FINAL REGISTRATION REPORT

Part B

Section 3

Efficacy Data and Information

Concise summary

Product code: SHA 7216 A

Product name(s): CIAZ

Chemical active substance:

Boscalid, 233 g/L

Difenoconazole, 66 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: Sharda Cropchem España

Submission date: August 2021

MS Finalisation date: March 2022, December 2022

Version history

When	What
December, 2021	Updated by applicant
March 2022	ZRMs evaluated dRR updated by Applicant.
December 2022	ZRMs made corrections according to reviewed comments.

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3 Efficacy Data and Information (including Value Data) on the Plant Protection Product (KCP 6)

Transformation of the dRR (applicant version) into the RR (zRMS version)

The process chosen by the zRMS to transform the dRR into a RR should be explained. Options are to rewrite the document (with track change or not) or to use commenting boxes such as the following:

Comments of zRMS:	Comments of zRMS are presented in commenting boxes at the end of each chapter. The text of dRR was generally not changed or rewritten (small changes in the document are marked by grey colour). Corrections done during commenting period were marked by yellow.

3.1 Summary and conclusions of zRMS on Section 3: Efficacy (KCP 6)

Abstract

Comments of zRMS: Overall summaries are not necessary here. It was provided at the end of each chapter of the dRR.

Table 3.1-1: Acceptability of intended uses (and respective fall-back GAPs, if applicable)

1	2	3	4	5	6	7	8	9	10	11	12	13	14
Use-No. [e]	**Member state(s)**	**Crop and/ or situation** **(crop destination / purpose of crop)**	**F, Fn, Fpn G, Gn, Gpn or I**	**Pests or Group of pests controlled** (additionally: developmental stages of the pest or pest group)	**Application**				**Application rate**			**PHI** (days)	**Remarks:** e.g. g safener/synergist per ha [f]
					Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	kg or L product / ha a) max. rate per appl. b) max. total rate per crop/season	g or kg as/ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min / max		
Zonal uses (field or outdoor uses, certain types of protected crops)													
1	CEU	**Winter wheat**	F	*Septoria spp.*(SEPTSP and/or SEPTTR)	Foliar Spray	BBCH 30-59	a) 2 b) 2	14	a) 1.5 b) 3	a) 0.35 boscalid + 0.11 difenoconazole b) 0.7 boscalid + 0.2 difenoconazole	200-400	-	To be confirmed by cMS In PL – water 200-300 L/ha should be applied. Only SEPTTR can be conditional registered in PL.
2	CEU	**Winter wheat**	F	*Puccinia spp* (PUCCST and/or PUCCRE)	Foliar Spray	BBCH 30-59	a) 2 b) 2	14	a) 1.5 b) 3	a) 0.35 boscalid + 0.1 difenoconazole b) 0.7 boscalid + 0.2 difenoconazole	200-400	-	To be confirmed by cMS In PL – water 200-300 L/ha should be applied.. Only PUCCST can be conditional registered in PL.
3	CEU	**Winter wheat**	F	*Fusarium spp.* (FUSASP)	Foliar Spray	BBCH 39-59	a) 2 b) 2	14	a) 1.5 b) 3	a) 0.35 boscalid + 0.1 difenoconazole b) 0.7 boscalid + 0.2 difenoconazole	200-400	-	To be confirmed by cMS In PL – use not accepted.

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1.

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

A	Acceptable

R	Acceptable with further restriction
C	To be confirmed by cMS
N	Not acceptable / evaluation not possible
n.r.	Not relevant for section 3

3.2 Efficacy data (KCP 6)

Introduction

This document summarises the information related to the efficacy data of the plant protection product **Boscalid 23.3% + Difenoconazole 6.6% SC (CIAZ; Product code: SHA 7216 A)** containing the active substances boscalid and difenoconazole, which both have been included into Annex I of Council Directive 91/414/EEC.

The SANCO reports for boscalid (SANCO/3919/2007 final) and difenoconazole (SANCO/830/08, rev. 3) are considered to provide the relevant review information or a reference to where such information can be found.

For the implementation of the uniform principles of Annex VI, the conclusions of the review reports on the active substances boscalid and difenoconazole, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health on 21th January 2008 and 14th March 2008, respectively, shall be taken into account. Consideration of active substances for Annex I inclusion does not include an evaluation of efficacy. Therefore, there are no concerns to address arising from the inclusion directive of boscalid and difenoconazole relating to efficacy.

These concerns have been addressed within the current submission.

Appendix 1 of this document contains the list of references included in this document for support of the evaluation.

The detailed assessment of the individual trial and study data is located in the following report:

Report:	**KCP 6.0/001 Biological Assessment Dossier Boscalid 23.3% + Difenoconazole 6.6% SC, Central**

Description of the plant protection product

Boscalid 23.3% + Difenoconazole 6.6% SC is an Suspension Concentrate (SC) formulation containing 233 grams per liter (g/L) boscalid and 66 grams per liter (g/L) difenoconazole for use in winter wheat – please refer to Appendix 2 to see the GAP covered by this BAD.

To support the registration of Boscalid 23.3% + Difenoconazole 6.6% SC in the GAP claimed crops, trials have been set up in winter wheat. In winter wheat efficacy trials conducted in Italy, Poland, Germany, France, United Kingdom, Czech Republic and Hungary, the boscalid + difenoconazole formulation prepared by Sharda Cropchem España – Boscalid 23.3% + Difenoconazole 6.6% SC – was compared against a reference boscalid + difenoconazole co-formulation currently on the market in South- and Central Europe.

According to the GAP, the proposed application rate of Boscalid 23.3% + Difenoconazole 6.6% SC is 1.5 L per hectare (L/ha), with up to two applications per season. This will deliver 233 g boscalid and 66 g difenoconazole per hectare. In the current document, results obtained in field trials with Boscalid 23.3% + Difenoconazole 6.6% SC applied at 1.5 L/ha to 3.0 L/ha will be presented where these have been tested against similar dose rates of boscalid + difenoconazole reference product currently marketed in the countries where the trials were conducted.

The data presented in this dossier fully support the label claim of Boscalid 23.3% + Difenoconazole 6.6% SC for the control of *Septoria spp.*, *Puccinia spp.* and *Fusarium spp.* in winter wheat as listed in the table below;

Table 3.2-1: Simplified table of currently registered uses and requested uses for the product code.

Crop / *disease*	Application method	Spray volume (L/ha)	Max. individual application rate (kg f.p./ha) [kg a.s./ha]	Max. number of applications	Application timing (e.g. BBCH)
Winter wheat / Puccinia	Spray	200-400	(1.5) [0.350+0.100]	2	BBCH 30-59
Winter wheat / Septoria	Spray	200-400	(1.5) [0.350+0.100]	2	BBCH 30-59
Winter wheat / Fusarium	Spray	200-400	(1.5) [0.350+0.100]	2	BBCH 30-59

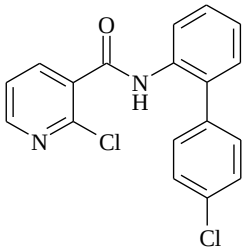
Further details are in the table "All intended uses" in Part B - Section 0.

Description of active substance boscalid

Boscalid is a member of the class of pyrazine-carboxamide fungicides. Boscalid effectively controls several fungal pathogens belonging to the four major classes of plant pathogenic fungi.

Today, boscalid is registered and commercialised in several formulations, as straight product as well as in mixtures, around the world.

Table 3.2-2: Identity of boscalid

Common name	Boscalid
IUPAC name	2-Chloro-*N*-(4'-chlorobiphenyl-2-yl)nicotinamide
CA name	2-Chloro-*N*-(4'-chloro[1,1'-biphenyl]-2-yl)-3-pyridinecarboxamide
CIPAC No	673
CAS Registry No.	188425-85-6
EEC No	not assigned
Minimum purity	≥ 960 g/kg
Structural formula[1]	
Empirical formula	$C_{18}H_{12}Cl_2N_2O$
Molecular mass	343.21 g/mol

Mode of action, boscalid

Boscalid has preventative and curative properties. It inhibits spore germination, germ tube elongation, mycelial growth, and sporulation (all major stages of fungal growth and reproduction necessary for dis-

[1] Source: Chem Service Inc. Internet, Tuesday March 20th, 2019. URL: https://www.chemservice.com/

ease development). Boscalid is a systemic compound. Depending on the type of formulation, it penetrates into the plant when applied to leaves (or roots), and it is then translocated acropetally.

The mode of action of boscalid at the molecular level is the inhibition of the mitochondrial succinate dehydrogenase (SDH, complex II). This enzyme is part of tricarboxylic acid cycle (citrate cycle, Krebs cycle). It belongs also to a class of flavoproteins, which enter electrons into the mitochondrial respiration chain. Therefore, inhibition of succinate dehydrogenase by boscalid affects both the carbon flow into crucial metabolites and the yield of ATP. The shortage of building blocks for amino acids and sugars together with the reduced energy yield severely interferes with basic principles of growth and maintenance of a living cell.

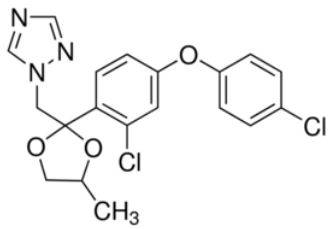
The efficacy of inhibition of SDH strongly depends on the species. In phytopathogenic fungi as *Botrytis cinerea*, SDH is strongly inhibited by a low concentration of Boscalid. In the yeast *Saccharomyces cerevisiae*, inhibition is still observed but a higher concentration is necessary and the mammalian enzyme from pig liver is almost resistant to boscalid.

Boscalid has preventative and curative properties. It inhibits spore germination, germ tube elongation, mycelial growth, and sporulation (all major stages of fungal groth and reproduction necessary for disease development).

Description of active substance difenoconazole

The active substance difenoconazole is a systemic triazole fungicide and is active as a systemic broad-spectrum fungicide with long-lasting preventative and curative action.

Table 3.2-3: Identity of difenoconazole

Common name	Difenoconazole
IUPAC name	3-chloro-4-[(2*RS*,4*RS*;2*RS*,4*SR*)-4-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-2-yl]phenyl 4-chlorophenyl ether
CA name	1-(2-(2-chloro-4-(4-chlorophenoxy)phenyl)-4-methyl-1,3-dioxolan-2-ylmethyl)-1*H*-1,2,4-triazole
CIPAC No	687
CAS Registry No.	119446-68-3
EEC No	Not allocated
Minimum purity	≥ 940 g/kg
Structural formula[2]	
Empirical formula	$C_{19}H_{17}CL_2N_3O_3$
Molecular mass	406.26 g/mol

Mode of action, difenoconazole

Difenoconazole is a broad-spectrum fungicide that controls a wide variety of fungi – including members of the Aschomycetes, Basidomycetes and Deuteromycetes families. It acts as a seed treatment, foliar

[2] Source: Chem Service Inc. Internet, Thursday June 15th, 2017. URL: https://www.chemservice.com/

spray and systemic fungicide. It is taken up through the surface of the infected plant and is translocated to all parts of the plant. It has a curative effect and a preventative effect. Difenoconazole can be applied to a range of crops, including cereals, vegetables and fruits. It controls various fungi including powdery mildew, rust, scab and leaf spots. The mode of action of difenoconazole is that it is a sterol demethylation inhibitor which prevents the development of the fungus by inhibiting cell membrane ergosterol biosynthesis.

FRAC (Fungicide Resistance Action Committee) presents difenoconazole together with the other triazoles into the fungicide group that comprises the Sterol Biosynthesis Inhibitor's (abbreviated SBI's) and into the class I for DeMethylation Inhibitor (abbreviated DMI). Due to its primary target site and its chemical family, in the FRAC mode of action classification, it is classified as group G1 Fungicide (FRAC MOA G1, Group code 3).

Information on similar formulations and current approvals

Boscalid 23.3% + Difenoconazole 6.6% SC is an SC formulation containing 233 g/L boscalid and 66 g/L difenoconazole. Data presented in this dossier is generated using this formulation in comparison with e.g. the Syngenta reference product containing boscalid and difenoconazole. Boscalid as well as difenoconazole are currently registered under a variety of trade names and formulations throughout Europe and a selection of these are described in table below.

Table 3.2-4: Current approvals of products in the EU Central zone as well as connected EPPO zones where trials were conducted. Reference products used in trials are also included

Country	Product	Active ingredient	Approval number
Austria	Prosaro	Prothioconazole 125 g/L + Tebuconazole 125 g/L EC	3054-0
	Difenzone	**Difenoconazole 250 g/L EC**	**3285**
Croatia	Cantus	Boscalid 500 g/L	UP/I-320-20/04-01/209
	Difenzone	**Difenoconazole 250 g/L**	**UP/I-320-20/12-01/323**
	Bellis	Piraklostrobin 128 g/L + Boskali 252 g/L	UP/I-320-20/06-01/289
Czech Republic	Prosaro	Prothioconazole 125 g/L + Tebuconazole 125 g/L EC	4561-2V
	Elanza	**Boscalid 23.3% + Difenoconazole 6.6% SC**	**5952-0**
	Atos	**Difenoconazole 250 g/L EC**	**4838-1**
Denmark	Prosaro	Prothioconazole 125 g/L + Tebuconazole 125 g/L EC	18-527
Estonia	Prosaro	Prothioconazole 125 g/L + Tebuconazole 125 g/L EC	38089250
France	Bell Star	Boscalid 140 g/L + epoxiconazole 50 g/L EC	2110194
	Pulco	Boscalid 50 g/L EC	2150267
Germany	Champion	Boscalid 233 g/L + epoxiconazole 50 g/L EC	025757-00
	Score	Difenoconazole 250 g/L EC	024353-00
	Cantus	Boscalid 500 g/L WG	025180-00
Greece	Bellis Gold	Boscalid 267 g/L WG	60426
	Disco 25 EC	**Boscalid 250 g/L EC**	**60617**
Ireland	Bellis	Boscalid 267 g/L WG	03798
	Difcor 250 EC	Boscalid 250 g/L Ec	04983
Italy	Proline Star	Prothioconazole 125 g/L + Tebuconazole 125 g/L EC	015640
	Filan WG	Boscalid 500 g/L EC	015344
	Agridif 250	**Difenoconazole 232 g/L EC**	**013225**

Description of winter wheat

Common wheat (*Triticum aestivum* ssp. *vulgare*) is the most widely cultivated species of wheat in Poland (besides this, spelt, durum, flatbread, and small spelt are grown). Area-wise, wheat sowing ranks third in the world after rice and corn. Wheat is grown for consumption: flours, groats, flakes, bran and for feed purposes. Wheat varieties have very different soil requirements, which is why good winter wheat varieties - their list is usually given on a provincial basis. Some yield well only on good sites (soils of classes I, II, III), but there are also varieties with lower requirements that yield quite well on soils of classes IV a or IV b. In choosing a site for wheat, medium to heavy soils with high humus content, proper air-water relations and good pH are preferred. Wheat generally does not tolerate soils with a pH below 5.5. However, there are varieties, e.g., Pokusa, Artist, Janosh, Chiron, which will still grow well up to pH 5.2. Below pH 5.0 wheat will never yield well.

