1 - available	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	0 - not available	-	0 - not applied	-
	calcium chloride	0 - not available	-	0 - not applied	-
	Urtica spp.	0 - not available	-	0 - not applied	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	-	-	-	-

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

A discussion of non-chemical alternatives for controlling downy mildew in onion is provided under point 2.2.

Table 2.4.3-2 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	-	-	-	-
	intercropping	1 - available	1 - moderate	0 - not applied	0 - not feasible
	sowing/planting date	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	plant density	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	fertilizers	1 - available	0 - none	-	-
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	1 - available	0 - none	-	-
	micro-climate	1 - available	1 - moderate	3 - applied (≥ 50%)	2 - feasible
	organic matter	1 - available	0 - none	-	-
	crop burning	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
Host resistance	resistant genotypes	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	variety mixtures	-	-	-	-
	multiline cultivar	-	-	-	-
	genetic engineering	-	-	-	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	-	0 - not applied	-
	predation	-	-	-	-
	soil management	-	-	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	1 - available	1 - moderate	3 - applied (≥ 50%)	2 - feasible
	cold	-	-	-	-
	water	1 - available	1 - moderate	3 - applied (≥ 50%)	2 - feasible
	radiation	1 - available	1 - moderate	0 - not applied	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	1 - available	0 - none	0 - not applied	-
	calcium chloride	1 - available	0 - none	0 - not applied	-
	Urtica spp.	-	-	-	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	1 - available	1 - moderate	0 - not applied	-

2.4.4 Evaluation of fungicide/pathogen resistance management strategy based on remaining fungicide and non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Since $Z/X = 0.80$, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Since $Z/X = 1.14$, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

THE CZECH REPUBLIC (CZ)

VALBON (15.6 g/kg benthiavalicarb + 700 g/kg mancozeb) and VERSILUS (133.5 g/kg benthiavalicarb) are authorised for controlling *Phytophthora infestans* in potato. The evaluation of the necessity for benthiavalicarb in the Czech Republic focusses on a) the control of late blight in potato.

1 List of authorised fungicide active substances on crop/pest combinations

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:
- ametoctradin
- amisulbrom
- azoxystrobin
- chlorothalonil
- copper compounds
- cyazofamid
- difenoconazole ([2])
- dithiocarbamates
- famoxadone
- fluazinam
- zoxamide

Translaminar fungicides:
- benthiavalicarb
- cymoxanil
- dimethomorph
- fenamidone
- fluopicolide
- mandipropamid
- valifenalate

Systemic fungicides:
- benalaxyl-M
- metalaxyl-M
- propamocarb
- oxathiapiprolin

2 Data on fungicide resistance risk

2.1 Step 1: Evaluation of fungicide alternatives with the same mode of action (MoA)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb, plant protection products containing dimethomorph, mandipropamid and valifenalate that have the same mode of action (cellulose synthase inhibition) are authorised for the control of late blight in potato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a "presumed reproductive toxicant (Cat 1B)". As a result dimethomorph may be banned from the European market according to current legislation.

VERSILUS (150 g/kg benthiavalicarb-isopropyl) applied at 75 g as/ha has a similar efficacy than VALIS M (600 g/kg mancozeb + 60 g/kg valifenalate) and REVUS (250 g/l mandipropamid) both applied at 150 g as/ha. These results suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than valifenalate and mandipropamid.

2.2 Step 2: Evaluation of alternative non-fungicide programs

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Sustainable management strategies for late blight control in potato production were identified based on a literature review by Pacilly *et al*. (2016). Research on the control of potato late blight focusses on cultural practices and plant breeding for resistance. Biological antifungal products based on *Pythium oligandrum* strain M1 are authorised for controlling late blight in potato.

Crop rotation

Infections originating from oospores are mainly found in regions with narrow rotation schemes and therefore a bigger rotation scheme should prevent such sources of infection. Producers of

([2]) DMI fungicides have no activity against oomycetes and are not further considered in the evaluation.

starch potatoes however have a rotation plan with fewer crops, which results in a larger risk on initial infection from surviving oospores in the soil.

Intercropping

Field experiments with intercropping systems often resulted in significant reductions of late blight in potato but were not able to eradicate the disease completely. Current potato production is however based on mono-cropping and the machinery used for planting and harvesting cannot be used in intercropping systems.

Harvesting dates

The time of harvesting can affect the spread of *Phytophthora infestans* because early harvesting results in lower crop densities later in the season slowing down a late blight epidemic. Compared to seed potatoes, starch and ware potatoes are harvested later in the season.

Crop density

High potato densities contribute to disease dispersal and corresponding late blight severity. A high density of potatoes is however the result of profit maximisation.

Fertilizers

In vitro studies have shown that nitrogen supply increased susceptibility of potato crops to *P. infestans*. However no effect was observed under field conditions.

Resistant plant genotypes

The use of resistant cultivars is an important aspect in sustainable management strategies. Breeding for resistance to late blight started a long time ago. The classical breeding process is time consuming and many resistant genes have already been overcome by the pathogen. Furthermore, recently introduced resistant cultivars were not attractive to the farmers because they lack some of the preferred market characteristics and are not as high yielding.

Cultivar mixtures

Mixing susceptible and resistant potato cultivars on small scales, *e.g.* in plant rows, has been shown to be most effective in decreasing the spread of the disease. Applying cultivar mixtures is however economically not interesting for farmers. A change in market demands for specific potato cultivars could limit these economic losses when moving towards cultivar mixtures.

Genetically engineered crops

Genetic engineering is faster than classical breeding. However, the production of genetically modified potatoes is strictly regulated and also under political and social debate. Besides the possible negative effects on the environment, one other issue is related to the intellectual property rights.

Biological control

Although some biological control agents, plant extracts and biopesticides have been proven to be effective, none of them work as well as chemical fungicides. Because many biological control strategies result in ineffective control, these can be combined with conventional use of chemical fungicides to improve disease management.

2.3 Step 3: Evaluation of alternative modes of action

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fenamidone, fluopicolide, mandipropamid and valifenalate.

2.4 Step 4: Evaluation of fungicide risk of resistance, pathogen risk of resistance and evaluation of non-fungicide alternatives

2.4.1 Evaluation of fungicide risk of resistance (X)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

In case of high disease pressure during the main growth phase it is recommended to use translaminar or systemic fungicides containing active substances such as benthiavalicarb, cymoxanil, dimethomorph, fenamidone, fluopicolide, mandipropamid, oxathiapiproline, propamocarb and valifenalate. Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Due to frequent resistance against metalaxyl-M and benalaxyl-M, these fungicides should be applied only once at the early growth stages to seize the upward growth of the fungus through the stem and are not taken into account. Active substances with contact activity such as ametoctradin, mancozeb, cyazofamid, fluazinam, zoxamide, *etc.*, are also not considered in the calculation.

Table 2.4.1-1 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in potatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl-M metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	fenamidone	C3 - Respiration complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b gene*)	QoI fungicides (Quinone outside Inhibitors)	11	high
3	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
4	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
5	fluopicolide	B5 - Cytoskeleton and motor proteins delocalisation of spectrin-like proteins	benzamides	43	medium *
6	benthiavalicarb valifenalate dimethomorph mandipropamid	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
7	oxathiapiprolin	F9 - Lipid synthesis or membrane integrity lipid homeostasis and transfer/storage	OSBPI oxysterol binding protein homologue inhibition	49	high

* not counted

Four alternative modes of action were identified. Two modes of action are classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. The risk of resistance for fungicides (X) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be $2 \times 0.50 + 2 \times 0.75 = 2.50$.

2.4.2 Evaluation of fungal pathogen risk (Z)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Phytophthora infestans developed resistance quite rapidly to the phenylamide fungicides (metalaxyl and benalaxyl) but not to the CAA fungicides, QoI fungicides, cymoxanil and carbamates. Therefore, the Fungicide Resistance Action Committee classified *P. infestans* as a medium risk pathogen ($Z = 2$) for all modes of action.

2.4.3 Evaluation of non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in potato is provided under point 2.2.

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	1 - available	1 - moderate	3 - applied (≥ 50%)	1 - feasible with restrictions
	intercropping	1 - available	1 - moderate	-	0 - not feasible
	harvesting date	1 - available	1 - moderate	-	1 - feasible with restrictions
	crop density	1 - available	1 - moderate	-	0 - not feasible
	fertilizers	1 - available	0 - none	-	0 - not feasible
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	-	1 - feasible with restrictions
	cultivar mixtures	1 - available	1 - moderate	-	0 - not feasible
	multiline cultivar	-	-	-	-
	genetic engineering	0 - not available	-	0 - not applied	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	1 - moderate	0 - not applied	-
	predation	-	-	-	-
	soil management	-	-	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	-	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	-	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	0 - not available	-	0 - not applied	-
	calcium chloride	0 - not available	-	0 - not applied	-
	Urtica spp.	0 - not available	-	0 - not applied	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	-	-	-	-

2.4.4 Evaluation of fungicide/pathogen resistance management strategy based on remaining fungicide and non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Since $Z/X = 0.80$, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

GERMANY (DE)

VALBON (15.6 g/kg benthiavalicarb + 700 g/kg mancozeb) and VERSILUS (133.5 g/kg benthiavalicarb) are authorised for controlling late blight (*Phytophthora infestans*) in potato. The evaluation of the necessity for benthiavalicarb in Germany focusses on a) the control of late blight in potato.