Varieties: genetic progress is so great today that every year there are higher and higher yielding varieties with better parameters, achieving the required parameters more easily and maintaining them more easily. In research whether German, Austrian that is also confirmed by Polish research at COBORU, varieties such as Artist, Patras, Janosh, Tobak, Pokusa, and novelties Chiron and Balitus are in high positions.

For our dreams of high yields and good quality to come true, we need to protect wheat from weeds, viral diseases, fungal diseases, and pests.

Wheat - protection against diseases

Viral diseases are prevented by controlling their vectors - aphids and jumpers already in autumn. The threat of fungal diseases depends largely on the course of the weather, the susceptibility of the variety to the disease, crop rotation, fertilization. The greatest disease threat is in southern Poland due to the amount of rainfall, frequent fog and dew. Shortened or no crop rotation means increased development of diseases such as brown leaf spot, septoria, fusariosis and stem base rot.

Description of the target pests

Key targets for this product are foliar- and ear diseases of winter wheat. The listed pests are present throughout or in parts of the Central zone and in relevant EPPO zones. The key targets for this product are described in detail in the Biological Assessment dossier.

Yellow rust (*Puccinia striiformis* - PUCCST)

Yellow rust affects wheat, barley and oats, although it occurs more frequently on wheat. The forms of *P. striiformis* that affect wheat are distinct from those which affect barley and rye, so that the disease cannot spread from one crop species to the other. The fungus exists as many physiologic races, adapted to different cereal varieties. Symptoms consist of orange-yellow pustules, which form characteristic stripes on the leaf surface. Ears may also become infected, with pustules developing within the glumes and on the awns of barley. Destruction of the leaf and ear reduces photosynthesis leading to yield losses of 30% or more. Cereal varieties differ markedly in their resistance to yellow rust. Epidemic risk can be reduced further by sowing adjacent fields with different varieties chosen in accordance with the Diversification Scheme. Stubble should be ploughed or desiccated and cultivated soon after harvest to destroy the “green-bridge” on which the pathogen is dependant for survival.

Brown rust (*Puccinia recondita* – PUCCRE)

Brown rust (*Puccinia recondita*) is a common foliar disease, particularly in temperate climates. It is encouraged by warm temperatures (15-22 ºC) combined with periods of extreme (100%) humidity. The disease often appears at a late stage and can develop rapidly with a latent period of just 6 days in ideal conditions. The need for warmer temperatures means that the disease tends to occur in mid to late summer in most of Northern Europe. Severe infestations are rare, but can be devastating with yield losses of up to 60%. Damage may vary on average from 5 to 30 dt/ha.

Blotch of wheat (*Septoria tritici* – SEPTTR)

Septoria leaf caused by *Septoria tritici* is the most frequent diseases on wheat. *Septoria tritici* mainly develops on leaves. *Septoria tritici* is the major pathogen of wheat crops and is particularly prevalent in regions with wet summers such as Northern Europe. Initial infection over the winter and spring is via wind-dispersed ascospores, though rainfall plays a critical role in subsequent development of the disease by facilitating transmission within the crop as splash-dispersed pycnospores. The disease is characterized by a protracted latent period (21-28 days under ideal conditions) where the fungus develops unseen in the leaf. Visible symptoms of *Septoria tritici are* characterized by pale brown to greenish grey oval lesions, which have black pycnidia visible to the naked eye, parallel to the veins of the leaves. Damages due to *Septoria* attacks are often severe and impacting the yield and quality of wheat.

Fusarium species (*Fusarium spp.* – FUSASP)

Fusarium is a large genus of filamentous fungi widely distributed in soil and in association with plants. Most species are harmless saprobes and are relatively abundant members of the soil microbial community. Some species produce mycotoxins in cereal crops that can affect human and animal health if they enter the food chain. The main toxins produced by these Fusarium species are fumonisins and trichothecenes. The genus includes a number of economically important plant pathogenic species.

Fusarium graminearum commonly infects barley if there is rain late in the season. It is of economic impact to the malting and brewing industries as well as feed barley. Fusarium contamination in barley can result in head blight. The genome of this wheat and maize pathogen has been sequenced. Fusarium graminearum can also cause root rot and seedling blight.

Table 3.2-5: Glossary of pests mentioned in the dossier.

EPPO code	Scientific name	Common name
PUCCRE	*Puccinia recondita*	Brown rust of cereals
PUCCST	*Puccinia striiformis*	Yellow rust of wheat
PUCCSP	*Puccinia spp.*	Rust species
SEPTTR	*Zymoseptoria tritici*	Leaf spot of wheat
SEPTSP	*Septoria spp.*	Leaf spot diseases
FUSASP	*Fusarium spp.*	-

Table 3.2-6: Major / minor status of intended uses (for all cMS and zRMS).

Crop and/or situation	Crop status		Pests or group of pests controlled	Pest status	
	Major	Minor		Major	Minor
Winter wheat	CEU	-	Puccinia	CEU	-
Winter wheat	CEU	-	Septoria	CEU	-
Winter wheat	CEU	-	Fusarium	CEU	-

Compliance with the Uniform Principles

Comprehensive field trials were conducted in Italy, France, Czech Republic, Poland, Germany and Hungary in 2016, 2017 and 2019. The trials followed the corresponding EPPO guidelines. The GEP-requirement and the Uniform Principles are taken care of.

Information on trials submitted (3.1 Efficacy data)

Trials in this dossier were carried out by contractor companies and Official Research institutes, all of which follow the EPPO guidelines and are officially recognized by the competent authorities to carry out field registration trials in accordance with the principles of Good Experimental Practice (GEP). The GEP-requirement and the Uniform Principles are therefore taken care of.

On the basis of the EPPO guideline 1/241(1) "Guidance on comparable climates", the trials included in this dossier have been grouped and summarized by EPPO zones. EPPO zones have been defined by taking into account differences between the agro-climatic sub-areas of the EPPO region.

In general, the trials were conducted according to the respective EPPO guidelines.

In support of the current application for registration of Boscalid 23.3% + Difenoconazole 6.6% SC, 21 efficacy trials were conducted in the Maritime, the North-east, the South-east and the Mediterranean EPPO zones.

In the trials used to assess the level of control obtained with Boscalid 23.3% + Difenoconazole 6.6% SC, a different number of assessments were conducted during the course of the trials. In some trials, a single assessment was conducted on the specific plant part and in others, two or more assessments were conducted. Therefore, not to bias the data from any trial with more than one assessment, the summary tables contain the data from one assessment per plant part per trial. An assessment is only considered valid for evaluation if the level of pest severity (PESSEV) is minimum 1% in the untreated check or if pest incidence (PESINC) is minimum 5% in the untreated check. The data selected from each trial is either the final assessment timing on each plant part or the assessment conducted at the most relevant timing.

Table 3.2-7: Presentation of efficacy trials (efficacy trials, preliminary trials...)

Crop(s) *	Target(s)*	Country	Years	Type of trial**	Number of trials (number of valid trials)				GEP, non-GEP, official***	Comments (any other relevant information)
					EPPO zone					
					MAR	MED	S-E	N-E		
TRZAW	SEPTTR SEPTSP PUCCRE PUCCST PUCCSP FUSASP	Italy	2017	MED + E	-	4 (4)	-	-	GEP	
		France	2017	P + MED + E	4 (4)	1 (1)	-	-	GEP	
		Germany	2017	P + MED + E	1 (1)	-	-	-	GEP	
		Czech Rep.	2016	P + MED + E	4 (4)	-	-	-	GEP	
			2019	MED + E	6 (6)	-	-	-	GEP	
		Hungary	2016	P + MED + E	-	-	4 (4)	-	GEP	
		Poland	2016	P + MED + E	-	-	-	2	GEP	
			2017	P + MED + E	-	-	-	2	GEP	
					15 (15)	5 (5)	4 (4)	4 (4)	-	
		Total, all crops			15 (15)	5 (5)	4 (4)	4 (4)	-	

Climatic zones

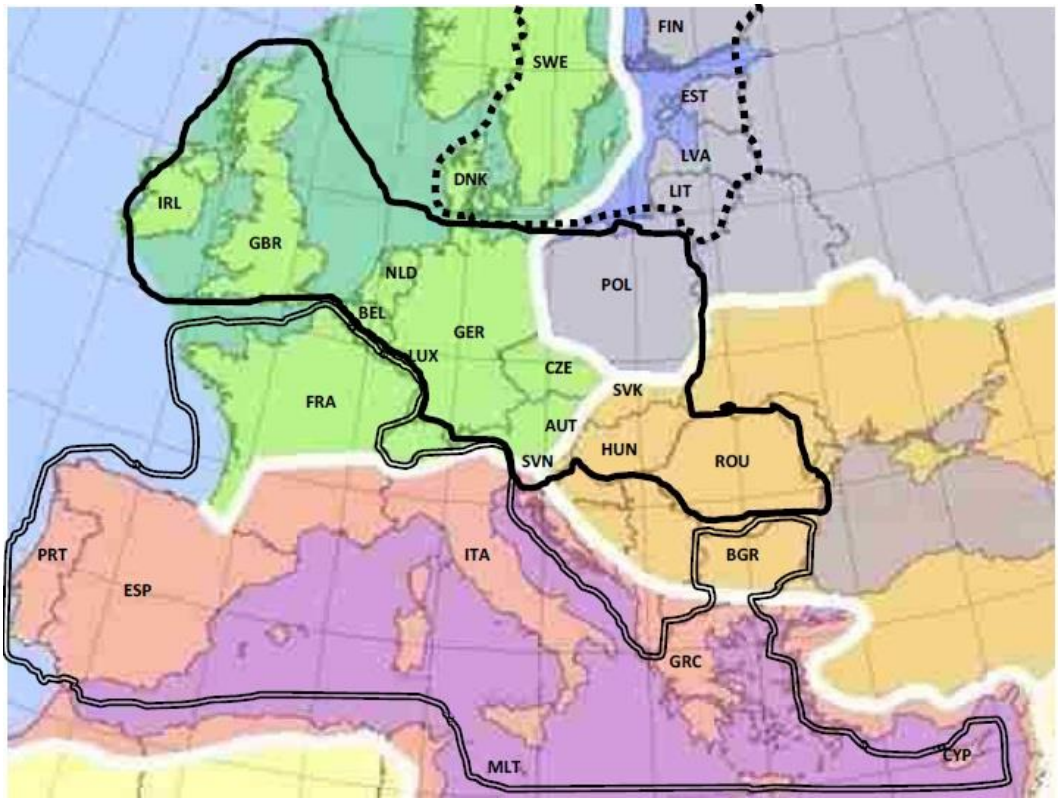
Europe is divided into four climatic zones, according to EPPO standard PP 1/241 (1). Besides providing guidance in determining comparability of climatic conditions between geographical areas where efficacy evaluation trials are performed, the standard also supports the use of data generated in one country to support registration in another country[3].

[3] Development of Comparable Agro-Climatic Zones for the International Exchange of Data on the Efficacy and Crop Safety of Plant Protection Products, E. Bouma, 2005 OEPP/EPPO, Bulletin OEPP/EPPO Bulletin 35, 233-238.

Czech Republic, Germany and N-France are located in the Maritime EPPO zone; Poland is located in the North-east EPPO zone; Hungary is located in the South-east EPPO zone; Italy and S-France are located in the Mediterranean EPPO zone (Figure 3.2-1).

This document is prepared to support the submission of Boscalid 23.3% + Difenoconazole 6.6% SC throughout the Central Registration zone, therefore data from the Maritime, North-east and South-east EPPO zones are included. Data obtained in the Mediterranean EPPO zone zone has also been added as supporting information, however, the data from each climatic zone is summarised separately.

Figure 3.2-1: Representation of EPPO climatic zones (in colour: EPPO Standard PP1/241, Guidance on comparable climates) superimposed with the 3 European zones (EC Regulation 1107/2009) (Source: EPPO)



Agronomic conditions

Cultural conditions of winter wheat and agronomy (e.g. cultivations used, application methods, cultivars, fertilizer regime, relative times of planting and harvest) do not differ significantly between the countries in the EU, but common is that rust, Fusarium and Septoria attack winter wheat and other cereals from the South to the North, from East to West when the weather conditions are favourable for the pests to infest the crops.

The same boscalid and difenoconazole containing fungicides are already registered and used in the countries where the trials were conducted to support the current application for registration. Please refer to **Błąd! Nie można odnaleźć źródła odwołania.** for the registration numbers in the different countries. In all countries, the products are registered for the same use. In each country, these are used protectively at similar application timings when the crops are at similar growth stages

(i) *Pest physiology*

The physiology of individual pathogens presented is common throughout Southern and Central Europe. Although trials were performed in different countries, sites were selected to exert maximum disease pressure and to exacerbate treatment differences. No difference in the level of control was apparent between the different countries or regions in which the trials were conducted.

(ii) *Site selection*

Although trials were performed throughout the Southern and Central EU, in each country the sites were carefully selected to ensure that for each fungal disease, the level of control was assessed on a range of populations, when treated at the recommended application timings. To exert maximum control pressure and to exacerbate treatment differences in each country this included some trials which contained high infestation levels. No differences in the level of control were apparent between the different countries or regions in which the trials were conducted.

(iii) *Agronomic practices*

Agronomic practices for growing wheat are similar throughout the Central zone as well as in the countries in the connected EPPO zones where trials were conducted. The levels of inorganic fertilizers and other crop inputs are also generally similar between the countries.

(iv) *Varieties*

Although crop varieties tend to differ between countries, observations on efficacy have not indicated any particular varietal sensitivity. The crop safety of Boscalid 23.3% + Difenoconazole 6.6% SC has been tested on a wide range of varieties in efficacy trials. The results from these trials show that there are no particularly sensitive varieties. Crop tolerance and yield data generated in one country is therefore relevant in another Member state. To increase the probability of high levels of disease in the trials, the varieties chosen in each country were the ones with the least resistance to the selected disease. Therefore, the results from each country can be considered as the worst case.

(v) *Trial methodology*

Similar trial methodology was used in all countries. All trials were conducted to GEP by officially recognised testing organisations and in accordance with relevant EPPO standards.

(vi) *Locations*

Trials were performed in the major crop growing areas in each respective country. These areas have been found to be particularly suitable for cereal production due to their innate similarity in terms of soil type and climate.

(vii) *Soil*

It is not expected that a foliar applied fungicide will be affected in any way by soil type and so this factor can be ignored for the purposes of this dossier.

On the basis that the above factors do not influence the overall performance of Boscalid 23.3% + Difenoconazole 6.6% SC, it is the applicant's contention that data from Czech Republic, Poland, Germany and Hungary is equally valid in demonstrating the products performance throughout the Central EU zone and the data from the France and Italy is valid as supporting data.

In all 21 efficacy trials conducted in winter wheat, the performance of Boscalid 23.3% + Difenoconazole 6.6% SC was measured against a commercial standard co-formulation with diferents products.

Table 3.2-8: Presentation of reference standards used in trials (efficacy trials, preliminary trials...)

Trade name	Formulation	Composition	Rates	Country	N° of Trials
National reference product					
PROLINE STAR	EC	125 g/L prothioconazole + 125 g/L tebuconazole	1.0	IT CZ	4 4
BELL STAR	SC	140 g/L Boscalid + 50 g/L Epoxiconazole	2.5	FR	~~4~~ 5

Trade name	Formulation	Composition	Rates	Country	N° of Trials
CHAMPION	SC	233 g/L Boscalid + 67 g/L Epoxiconazole	1.5	DE	1
PROSARO	EC	125 g/L prothioconazole + 125 g/L tebuconazole	1.0	CZ HU	6 4
VENTUR 300	SC	233 g/L Boscalid + 67 g/L Epoxiconazole	1.5	PL	4

Comments of zRMS:	This document was prepared by Applicant for CIAZ (product code: SHA 7216A) containing boscalid (233 g/l) and difenoconazole (66 g/l). The formulation of this product is a suspension concentrate (SC) for used in winter wheat against SEPTTR, SEPTSP, PUCCST and PUCCRE, and FUSASP. All necessary information's were presented by Applicant in this dRR (ex., description of the target pests, active compounds, standard reference products, etc.). This document summarises the information related to the efficacy of the plant protection product – CIAZ (product code: SHA 7216 A), according to Article 33 of Regulation 1107/2009. Both, boscalid and difenoconazole are on the list of approved active substances. Boscalid has preventative and curative properties. It inhibits spore germination, germ tube elongation, mycelial growth, and sporulation (all major stages of fungal growth and reproduction necessary for disease development). Boscalid is a systemic compound. Depending on the type of formulation, it penetrates into the plant when applied to leaves (or roots), and it is then translocated acropetally. It inhibits spore germination, germ tube elongation, mycelial growth, and sporulation (all major stages of fungal growth and reproduction necessary for disease development). Difenoconazole is a broad-spectrum fungicide that controls a wide variety of fungi. It acts as a seed treatment, foliar spray and systemic fungicide. It is taken up through the surface of the infected plant and is translocated to all parts of the plant. It has a curative effect and a preventative effect. Difenoconazole can be applied to a range of crops, including cereals, vegetables, and fruits. It controls various fungi including powdery mildew, rust, scab, and leaf spots. The mode of action of difenoconazole is that it is a sterol demethylation inhibitor which prevents the development of the fungus by inhibiting cell membrane ergosterol biosynthesis. In Poland 35 plant protection products with boscalid as active compound and 78 plant protection products with difenoconazole are registered and commonly used for protection plants (dated 28.01.2022). No plant protection product with both compound in one plant protection product is registered in Poland. For example, in Czech Republic is registered Elanza with boscalid 23,3% and difenoconazole 6,6%. Elanza (approval number: 5952-0) was used in efficacy trials by Applicant as reference product in some trials from Czech Republic. Poland is a ZRMs.

3.2.1 Preliminary tests (KCP 6.1)

The activity of boscalid as well as difenoconazole are both well known; both actives have been marketed by e.g. Syngenta ans BASF, for the use in cereals and other crops to control a wide range of foliar diseases for a number of years, i.e. difenoconazole has been used since 1989 and difenoconazole has been marketed a since 2001. Based on the knowledge about the active substances and the experiences with the actives in the GAP claimed crops at the proposed dose rates, the necessary application rates to obtain

sufficient control of the pest organism are already known. Therefore, preliminary tests in glasshouses and field trials to assess the biological activity of the active substance or dose range for the plant protection product were not deemed necessary.

Comments of zRMS:	No results of the preliminary range-finding tests were submitted by the Applicant which is acceptable. The active substances of CIAZ (product code: SHA 7216 A) – boscalid and difenoconazole are registered and has been commonly used in agricultural practice for many years. So, a large-scale efficacy trials are available to evaluate the effectiveness of products containing those active compounds. Therefore, there was no need for preliminary range-finding tests in the opinion of Evaluator. No specific trials against justification of ratio of active ingredients in the mixture was submitted by Applicant. However, during efficacy trials different standards reference products were used. Also, with both – boscalid (233 g/l) and difenoconazole (Elanza) (66 g/l). Elanza have the same formulation and content of active compounds as studied product – CIAZ. No data to justify the ratio of active substance in the product are available. This is not in line with the guidance document SANTE/6895/2009. The submitted data can lead only to an assumption, that the ratio of boscalid 233 g/l + difenoconazole 66 g/l is required. The Concerned Member states should consider whether this is acceptable for them.

3.2.2 Minimum effective dose tests (KCP 6.2)

Boscalid 23.3% + Difenoconazole 6.6% SC was tested at a range of dose rates, but to demonstrate minimum effective dose rate, the control obtained with Boscalid 23.3% + Difenoconazole 6.6% SC applied at 0.8 L/ha, 1.0 L/ha and 1.5 L/ha was evaluated in ~~27~~ 28 winter wheat trials for the control of *Septoria*, *Puccinia* and *Fusarium*. The dose rates tested reflects 53%, 67% and 100% of the recommended rate of Boscalid 23.3% + Difenoconazole 6.6% SC, in accordance with the EPPO guideline PP 1/225(2) "Minimum effective dose". The dose is selected on the basis of its efficacy performance, product safety parameters and environmental limitations. Efficacy was tested under a range of environmental conditions to fully challenge the product. Data are presented from trials conducted in the Maritime EPPO zone (i.e. N-France, Czech Republic and Germany), the North-east EPPO zone (i.e. Poland), the South-east EPPO zone (i.e. Hungary) and the Mediterranean EPPO zone (i.e. Italy and S-France).

Control of Septoria in winter wheat

To prove and to support the proposed dose rate of 1.5 L/ha Boscalid 23.3% + Difenoconazole 6.6% SC [233 g boscalid + 66 g difenoconazole per hectare, per application] for the control of *Septoria spp.* ~~(SEPTTR)~~ in winter wheat, the assessment results from 13 efficacy trials performed in the Maritime EPPO zone (7), the North-east EPPO zone (2), the South-east EPPO zone (2) and the Mediterranean EPPO zone (1) are reported. The trials were conducted in S-France (1), N-France (3), Poland (2), Czech Republic (4) and Hungary (2) in 2016, 2017 and 2019. Boscalid 23.3% + Difenoconazole 6.6% SC was included in these trials at 1.5 L/ha to demonstrate the recommended dose rate as well as at the lower dose rates (1.5 L/ha [233 g boscalid + 66 g difenoconazole per hectare, per application]). In the trials, specifically targeted for this pathogen, one or two applications were applied in the spring (April-June) at growth stages ranging between BBCH 31 and BBCH 61.

The results obtained with Boscalid 23.3% + Difenoconazole 6.6% SC applied for the control of *Septoria spp*. ~~rust~~ in winter wheat are presented in Table 3.2-9, Table 3.2-10, Table 3.2-11 and Table 3.2-12 for results obtained in the Maritime zone (7 trials), the North-east (3 trials), the South-east zone (2 trials) and the Mediterranean zone (1 trial) respectively.

Table 3.2-9: Minimum effective dose – Maritime zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against ~~SEPTTR~~ *Septoria spp*. in winter wheat.

Target: ~~SEPTTR~~ SEPTSP	No. of trials	Mean % Control from 5 trial in the Maritime EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
		Mean % PESSEV (range)	Mean	Range	Mean	Range
Winter wheat						
Mean % control, one observation on **LEAF 1** per trial, **PESSEV** at 21-35 DAT2	2	40.7 (0.65-80.7)	**45.9**	35.9-55.8	**53.4**	51.3-55.5
Mean % control, one observation on **LEAF 2** per trial, **PESSEV** at 21-28 DAT2	3	19.1 (1.9-40.2)	**79.8**	40.1-100	**82.2**	46.5-100
Mean % control, one observation on **LEAF 3** per trial, **PESSEV** at 21-28 DAT2	3	27.1 (13.1-44.8)	**83.0**	55.9-98.2	**88.2**	68.4-99.2
Target: SEPTTR		**Mean % PESINC**	**Mean**	**Range**	**Mean**	**Range**
Mean % control, one observation on **LEAF 1** per trial, **PESINC** at 25-35 DAT2	2	16.7 (8.33-25.0)	**13.4**	0.0-26.7	**43.4**	40.0-46.7
Mean % control, one observation on **LEAF 2** per trial, **PESINC** at 25 DAT2	1	16.7	**10.0**	-	**40.0**	-

Table 3.2-10: Minimum effective dose – South-east zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against ~~SEPTTR~~ SEPTSP in winter wheat.

Target: ~~SEPTTR~~ SEPTSP	No. of trials	Mean % Control from 2 trial in the South-east EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
		Mean % PESSEV (range)	Mean	Range	Mean	Range
Winter wheat						
Mean % control, one observation on **LEAF 1** per trial, **PESSEV** at 20 DAT2	2	63.0 (39.8-86.1)	**64.0**	49.3-78.6	**69.5**	62.8-76.1

Table 3.2-11: Minimum effective dose – North-east zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against SEPTTR in winter wheat.

Target: SEPTTR	No. of trials	Mean % Control from 3 trial in the North-east EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
		Mean % PESSEV (range)	Mean	Range	Mean	Range
Winter wheat						

Mean % control, one observation on **LEAF 3** per trial, **PESSEV** at 12-18 DAT1	3	22.2 (16.3-28.3)	**62.7**	37.9-77.2	**67.6**	53.9-76.5

Table 3.2-12: Minimum effective dose – Mediterranean zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against SEPTTR in winter wheat.

		Mean % Control from 1 trial in the Mediterranean EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	**1.0 L/ha**		**1.5 L/ha**	
Target: SEPTTR	**No. of trials**	**Mean % PESSEV (range)**	**Mean**	**Range**	**Mean**	**Range**
Winter wheat						
Mean % control, one observation on **LEAF 2** per trial, **PESSEV** at 35 DAT2	1	80.1	**63.9**	-	**79.5**	-
Target: SEPTTR		**Mean % PESINC**	**Mean**	**Range**	**Mean**	**Range**
Mean % control, one observation on **LEAF 1** per trial, **PESINC** at 35 DAT2	1	10.0	**83.3**	-	**83.3**	-

The data from the eleven trials proves that the minimum effective dose rate of Boscalid 23.3% + Difenoconazole 6.6% SC to control Septoria in winter wheat is 1.5 L/ha, with up to two applications per season. Furthermore, the data demonstrated that if the application rate is reduced below this, a decrease in control as well as in persistence is observed.

Control of Puccinia in winter wheat

To prove and to support the proposed dose rate of 1.5 L/ha Boscalid 23.3% + Difenoconazole 6.6% SC [233 g boscalid + 66 g difenoconazole per hectare, per application] for the control of *Puccinia* spp. ~~(PUCCRT)~~ in winter wheat, the assessment results from nine efficacy trials performed in the Maritime, the North-east and Mediterranean EPPO zones are reported. The trials were conducted in Czech Republic (4), Poland (2), Italy (2) and S-France (1) in 2017 and 2019. Boscalid 23.3% + Difenoconazole 6.6% SC was included in these trials at 1.5 L/ha to demonstrate the recommended dose rate as well as at the lower doses rates (0.8 L/ha [186,4 g boscalid + 52.8 g difenoconazole per hectare, per application and 1.0 L/ha [233 g boscalid + 66 g difenoconazole per hectare, per application]). In the trials, specifically targeted for this pathogen, two applications were applied in the spring (Mar-April) at growth stages ranging between BBCH 31 and BBCH 43.

The results obtained with Boscalid 23.3% + Difenoconazole 6.6% SC applied for the control of *Puccinia spp*. ~~septoria~~ in winter wheat are presented in Table 3.2-13, Table 3.2-14 and Table 3.2-15 for results obtained in the Maritime zone (four trials), North-east zone (two trials) and Mediterranean zone (three trials), respectively.

Table 3.2-13: Minimum effective dose – Maritime zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against PUCCST in winter wheat.

		Mean % Control from 4 trial in the Maritime EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC						
		Untreated	**0.8 L/ha**		**1.0 L/ha**		**1.5 L/ha**	
Target: ~~PUCCRT~~ PUCCST	**No. of trials**	**Mean % PESSEV (range)**	**Mean**	**Range**	**Mean**	**Range**		
Winter wheat								
Mean % control, one observation on **LEAF 1** per trial, **PESSEV** at 14-28 DAT2	4	24.5 (15.0-29.7)	**73.4**	44.8-98.9	**87.3**	74.8-99.2	**92.6**	80.0-100

Mean % control, one observation on **LEAF 2** per trial, **PESSEV** at 14-28 DAT2	3	30.5 (5.9-44.8)	**85.4**	60.0-98.3	**94.7**	88.0-98.2	**97.0**	92.5-99.4
Mean % control, one observation on **LEAF 3** per trial, **PESSEV** at 14 DAT2	1	5.7	**73.2**	-	**89.4**	-	**92.6**	-

Table 3.2-14: **Minimum effective dose – North-east zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against PUCCRE~~T~~ and PUCCST in winter wheat.**

		Mean % Control from 2 trial in the North-east EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
Target: PUCCRE~~T~~ and PUCCST	**No. of trials**	**Mean % PESSEV (range)**	**Mean**	**Range**	**Mean**	**Range**
Winter wheat						
Mean % control, one observation on **LEAF 1** per trial, **PESSEV** at 14-21 DAT1	2	9.7 (5.9-13.5)	**36.0**	17.8-54.2	**63.4**	55.6-71.2

Table 3.2-15: **Minimum effective dose – Mediterranean zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against ~~PUCCRT~~ PUCCSP and PUCCRE in winter wheat.**

		Mean % Control from 3 trial in the Mediterranean EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
Target: ~~PUCCRT~~ PUCCSP and PUCCRE	**No. of trials**	**Mean % PESSEV (range)**	**Mean**	**Range**	**Mean**	**Range**
Winter wheat						
Mean % control, one observation on **LEAF 1** per trial, **PESSEV** at 14-21 DAT2	3	4.21 (1.37-6.04)	**74.4**	68.2-82.9	**77.3**	69.0-90.2
Mean % control, one observation on **LEAF 2** per trial, **PESSEV** at 21 DAT1	1	10.03	**34.9**	-	**48.3**	-
Mean % control, one observation on **LEAF 2** per trial, **PESSEV** at 21 DAT2	1	5.77	**39.6**	-	**48.6**	-
Target: PUCCRT		**Mean % PESINC**	**Mean**	**Range**	**Mean**	**Range**
Mean % control, one observation on **LEAF 1** per trial, **PESINC** at 14-21 DAT2	3	29.14 (20.75-41.7)	**68.6**	64.0-73.9	**74.7**	68.4-80.0

The data from the three trials proves that the minimum effective dose rate of Boscalid 23.3% + Difenoconazole 6.6% SC to control Puccinia in winter wheat is 1.5 L/ha, with up to two applications per season. Furthermore, the data demonstrated that if the application rate is reduced below this, a decrease in control as well as in persistence is observed.