1 List of authorised fungicide active substances on crop/pest combinations

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:

- ametoctradin
- amisulbrom
- copper compounds
- cyazofamid
- difenoconazole ([3])
- dithiocarbamates ([4])
- famoxadone
- fluazinam
- zoxamide

Translaminar fungicides:

- benthiavalicarb
- cymoxanil
- dimethomorph
- fluopicolide
- mandipropamid
- valifenalate

Systemic fungicides:

- benalaxyl-M
- metalaxyl-M
- oxathiapiprolin
- propamocarb

2 Data on fungicide resistance risk

2.1 Step 1: Evaluation of fungicide alternatives with the same mode of action (MoA)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb, plant protection products containing dimethomorph, mandipropamid and valifenalate that have the same mode of action (cellulose synthase inhibition) are authorised for the control of late blight in potato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a “presumed reproductive toxicant (Cat 1B)”. As a result dimethomorph may be banned from the European market according to current legislation.

VERSILUS (150 g/kg benthiavalicarb-isopropyl) applied at 75 g as/ha has a similar efficacy than VALIS M (600 g/kg mancozeb + 60 g/kg valifenalate) and REVUS (250 g/l mandipropamid) both applied at 150 g as/ha. These results suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than valifenalate and mandipropamid.

2.2 Step 2: Evaluation of alternative non-fungicide programs

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Sustainable management strategies for late blight control in potato production were identified based on a literature review by Pacilly *et al*. (2016). Research on the control of potato late blight focusses on cultural practices and plant breeding for resistance.

Crop rotation

Infections originating from oospores are mainly found in regions with narrow rotation schemes and therefore a bigger rotation scheme should prevent such sources of infection. Producers of starch potatoes however have a rotation plan with fewer crops, which results in a larger risk on initial infection from surviving oospores in the soil.

([3]) DMI fungicides have no activity against oomycetes and are not further considered in the evaluation.
([4]) including mancozeb and metiram

Intercropping

Field experiments with intercropping systems often resulted in significant reductions of late blight in potato but were not able to eradicate the disease completely. Current potato production is however based on mono-cropping and the machinery used for planting and harvesting cannot be used in intercropping systems.

Harvesting dates

The time of harvesting can affect the spread of *Phytophthora infestans* because early harvesting results in lower crop densities later in the season slowing down a late blight epidemic. Compared to seed potatoes, starch and ware potatoes are harvested later in the season.

Crop density

High potato densities contribute to disease dispersal and corresponding late blight severity. A high density of potatoes is however the result of profit maximisation.

Fertilizers

In vitro studies have shown that nitrogen supply increased susceptibility of potato crops to *P. infestans*. However no effect was observed under field conditions.

Resistant plant genotypes

The use of resistant cultivars is an important aspect in sustainable management strategies. Breeding for resistance to late blight started a long time ago. The classical breeding process is time consuming and many resistant genes have already been overcome by the pathogen. Furthermore, recently introduced resistant cultivars were not attractive to the farmers because they lack some of the preferred market characteristics and are not as high yielding.

Cultivar mixtures

Mixing susceptible and resistant potato cultivars on small scales, *e.g.* in plant rows, has been shown to be most effective in decreasing the spread of the disease. Applying cultivar mixtures is however economically not interesting for farmers. A change in market demands for specific potato cultivars could limit these economic losses when moving towards cultivar mixtures.

Genetically engineered crops

Genetic engineering is faster than classical breeding. However, the production of genetically modified potatoes is strictly regulated and also under political and social debate. Besides the possible negative effects on the environment, one other issue is related to the intellectual property rights.

Biological control

Although some biological control agents, plant extracts and biopesticides have been proven to be effective, none of them work as well as chemical fungicides. Because many biological control strategies result in ineffective control, these can be combined with conventional use of chemical fungicides to improve disease management.

2.3 Step 3: Evaluation of alternative modes of action

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fluopicolide, mandipropamid and valifenalate.

2.4 Step 4: Evaluation of fungicide risk of resistance, pathogen risk of resistance and evaluation of non-fungicide alternatives

2.4.1 Evaluation of fungicide risk of resistance (*X*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

In case of high disease pressure during the main growth phase it is recommended to use translaminar or systemic fungicides containing active substances such as benthiavalicarb, cymoxanil, dimethomorph, fluopicolide, mandipropamid, oxathiapiproline, propamocarb and valifenalate. Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Due to frequent resistance against metalaxyl and benalaxyl, these fungicides should be applied only once at the early growth stages to seize the upward growth of the fungus through the stem and are not taken into account ([5]). Active substances with contact activity (mancozeb, cyazofamid, fluazinam and zoxamide) are also not considered in the calculation.

Table 2.4.1-1 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in potatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl-M metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
3	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
4	fluopicolide	B5 - Cytoskeleton and motor proteins delocalisation of spectrin-like proteins	benzamides	43	medium *
5	benthiavalicarb valifenalate dimethomorph mandipropamid	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
6	oxathiapiprolin	F9 - Lipid synthesis or membrane integrity lipid homeostasis and transfer/storage	OSBPI oxysterol binding protein homologue inhibition	49	high

* not counted

The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be $1 \times 0.50 + 2 \times 0.75 = 2.00$.

2.4.2 Evaluation of fungal pathogen risk (*Z*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Phytophthora infestans developed resistance quite rapidly to the phenylamide fungicides (metalaxyl and benalaxyl) but not to the CAA fungicides, QoI fungicides, cymoxanil and carbamates. Therefore, the Fungicide Resistance Action Committee classified *P. infestans* as a medium risk pathogen ($Z = 2$) for all modes of action.

2.4.3 Evaluation of non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in potato is provided under point 2.2.

([5]) from: https://www.lfl.bayern.de/ips/blattfruechte/034444/index.php

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	1 - available	1 - moderate	3 - applied (≥ 50%)	1 - feasible with restrictions
	intercropping	1 - available	1 - moderate	-	0 - not feasible
	harvesting date	1 - available	1 - moderate	-	1 - feasible with restrictions
	crop density	1 - available	1 - moderate	-	0 - not feasible
	fertilizers	1 - available	0 - none	-	0 - not feasible
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	-	1 - feasible with restrictions
	cultivar mixtures	1 - available	1 - moderate	-	0 - not feasible
	multiline cultivar	-	-	-	-
	genetic engineering	0 - not available	-	0 - not applied	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	1 - moderate	0 - not applied	-
	predation	-	-	-	-
	soil management	1 - available	1 - moderate	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	-	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	-	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	0 - not available	-	0 - not applied	-
	calcium chloride	0 - not available	-	0 - not applied	-
	Urtica spp.	0 - not available	-	0 - not applied	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	-	-	-	-

2.4.4 Evaluation of fungicide/pathogen resistance management strategy based on remaining fungicide and non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Since Z/X = 1.0, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

SPAIN (ES)

VALBON (17.5g/kg benthiavalicarb-isopropyl + 700g/kg mancozeb) is authorised for controlling late blight (*Phytophthora infestans*) in potato and tomato, early blight (*Alternaria solani*) in potato and peacock spot (*Fusicladium oleagineum*) in olives. VINCARE (17.5g/kg benthiavalicarb-isopropyl + 500 g/kg folpet) is authorised for controlling late blight (*Phytophthora infestans*) in tomato. VINTAGE C DISPERSS (17.5g/kg benthiavalicarb-isopropyl + 375g/kg tetracopper hexahydroxide sulphate) is authorised for controlling late blight (*Phytophthora infestans*) in tomato. The evaluation of the necessity for benthiavalicarb in Spain focusses on the control of a) late blight in potato, b) early blight in potato, c) late blight in tomato and d) and peacock spot in olive.

1 List of authorised fungicide active substances on crop/pest combinations

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:
- ametoctradin
- amisulbrom
- chlorothalonil
- copper compounds
- cyazofamid
- difenoconazole ([6])
- dithiocarbamates
- famoxadone
- fluazinam
- folpet
- pyraclostrobin
- zoxamide

Translaminar fungicides:
- benthiavalicarb
- cymoxanil
- dimethomorph
- fenamidone
- fluopicolide
- mandipropamid
- valifenalate

Systemic fungicides:
- benalaxyl
- benalaxyl-M
- fosetyl-Al
- metalaxyl
- metalaxyl-M
- propamocarb

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

Contact fungicides:
- azoxystrobin
- chlorothalonil
- copper compounds
- difenoconazole
- dithiocarbamates
- famoxadone
- folpet
- pyraclostrobin
- zoxamide

Translaminar fungicides:
- benthiavalicarb
- cymoxanil
- dimethomorph
- fenamidone
- mandipropamid

Systemic fungicides:
- benalaxyl
- fosetyl-Al
- metalaxyl
- metalaxyl-M
- propamocarb
- tebuconazole

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:
- ametoctradin
- amisulbrom
- azoxystrobin
- captan
- chlorothalonil
- copper compounds
- cyazofamid
- difenoconazole ([6])
- dithiocarbamates
- famoxadone
- folpet
- pyraclostrobin
- zoxamide

Translaminar fungicides:
- benthiavalicarb
- cymoxanil
- dimethomorph
- fenamidone
- mandipropamid
- valifenalate

Systemic fungicides:
- benalaxyl
- benalaxyl-M
- fosetyl-Al
- metalaxyl
- metalaxyl-M
- propamocarb

([6]) DMI fungicides have no activity against oomycetes and are not further considered in the evaluation.