Control of Fusarium in winter wheat

To prove and to support the proposed dose rate of 1.5 L/ha Boscalid 23.3% + Difenoconazole 6.6% SC

[233 g boscalid + 66 g difenoconazole per hectare, per application] for the control of *Fusarium spp.* (FUSASP) in winter wheat, the assessment results from seven efficacy trials performed in the Maritime, South-east and Mediterranean EPPO zones are reported. The trials were conducted in Italy (2), Germany (1), Czech Republic (2) and Hungary (2) in 2016 and 2017. Boscalid 23.3% + Difenoconazole 6.6% SC was included in these trials at 1.5 L/ha to demonstrate the recommended dose rate as well as at the lower dose rate (1.0 L/ha [233 g boscalid + 66 g difenoconazole per hectare, per application]). In the trials, specifically targeted for this pathogen, two applications were applied in the spring (Mar-April) at growth stages ranging between BBCH 31 and BBCH 65.

The results obtained with Boscalid 23.3% + Difenoconazole 6.6% SC applied for the control of fusarium in winter wheat are presented in Table 3.2-16, Table 3.2-16 and Table 3.2-18 for results obtained in the Maritime zone (three trials), the South-east zone (two trials) and Mediterranean zone (two trials), respectively.

Table 3.2-16: Minimum effective dose – Maritime zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against FUSASP in winter wheat.

		Mean % Control from 3 trial in the Mediterranean EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
Target: FUSASP	**No. of trials**	**Mean % PESSEV (range)**	**Mean**	**Range**	**Mean**	**Range**
Winter wheat						
Mean % control, one observation on **Ear** per trial, **PESSEV** at 13-30 DAT2	3	12.7 (2.23-24.5)	**58.4**	40.0-75.0	**62.1**	51.1-75.0
Target: FUSASP		**Mean % PESINC**	**Mean**	**Range**	**Mean**	**Range**
Mean % control, one observation on **Ear** per trial, **PESINC** at 13-16 DAT2	2	16.4 (7.81-25.0)	**92.4**	91.0-93.8	**92.9**	92.0-93.8

Table 3.2-17: Minimum effective dose – South-east zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against FUSASP in winter wheat.

		Mean % Control from 2 trial in the South-east EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
Target: FUSASP	**No. of trials**	**Mean % PESSEV (range)**	**Mean**	**Range**	**Mean**	**Range**
Winter wheat						
Mean % control, one observation on **Ear** per trial, **PESSEV** at 8-9 DAT2	2	31.2 (23.3-39.1)	**77.5**	72.2-82.8	**77.8**	73.1-82.5
Target: FUSASP		**Mean % PESINC**	**Mean**	**Range**	**Mean**	**Range**
Mean % control, one observation on **Ear** per trial, **PESINC** at 8-9 DAT2	2	55.0 (49.0-61.0)	**63.4**	61.5-65.3	**61.2**	61.1-61.2

Table 3.2-18: **Minimum effective dose – Mediterranean zone: Minimum effective dose of Boscalid 23.3% + Difenoconazole 6.6% SC against FUSASP in winter wheat.**

Target: FUSASP	No. of trials	Mean % Control from 2 trial in the Mediterranean EPPO Zone at a range of doses of Boscalid 23.3% + Difenoconazole 6.6% SC				
		Untreated	1.0 L/ha		1.5 L/ha	
		Mean % PESSEV (range)	Mean	Range	Mean	Range
Winter wheat						
Mean % control, one observation on **Ear** per trial, **PESSEV** at 14 DAT2	2	24.4 (22.6-26.2)	**71.8**	68.5-75.2	**73.3**	70.0-76.5
Target: FUSASP		**Mean % PESINC**	**Mean**	**Range**	**Mean**	**Range**
Mean % control, one observation on **Ear** per trial, **PESINC** at 14 DAT2	2	36.4 (33.8-39.0)	**73.0**	70.6-75.5	**74.2**	71.5-76.8

The data from the seven trials proves that the minimum effective dose rate of Boscalid 23.3% + Difenoconazole 6.6% SC to control fusarium in winter wheat is 1.5 L/ha, with up to two applications per season. Furthermore, the data demonstrated that if the application rate is reduced below this, a decrease in control as well as in persistence is observed.

Summary and conclusions on the minimum effective dose

In summary, reducing the application rate of Boscalid 23.3% + Difenoconazole 6.6% SC from the proposed dose rate resulted in decreased efficacy against the causal agents.

According to the presented results, the dose of 1.5 L/ha per application for septoria, fusarium and puccinia in winter wheat provided the optimal overall control and should be considered as effective against the diseases, for which activity of Boscalid 23.3% + Difenoconazole 6.6% SC is claimed. As diseases often occur as complexes of several pathogens throughout a season, up to two applications of Boscalid 23.3% + Difenoconazole 6.6% SC at the proposed rate should be used to efficiently control all pathogens claimed on the label.

This document clearly demonstrates – as will be demonstrated in the following sections – that the efficacy and crop safety of Boscalid 23.3% + Difenoconazole 6.6% ES is equivalent to the standard reference products to which it was compared. The applicant therefore wishes to cite the data on boscalid and difenoconazole now out of protection in additional support of those recommendations on the draft label that are not adequately supported by the applicant's data and requests that the zonal and national evaluators extrapolate from those data.

Comments of zRMS:	To provide information to establish the minimum effective dose, some of the trials conducted to demonstrate efficacy should include at least one lower dose(s) (for example 60–80% of the recommended dose) to that which would be recommended. It is utilized to achieve the desired effect. In the appropriate research of efficacy were tested differ doses and to register was chosen the lowest effective, which is in accordance with EPPO 1/225 (2). Applicant for support the MED (minimum effective dose) was studied following doses: • **Maritime EPPO zone against FUSASP, ~~PUCCRT~~ PUCCST and ~~SEPTTR~~ SEPTSP** – three different doses were studied: 0,8 l/ha (0,53N); 1,0 l/ha (0,67N) and 1,5 l/ha (N) in during 4 trials and two doses: 1,0 l/ha (0,67N) and

	1,5 l/ha (N) in 11 trials • **N-E EPPO zone against PUCCRE~~T~~, PUCCST and SEPTTR** – two different doses were studied: 1,0 l/ha (0,67N) and 1,5 l/ha (N) during trials. Lack of trials against FUSASP. • **S-E EPPO zone against ~~SEPTTR~~ SEPTSP and FUSASP** – two different doses were studied: 1,0 l/ha (0,67N) and 1,5 l/ha (N) during trials. Lack of trials against PUCCRT. • **MED EPPO zone against SEPTTR, PUCCRE~~T~~, PUCCSP and FUSASP** - two different doses were studied: 1,0 l/ha (0,67N) and 1,5 l/ha (N) during trials. According to the presented results, the dose rate of 1.5 L/ha per application, for control of SEPTTR, SEPTSP, PUCCRE~~T~~, PUCCST and FUSASP in winter wheat provided the optimal overall control and should be considered as effective against the diseases, for which activity of CIAZ (product code: SHA 7216 A) is claimed. The efficacy and crop safety of CIAZ is equivalent to the standard reference products to which it was compared. In the opinion of ZRMs, registered the same dose (1.5 L/ha) for all diseases will make it easier for farmers to stand the product. Wheat is not endangered only by FUSASP, but also by other diseases. The dose of 1.0 L/ha was much less effective than the dose of 1.5 L/ha in the case of SEPTTR, SEPTSP, PUCCRE and PUCCST. Therefore, in our opinion, the recommended dose should be 1.5 L/ha (which showed a low, but still better efficacy than the dose of 1.0 L/ha). The concerned member states should consider an acceptability of extrapolation from other EPPO zones results which was characterized by limited number of trials or lack of them.

3.2.3 Efficacy tests (KCP 6.2)

Data from ~~22~~ 23 efficacy trials conducted in winter wheat in the Maritime EPPO zone (15 ~~14~~; i.e. N-France (~~3~~ 4), Germany (1) and the Czech Republic (10)), the North-east EPPO zone (4; i.e. Poland) and the South-east (4; i.e. Hungary) have been included in this biological assessment dossier to support the label claims and recommendations on efficacy in the EU Central Registration zone.

To give additional support to the label claims in regards to efficacy, the data obtained from five efficacy trials conducted in winter wheat in the Mediterranean EPPO zone (i.e. Italy (4) and S-France (1)) has also been included. Data from the Mediterranean trials has been added as the same diseases that are affecting cereals crops in the South zone may also affect the cereal cultivation in the Central zone as well. Therefore, to demonstrate the wide range of control obtained with boscalid and difenoconazole, the Mediterranean data has been added to the current evaluation.

In the ~~27~~ 28 trials, the level of control obtained by Boscalid 23.3% + Difenoconazole 6.6% SC was assessed on Septoria, Puccinia and Fusarium in winter wheat.

Table 3.2-19: Details on trial methodology

Guidelines	General guidelines	EPPO PP 1/152(3/4), PP 1/181(3/4), PP 1/135(3/4), PP 1/225(2), PP 1/239(2); PP 1/226 (3)
	Specific guidelines	PP 1/26(4)
Experimental	Plot design	RCBD (~~27~~ 28)

design	Plot size	12-25 m²
	Number of replications	4 (~~27~~ 28)
Crop	Trials per crop	Winter wheat (~~27~~ 28)
	Varieties per crop	Winter wheat: SY Ideo, Ovidio, Simeto, Anapo, Bologna, SY-Moisson, Diametro, Aspache, Cellule, Svitava (2), Rumor, Bodycek, Tobak (2), GK körös, MV kokárda, Genius, Balaton, Arkadia, Sailor, Legenda, Bohemia (3), Toras (2).
	Sowing period	Winter wheat: September 29th to December 17th
Application	Crop stage (BBCH)* at application	Winter wheat: BBCH 31-51 (1st appl.) and BBCH 37-65 (2nd appl.)
	Timing Pest stage at appl. (1)	Please refer to detailed summary tables in Appendix 5.
	Number of appl. Intervals between appl.	1 (5); 2 (~~22~~ 23) n.r.; 8-28 days
	Spray volumes	200-400 L/ha
Assessment	Assessment types	- Visual estimation of Pest severity, compared to 'untreated' ('untreated' = 0 % control); total control = 100 % control) – based on the assessment of attacked plant area, as compared to the untreated check. - Visual estimation of Pest incidence, compared to 'untreated' ('untreated' = 0 % control); total control = 100 % control) – based on the percentage of attacked plants or plant parts on a sample of a defined number of plants/plant parts per plot, as compared to the untreated check. - Crop yield was assessed in 17 efficacy trials conducted on TRZAW. Yield assessments included grain yield [T/ha] as well as different quality parameters (i.e. TGW and HLW).
	Assessment dates	Please refer to the summary tables in the following section
Other relevant information	Soil type	Light to heavy soils
	Natural / artificial innoculation…	Natural
	Field / Greenhouse...	Field

Control of Septoria in winter wheat

The efficacy trials were conducted to prove the following label claims:

Crop	Winter wheat
Use rate Use frequency Application timing	1.5 L/ha Boscalid 23.3% + Difenoconazole 6.6% SC Up to 2x BBCH 30-59
Target disease	*Septoria spp.*

The effectiveness of applying Boscalid 23.3% + Difenoconazole 6.6% SC against Septoria was evaluated in 13 winter wheat trials assessed for pest severity and pest incidence. These trials were carried out in 2016, 2017 and 2019 in the Maritime EPPO zone (7; i.e. Czech Republic (4) and N-France (3)), the North-east EPPO zone (3; i.e. Poland), the South-east EPPO zone (2; i.e. Hungary) and the Mediterranean EPPO zone (1; i.e. S-France). The objective was to confirm the performance of Boscalid 23.3% + Difenoconazole 6.6% SC at the proposed dose rate of 1.5 L/ha (i.e. 350 g boscalid and 100 g difenoconazole

per hectare). In the trials specifically targeted for this pathogen, one (4) or two (9) applications were applied in the spring (April-June) at growth stages ranging between BBCH 31 and BBCH 61.

In Italian and Hungarian trials, Boscalid 23.3% + Difenoconazole 6.6% SC was tested alongside an EU approved prothioconazole + tebuconazole co-formulation, i.e. Prosaro and Proline Star (125 g/L prothioconazole + 125 g/L tebuconazole SC) and in French and Poland trials, Boscalid 23.3% + Difenoconazole 6.6% SC was tested against Bell Star and Ventur 300 SC (Boscalid + Epoxiconazole SC).

Maritime zone

In the Maritime trials, Septoria was assessed at 8 assessments, which were considered valid (i.e. PESSEV ≥ 1%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-20 therefore only contains one assessment per plant part from the Maritime trials assessed repeatedly.

In 6 of the 11 assessments carried out show statistically significant differences between the two tested products at where these were compared. In all trials where Boscalid 23.3% + Difenoconazole 6.6% SC was compared or even better against Bell Star (Boscalid 140 g/L + epoxiconazole 67 g/L SC reference product).

Table 3.2-20: Efficacy - Maritime zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against Septoria *spp.* (SEPTSP) in winter wheat in the efficacy tests – 14-36 DAT2.

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
LEAF1	21-35 DAT2	2	40.7 (0.65-80.7)	53.4 (51.3-55.5)	36.9 (23.1-50.8)	2			>
LEAF2	21-28 DAT2	3	19.1 (1.9-40.2)	82.2 (46.5-100)	85.0 (55.4-100)	1	2		=
LEAF3	21-28 DAT2	3	27.1 (13.1-44.8)	88.2 (68.4-99.2)	88.3 (66.5-99.4)		3		=
Pest incidence			**PESINC**						
LEAF1	25-35 DAT2	2	16.7 (8.33-25.0)	43.4 (40.0-46.7)	19.2 (0.0-38.3)	2			>
LEAF2	25 DAT2	1	16.7	40.0	30.0	1			>

North-east zone

In the North-east trials, Septoria *tritici* was assessed at 3 assessments, which were considered valid (i.e. PESSEV ≥ 1%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-21 therefore only contains one assessment per plant part from the North-east trials assessed repeatedly.