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

Contact fungicides:
- copper compounds
- difenoconazole
- dithiocarbamates
- folpet
- kresoxim-methyl
- pyraclostrobin

Translaminar fungicides:
- benthiavalicarb
- dodine
- trifloxystrobin

Systemic fungicides:
- tebuconazole
- fenbuconazole

2 Data on fungicide resistance risk

2.1 Step 1: Evaluation of fungicide alternatives with the same mode of action (MoA)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb, plant protection products containing dimethomorph, mandipropamid and valifenalate that have the same mode of action (cellulose synthase inhibition) are authorised for controlling late blight in potato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a "presumed reproductive toxicant (Cat 1B)". As a result dimethomorph may be banned from the European market according to current legislation.

Benthiavalicarb-isopropyl applied at 75g as/ha has a similar efficacy than mandipropamid applied at 150 g as/ha ([7]). Additionally, VALBON (17.5 g/kg benthiavalicarb-isopropyl+ 700 g/kg mancozeb) is applied at a maximum rate of 1.8 kg/ha, equivalent to 31.5 g/ha of benthiavalicarb-isopropyl, in potato for controlling late blight while VALIS M (60g/kg valifenalate + 600 g/kg mancozeb) is applied at a dose rate of 2.5 kg/ha, equivalent to 150 g/ha of valifenalate. These results suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than mandipropamid and valifenalate.

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

Since benthiavalicarb, cymoxanil, dimethomorph, mandipropamid, metalaxyl, metalaxyl-M benalaxyl and benalaxyl-M have no activity against *Alternaria solani*, this crop/disease pathogen combination is not further evaluated.

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

As for late blight in potato, there are plant protection products containing dimethomorph, mandipropamid and valifenalate with the same mode of action (cellulose synthase inhibition) as benthiavalicarb which are authorised for controlling late blight in tomato.

Dimethomorph may be banned from the European market according to current legislation in the future (*cf. supra*).

Additionally, benthiavalicarb-isopropyl applied at 75 g/ha has a similar efficacy than mandipropamid applied at 150g as/ha ([7]). Furthermore, VALBON (17.5g/kg benthiavalicarb-isopropyl + 700g/kg mancozeb) is applied at a maximum application rate of 2.0 kg/ha, equivalent to 35 g as/ha of benthiavalicarb-isopropyl, for controlling late blight in tomato while VALIS M (60g/kg valifenalate + 600g/kg mancozeb) is applied at a dose rate of 2.5 kg /ha, equivalent to 150 g/ha of valifenalate. These results suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than mandipropamid and valifenalate.

([7]) A solo product VERSILUS containing 150 g/kg of benthiavalicarb-isopropyl applied at 75g as/ha is rated with a score of 4.2 for controlling leaf blight in the EuroBlight Fungicide Table (rev. 5-Feb-2019) and has a 0.2 points higher rating than REVUS (250 g/l mandipropamid) applied at 150g as/ha. The plant protection product is authorised in Belgium, the Czech Republic, Germany and the Netherlands.

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

There are no plant protections products containing active substances with the same mode of action as benthiavalicarb against peacock spot in olive.

2.2 Step 2: Evaluation of alternative non-fungicide programs

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

The Ministerio de Agricultura, Alimentación y Medio Ambiente (MAGRAMA) published a guide for Integrated Pest Management in potato crops in Spain (MAGRAMA, 2015). Preventive cultural measures for controlling *P. infestans* described in the guide are given here below:
- use potato seed or plants which are certified to be free of infection and destroy the possible source of inoculation such as heaps of waste;
- maintain good coverage for the tubers with proper hilling or with burning the plant foliage in the most affected plots;
- withdraw affected tubers before storage and in the warehouse maintain good air circulation and temperature as low as possible considering the others factors;
- destroy the plants at the end of the cultivation cycle if the pest is observed in order to avoid its multiplication;
- use varieties that have a low sensitivity to late blight.

The guide states that apart from those means, *Phytophthora infestans* infestations can be treated with chemical fungicides.

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

Since benthiavalicarb, cymoxanil, dimethomorph, mandipropamid, metalaxyl, metalaxyl-M benalaxyl and benalaxyl-M have no activity against *Alternaria solani*, this crop/disease pathogen combination is not further evaluated.

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

The Sociedad Española de Agricultura Ecológica (SEAE) published a technical notebook about organic cultivation of tomato and pepper (Roselló I Oltra *et* Porcuna, 2012). Different measures to control *Phytophthora infestans* in tomato are described in this technical notebook and are given below:

Cultural methods

- avoid free water in the crops;
- use healthy seeds or seedlings;
- remove the affected fruits and plants from the plots;
- proper management of ventilation and irrigation to reduce humidity.

Natural products and basic substances:

- copper oxychloride;
- phosphites;
- yeast extracts;
- silicon-based desiccants.

Biological control

There are three microbial plant protection products authorised for controlling late blight in tomato containing *Gliocladium catenulatum*, *Trichoderma asperellum* plus *Trichoderma gamsii* and *Trichoderma asperellum* plus *Trichoderma atrovirid*.

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

The Ministerio de Agricultura, Alimentación y Medio Ambiente (MAGRAMA) published a guide for Integrated Pest Management in olive crops in Spain (MAGRAMA, 2014). The preventive cultural measures against *F. oleagineum* described are given below:

- perform pruning that favours aeration for the trees and drying of the humid leaves;
- do not apply an excess of nitrogen fertilizer in areas having favourable environmental characteristics for this fungus;
- in new plantations in areas with very favourable environmental conditions for the development of the disease, use varieties resistant to the peacock spot, e.g. Lechín de Sevilla, Manzanilla de Hellín, *etc*. and, if possible, arrange the rows in order to reduce the hours of shade in the trees.

The guide states that apart from those means, *Fusicladium oleagineum* infestations can be treated with chemical fungicides.

2.3 Step 3: Evaluation of alternative modes of action

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fenamidone, fluopicolide, mandipropamid and valifenalate.

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

Since benthiavalicarb, cymoxanil, dimethomorph, mandipropamid, metalaxyl, metalaxyl-M benalaxyl and benalaxyl-M have no activity against *Alternaria solani*, this crop/disease pathogen combination is not further evaluated.

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fenamidone, mandipropamid and valifenalate.

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are dodine and trifloxystrobin

2.4 Step 4: Evaluation of fungicide risk of resistance, pathogen risk of resistance and evaluation of non-fungicide alternatives

2.4.1 Evaluation of fungicide risk of resistance (*X*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

In case of high disease pressure during the main growth phase it is recommended to use translaminar or systemic fungicides containing active substances such as benthiavalicarb, cymoxanil, dimethomorph, fenamidone, fluopicolide, mandipropamid, valifenalate, benalaxyl, benalaxyl-M, fosetyl-Al, metalaxyl, metalaxyl-M and propamocarb.

Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Due to frequent resistance against metalaxyl, metalaxyl-M, benalaxyl and benalaxyl-M, these fungicides should be applied only once at the early growth stages to seize the upward growth of the fungus through the stem and are not taken into account. Active substances with contact activity are also not considered in the calculation.

Table 2.4.1-1 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in potatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl benalaxyl-M metalaxyl metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	fenamidone	C3 - Respiration complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b gene*)	QoI fungicides (Quinone outside Inhibitors)	11	high
3	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
4	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
5	fluopicolide	B5 - Cytoskeleton and motor proteins delocalisation of spectrin-like proteins	benzamides	43	medium *
6	benthiavalicarb dimethomorph mandipropamid valifenalate	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
7	fosetyl-Al	P7 – Host plant defence induction phosphanates	phosphonates	33	low

* not counted

Four alternative modes of action were identified. One mode of action is classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. One mode of action is classified with a low risk for resistance and weighed with a factor of 1.0. The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be $1 \times 0.50 + 2 \times 0.75 + 1 \times 1.00 = 3.00$.

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

Since benthiavalicarb, cymoxanil, dimethomorph, mandipropamid, metalaxyl, metalaxyl-M benalaxyl and benalaxyl-M have no activity against *Alternaria solani*, this crop/disease pathogen combination is not further evaluated.

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

The same process as done previously is followed.

Table 2.4.1-2 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in tomatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl benalaxyl-M metalaxyl metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	fenamidone	C3 - Respiration complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b gene*)	QoI fungicides (Quinone outside Inhibitors)	11	high
2	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
3	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
4	benthiavalicarb dimethomorph mandipropamid valifenalate	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
5	fosetyl-Al	P7 – Host plant defence induction phosphanates	phosphonates	33	low

* not counted

Four alternative modes of action were identified. One mode of action is classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. One mode of action is classified with a low risk for resistance and weighed with a factor of 1.0.The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be 1 × 0.50 + 2 × 0.75 + 1 × 1.00 = 3.00.

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

The same process as done previously is followed.

Table 2.4.1-3 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting peacock spot in olives

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	tebuconazole fenbuconazole	G1 - Sterol biosynthesis in membranes C^{14}- demethylase in sterol biosynthesis (erg11/cyp51)	DMI-fungicides (DeMethylation Inhibitors)	3	medium
2	trifloxystrobin	C3 – Respiration complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b gene*)	QoI fungicides (Quinone outside Inhibitors)	11	high
3	benthiavalicarb	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
4	dodine	U – Unknow mode of action cell membrane disruption (proposed)	guanidines	U 12	medium

* not counted

Three alternative modes of action were identified. One mode of action is classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be 1 × 0.50 + 2 × 0.75 = 2.00.

2.4.2 Evaluation of fungal pathogen risk (Z)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Phytophthora infestans developed resistance quite rapidly to the phenylamide fungicides (metalaxyl and benalaxyl) but not to the CAA fungicides, QoI fungicides, cymoxanil and carbamates. Therefore, the Fungicide Resistance Action Committee classified *P. infestans* as a medium risk pathogen (*Z* = 2) for all modes of action.

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

The control of early blight in potato is not evaluated (*cf. supra*).

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

The Fungicide Resistance Action Committee classified *Phytophthora infestans* as a medium risk pathogen (*Z* = 2) for all modes of action.

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

Fusicladium oleagineum is classified by the Fungicide Resistance Action Committee as a low risk pathogen (*Z* = 1) for all modes of action.

2.4.3 Evaluation of non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in potato is provided under point 2.2.

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	-	-	-	-
	intercropping	-	-	-	-
	harvesting date	-	-	-	-
	crop density	-	-	-	-
	fertilizers	-	-	-	-
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds/hilling	1 - available	1 - moderate	-	1 - feasible with restrictions
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	-	1 - feasible with restrictions
	variety mixtures	-	-	-	-
	multiline cultivar	-	-	-	-
	genetic engineering	-	-	-	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	-	-	-	-
	predation	-	-	-	-
	soil management	-	-	-	-
	hypovirulence	-	-	-	-
Physical methods	heat/burning	1 - available	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	-	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	-	-	-	-
	calcium chloride	-	-	-	-
	Urtica spp.	-	-	-	-
Resistance inducers	synthetic inducers	-	-	-	-
	natural inducers	-	-	-	-

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

The control of early blight in potato is not evaluated (*cf. supra*).

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in tomato is provided under point 2.2.

Table 2.4.3-2 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	-	-	-	-
	intercropping	-	-	-	-
	harvesting date	-	-	-	-
	crop density	-	-	-	-
	fertilizers	-	-	-	-
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	-	-	-	-
	organic matter	-	-	-	-

Table 2.4.3-3 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Host resistance	resistant genotypes	-	-	-	-
	variety mixtures	-	-	-	-
	multiline cultivar	-	-	-	-
	genetic engineering	-	-	-	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	1 - moderate	1 - applied (< 10%)	2 -feasible
	predation	-	-		-
	soil management	-	-	-	-
	hypovirulence	-	-	-	-
Physical methods	heat		-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	-	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	phosphites	1- available	1 - moderate	-	-
	yeast extract	1- available	1 - moderate	-	-
	silicon-based desicants	1- available	-	-	-
Resistance inducers	synthetic inducers	-	-	-	-
	natural inducers	-	-	-	-

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

Table 2.4.3-4 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	-			
	intercropping	-			
	harvesting date				
	crop density	1 - available	1 - moderate	-	1 - feasible with restrictions
	fertilizers	1 - available	1 - moderate	-	-
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds/hilling	-			
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	1 - moderate	-	1 - feasible with restrictions
	variety mixtures	1 - available	1 - moderate		0 - not feasible
	multiline cultivar	-	-	-	-
	genetic engineering				-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis				-
	predation	-	-	-	-
	soil management			-	-
	hypovirulence	-	-	-	-
Physical methods	heat			-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation			-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate				-
	calcium chloride				-
	Urtica spp.				-
Resistance inducers	synthetic inducers				-
	natural inducers	-	-	-	-

2.4.4 Evaluation of fungicide/pathogen resistance management strategy based on remaining fungicide and non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Since Z/X = 0.67, a derogation may not be scientifically supported.

b) Potato, *Solanum tuberosum* (SOLTU) / early blight, *Alternaria solani* (PHYTIN)

Control of early blight in potato was not evaluated.

c) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Since Z/X = 0.67, a derogation may not be scientifically supported.

d) Olive, *Olea europaea* (OLVEU) / peacock spot, *Fusicladium oleagineum* (CYCLOL)

Since Z/X = 0.5, a derogation may not be scientifically supported.

IRELAND (IE)

VALBON (17.5 g/kg benthiavalicarb-isopropyl + 700 g/kg mancozeb) is authorised for controlling *Phytophthora infestans* in potato. The evaluation of the necessity for benthiavalicarb in Ireland focusses on a) the control of late blight in potato.

1 List of authorised fungicide active substances on crop/pest combinations

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:	Translaminar fungicides:	Systemic fungicides:
- ametoctradin	- benthiavalicarb	- benalaxyl-M
- amisulbrom	- cymoxanil	- metalaxyl-M
- chlorothalonil	- dimethomorph	- oxathiapiprolin
- cyazonfamid	- fenamidone	- propamocarb
- famoxadone	- fluopicolide	
- fluazinam	- mandipropamid	
- mancozeb		
- zoxamide		

2 Data on fungicide resistance risk

2.1 Step 1: Evaluation of fungicide alternatives with the same mode of action (MoA)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb, plant protection products containing dimethomorph and mandipropamid that have the same mode of action (cellulose synthase inhibition) are authorised for the control of late blight in potato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a “presumed reproductive toxicant (Cat 1B)”. As a result dimethomorph may be banned from the European market according to current legislation.

Benthiavalicarb-isporopyl applied at 75 g/ha is rated with a score of 4.2 for controlling leaf blight in the EuroBlight Fungicide Table (rev. 5-Feb-2019) and has a 0.2 points higher rating than REVUS (250 g/l mandipropamid) applied at 150 g as/ha. These results suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than mandipropamid.

2.2 Step 2: Evaluation of alternative non-fungicide programs

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Sustainable management strategies for late blight control in potato production were identified based on a literature review by Pacilly *et al*. (2016). Research on the control of potato late blight focusses on cultural practices and plant breeding for resistance. Biological antifungal products based on *Bacillus amyloliquefaciens* strain QST713 are authorised for use in potato.

Crop rotation

Infections originating from oospores are mainly found in regions with narrow rotation schemes and therefore a bigger rotation scheme should prevent such sources of infection. Producers of starch potatoes however have a rotation plan with fewer crops, which results in a larger risk on initial infection from surviving oospores in the soil.

Intercropping

Field experiments with intercropping systems often resulted in significant reductions of late blight in potato but were not able to eradicate the disease completely. Current potato production is however based on mono-cropping and the machinery used for planting and harvesting cannot be used in intercropping systems.

Harvesting dates

The time of harvesting can affect the spread of *Phytophthora infestans* because early harvesting results in lower crop densities later in the season slowing down a late blight epidemic. Compared to seed potatoes, starch and ware potatoes are harvested later in the season.

Crop density

High potato densities contribute to disease dispersal and corresponding late blight severity. A high density of potatoes is however the result of profit maximisation.

Fertilizers

In vitro studies have shown that nitrogen supply increased susceptibility of potato crops to *P. infestans*. However no effect was observed under field conditions.

Resistant plant genotypes

The use of resistant cultivars is an important aspect in sustainable management strategies. Breeding for resistance to late blight started a long time ago. The classical breeding process is time consuming and many resistant genes have already been overcome by the pathogen. Furthermore, recently introduced resistant cultivars were not attractive to the farmers because they lack some of the preferred market characteristics and are not as high yielding.

Cultivar mixtures

Mixing susceptible and resistant potato cultivars on small scales, *e.g.* in plant rows, has been shown to be most effective in decreasing the spread of the disease. Applying cultivar mixtures is however economically not interesting for farmers. A change in market demands for specific potato cultivars could limit these economic losses when moving towards cultivar mixtures.

Genetically engineered crops

Genetic engineering is faster than classical breeding. However, the production of genetically modified potatoes is strictly regulated and also under political and social debate. Besides the possible negative effects on the environment, one other issue is related to the intellectual property rights.

Biological control

Although some biological control agents, plant extracts and biopesticides have been proven to be effective, none of them work as well as chemical fungicides. Because many biological control strategies result in ineffective control, these can be combined with conventional use of chemical fungicides to improve disease management.

2.3 Step 3: Evaluation of alternative modes of action

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fenamidone, fluopicolide and mandipropamid.