No significant differences were observed between the two tested products at any of the 3 assessments where these were compared. In all trials where Boscalid 23.3% + Difenoconazole 6.6% SC was compared against Ventur 300 (Boscalid 233 g/L + epoxiconazole 67 g/L SC reference product) and in none of them statistically significant differences were observed.

Table 3.2-21: **Efficacy – North-east zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against septoria *tritici* in winter wheat in the efficacy tests – 20 DAT1.**

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at: Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
LEAF1	12-18 DAT1	3	22.2 (16.3-28.3)	67.6 (53.9-76.5)	64.7 (41.1-82.2)	1	2		=

South-east zone

In the South-east trials, Septoria was assessed at 2 assessments, which were considered valid (i.e. PESSEV ≥ 1%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-22 therefore only contains one assessment per plant part from the South-east trials assessed repeatedly.

Some differences were observed between the two tested products at the 2 assessments where these were compared. In all trials where Boscalid 23.3% + Difenoconazole 6.6% SC was compared against Prosaro (Prothioconazole 125 g/L + tebuconazole 125 EC reference product) but the product showed a sufficient efficacy result.

Table 3.2-22: **Efficacy – South-east zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against septoria *spp.* (SEPTSP) in winter wheat in the efficacy tests – 20 DAT2.**

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at: Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
LEAF1	20 DAT2	2	63.0 (39.8-86.1)	69.5 (62.8-76.1)	80.4 (72.3-88.4)			2	<

Mediterranean zone

In the Mediterranean trials, Septoria was assessed at 2 assessments, which were considered valid (i.e. PESSEV ≥ 1% or PESINC ≥ 5%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-23 therefore only contains one assessment per plant part from the Mediterranean trials assessed repeatedly.

The individual trial results show that Boscalid 23.3% + Difenoconazole 6.6% SC gave excellent control of Septoria, equivalent to that achieved by Bell Star (Boscalid 140 g/L + epoxiconazole 50 g/L SC reference product). No significant differences were observed between the two tested products at any of the 2 assessments where these were compared.

Table 3.2-23: **Efficacy - Mediterranean zone: Efficacy of 1.5 L/ha Boscalid 23.3% + Difenoconazole 6.6% SC and reference products at comparable dose rate applied against Septoria *tritici* in winter wheat in the efficacy tests – 35 DAT2.**

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
LEAF2	35 DAT2	1	80.1	79.5	99.1			1	<
Pest incidence			**PESINC**						
LEAF1	35 DAT2	1	10.0	83.3	100			1	<

Control of Puccinia in winter wheat

The efficacy trials were conducted to prove the following label claims:

Crop	Winter wheat
Use rate Use frequency Application timing	1.5 L/ha Boscalid 23.3% + Difenoconazole 6.6% SC Up to 2x BBCH 30-59
Target disease	*Puccinia spp.*

The effectiveness of applying Boscalid 23.3% + Difenoconazole 6.6% SC against Puccinia was evaluated in nine winter wheat trials assessed for pest severity and pest incidence. These trials were carried out in 2017 and 2019 in the Maritime EPPO zone (4; i.e. Czec Republic), in the North-east EPPO zone (2; i.e. Poland) and Mediterranean EPPO zone (3; i.e. S-France(1) and Italy (2)). The objective was to confirm the performance of Boscalid 23.3% + Difenoconazole 6.6% SC at the proposed dose rate of 1.5 L/ha (i.e. 350 g boscalid and 100 g difenoconazole per hectare). In the trials specifically targeted for this pathogen, two applications were applied in the spring (March-June) at growth stages ranging between BBCH 31 and BBCH 51.

In Italian Boscalid 23.3% + Difenoconazole 6.6% SC was tested alongside an EU approved prothioconazole + tebuconazole co-formulation, i.e. Prosaro and Proline Star (125 g/L prothioconazole + 125 g/L tebuconazole EC) and in the French and Poland trials, Boscalid 23.3% + Difenoconazole 6.6% SC was tested against Bell Star and Ventur 300 (Boscalid g/L+ Epoxiconazole SC).

Maritime zone

In the Maritime trials, Puccinia *striformis* was assessed at 8 assessments, which were considered valid (i.e. PESSEV ≥ 1%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-24 therefore only contains one assessment per plant part from the Maritime trials assessed repeatedly.

Some differences were observed between the two tested products at the 8 assessments where these were compared. In all trials where Boscalid 23.3% + Difenoconazole 6.6% SC was compared against Prosaro 250 (Boscalid 125 g/L + tebuconazole 125 g/L SC reference product) but the product showed a sufficient efficacy result.

Table 3.2-24: Efficacy – Maritime zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against Puccinia *striformis* (PUCCST) in winter wheat in the efficacy tests – 14-28 DAT2.

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at: Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
LEAF1	14-28 DAT2	4	24.5 (15.0-29.7)	92.6 (80.0-100)	96.6 (91.1-100)		3	1	=
LEAF2	14-28 DAT2	3	30.5 (5.9-44.8)	97.0 (92.5-99.4)	97.2 (92.5-99.7)		3		=
LEAF3	14 DAT2	1	5.7	92.6	93.6		1		=

North-east zone

In the North-east trials, Puccinia *striformis* and *P. recondita* was assessed at 2 assessments, which were considered valid (i.e. PESSEV ≥ 1%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-25 therefore only contains one assessment per plant part from the North-east trials assessed repeatedly.

Some differences were observed between the two tested products at the 2 assessments where these were compared. In all trials where Boscalid 23.3% + Difenoconazole 6.6% SC was compared against Ventur 300 (Boscalid 233 g/L + epoxiconazole 67 g/L SC reference product) but the product showed a sufficient efficacy result.

Table 3.2-25: Efficacy – North-east zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against Puccinia *striformis* (PUCCST) and *P. recondita* (PUCCRE) in winter wheat in the efficacy tests – 14-21 DAT2.

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at: Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
LEAF1	14-21 DAT1	2	9.7 (5.9-13.5)	63.4 (55.6-71.2)	93.8 (89.8-97.8)			2	<

Mediterranean zone

In the Mediterranean trials, Puccinia was assessed at 8 assessments, which were considered valid (i.e. PESSEV ≥ 1% or PESINC ≥ 5%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-26 therefore only contains one assessment per plant part from the Mediterranean trials assessed repeatedly.

No significant differences were observed between the two tested products at any of the 8 assessments where these were compared. In all trials where Boscalid 23.3% + Difenoconazole 6.6% SC was compared against Bell Star (Boscalid 140 g/L + epoxiconazole 50 g/L SC reference product) and Proline Star (Prothioconazole 125 g/L + Tebuconazole 125 g/L EC reference product) and in none of them statistically significant differences were observed.

Table 3.2-26: **Efficacy - Mediterranean zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against Puccinia *spp.* (PUCCSP) and *P. recondita* (PUCCRE) in winter wheat in the efficacy tests – 14-21 DAT2.**

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
LEAF1	14-21 DAT2	3	4.21 (1.37-6.04)	77.3 (69.0-90.2)	83.8 (73.4-100)		1	2	<
LEAF2	21 DAT2	1	10.03	48.3	98.5			1	<
LEAF3	21 DAT2	1	5.77	48.6	96.8			1	<
Pest incidence			**PESINC**						
LEAF1	14-21 DAT2	3	29.14 (20.75-41.7)	74.7 (68.4-80.0)	55.5 (16.7-77.1)	1	2	1	=

Control of Fusarium in winter wheat

The efficacy trials were conducted to prove the following label claims:

Crop	Winter wheat
Use rate Use frequency Application timing	1.5 L/ha Boscalid 23.3% + Difenoconazole 6.6% SC Up to 2x BBCH 30-59
Target disease	Fusarium

The effectiveness of applying Boscalid 23.3% + Difenoconazole 6.6% SC against Fusarium was evaluated in seven winter wheat trials assessed for pest severity and pest incidence. These trials were carried out in 2016 or 2017 in the Maritime EPPO zone (3; i.e. Czech Republic (2) and Germany (1)), the Southeast EPPO zone (2; i.e. Hungary (2)) and the Mediterranean EPPO zone (2; i.e. Italy). The objective was to confirm the performance of Boscalid 23.3% + Difenoconazole 6.6% SC at the proposed dose rate of 1.5 L/ha (i.e. 350 g boscalid and 100 g difenoconazole per hectare). In the trials specifically targeted for this pathogen, two applications were applied in the spring (March-April) at growth stages ranging between BBCH 31 and BBCH 65.

In Italian Boscalid 23.3% + Difenoconazole 6.6% SC was tested alongside an EU approved prothioconazole + tebuconazole co-formulation, i.e. Prosaro and Proline Star (125 g/L prothioconazole + 125 g/L tebuconazole EC) and in the French trial, Boscalid 23.3% + Difenoconazole 6.6% SC was tested against Bell Star (Boscalid 140 g/L+ Epoxiconazole 50 g/L SC).

Maritime zone

In the Maritime trials, Puccinia was assessed at 5 assessments, which were considered valid (i.e. PESSEV ≥ 1% and PESINC ≥ 5%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-27 therefore only contains one assessment per plant part from the Maritime trials assessed repeatedly.

Some differences were observed between the two tested products at the 3 assessments where these were compared. In all trials where Boscalid 23.3% + Difenoconazole 6.6% SC was compared against reference product but the product showed a sufficient efficacy result.

Table 3.2-27: **Efficacy - Maritime zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against ~~Puccinia~~ *Fusarium* in winter wheat in the efficacy tests – 13-30 DAT2.**

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
EAR	13-30 DAT2	3	12.7 (2.23-24.5)	62.1 (51.1-75.0)	84.1 (72.4-100)			3	<
Pest incidence			**PESINC**						
EAR	13-16 DAT2	2	16.4 (7.81-25.0)	92.9 (92.0-93.8)	91.5 (83.0-100)	1		1	=

South-east zone

In the South-east trials, Puccinia was assessed at 4 assessments, which were considered valid (i.e. PESSEV ≥ 1% and PESINC ≥ 5%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-28 therefore only contains one assessment per plant part from the South-east trials assessed repeatedly.

No significant differences were observed between the two tested products at three of the 4 assessments where these were compared. In all trials where Boscalid 23.3% + difenoconazole 6.6% EC was compared against Prosaro (Prothioconazole 125 g/L + tebuconazole 125 EC reference product) and in none of them statistically significant differences were observed.

Table 3.2-28: **Efficacy – South-east zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against ~~Puccinia~~ *Fusarium* in winter wheat in the efficacy tests – 8-9 DAT2.**

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 125 + 125 g ai/ha	Efficacy obtained with: Reference product at Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
EAR	8-9 DAT2	2	31.2 (23.3-39.1)	77.8 (73.1-82.5)	88.5 (85.6-91.3)		1	1	<
Pest incidence			**PESINC**						
EAR	8-9 DAT2	2	55.0 (49.0-61.0)	61.2 (61.1-61.2)	65.3 (62.3-68.3)		1	1	=

Mediterranean zone

In the Mediterranean trials, Puccinia was assessed at 4 assessments, which were considered valid (i.e. PESSEV ≥ 1% and PESINC ≥ 5%). In order not to bias the data from any trials with data from more than one assessment on each plant part, repeated assessments were excluded from summary. Table 3.2-29 therefore only contains one assessment per plant part from the Mediterranean trials assessed repeatedly.

No significant differences were observed between the two tested products at any of the 4 assessments where these were compared. In all trials where Boscalid 23.3% + difenoconazole 6.6% SC was compared against Proline Star (Prothioconazole 125 g/L + tebuconazole 125 g/L EC reference product) and in none of them statistically significant differences were observed.

Table 3.2-29: **Efficacy - Mediterranean zone: Efficacy of 1.5 L/ha Boscalid 23.3% + difenoconazole 6.6% SC and reference products at comparable dose rate applied against ~~Puccinia~~ *Fusarium* in winter wheat in the efficacy tests – 14 DAT2.**

Part assessed	Days after Last Treatment. (DALT)	No. of trials	Mean infestation level (%)	Efficacy obtained with: Boscalid 23.3% + Difenoconazole 6.6% SC at: Mean (min-max) 350 + 100 g ai/ha	Efficacy obtained with: Reference product at: Mean (min-max) 1N	No. of trials where Boscalid 23.3% + Difenoconazole 6.6% SC at 233 + 66 g ai/ha is >, < or =, compared to the Reference product at 1N = : ± 5% control: >	=	<	Overall
Pest severity			**PESSEV**						
EAR	14 DAT2	2	24.4 (22.6-26.2)	73.3 (70.0-76.5)	75.7 (72.5-78.8)		2		=
Pest incidence			**PESINC**						
EAR	14 DAT2	2	36.4 (33.8-39.0)	74.2 (71.5-76.8)	76.4 (73.6-79.1)		2		=

Summary and conclusion

Based on the results of ~~27~~ 28 field efficacy trials carried out in 2016, 2017 and 2019 season, the following can be concluded for the intended use of Boscalid 23.3% + difenoconazole 6.6% SC applied at 1.5 L/ha per application in winter wheat:

- Boscalid 23.3% + difenoconazole 6.6% SC applied in winter wheat provided a moderate to high level control of *Puccinia* spp., Fusarium and *Septoria* spp. with the recommended dose rate of 1.5 L/ha. As diseases often occur as a complex of several diseases with different susceptibility towards boscalid and/or difenoconazole, up to 2 applications per season of Boscalid 23.3% + difenoconazole 6.6% SC at the 1.5 L/ha rate should be used to efficiently control the diseases claimed on the label.

- Compared to the differents reference products tested, the efficacy obtained with Boscalid 23.3% + difenoconazole 6.6% SC is comparable against the key diseases tested.

- The trial results are considered valid for all intended Central zone countries.

This document clearly demonstrates that the efficacy and crop safety of Boscalid 23.3% + difenoconazole 6.6% SC is equivalent to the standard reference products to which the test product was compared. The applicant therefore wishes to cite the data on boscalid and difenoconazole containing products now out of protection in additional support of those recommendations on the draft label that are not adequately supported by the applicant's data and requests that the zonal and national evaluators extrapolate from those data.

Comments of zRMS:	Details of experiment are presented above by Applicant. All used methodology is in accordance with GEP rules, in exception of conduction studies during one growing season in MED (2017) and S-E EPPO zone (2016). Three different growing seasons were studied in the Maritime EPPO zone (2016, 2017 and 2019) and two growing seasons (2016 and 2017) in N-E EPPO zone. All trials were performed on winter wheat on different varieties. The presented data and information about the plant protection product, active substances, crops and pests and the intended uses correspond with the provided EPPO Standards. It can be concluded to accept these data and information. Applicant submitted in total 28 efficacy trials carried out on winter wheat in four EPPO zones: Maritime EPPO zone (15 trials: FR-4, DE-1, CZ-10), North-East EPPO zone (4 trials: PL), MED EPPO zone (5 trials: IT-4, FR-1) and South-East EPPO zone (4 trials: HU). The number of trials is sufficient and fulfil EPPO requirements for a major crop for Maritime EPPO zone. cMS form S-E should decide if 5 studies and cMS from S-E and N-E EPPO zone should decide if only 4 trials can be acceptable considering the importance of this crop. For Poland – number of trials is acceptable, because we can use trials from neighbouring countries (CZ-10 and DE-1). The following efficacy scale was used: - L – limiting (0-60% efficacy)

- ME – moderately efficiency (60-80%)
- E – efficiently (>80%)

We are dealing with the active substances used commonly for many years in many countries. We must emphasize that each pest should been representative by sufficient number of field efficacy tests (at least 6 for major pest and at least 3 for minor pest). PESSEV and PESINC was acceptable in all submitted trials by Applicant. Results were presented by the Applicant in the tables above and in the BAD in appendixes.

Efficacy of CIAZ (product code: SHA 7216 A):

- ***Septoria spp.***

Maritime EPPO zone – 7 trials were submitted (CZ-4, FR-3). All trials were performed on SEPTSP
N-E EPPO zone – 3 trials were submitted (PL). Trials were performed on SEPTTR
S-E EPPO zone – 2 trials were submitted (HU). Trials were performed on SEPTSP.
MED EPPO zone -1 trial was submitted (FR). Trial was carried out in SEPTTR.

Only in Maritime EPPO zone, Applicant submitted enough number of trials. cMS from N-E, S-E and MED EPPO zone should decide if limited number of trials can be acceptable or should consider possibility od extrapolation results from other EPPO zone. ~~In Poland on the basis on 7 trials (CZ-4, PL-3), SEPTTR can be included in Polish label project~~

Septoria is the collective name for fungal diseases caused by fungi formerly classified as *Septoria*. And although current research based on molecular techniques has made it possible to accurately classify individual species, the name of the diseases has remained common. In Poland, two diseases belonging to this group are the most important in cereal crops. Septoriasis is caused by fungi that overwinter in crop residues, and their spores are carried with raindrops. It is worth mentioning that similar symptoms to stripe *septoria* are also observed in wheat chaff *septoria* caused by the fungus *Septoria nodorum* (the bag stage of *Phaeosphaeria nodorum*), whose current name is Septoria glumarum. Symptoms of this disease can also be observed already on seedlings, later on leaves, stems and ears. In the case of septoria glumarum, the spots on the leaves are usually light brown, lenticular, initially with a chlorotic border. On leaves, too, they can form very extensive necroses leading to leaf dieback. Here, however, pycnidia are less frequently observed, and are not arranged in rows, but their arrangement is usually irregular or concentric. In the opinion of ZRMS, SEPTTR can be conditionally registered in Poland on the basis on 3 trials carried out in N-E against SEPTTR and 4 trials against SEPTSP in Maritime EPPO zone. It can be concluded that CIAZ at recommended dose (1,5 L/ha) moderately effective control SEPTTR on winter wheat.

The following is a detailed assessment of the effectiveness of individual *Septoria species*.

✓ **N-E EPPO zone**:

				Assessm. Days after							Un-treated		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha			Boscalid + Difeno. Ref. product 1 N		
Trial no.	Country	Variety	No. of appl.	1st appl.	2nd appl.	Pest	Assess. Type	Part assess.	Crop GS at Assess. BBCH		Mean		Mean		% Control	Mean		% Control
322_Sharda_SF17PZ312W	PL	Sailor	1	18	-	SEPTTR	PESSEV	Leaf 3	75		21.9	a	10.1	b	53.9	12.9	b	41.1
347_Sharda_SF17PZ306W	PL	Legenda	1	15	-	SEPTRR	PESSEV	Leaf 3	73		28.3	a	6.63	b	76.5	5.03	b	82.2
348_Sharda_SF17PZ307W	PL	Sailor	1	12	-	SEPTRR	PESSEV	Leaf 3	73		16.3	a	4.50	b	72.3	4.75	b	70.8
										min	16.3		4.50		53.9	4.75		41.1
										max	28.3		10.1		76.5	12.9		82.2
Mean % Control (Last observation on Leaf 3 / One observation per trial, PESSEV), n=3											22.2		7.08		67.6	7.56		64.7

✓ **Maritime EPPO zone:**

Trial no.	Country	Variety	No. of appl.	1st appl.	2nd appl.	Pest	Assess. Type	Part assess.	Crop GS at Assess. BBCH	Untreated Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha Mean		% Control	Boscalid + Difeno. Ref. product 1 N Mean		% Control
PC 17-05-32-NE1	FR	SY-Moisson	2	63	35	SEPTSP	PESSEV	Leaf 1	75	0.65	a	0.32	a	51.3	0.57	a	23.1
PC 17-05-32-NE01	FR	Aspache	2	40	21	SEPTSP	PESSEV	Leaf 1	73	80.7	a	35.9	a	55.5	39.7	b	50.8
									min	0.65		0.32		51.3	0.57		23.1
									max	80.7		35.9		55.5	39.7		50.8
Mean % Control (Last observation on Leaf 1 / One observation per trial, PESSEV), n=2										40.7		18.1		53.4	20.1		36.9
SWEPL-CZE16-BOTR-TRZAW-KUJ23	CZ	Svitava	1	14	-	SEPTSP	PESSEV	Leaf 2	56	15.3	a	7.1	ab	46.5	5.7	b	55.4
F1914-TRZAW-DOM45	CZ	Bohemia	2	35	21	SEPTSP	PESSEV	Leaf 2	75	1.9	a	0.0	b	100	0.0	b	100
SWEPL-F1914-RYMA	CZ	Toras	2	49	28	SEPTSP	PESSEV	Leaf 2	73	40.2	a	0.0	d	100	0.1	c	99.5
									min	1.9		0.0		46.5	0.0		55.4
									max	40.2		7.1		100	5.7		100
Mean % Control (Last observation on Leaf 2 / One observation per trial, PESSEV), n=3										19.1		2.4		82.2	1.9		85.0
SWEPL-CZE16-BOTR-TRZAW-RYM1	CZ	Rumor	2	49	28	SEPTSP	PESSEV	Leaf 3	59	23.3	a	0.60	c	97.1	0.20	d	98.9
F1914-TRZAW-DOM45	CZ	Bohemia	2	35	21	SEPTSP	PESSEV	Leaf 3	75	13.1	a	4.1	c	68.4	4.4	c	66.5
SWEPL-F1914-RYMA	CZ	Toras	2	49	28	SEPTSP	PESSEV	Leaf 3	73	44.8	a	0.3	c	99.2	0.2	c	99.4
									min	13.1		0.3		68.4	0.2		66.5
									max	44.8		4.1		99.2	4.4		99.4
Mean % Control (Last observation on Leaf 3 / One observation per trial, PESSEV), n=3										27.1		1.7		88.2	1.6		88.3
PC 17-05-32-NE1	FR	SY-Moisson	2	63	35	SEPTSP	PESINC	Leaf 1	75	25.0	a	13.3	a	46.7	20.0	a	38.3
PC 17-05-32-NE2	FR	Diametro	2	47	25	SEPTSP	PESINC	Leaf 1	60	8.33	a	5.0	a	40.0	13.3	a	0.0
									min	8.33		5.0		40.0	13.3		0.0
									max	25.0		13.3		46.7	20.0		38.3
Mean % Control (Last observation on Leaf 1 / One observation per trial, PESINC), n=2										16.7		9.2		43.4	16.7		19.2
PC 17-05-32-NE2	FR	Diametro	2	47	25	SEPTSP	PESINC	Leaf 2	60	16.7	a	10.0	a	40.0	11.7	a	30.0
									min	16.7		10.0		40.0	11.7		30.0
									max	16.7		10.0		40.0	11.7		30.0
Mean % Control (Last observation on Leaf 2 / One observation per trial, PESINC), n=1										16.7		10.0		40.0	11.7		30.0

✓ S-E EPPO zone:

Trial no.	Country	Variety	No. of appl.	1st appl.	2nd appl.	Pest	Assess. Type	Part assess.	Crop GS at Assess. BBCH	Untreated Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha Mean		% Control	Boscalid + Difeno. Ref. product 1 N Mean		% Control
SWEPL-HU16-BOTR-TRZAW-PLA17	HU	GK Körös	2	32	20	SEPTSP	PESSEV	Leaf 1	77	86.1	a	31.9	c	62.8	23.9	c	72.3
SWEPL-HU16-BOTR-TRZAW-PLA18	HU	MV Kokárda	2	35	20	SEPTSP	PESSEV	Leaf 1	77	39.8	a	9.50	b	76.1	4.6	bc	88.4

												min	39.8		9.50		62.8	4.6	72.3
												max	86.1		31.9		76.1	23.9	88.4
												Mean % Control (Last observation on Leaf 1 / One observation per trial, PESSEV), n=2	63.0		20.7		69.5	14.3	80.4

✓ **MED EPPO zone:**

Trial no.	Country	Variety	No. of appl.	Assessm. Days after 1st appl.	Assessm. Days after 2nd appl.	Pest	Assess. Type	Part assess.	Crop GS at Assess. BBCH	Untreated Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha % Control	Boscalid + Difeno. Ref. product 1 N Mean		Boscalid + Difeno. Ref. product 1 N % Control
PC 17-05-32-SW1	FR	Bologna	2	43	35	SEPTTR	PESSEV	Leaf 2	75-83	80.1	a	16.5	c	79.5	0.7	c	99.1
									min	80.1		16.5		79.5	0.7		99.1
									max	80.1		16.5		79.5	0.7		99.1
									Mean % Control (Last observation on Leaf 2 / One observation per trial, PESSEV), n=1	80.1		16.5		79.5	0.7		99.1
PC 17-05-32-SW1	FR	Bologna	2	43	35	SEPTTR	PESINC	Leaf 1	75-83	10.0	a	1.67	a b	83.3	0.0	b	100
									min	10.0		1.67		83.3	0.0		100
									max	10.0		1.67		83.3	0.0		100
									Mean % Control (All observations on Leaf 1, PESINC), n=1	10.0		1.67		83.3	0.0		100

- ***Puccinia spp.***

Maritime EPPO zone – 4 trials were submitted (CZ). Trials were carried out on PUCCST

N-E EPPO zone – 2 trials were submitted (PL). 1 trial was performed against PUCCST and 1 trial against PUCCRE.

S-E EPPO zone – 0 trials

MED EPPO zone -3 trials was submitted (FR-1, IT-2). 2 trials were performed on PUCCSP and 1 on PUCCRT.

All EPPO zones were characterized by limited number of efficacy trials against ~~PUCCRT~~ *Puccinia sp*. So, cMS from N-E, S-E, Maritime and MED EPPO zone should decide if limited number of trials can be acceptable or should consider possibility of extrapolation results from other EPPO zone. In Poland on the basis on ~~6~~ 5 trials (CZ-4, PL-~~2~~1), ~~PUCCRT~~ PUCCST can be included in Polish label project and conditionally registered. PUCCRE should be deleted from Polish label (only 1 trial is not accepted). In Polish label PUCCST should be registered as moderately sensitive against CIAZ used at recommended dose (in N-E efficacy was at level <60% and in Maritime at level >90%).

The following is a detailed assessment of the effectiveness of individual *Puccinia species*.

✓ N-E EPPO zone:

Trial no.	Country	Variety	No. of appl.	Assessm. Days after 1st appl.	Assessm. Days after 2nd appl.	Pest	Assess. Type	Part assess.	Crop GS at Assess. BBCH	Untreated Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha % Control	Boscalid + Difeno. Ref. product 1 N Mean		Boscalid + Difeno. Ref. product 1 N % Control
321_Sharda_SF17PZ311W	PL	Arkadia	1	34	-	PUCCST	PESSEV	Leaf 1	77	13.5	a	6.0	b	55.6	0.3	c	97.8
322_Sharda_SF17PZ312W	PL	Sailor	1	32	-	PUCCRE	PESSEV	Leaf 1	77	5.9	a	1.7	b c	71.2	0.6	c	89.8
									min	5.9		1.7		55.6	0.3		89.8
									max	13.5		6.0		71.2	0.6		97.8

Mean % Control (Last observation on Leaf 1 / One observation per trial, PESSEV), n=2											9.7		3.9		63.4	0.45		93.8		

✓ Maritime EPPO zone:

Trial no.	Country	Variety	No. of appl.	Assessm. Days after 1st appl.	Assessm. Days after 2nd appl.	Pest	Assess. Type	Part assess.	Crop GS at Asses. BBCH	Untreated Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha Mean		% Control	Boscalid + Difeno. Ref. product 1 N Mean		% Control
F1914-TRZAW-DOM46	CZ	Bohemia	2	18	14	PUCCST	PESSEV	Leaf 1	65	15.0	a	1.3	b	90.1	1.2	b	91.1
SWEPL-CZE19-BDC-TRZAW-TRU14	CZ	Tobak	2	32	18	PUCCST	PESSEV	Leaf 1	77	25.0	a	5.0	d	80.0	1.0	e	96.0
SWEPL-F1914-RYMC	CZ	Toras	2	49	28	PUCCST	PESSEV	Leaf 1	73	28.3	a	0.0	d	100	0.1	c	99.3
SWEPL-F1914-RYMD	CZ	Bohemia	2	49	28	PUCCST	PESSEV	Leaf 1	73	29.7	a	0.0	c	100	0.0	c	100
									min	15.0		0.0		80.0	0.0		91.1
									max	29.7		5.0		100	1.2		100
Mean % Control (All observations on Leaf 1, PESSEV), n=4										24.5		1.5		92.6	0.58		96.6
F1914-TRZAW-DOM46	CZ	Bohemia	2	18	14	PUCCST	PESSEV	Leaf 2	65	5.9	a	0.4	c	92.5	0.4	c	92.5
SWEPL-F1914-RYMC	CZ	Toras	2	49	28	PUCCST	PESSEV	Leaf 2	73	40.8	a	0.3	c	99.1	0.2	c	99.4
SWEPL-F1914-RYMD	CZ	Bohemia	2	49	28	PUCCST	PESSEV	Leaf 2	73	44.8	a	0.2	c	99.4	0.1	c	99.7
									min	5.9		0.2		92.5	0.1		92.5
									max	44.8		0.4		99.4	0.4		99.7
Mean % Control (All observations on Leaf 2, PESSEV), n=3										30.5		1.3		97.0	0.23		97.2
F1914-TRZAW-DOM46	CZ	Bohemia	2	18	14	PUCCST	PESSEV	Leaf 3	65	5.7	a	0.4	c	92.6	0.4	c	93.6
									min	5.7		0.4		92.6	0.4		93.6
									max	5.7		0.4		92.6	0.4		93.6
Mean % Control (All observations on Leaf 3, PESSEV), n=1										5.7		0.4		92.6	0.4		93.6