2.4 Step 4: Evaluation of fungicide risk of resistance, pathogen risk of resistance and evaluation of non-fungicide alternatives

2.4.1 Evaluation of fungicide risk of resistance (*X*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

In case of high disease pressure during the main growth phase it is recommended to use translaminar or systemic fungicides containing active substances such as benthiavalicarb, cymoxanil, dimethomorph, fenamidone, fluopicolide, mandipropamid, oxathiapiproline, propamocarb and valifenalate. Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Due to frequent resistance against metalaxyl-M and benalaxyl-M, these fungicides should be applied only once at the early growth stages to seize the upward growth of the fungus through the stem and are not taken into account. Active substances with contact activity such as ametoctradin, mancozeb, cyazofamid, fluazinam, zoxamide, *etc*., are also not considered in the calculation.

Table 2.4.1-1 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in potatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl-M metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	fenamidone	C3 - Respiration complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b gene*)	QoI fungicides (Quinone outside Inhibitors)	11	high
3	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
4	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
5	fluopicolide	B5 - Cytoskeleton and motor proteins delocalisation of spectrin-like proteins	benzamides	43	medium *
6	benthiavalicarb dimethomorph mandipropamid	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
7	oxathiapiprolin	F9 - Lipid synthesis or membrane integrity lipid homeostasis and transfer/storage	OSBPI oxysterol binding protein homologue inhibition	49	high

* not counted

Four alternative modes of action were identified. Two modes of action are classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be $2 \times 0.50 + 2 \times 0.75 = 2.50$.

2.4.2 Evaluation of fungal pathogen risk (*Z*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Phytophthora infestans developed resistance quite rapidly to the phenylamide fungicides (metalaxyl and benalaxyl) but not to the CAA fungicides, QoI fungicides, cymoxanil and carbamates. Therefore, the Fungicide Resistance Action Committee classified *P. infestans* as a medium risk pathogen ($Z = 2$) for all modes of action.

2.4.3 Evaluation of non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in potato is provided under point 2.2.

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	1 - available	1 - moderate	3 - applied (≥ 50%)	1 - feasible with restrictions
	intercropping	1 - available	1 - moderate	-	0 - not feasible
	harvesting date	1 - available	1 - moderate	-	1 - feasible with restrictions
	crop density	1 - available	1 - moderate	-	0 - not feasible
	fertilizers	1 - available	0 - none	-	0 - not feasible
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	-	1 - feasible with restrictions
	cultivar mixtures	1 - available	1 - moderate	-	0 - not feasible
	multiline cultivar	-	-	-	-
	genetic engineering	0 - not available	-	0 - not applied	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	predation	-	-	-	-
	soil management	-	-	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	-	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	-	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	0 - not available	-	0 - not applied	-
	calcium chloride	0 - not available	-	0 - not applied	-
	Urtica spp.	0 - not available	-	0 - not applied	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	-	-	-	-

2.4.4 Evaluation of fungicide/pathogen resistance management strategy based on remaining fungicide and non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Since $Z/X = 0.80$, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

THE NETHERLANDS (NL)

VALBON (12.5 g/kg benthiavalicarb-isopropyl + 700 g/kg mancozeb), VALBON START (17.5 g/kg benthiavalicarb-isopropyl + 700 g/kg mancozeb) and VERSILUS (150 g/kg benthiavalicarb-isopropyl) are authorised for controlling *Phytophthora infestans* in potato. VALBON is also authorised for controlling *Peronospora destructor* in onions and shallots. The evaluation of the necessity of benthiavalicarb in the Netherlands focusses on the control of a) late blight in potato and b) downy mildew in onions.

1 List of authorised fungicide active substances on crop/pest combinations

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:

- ametoctradin
- amisulbrom
- azoxystrobin
- chlorothalonil
- cyazofamid
- difenoconazole ([8])
- fluazinam
- mancozeb
- zoxamide

Translaminar fungicides:

- benthiavalicarb
- cymoxanil
- dimethomorph
- fluopicolide
- mandipropamid
- valifenalate

Systemic fungicides:

- benalaxyl-M
- metalaxyl-M
- oxathiapiprolin
- propamocarb

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Phytophthora infestans* (PHYTIN)

Contact fungicides:

- azoxystrobin
- chlorothalonil
- mancozeb
- pyraclostrobin

Systemic fungicides:

- benthiavalicarb
- dimethomorph
- fluopicolide
- fluoxastrobin
- metalaxyl-M
- oxathiapiprolin
- propamocarb
- prothioconazole ([8])

2 Data on fungicide resistance risk

2.1 Step 1: Evaluation of fungicide alternatives with the same mode of action (MoA)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb, plant protection products containing dimethomorph and mandipropamid that have the same mode of action (cellulose synthase inhibition) are authorised for controlling late blight in potato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a “presumed reproductive toxicant (Cat 1B)”. As a result dimethomorph may be banned from the European market according to current legislation.

VERSILUS (150 g/kg benthiavalicarb-isopropyl) applied at 75 g as/ha has a similar efficacy than VALIS M (600 g/kg mancozeb + 60 g/kg valifenalate) and REVUS (250 g/l mandipropamid) both applied at 150 g as/ha. These results suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than valifenalate and mandipropamid.

([8]) DMI fungicides have no activity against oomycetes and are not further considered in the evaluation.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Besides benthiavalicarb, plant protection products containing dimethomorph, which has the same mode of action (cellulose synthase inhibition) is authorised for controlling downy mildew in onions.

As a result of a new proposal to classify the active substance dimethomorph as a "presumed reproductive toxicant (Cat 1B)", dimethomorph may be banned from the European market according to current legislation.

2.2 Step 2: Evaluation of alternative non-fungicide programs

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Sustainable management strategies for late blight control in potato production were identified based on a literature review by Pacilly *et al*. (2016). Research on the biological control of potato late blight focusses on cultural practices and plant breeding for resistance.

Crop rotation

Infections originating from oospores are mainly found in regions with narrow rotation schemes and therefore a bigger rotation scheme should prevent such sources of infection. Producers of starch potatoes however have a rotation plan with fewer crops, which results in a larger risk on initial infection from surviving oospores in the soil.

Intercropping

Field experiments with intercropping systems often resulted in significant reductions of late blight in potato but were not able to eradicate the disease completely. Current potato production is however based on mono-cropping and the machinery used for planting and harvesting cannot be used in intercropping systems.

Harvesting dates

The time of harvesting can affect the spread of *Phytophthora infestans* because early harvesting results in lower crop densities later in the season slowing down a late blight epidemic. Compared to seed potatoes, starch and ware potatoes are harvested later in the season.

Crop density

High potato densities contribute to disease dispersal and corresponding late blight severity. A high density of potatoes is however the result of profit maximisation.

Fertilizers

In vitro studies have shown that nitrogen supply increased susceptibility of potato crops to *P. infestans*. However no effect was observed under field conditions.

Resistant plant genotypes

The use of resistant cultivars is an important aspect in sustainable management strategies. Breeding for resistance to late blight started a long time ago. The classical breeding process is time consuming and many resistant genes have already been overcome by the pathogen. Furthermore, recently introduced resistant cultivars were not attractive to the farmers because they lack some of the preferred market characteristics and are not as high yielding.

Variety mixtures

Mixing susceptible and resistant potato cultivars on small scales, *e.g*. in plant rows, was most effective in decreasing the spread of the disease. Applying cultivar mixtures is economically not interesting for farmers. A change in market demands for specific potato cultivars could limit these economic losses when moving towards cultivar mixtures.

Genetically engineered crops

Genetic engineering is faster than classical breeding. However, the production of genetically modified potatoes is strictly regulated and also under political and social debate. Besides the possible negative effects on the environment, one other issue is related to the intellectual property rights.

Biological control

Although some biological control agents, plant extracts and biopesticides have been proven to be effective, none of them work as well as chemical fungicides. Because many biological control strategies result in ineffective control, these can be combined with conventional use of chemical fungicides to improve disease management.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Biological control of downy mildew in onion focusses primarily on preventive measures; *i.e.* reducing primary infections sources, for example by warm water treatment of plant onions, to delay the onset of the epidemic allowing a longer growth period (Evenhuis & Spruijt, 2011). Fungicide treatments are however most effective in case of high disease pressure (Meier *et al.*, 2005).

Crop burning

Burning of first-year plant onions can limit the transmission of downy mildew from the foliage into the bulbs but cannot be fully prevented. Burning contaminated areas can kill downy mildew spores and reduce their dispersion. For an optimal effect, the burner should be mounted at canopy level and trailed at a speed of 2 km/h. Under weather conditions that are favourable for downy mildew, sporulation can already take place soon after crop burning and it is therefore necessary to burn the crop several times per week (Evenhuis & Spruijt, 2011). Besides the costs, yield losses may occur when the crop foliage is burned early in the growing season.

Intercropping

Intercropping with coriander or mustard reduces the infestation of downy mildew in onions because of volatile compounds that may have an effect on the sporangia of downy mildew (Meier *et al*., 2005).