✓ MED EPPO zone:

Trial no.	Country	Variety	No. of appl.	Assessm. Days after 1st appl.	Assessm. Days after 2nd appl.	Pest	Assess. Type	Part assess.	Crop GS at Asses. BBCH	Untreated Mean		Boscalid 23,3 + Difenoconazole 6,6 SC 1.0 L/ha Mean		% Control	Boscalid 23,3 + Difenoconazole 6,6 SC 1.5 L/ha Mean		% Control
PC 15 SHR 238	IT	SY Ideo	2	28	14	PUCCSP	PESSEV	Leaf 1	61	5.24	a	1.46	b	72.1	1.42	b	72.5
PC 15 SHR 239	IT	Ovidio	2	28	14	PUCCSP	PESSEV	Leaf 1	61	6.04	a	1.92	b	68.2	1.87	b	69.0
PC 17-05-32-SW1	FR	Bologna	2	29	21	PUCCRE	PESSEV	Leaf 1	69	1.37	a	0.23	b	82.9	0.13	b	90.2
									min	1.37		0.23		68.2	0.13		69.0
									max	6.04		1.92		82.9	1.87		90.2
Mean % Control (All observations on Leaf 1, PESSEV), n=3										4.21		1.20		74.4	1.14		77.3
PC 17-05-32-SW1	FR	Bologna	2	29	21	PUCCRE	PESSEV	Leaf 2	69	10.03	a	6.53	b	34.9	5.18	b	48.3
									min	10.03		6.53		34.9	5.18		48.3
									max	10.03		6.53		34.9	5.18		48.3
Mean % Control (All observations on Leaf 2,										10.		6.5		34.9	5.1		48.3

								PESSEV), n=1			03			3				8		
PC 17-05-32-SW1	FR	Bo-logna	2	29	21	PUCCRE	PESSEV	Leaf 3	69		5.7 7	a		3.4 8	b	39.6		2.9 7	b	48.6
										min	5.7 7			3.4 8		39.6		2.9 7		48.6
										max	5.7 7			3.4 8		39.6		2.9 7		48.6
								Mean % Control (All observations on Leaf 3, PESSEV), n=1			5.7 7			3.4 8		39.6		2.9 7		48.6
PC 15 SHR 238	IT	SY Ideo	2	28	14	PUCCSP	PESINC	Leaf 1	65		20. 75	a		5.2 5	b	73.9 1		5.0	b	75.6
PC 15 SHR 239	IT	Ovid io	2	28	14	PUCCSP	PESINC	Leaf 1	65		25. 0	a		8.0	b	67.9		7.7	b	68.4
PC 17-05-32-SW1	FR	Bo-logna	2	29	21	PUCCRE	PESINC	Leaf 1	69		41. 67	a		15. 0	b	64.0		8.3 3	b	80.0
										min	20. 75			5.2 5		64.0		5.0		68.4
										max	41. 67			15. 0		73.9 1		8.3 3		80.0
								Mean % Control (All observations on Leaf 1, PESINC), n=2			29. 14			9.4 1		68.6 0		7.0 1		74.7

- ***Fusasp spp.***

Maritime EPPO zone – 3 trials were submitted (CZ-2, DE-1)

N-E EPPO zone – 0 trials

S-E EPPO zone – 2 trials were submitted (HU)

MED EPPO zone -2 trials was submitted (IT)

All EPPO zones were characterized by limited number of efficacy trials against FUSASP. So, cMS from N-E, S-E, Maritime, and MED EPPO zone should decide if limited number of trials can be acceptable or should consider possibility the extrapolation results from other EPPO zone. In Poland only 3 trials from neighbouring countries (DE-1, CZ-2) are not accepted, because FUSASP is a major disease in winter wheat, so at least 6 efficacy trials should be presented. FUSASP should be excluded from GAP table and Polish label project.

Boscalid 23.3% + difenoconazole 6.6% SC applied in winter wheat provided a moderate to high level control of *Puccinia spp*., *Fusarium* and *Septoria sp*p. with the recommended dose rate of 1.5 L/ha. Max. 2 application per season can be used. Results were comparable to standard reference products used during efficacy trials.

Interval between application:

- *MAR*: 7-28 days (in 5 trials interval: 13-14 days was studied)
- *N-E*: 0 days (only 1 appl. was studied)
- *MED*: 8-14 days
- *S*-E: 11-16 days

In the opinion of Evaluator, interval between application amounting to 14 days is acceptable for MAR, S-E and MED. cMS from N-E should decide if this interval (14 days) can be accepted, considering that such interval in this zone has not been tested, because only 1 application was studied. In the opinion of ZRMs, in Poland interval (14 days) can be accepted on the basis on trials from Maritime EPPO zone. During efficacy trials, assessment was made after 1st and 2nd application. Results has shown that CIAZ control fungal disease on winter wheat after 1st and 2nd application. Applicant submitted enough number of trials for efficacy after 1 application and limited number of trials for 2 applications. However, in our opinion CIAZ should be registered conditionally. Within 2 years after registration, it will be necessary to submit studies performed in Poland to show the effectiveness of 2 applications per season. In Poland, only in one selectivity trial (351_Sharda_SF16PZ310W) – 2 application per season were studied. No negative effects on yield or its quality was observed.

In the opinion of Evaluator if one application has enough efficiency, it also be used to confirm the effectiveness of two doses per season. The lack of dose harmonization (one or two applications) was due to the following issues, which are briefly described below. Some trials were performed with one application because of various reason like:[1)] other diseases appeared and trials had to be

stopped, [2)] disease pressure was reduced or weather conditions for which didn't make sense or institutes where not able to do a second application. It can be clearly observed in results over two seasons that product performed very good in all cases, and only can be expected that with a second application, the efficacy of the formulation would be increased in percentage of control and in time product protect the crop against diseases. The second application could only represent a phytotoxic problem, but as can be observed in results of trials presented, even in trials with two applications at double dose crops didn't present any phytotoxicity.
Also, trials with only one application would be even more challenging than trials with two applications, so the trials with one application should be considered as valid for registration according EPPO PP 1/226(3) extrapolation is possible "from more challenging control situations to ones that pose a lower challenge". According to this, Evaluator believes that all trials should be valid for registration purposes.

However, **in situation that we have not registered any plant protection product with boscalid and difenoconazole in Poland only conditional registration seems to pe possible against SEPTTR and PUCCST~~RT~~ on winter wheat for two years, after which the Applicant will be required to present the missing efficacy field tests carried out twice a season, optimally in the North-East EPPO zone.**

Application widow:

- *MAR*: BBCH 31-61
- *N-E*: BBCH 45-51
- *S-E*: BBCH 32-65
- *MED*: BBCH 31-47

In the opinion of Evaluator, window application amounting to BBCH 30-59 against SEPTTR (or/and SEPTSP), PUCCRE~~T~~ and/or PUCCST and BBCH 39-59 against FUSASP is acceptable.

Water volume:

- *MAR*: 200-300 L/ha
- *N-E*: 200 L/ha
- *S-E*: 250 L/ha
- *MED*: 250-400 L/ha

cMS from MAR, S-E, N-E and MED should decide if this water volume can be accepted, considering that such range of water volume in this zone has not been tested. In the opinion of ZRMS, water volume for Poland should be 200-300 L/ha (because this volume was studied in trials, volume of 400 L/ha was not studied).

ZRMs agree with Applicant that: *Boscalid 23.3% + difenoconazole 6.6% SC applied in winter wheat provided a moderate to high level control of Puccinia spp., Fusarium and Septoria spp. with the recommended dose rate of 1.5 L/ha. As diseases often occur as a complex of several diseases with different susceptibility to-wards boscalid and/or difenoconazole, up to 2 applications per season of Boscalid 23.3% + difenoconazole 6.6% SC at the 1.5 L/ha rate should be used to efficiently control the diseases claimed on the label*

The applicant wishes to cite the original registrant's data on boscalid and difenoconazole now out of protection in support of those recommendations on the draft label that are not adequately supported by the applicant's data and requests that the Zonal Rapporteur extrapolate from those data. However, in the opinion of Evaluator it is not possible according to Polish regulations.

Concerned Member States will need to consider the relevance of the submitted formulation comparability data in relation to the current authorized uses for the reference product (a.s. boscalid and difenoconazole) in their own Member State. It is recommended to authorize the product CIAZ (product code: SHA 7216 A) in the extent of the authorization of the reference product (a.s. boscalid and difenoconazole) at the equivalent dose rate.

3.3 Information on the occurrence or possible occurrence of the development of resistance (KCP 6.3)

The following dossier section follows EPPO standard PP 1/213(4) *Resistance risk analysis* in particular point 6. *Registration requirements* and Appendix I of the standard.

Introduction

Resistance to crop protection chemicals is a natural biological phenomenon that occurs in insects, weeds and fungi. It usually becomes evident after the repeated use of a particular pesticide selects the naturally-occurring resistant strains within the wild population and allows them to multiply over several seasons until they become dominant in the population and pose a control problem.

The fungicide-resistant population develops because the sensitive population is suppressed and the rare fungicide-resistant individual can multiply and occupy the biological niche previously filled by the sensitive population. An increase in the frequency of such resistant strains may result in loss of disease control. As a general principle, resistance develops at different rates depending on the pathogen type, nature of the epidemic (or disease severity) and use pattern of the fungicide.

Reports of the appearance of resistant strains in laboratory studies do not necessarily imply that any loss of control is expected in the field. Likewise, the appearance of less-sensitive strains in the field does not always result in failure of disease control. When the frequency of resistant individuals is low and/or the level of resistance is moderate, fungicide applications in most cases will provide satisfactory control.

To avoid the misinterpretation of potential and/or possible resistance cases, the Fungicide Resistance Action Committee (FRAC) states that the term resistance be limited to situations where the conditions in both (a) and (b) below are met:

(a) the development of resistance leads to failure of disease control under practical field conditions following application of a fungicide correctly and according to the label and

(b) a demonstration that a loss of control is due to the presence of pathogenic strains with reduced fungicide sensitivity.

3.3.1 Mode of action

Mode of Action of Boscalid

The active substance boscalid is a systemic compound. Depending on the type of formulation, it penetrates into the plant when applied to leaves (or roots), and it is then translocated acropetally. Boscalid belongs to the chemical class of pyridinecarboxamides in the group of complex II: succinate-dehydrogenase fungicides and is classified in Group 7 by FRAC (FRAC MOA Code: complex II :succinate-dehydrogenase, Group code 7).

Boscalid acts by blocking the enzyme succinate dehydrogenase, and by inhibiting the cytochrome II complex, prevents the development of the fungus by depriving the cells of their energy source and eliminates the formation of blocks for the synthesis of the essential components of the cells. Boscalid is developed in a preventive way preventing both germination of spores and germinative tube growth: the activity of pathogenic fungi is blocked from the early stages of infection.

Boscalid is effective against fungi, e.g. *Leveillula taurica, Leptosphaeria maculans, Puccinia arachidis, Uromyces appendiculatus, Mycosphaerella arachidis, Alternaria brassicae, Septoria lycopersici, Mycosphaerella berkeleyi, Sclerotinia sclerotiorum, Botryotinia fuckeliana* and *Alternaria solani.*

Mode of Action of difenoconazole

Difenoconazole is a triazole fungicide. It belongs to the Sterol Biosynthesys Inhibitors (SBI fungicides), SBI class I, group name: DMI (**D**e-**M**ethilation **I**nhibitors), SBI Class I.

SBI fungicides inhibit the C14 demethylation step within fungal sterol biosynthesis. Chemically, DMI's belong to different classes. There are four classes of fungicides that comprise the Sterol Biosynthesis Inhibitor's (abbreviated SBI's): Only three classes (G1 to G3) are used as agricultural fungicides: DMI-fungicides, Amines (before called "Morpholine"- fungicides) and Hydroxyanilides. All classes inhibit targets within fungal sterol biosynthesis but differ in regard to the precise target sites they inhibit.

Figure 3.3-1: Overview on Sterol Biosynthesis Inhibitors

Sterol Biosynthesis Inhibitors				
SBI Class:	I	II	III	IV
FRAC serial code	3	5	17	18
FRAC target no.	G1	G2	G3	G4
Group name	**De-M**ethylation **I**nhibitors: **(DMI**s)	amines (formerly 'morpholines')	hydroxy-anilides	squalene-epoxidase inhibitors
Target in Sterol Biosynthesis	sterol C14 demethylase	Δ^{14} reductase and $\Delta^{7} \rightarrow \Delta^{8}$ isomerase	3-keto reductase	squalene-epoxidase
Chemistry	piperazines pyridines pyrimidines imidazoles triazoles	morpholines piperidines spiroketalamines	hydroxyanilides	thiocarbamates [1] allylamines [2]
Uses	agriculture (fungicide) material protection medicine (antimycotic)	agriculture (fungicide)	agriculture (fungicide)	agriculture (herbicide) [1] medicine [2] (antimycotic)

The SBI based fungicides have a broad spectrum of activity against a range of economically important pathogens on arable crops, top fruit, vines, plantation crops, etc and they represent an important class of agricultural fungicides. They make a major contribution to world agricultural production

3.3.2 Mechanism of resistance

Mechanisms of Resistance, Boscalid

The FRAC SDHI Working Group was working in the resistance management recommendations for the SDHI fungicides and they have shown that target site mutations in sdh gene, e.g. H/Y (or H/L) at 257 *Ustilago maydis*, homolog to 267 in *Zymoseptoria tritici* and 272 in *Botrytis cinerea*.

SDHI fungicides were discovered more than 40 years ago. Due to the limited disease and application spectrum of the "first generation" carboxamides, resistance under commercial conditions remained limited to a few crop/pathosystems (primarily Basidiomycetes), e.g.*Puccinia horiana*, chrysanthemum rust, and *Ustilago nuda*, loose smut in barley.

In addition to these "first generation" molecules, SDHIs with increased spectrum and potency were launched starting in 2003 and new ones continue to be launched today. These modern generation SDHIs are rapidly achieving market share in many crops and new SDHIs are currently in development.

The target enzyme of SDH inhibitors is succinate dehydrogenase (SDH, so-called complex II in the mitochondrial respiration chain), which is a functional part of the tricarboxylic cycle and linked to the mitochondrial electron transport chain (Keon et al., 1991). SDH consists of four subunits (A, B, C and D) and

the binding site of the SDHIs (the ubiquinone binding site) is formed by the subunits B, C and D. Target site mutations conferring reduced sensitivity can develop in all three subunits.