Change in planting dates

Late cultures (May-Aug) have a higher risk of infestation with downy mildew. Depending on the weather conditions, onions can be planted mid-March to avoid early infestations of downy mildew resulting in high yield losses. As regards sowing, there are however many cases in which late sowing prevented downy mildew infestations due to early growth stage resistance (Meier *et al*, 2005).

Plant density

A lower plant density is an important option to delay downy mildew infestations. Several observations have shown that in cases of lower plant densities, the crop growth period would be longer compensating the overall field production loss (Meier *et al*, 2005). Optimal plant density was determined to be 70-80 plants per m^2 sown in 5 rows per seedbed with a width of 1.5 m (van den Broek, 2008).

Fertilizers

Nutrient deficient soils can result in early infestations of downy mildew. Soil fertilization, including nitrogen fixation by preceding crops, can increase crop vigour and disease resistance. However, higher fertilizer application rates can result in a lush crop in which bulb production is delayed. (Meier *et al*, 2005). Nitrogen fertilization should be limited (van den Broek, 2008).

Raised beds

Some growers cultivate onions on raised beds. It is believed that the circulation of more air between the plants reduces the infestation risk (Meier *et al*, 2005); infestation risk is also believed to be reduced because the top soil remains drier. Cultivation on raised beds in field research had however no quantitative and qualitative effects on yield. Cultural control measures are not sufficient in case of high disease pressure (van den Broek, 2008).

Temperature and humidity management (micro-climate)

The presence of weeds in the crops causes a higher air humidity, which increases the infestation risk. Mechanical and thermal weed control may be advised in organic farming or chemical weed control in a conventional production system.

Organic matter

Literature data suggest that compost could strengthen onion plants because of the soil-improving activity and stimulation of soil functions. The potential effects of different compost types on plant growth and control of downy mildew infestations in onions have been assessed but no significant effects were observed (Zanen & Hospers-Brands, 2007).

Resistant plant genotypes

There are a few onion varieties available that are resistant to downy mildew. The resistance is based on one gene. Although the resistance is believed to be strong and durable, increased selection pressure on the resistance gene can lead to resistance breakdown.

Soil suppressiveness enhancement

Resistance against downy mildew in onions can be induced by treating seeds and bulbs with metabolites produced by *Fusarium solani*. These metabolites activate phytoalexins in onion plants.

Heat

Warm water treatment of first year plant onions prevents systemic infection. Plant onions should be treated for at least one hour at temperatures at or above 40°C. The water temperatures should not exceed 43°C because it can inhibit the germination capacity of more heat-sensitive plant onions (Evenhuis & Spruijt, 2011).

Water

Overhead irrigation during the night could prevent the dispersion of downy mildew. Field research showed that overhead irrigation during the early morning suppressed downy mildew epidemics. However, applying overhead irrigation every night could have adverse effects, such as the development of other fungal leaf diseases (Meier *et al*., 2009).

Radiation

Laboratory experiments have shown that downy mildew spores can be killed by UV-radiation (Lamers & van Rozen, 2009). Under field conditions, sporulation was inhibited by UV-irradiation between the rows. UV-irradiation above the crop canopy led to an infestation at the end of the season. Application frequency is important to achieve a high effectiveness. Further research is necessary into sporulation prediction models to determine the appropriate application timing.

Natural products and basic substances

It is suggested that some natural products and basic substances (sulphur, whey, seaweed extract, calcium chloride and potassium bicarbonate) can control downy mildew except in case of a high disease pressure. Based on further field investigations it was concluded that whey could control downy mildew infestations but not to an extent that is practically feasible (Termorshuizen & Volker, 2007). Algae extracts, lecithin and rape seed oil have no effect on downy mildew. Sodium hydrocarbonate, sulphur, calcium chloride and plant extracts have little effect on downy mildew infestations. Although garlic extract is used to disinfect onion seeds, the effect on downy mildew infestation has not been proven (Meier *et al*., 2005).

Natural inducers

Siberian fir extract induces the natural resistance and has been reported to be effective against downy mildew in onions. It is recommended spraying from the 4th true leaf stage and repeating the spray application 15 days later (Meier *et al*., 2005).

2.3 Step 3: Evaluation of alternative modes of action

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fluopicolide, mandipropamid and valifenalate.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Besides benthiavalicarb, other systemic fungicides are dimethomorph, fluopicolide, propamocarb, fluoxastrobin, metalaxyl-M and oxathiapiprolin. Prothioconazole has no activity against downy mildew and is not further considered in the evaluation.

2.4 Step 4: Evaluation of fungicide risk of resistance, pathogen risk of resistance and evaluation of non-fungicide alternatives

2.4.1 Evaluation of fungicide risk of resistance (*X*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

In case of high disease pressure during the main growth phase it is recommended to use translaminar or systemic fungicides containing active substances such as benthiavalicarb, cymoxanil, dimethomorph, fluopicolide, propamocarb, mandipropamid, oxathiapiproline and valifenalate. Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Due to frequent resistance against metalaxyl-M and benalaxyl-M, these fungicides should be applied only once at the early growth stages to seize the upward growth of the fungus through the stem and are not taken into account. Active substances with contact activity (amisulbrom, mancozeb, cyazofamid, fluazinam and zoxamide) are also not considered in the calculation.

Table 2.4.1-1 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in potatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl-M metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
3	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
4	fluopicolide	B5 - Cytoskeleton and motor proteins delocalisation of spectrin-like proteins	benzamides	43	medium *
5	benthiavalicarb valifenalate dimethomorph mandipropamid	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
6	oxathiapiprolin	F9 - Lipid synthesis or membrane integrity lipid homeostasis and transfer/storage	OSBPI oxysterol binding protein homologue inhibition	49	high

* not counted

Three alternative modes of action were identified. One mode of action is classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be $1 \times 0.50 + 2 \times 0.75 = 2.00$.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Fungicide active substances with a systemic or local systemic activity are considered in the calculation. Fluopicolide is only used in combination with propamocarb and is not counted. Three alternative modes of action were identified. Two modes of action are classified with a high risk for resistance and weighed with a factor of 0.5. One mode of action is classified with a medium risk for resistance and multiplied with a factor of 0.75. Accordingly, the risk of resistance for fungicides (*X*) with (local) systemic activity is calculated to be $2 \times 0.50 + 1 \times 0.75 = 1.75$.

Table 2.4.1-2 Mode of action and resistance risk for (local) systemic fungicides used in combatting downy mildew in onions

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	fluoxastrobin	C3 - Respiration complex III: cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b* gene)	QoI fungicides (Quinone outside Inhibitors)	11	high *
2	metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high
3	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
4	fluopicolide	B5 - Cytoskeleton and motor protein delocalisation of spectrin-like proteins	benzamides	43	medium *
5	benthiavalicarb dimethomorph	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
6	oxathiapiprolin	F9 - Lipid synthesis or membrane integrity lipid homeostasis and transfer/storage	OSBPI oxysterol binding protein homologue inhibition	49	high

* not counted

2.4.2 Evaluation of fungal pathogen risk (*Z*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Phytophthora infestans developed resistance quite rapidly to the phenylamide fungicides (metalaxyl and benalaxyl) but not to the CAA fungicides, QoI fungicides, cymoxanil and carbamates. Therefore, the Fungicide Resistance Action Committee classified *P. infestans* as a medium risk pathogen (*Z* = 2) for all modes of action.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Downy mildew (*Peronospora* spp.) is regarded as posing a medium risk of development of resistance to fungicides (*Z* = 2).

2.4.3 Evaluation of non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in potato is provided under point 2.2.

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	1 - available	1 - moderate	3 - applied (≥ 50%)	1 - feasible with restrictions
	intercropping	1 - available	1 - moderate	-	0 - not feasible
	harvesting date	1 - available	1 - moderate	-	1 - feasible with restrictions
	crop density	1 - available	1 - moderate	-	0 - not feasible
	fertilizers	1 - available	0 - none	-	0 - not feasible
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	-	1 - feasible with restrictions
	variety mixtures	1 - available	1 - moderate	-	0 - not feasible
	multiline cultivar	-	-	-	-
	genetic engineering	0 - not available	-	0 - not applied	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	1 - moderate	0 - not applied	-
	predation	-	-	-	-
	soil management	1 - available	1 - moderate	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	1 - available	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	1 - available	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	0 - not available	-	0 - not applied	-
	calcium chloride	0 - not available	-	0 - not applied	-
	Urtica spp.	0 - not available	-	0 - not applied	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	-	-	-	-

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

A discussion of non-chemical alternatives for controlling downy mildew in onion is provided under point 2.2.

Table 2.4.3-2 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	-	-	-	-
	intercropping	1 - available	1 - moderate	0 - not applied	0 - not feasible
	sowing/planting date	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	plant density	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	fertilizers	1 - available	0 - none	-	-
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	1 - available	0 - none	-	-
	micro-climate	1 - available	1 - moderate	3 - applied (≥ 50%)	2 - feasible
	organic matter	1 - available	0 - none	-	-
	crop burning	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
Host resistance	resistant genotypes	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	variety mixtures	-	-	-	-
	multiline cultivar	-	-	-	-
	genetic engineering	-	-	-	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	-	0 - not applied	-
	predation	-	-	-	-
	soil management	-	-	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	1 - available	1 - moderate	3 - applied (≥ 50%)	2 - feasible
	cold	-	-	-	-
	water	1 - available	1 - moderate	3 - applied (≥ 50%)	2 - feasible
	radiation	1 - available	1 - moderate	0 - not applied	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	1 - available	0 - none	0 - not applied	-
	calcium chloride	1 - available	0 - none	0 - not applied	-
	Urtica spp.	-	-	-	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	1 - available	1 - moderate	0 - not applied	-

2.4.4 Evaluation of fungicide/pathogen resistance management strategy based on remaining fungicide and non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Since Z/X = 1.0, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

b) Onion, *Allium cepa* (ALLCE) / downy mildew, *Peronospora destructor* (PERODE)

Since Z/X = 0.80, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

POLAND (PL)

VALBON (17.5 g/kg benthiavalicarb-isopropyl + 700 g/kg mancozeb) is authorised for controlling *Phytophthora infestans* in potato and tomato. The evaluation of the necessity for benthiavalicarb in Poland focusses on a) the control of late blight in potato and b) late blight in tomato.

1 List of authorised fungicide active substances on crop/pest combinations

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Contact fungicides:

- ametoctradin
- chlorothalonil
- copper compounds
- cyazofamid
- dithiocarbamates ([9])
- difenoconazole ([10])
- famoxadone
- fluazinam
- folpet
- pyraclostrobin
- zoxamide

Translaminar fungicides:

- benthiavalicarb
- cymoxanil
- dimethomorph
- fenamidone
- fluopicolide
- mandipropamid
- valifenalate

Systemic fungicides:

- benalaxyl
- benalaxyl-M
- metalaxyl
- metalaxyl-M
- oxathiapiproline
- propamocarb

b) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phythophthora infestans* (PHYTIN)

Contact fungicides:

- ametoctradin
- azoxystrobin
- chlorothalonil
- copper compounds
- cyazofamid
- difenoconazole ([10])
- dithiocarbamates ([9])
- pyraclostrobin

Systemic fungicides:

- boscalid ([10])
- benalaxyl-M
- benthiavalicarb
- cymoxanil
- dimethomorph
- fenamidone
- fosetyl-Al
- mandipropamid
- metalaxyl
- metalaxyl-M

2 Data on fungicide resistance risk

2.1 Step 1: Evaluation of fungicide alternatives with the same mode of action (MoA)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb-isopropyl, plant protection products containing dimethomorph, mandipropamid and valifenalate that have the same mode of action (cellulose synthase inhibition) are authorised for the control of late blight in potato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a “presumed reproductive toxicant (Cat 1B)”. As a result dimethomorph may be banned from the European market according to current legislation.

Benthiavalicarb-isopropyl applied at 75 g as/ha has a similar efficacy than mandipropamid and valifenalate both applied at 150 g as/ha. These results suggest that benthiavalicarb has an

([9]) including mancozeb, metiram and propineb
([10]) DMI and SDHI fungicides have no activity against oomycetes and are not further considered in the evaluation.

excellent ability to control late blight at significantly lower dose rates than valifenalate and mandipropamid.

b) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Besides benthiavalicarb-isopropyl, plant protection products containing dimethomorph, and mandipropamid that have the same mode of action (cellulose synthase inhibition) are authorised for the control of late blight in tomato.

A new proposal to harmonize the classification and labelling has been submitted for dimethomorph. Based on effects on fertility and development observed in an extended one-generation reproduction toxicity study, it is proposed to classify dimethomorph as a "presumed reproductive toxicant (Cat 1B)". As a result dimethomorph may be banned from the European market according to current legislation.

Benthiavalicarb-isopropyl applied at 75 g as/ha has a similar efficacy than mandipropamid applied at 150 g as/ha. These results suggest that benthiavalicarb has an excellent ability to control late blight at significantly lower dose rates than mandipropamid.

2.2 Step 2: Evaluation of alternative non-fungicide programs

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Sustainable management strategies for late blight control in potato production were identified based on a literature review by Pacilly *et al*. (2016). Research on the control of potato late blight focusses on cultural practices and plant breeding for resistance.

Crop rotation

Infections originating from oospores are mainly found in regions with narrow rotation schemes and therefore a bigger rotation scheme should prevent such sources of infection. Producers of starch potatoes however have a rotation plan with fewer crops, which results in a larger risk on initial infection from surviving oospores in the soil.

Intercropping

Field experiments with intercropping systems often resulted in significant reductions of late blight in potato but were not able to eradicate the disease completely. Current potato production is however based on mono-cropping and the machinery used for planting and harvesting cannot be used in intercropping systems.

Harvesting dates

The time of harvesting can affect the spread of *Phytophthora infestans* because early harvesting results in lower crop densities later in the season slowing down a late blight epidemic. Compared to seed potatoes, starch and ware potatoes are harvested later in the season.

Crop density

High potato densities contribute to disease dispersal and corresponding late blight severity. A high density of potatoes is however the result of profit maximisation.

Fertilizers

In vitro studies have shown that nitrogen supply increased susceptibility of potato crops to *P. infestans*. However no effect was observed under field conditions.

Resistant plant genotypes

The use of resistant cultivars is an important aspect in sustainable management strategies. Breeding for resistance to late blight started a long time ago. The classical breeding process is time consuming and many resistant genes have already been overcome by the pathogen.

Furthermore, recently introduced resistant cultivars were not attractive to the farmers because they lack some of the preferred market characteristics and are not as high yielding.

Cultivar mixtures

Mixing susceptible and resistant potato cultivars on small scales, *e.g.* in plant rows, has been shown to be most effective in decreasing the spread of the disease. Applying cultivar mixtures is however economically not interesting for farmers. A change in market demands for specific potato cultivars could limit these economic losses when moving towards cultivar mixtures.

Genetically engineered crops

Genetic engineering is faster than classical breeding. However, the production of genetically modified potatoes is strictly regulated and also under political and social debate. Besides the possible negative effects on the environment, one other issue is related to the intellectual property rights.

Biological control

Although some biological control agents, plant extracts and biopesticides have been proven to be effective, none of them work as well as chemical fungicides. Because many biological control strategies result in ineffective control, these can be combined with conventional use of chemical fungicides to improve disease management.

b) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Below measures are applied in biological cultivation of fruiting vegetables, including tomatoes.

Crop rotation

A three-year crop rotation is often used with a continuous tomato cultivation throughout the first year, cultivation of cucumber followed by a leafy vegetable crop or green manure crop during the second year and cultivation of sweet peppers in the third year. The greenhouse needs to be compartmentalized.

Fertilizers

It is advisable to reduce the N-NO_3 levels for a more generative start of the crop.

Temperature and humidity management in protected cultivation

Humidity management is important to control diseases in case fungicides cannot be used. Drip irrigation, which keeps the relative air humidity low, is preferred.

Resistant plant genotypes

Phytophthora infestans resistant varieties are available. Seven tomato varieties were tested in a biological assay conducted in a walk-in tunnel and under open-field conditions in Belgium (Buysens & Gobin, 2018). When cultivated in walk-in tunnels, no disease symptoms were observed in any of the varieties examined. Significant differences in resistance amongst the varieties occurred under open-field conditions. Economic yields were 2 to 3 times higher in walk-in tunnel than in open-field cultivation.

2.3 Step 3: Evaluation of alternative modes of action

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a translaminar fungicide. Other active substances with translaminar or local systemic activity are cymoxanil, dimethomorph, fenamidone, fluopicolide, mandipropamid and valifenalate.

b) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Benthiavalicarb is a local systemic fungicide. Other active substances with (local) systemic activity are benalaxyl-M, cymoxanil, dimethomorph, fenamidone, fosetyl-Al, mandipropamid, metalaxyl and metalaxyl-M. Boscalid has no activity against late blight in tomato.

2.4 Step 4: Evaluation of fungicide risk of resistance, pathogen risk of resistance and evaluation of non-fungicide alternatives

2.4.1 Evaluation of fungicide risk of resistance (*X*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

In case of high disease pressure during the main growth phase it is recommended to use translaminar or systemic fungicides containing active substances such as benthiavalicarb, cymoxanil, dimethomorph, fenamidone, fluopicolide, mandipropamid, oxathiapiproline, propamocarb and valifenalate. Since fluopicolide is only authorised in combination with propamocarb, this mode of action is not counted. Due to frequent resistance against benalaxyl / benalaxyl-M and metalaxyl / metalaxyl-M, these fungicides should be applied only once at the early growth stages to seize the upward growth of the fungus through the stem and are not taken into account. Active substances with contact activity such as ametoctradin, cyazofamid, dithiocarbmates, fluazinam, zoxamide *etc*. are also not considered in the calculation.

Table 2.4.1-1 Mode of action and resistance risk for translaminar and systemic fungicides used in combatting late blight in potatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl benalaxyl-M metalaxyl metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high *
2	fenamidone	C3 - Respiration complex III cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b* gene)	QoI-fungicides (Quinone outside Inhibitors)	11	high
3	cymoxanil	unknown	cyanoacetamide-oxime	27	medium
4	propamocarb	F4 - Lipid synthesis or membrane integrity cell membrane permeability, fatty acids	carbamates	28	medium
5	fluopicolide	B5 - Cytoskeleton and motor proteins delocalisation of spectrin-like proteins	benzamides	43	medium *
6	benthiavalicarb dimethomorph mandipropamid valifenalate	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *
7	oxathiapiprolin	F9 - Lipid synthesis or membrane integrity lipid homeostasis and transfer/storage	OSBPI oxysterol binding protein homologue inhibition	49	high

* not counted

Four alternative modes of action were identified. Two modes of action are classified with a high risk for resistance and weighed with a factor of 0.5. Two modes of action are classified with a medium risk for resistance and multiplied with a factor of 0.75. The risk of resistance for fungicides (*X*) with translaminar and/or systemic activity that are applied during the main growth phase is calculated to be $2 \times 0.50 + 2 \times 0.75 = 2.50$.

b) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Fungicide active substances with a systemic or local systemic activity are considered in the calculation.

Table 2.4.1-2 Mode of action and resistance risk for (local) systemic fungicides used in combatting late blight in tomatoes

no	active substance	target site and code	group name	FRAC code	risk of resistance
1	benalaxyl-M metalaxyl metalaxyl-M	A1 - Nucleic acid metabolism RNA polymerase I	PA-fungicides (phenylamides)	4	high
2	fenamidone	C3 - Respiration complex III: cytochrome bc1 (ubiquinol oxidase) at Qo site (*cyt b gene*)	QoI fungicides (Quinone outside Inhibitors)	11	high
3	cymoxanil	U - unknown mode of action	cyanoacetamide-oxime	27	medium
4	fosetyl-Al	P7 - host plant defence induction phosphonates	phosphonates	33	low *
5	benthiavalicarb dimethomorph	H5 - Cell wall biosynthesis cellulose synthase	CAA-fungicides (Carboxylic Acid Amides)	40	medium *

* not counted

Since fosetyl-Al is only authorised in combination with fenamidone, this mode of action is not counted. Three modes of action are identified. Two modes of action are classified with a high risk for resistance and weighed with a factor of 0.5. One mode of action is classified with a medium risk for resistance and weighed with a factor of 0.75. Accordingly, the risk of resistance for fungicides (*X*) with (local) systemic activity is calculated to be $2 \times 0.50 + 1 \times 0.75 = 1.75$.

2.4.2 Evaluation of fungal pathogen risk (*Z*)

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)
b) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Phytophthora infestans developed resistance quite rapidly to the phenylamide fungicides (metalaxyl and benalaxyl) but not to the CAA fungicides, QoI fungicides, cymoxanil and carbamates. Therefore, the Fungicide Resistance Action Committee classified *P. infestans* as a medium risk pathogen ($Z = 2$) for all modes of action.

2.4.3 Evaluation of non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of non-chemical alternatives for controlling late blight in potato is provided under point 2.2.

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	1 - available	1 - moderate	3 - applied (≥ 50%)	1 - feasible with restrictions
	intercropping	1 - available	1 - moderate	-	0 - not feasible
	harvesting date	1 - available	1 - moderate	-	1 - feasible with restrictions
	crop density	1 - available	1 - moderate	-	0 - not feasible
	fertilizers	1 - available	0 - none	-	0 - not feasible
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	-	-	-	-
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	-	1 - feasible with restrictions
	cultivar mixtures	1 - available	1 - moderate	-	0 - not feasible
	multiline cultivar	-	-	-	-
	genetic engineering	0 - not available	-	0 - not applied	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-

Table 2.4.3-1 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	1 - available	1 - moderate	0 - not applied	-
	predation	-	-	-	-
	soil management	1 - available	1 - moderate	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	-	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	-	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	0 - not available	-	0 - not applied	-
	calcium chloride	0 - not available	-	0 - not applied	-
	Urtica spp.	0 - not available	-	0 - not applied	-
Resistance inducers	synthetic inducers	0 - not available	-	0 - not applied	-
	natural inducers	-	-	-	-

a) Tomato, *Solanum lycopersicum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

A discussion of preventive measures for controlling late blight in the biological cultivation of tomato is provided under point 2.2.

Table 2.4.3-2 Comments on the non-chemical alternatives for disease management

Method		Availability	Effectiveness	Practised usage	Feasibility
Cultural control	crop rotation	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	intercropping	-	-	-	-
	harvesting date	-	-	-	-
	crop density	-	-	-	-
	fertilizers	1 - available	1 - moderate	1 - applied (< 10%)	1 - feasible with restrictions
	soil tillage	-	-	-	-
	bio-fumigation	-	-	-	-
	raised beds	-	-	-	-
	micro-climate	1 - available	1 - moderate	1 - applied (< 10%)	1 - applied (< 10%)
	organic matter	-	-	-	-
Host resistance	resistant genotypes	1 - available	2 - high	1 - applied (< 10%)	1 - feasible with restrictions
	cultivar mixtures	-	-	-	-
	multiline cultivar	-	-	-	-
	genetic engineering	-	-	-	-
	gene editing	-	-	-	-
	gene silencing	-	-	-	-
Biological control	competition	-	-	-	-
	hyperparasitism	-	-	-	-
	antibiosis	-	-	-	-
	predation	-	-	-	-
	soil management	-	-	-	-
	hypovirulence	-	-	-	-
Physical methods	heat	-	-	-	-
	cold	-	-	-	-
	water	-	-	-	-
	radiation	-	-	-	-
	barriers and filters	-	-	-	-
Natural products and basic substances	sodium bicarbonate	-	-	-	-
	calcium chloride	-	-	-	-
	Urtica spp.	-	-	-	-
Resistance inducers	synthetic inducers	-	-	-	-
	natural inducers	-	-	-	-

2.4.4 Evaluation of fungicide/pathogen resistance management strategy based on remaining fungicide and non-fungicide alternatives

a) Potato, *Solanum tuberosum* (SOLTU) / late blight, *Phytophthora infestans* (PHYTIN)

Since Z/X = 0.80, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

b) Tomato, *Solanum lycopersicum* (LYPES) / late blight, *Phytophthora infestans* (PHYTIN)

Since Z/X = 1.14, a derogation may be supported for the use of benthiavalicarb in a conventional production system.

REFERENCES

Anon. (2014). Guía de gestion integrada de plagas: olivar. Ministerio de Agricultura, Alimentación y Medio Ambiente (MAGRAMA), Secretaria Técnica: Centro de Publicaciones, Madrid. https://www.mapa.gob.es/es/agricultura/temas/sanidad-vegetal/GUIAOLIVAR%20(2)_tcm30-57939.pdf

Anon. (2015). Guía de gestión integrada de plagas: patata. Ministerio de Agricultura, Alimentación y Medio Ambiente (MAGRAMA), Secretaria Técnica: Centro de Publicaciones, Madrid. https://www.mapa.gob.es/es/agricultura/temas/sanidad-vegetal/guiadepatata_tcm30-57961.pdf

Evenhuis B & Spruijt J (2011). Beheersing valse meeldauw in de uienteelt. bioKennis bericht nr. 34.

Lamers J & van Rozen K (2009). De mogelijkheden van UV-C straling voor de bestrijding van ziekten en plagen in de akkerbouw - Een literatuurstudie. Praktijkonderzoek Plant & Omgeving B.V. 26 pages.

Meier R, Evenhuis A, Spits HG & Waalwijk C (2009). Beheersing valse meeldauw (*Peronospora destructor*) in uien - Proefjaar 2008. Praktijkonderzoek Plant & Omgeving B.V., Projectnummer: 3252039500. 27 pages.

Meier R, Schepers HTAM, Wander JGN, Prins U, Hospers M & Bruin C (2005). Beheersing valse meeldauw (*Peronospora destructor*) in uien - Proefjaar 2004. Praktijkonderzoek Plant & Omgeving B.V., Projectnummer: 530395. 28 pages.

Pacilly FCA, Groot JCJ, Hofstede GJ, Schaap BF & Lammerts van Bueren ET (2016). Analysing potato late blight control as a social-ecological system using fuzzy cognitive mapping. *Agronomy for Sustainable Development*, 2016, 36(2), pp. 35.

Roselló I Oltra J & Porcuna JL(2012). Cultivo ecológico del tomate y del pimiento. Cuadernos Técnicos SEAE: Protección Vegetal Ecológica. Sociedad Española de Agricultura Ecológica (SEAE) https://www.icia.es/icia/download/Agroecología/Material/Cultivo_ecologico.pdf

Termorshuizen AAJ & Volker D (2007). Opties voor beheersing van valse meeldauw in ui zonder synthetische bestrijdingsmiddelen. Wetenschapswinkel Wageningen UR, rapportnummer 232.

van den Broek R (2008). Naar een optimal teeltsysteem voor biologische zaaiuien. bioKennis bericht nr. 17.

Zanen M & Hospers-Brands M (2007). Valse Meeldauw in biologische zaaiui, effecten van compost. Louis Bolk Insituut. 21 pages.