FRAC Guidelines for using SDH fungicides against *Sclerotinia sclerotiorum, Alternaria brassicae and Leptosphaeria maculans* on oilseed rape:

Long-term experience with SDH fungicides demonstrates that the resistance risk of *Sclerotinia sclerotiorum, Alternaria brassicae and Leptosphaeria maculans* to this fungicide group is of low to moderate and can be managed through appropriate use strategies.

- Apply SDHI fungicides always in mixtures
- The mixture partner should provide satisfactory disease control when used alone on the target disease and must have a different mode of action.
- Apply a maximum of 2 SDHI fungicide containing sprays per cereal crop.
- Apply the SDHI fungicide preventively or as early as possible in the disease cycle. Do not rely only on the curative potential of SDHI fungicides.
- Strongly reduced rate programs including multiple applications must not be used. Refer to manufacturers' recommendations for rates.

Mechanisms of Resistance, difenoconazole

Resistance is known in various fungal species. Several resistance mechanisms are known including a number of target site mutations on the cyp51 gene (cytochrome p450) and effects on ABC transporters.

In recent years, several point mutations in the cyp51 gene has been identified to influence the sensitivity towards DMI fungicides. Interestingly, differences in sensitivity patterns towards particular DMI's are observed. Wild-type isolates (group I) are highly sensitive to all DMI's. Isolates of group II (Y137F) have a slightly reduced sensitivity and isolates of group III (heterogeneous genotype) are clearly reduced in their sensitivity to all DMI's. Isolates of group IV (V136A) have a reduced sensitivity to all DMI's except tebuconazole, to which they are particularly sensitive. Isolates of group V (I381V) and group VI (A379G and I381V) are less sensitive to all DMI's except difenoconazole, which is particularly active against these two genotypes.

The resistance factors implied by these mutations are relative small, the variation of sensitivity within each genotype is rather big and all DMI's underwent a similar shift. This indicates that also other mechanisms are present in *Septoria tritici*. These resistance mechanisms have been associated with a fitness penalty in organisms like *Rhynchosporium secalis* and this is believed to be the case in other organisms. As a result, sensitivity levels have been seen to move over a period of time and then to stabilize. Unlike classic point mutations and the large changes in sensitivity observed in some groups of chemistry e.g. resistance to QoI's in *Septoria tritici*, resistance to DMI's has been shown to be in the form of small shifts occurring over a long period of time.

Resistance to SBI fungicides

Resistance to SBI fungicides has been well characterized during the last 25 years. Problems with SBI performance typically became obvious only after several years of intensive use with efficacy degrading stepwise. Following reduced selection pressure, a partial recovery in sensitivity is often observed. The mechanism of resistance is mostly controlled by the accumulation of several independent mutations and is generally referred to as "continuous selection", "quantitative resistance" or "shifting".

GENERAL RECOMMENDATIONS

The SBI fungicides represent one of the most potent classes of fungicides available to the grower for the control of many economically important pathogens. It is in the best interest of all those involved in recommending and using these fungicides that they are utilised in such a way that their effectiveness is maintained.

The recommendations are based upon data generated by members of the FRAC-SBI Working Group and upon the work of non-industry collaborators.

The following general recommendations can be made:

- Repeated application of SBI fungicides alone should not be used on the same crop in one season against a high-risk pathogen in areas of high disease pressure for that particular pathogen.
- Reduced rates of SBI fungicides can contribute to accelerate the shift to less sensitive populations. It is critical to use effective rates of SBI fungicides (DMI fungicides) in order to ensure robust disease control.
- When used in mixture recommended effective rates of the SBI (DMI fungicides) should be maintained. Split and reduced rate programmes, using multiple repeated applications at dose rates below manufacture's recommendations, provide continuous selection pressure and accelerate the development of resistant populations, and therefore must not be used.
- For crop/pathogen situations where repeated spray applications (e.g. orchard crops/powdery mildew) are made during the season, alternation (block sprays or in sequence) or mixtures with an effective non cross-resistant fungicide are recommended.
- Where alternation or the use of mixtures is not feasible because of lack of effective or compatible non cross-resistant partner fungicides, then input of SBI's should be reserved for critical parts of the season or crop growth stage.
- If the performance of SBIs should decline and sensitivity testing has confirmed the presence of less sensitive isolates, SBI's should only be used in mixture or alternation with effective non cross-resistant partner fungicides.
- The introduction of new classes of chemistry offers opportunities for more effective resistance management. The use of different modes of action should be maximised for the most effective resistance management strategies.
- Users must adhere to the manufacturers' recommendations. In many cases, reports of "resistance" have, on investigation, been attributed to cutting recommended use rates, or to poorly timed applications.
- Fungicide input is only one aspect of crop management. Fungicide use does not replace the need for resistant crop varieties, good agronomic practice, plant hygiene/sanitation, etc.
- Exclusive frequency measurements of single cyp51 mutations are not sufficient to describe the sensitivity situation towards DMIs but can help to better understand the background of sensitivity shifts.

3.3.3 Evidence of resistance

Evidence of Resistance, Boscalid

Members of the Fungicide Resistance Action Committee (FRAC) have monitored the occurrence of resistance to multisite fungicides across Europe. According to the FRAC, some records of practical resistance to boscalid have been recorded in certain regions.

Field isolates with target site mutations conferring reduced sensitivity were identified during routine monitoring in *Sclerotinia sclerotiorum* on oilseed rape. Many of the identified mutations have low to moder-

ate resistance factors for commercially available SDHIs and the frequency of the resistant mutations remains low in the population. Reports on field performance of the SDHIs remained good in 2014. These early monitoring reports of isolates with reduced sensitivity emphasize the need to abide by resistance management guidelines to prolong the life of the SDHIs.

Sclerotinia sclerotiorum

Extensive monitoring programs were carried out since 2006.
In 2014 and 2015, single resistant isolates were detected in France. No resistant isolates were detected in 2014 in Czech Republic, Germany, the United Kingdom and Poland.
In 2015, no resistance was detected in the Netherlands, Belgium, France, Poland, Czech Republic, Croatia and Germany.

In the season 2016, samples were tested from Germany, France, the United Kingdom, Czech Republic, Lithuania, Denmark and Poland.
No to low frequency of resistance was detected in France and Germany.
Analysis of samples including mutations is not yet completed and will be reported at the next working group meeting.

Leptosphaeria maculans

All isolates tested were sensitive, within the baseline (France, Germany, Poland, United Kingdom and Hungary).

Evidence of Resistance to SBI fungicides

The 2017 meeting minutes from the Sterol Biosynthesis Inhibitor (SBI) working group are giving a comprehensive summary of the situation relevant for use of the difenoconazole part of Boscalid 23.3% + Difenoconazole 6.6% SC:

A stable situation was found with DMI's and amines. For more information please refer to FRAC website http://www.frac.info/ :

Monitoring data (2016-2017) for crops supported for the product Boscalid 23.3% + Difenoconazole 6.6% SC:

- Cercospora Leaf spot of beets (*Cercospora beticola)*

- Monitoring data for 2016 are available for Austria, Belgium, Czech Republic, France, Germany, Italy, Netherlands, Poland, Sweden, Switzerland and United Kingdom. Based on this data, a stable situation was observed as in the last years.
- Monitoring in 2017 was carried out in France, Germany, Greece, Netherlands, Romania, Russia and Serbia. A stable situation was observed as in the last 5 years.
- Single isolates with slightly increased EC50 values were already detected 5 years ago in France and Germany but remain stable at a low frequency.
- Field performance can be affected when solo DMIs are used.
- The broad range of sensitivity leads to the assumption that a shift took place before routine monitoring was set up.

- Early blight of tomato and potato (*Alternaria solani* and *Alternaria alternata)*

- Monitoring was started in 2012 in Europe.

- Monitoring in 2017 was carried out in Belgium, Czech Republic, France, Germany, Hungary, Italy, Netherlands, Poland, Romania, Slovakia, Spain and Sweden.

Homogenous sensitivity of both pathogens was observed in different countries across Europe and no change occurring in 2017.

3.3.4 Cross-resistance

Cross Resistance among boscalid

Work with isolates from both field and lab studies suggests that cross-resistance patterns between SDHIs for different target site mutations are complex. Different target site mutations confer varying degrees of insensitivity between the different SDHIs. This suggests the effect of these target site mutations on field performance of specific SDHIs may vary if they were to spread in field populations. The various degrees of reduced sensitivity to different target site mutations may be explained by structural differences between classes of SDHIs and how they interact with the target site of a specific pathogen (Scalliet et al. 2012). Additionally, the magnitude of the effect conferred by a specific target site mutation can vary from species to species. In other words, the reduction in sensitivity conferred by specific target site mutations may vary between pathogen species, SDHI used and geographic location of the isolates (Sierotzki and Scalliet 2013).

Cross Resistance among SBI fungicides

The pattern of cross-resistance of the sterol biosynthesis inhibitor (SBI) fungicides, of which difenoconazole is a member, is complex and summarised as follows:

FRAC Code	SBI Class	Group Name	Chemical Group	Cross-resistance
G1/3	I	DMI (DeMethylation Inhibitors)	Piperazines, pyridines, pyrimidines, imidazoles, triazoles	Resistance within the DMI group but NOT to other SBI classes.
G2/5	II	Amines (morpholines)	Morpholines, piperidines, spiroketal-amines	Cross-resistance within the group generally found but not to other SBI classes.
G3/17	III	hydroxyanilides	hydroxyanilides	-
G4/18	IV	Squaline-epoxidase inhibitors	Thiocarbamates, allylamines	Resistance not know

Therefore, fungal pathogen strains that are resistant to DMI fungicides are unlikely to be cross-resistant to other SBI class fungicides and visa versa.

3.3.5 Sensitivity data

Diseases vary in their sensitivity towards fungicides both between and within populations, and this natural variation should be understood before shifts in sensitivity can be assessed. DMI fungicides have been tested and used worldwide for up to 30 years (or more), it is therefore difficult to find unexposed fungal populations. No true base line sensitivity data can therefore be established. FRAC has been monitoring the development in sensitivity in the most important diseases for a number of years, and Sharda will work closely together with FRAC to assist with this work.

3.3.6 Use pattern

Boscalid 23.3% + Difenoconazole 6.6% SC is composed of boscalid which is a systemic fungicide with protective, curative and eradicant activity as well as difenoconazole, which is a systemic fungicide with

preventive and curative activity. In the EU Central zone, the formulation is proposed for control of Rust, Septoria and Fusarium in winter wheat. The fungicide is proposed applied up to two times during the season at the recommended dose rate (1.5 L/ha).

The application may be employed when the climatically conditions are favourable for infestation or when warnings have been released in the different regions. Dependent on the crop and the pest to be controlled, this will deliver 350 g boscalid and 100 g difenoconazole per hectare, per application.

Boscalid as well as difenoconazole have both been used as straight product as well as in mixtures for many years.

3.3.7 Resistance risk assessment of unrestricted use pattern

The active substance

FRAC regards the resistance risk of the Group 7 (boscalid) as medium to low and Group G1 (difenoconazole) as medium.

The disease

The target organisms for the use of Boscalid 23.3% + Difenoconazole 6.6% SC have developed resistance to a range of fungicide groups including the DMIs and SDHI. Resistance to DMIs was the first time reported in 1990 in grapevine powdery mildew (*Erysiphe necator*; Steva et al., 1990) and resistance to SDHI rarely develop resistance towards boscalid. The resistance risk associated with any individual disease is dependent on a number of factors related to the disease epidemiology, these include:

- Life cycle; the shorter the generation time, the more frequent the need for exposure to the fungicide and the faster the build-up of resistance.
- Abundance of sporulation; the more spores that are released in the crop the greater the availability of individual genomes for mutation and selection and the faster the spread of resistant strains.
- Isolation of pathogen populations; the more isolated the crop, through geography, or protected crops, the less chance of ingress of sensitive forms or loss of resistant forms.
- Occurrence of a sexual stage in the life cycle; this may (e.g. *Septoria* spp.).

The intended disease target for Boscalid 23.3% + Difenoconazole 6.6% SC vary in terms of their intrinsic resistance risk. The resistance risk of target pathogens of Boscalid 23.3% + Difenoconazole 6.6% SC is available at www.frac.info.

Agronomic practice

In terms of agronomic practice, the selection pressure on the intended disease target for Boscalid 23.3% + Difenoconazole 6.6% SC may be low to high in annual cereal crops like wheat (depending on whether a successful crop rotation system is applied or mono-cropping is carried out in the crop, respectively).

The plant protection product

For optimum disease control, Boscalid 23.3% + Difenoconazole 6.6% SC is applied at the rates recommended on the proposed label. These have been shown to be the minimum effective dose for the major target pathogen (Section 3.2.2).

3.3.8 Test methods

There are several monitoring methods approved by FRAC (available on www.frac.info).

3.3.9 Acceptability of the resistance risk

In the absence of any potential resistance risk and in the absence of any other restrictions on the GAP (residues, toxicology etc.), the unrestricted use pattern for Boscalid 23.3% + Difenoconazole 6.6% SC would be season long usage with an unrestricted number of applications.

Overall it is clear that the unrestricted use of Boscalid 23.3% + Difenoconazole 6.6% SC presents an unacceptable resistance risk and therefore modifiers as part of a Management Strategy are proposed.

3.3.10 Resistance management strategy

As the unmodified use pattern is considered unacceptable, a number of modifiers are proposed which are entirely in accordance with the general recommendations made by FRAC.

- Use in alternation with fungicides with a different mode of action
- Use as recommended on the label. Do not use reduced doses.
- Application should be as a protective application.
- Use other measures such as resistant varieties, good agronomic practice

3.3.11 Implementation of the Management Strategy

Information on the management of resistance and the specific Resistance Management Strategy for Boscalid 23.3% + Difenoconazole 6.6% SC is disseminated by a number of routes including, but not exclusively:

- Product label has a clear statement regarding resistance risk and the management strategy
- Pack inserts for general information or to address a particular issue in a specific geographical area were it to occur.
- Leaflets available at, and distributed by distributors/wholesalers/merchants
- Information released by national and local advisory services re. monitoring
- FRAC publications including the web site www.frac.info
- Training for distributors/wholesalers/merchants and farmer groups
- Links from company web sites to FRAC and local Fungicide Resistance working groups for information and advice

3.3.12 Monitoring, reporting and reaction to the change in performance

Monitoring of field performance

Where field performance is significantly less than expected (relative to field trial results presented in section 3.2.3) and where no other explanation can be found for the reduced performance e.g. application errors, then samples may be taken for sensitivity testing. Where testing is carried out it will be conducted at laboratories experienced in carrying out such testing and using methods recommended by FRAC.

Analysis of performance-related complaints

Where no other reason for a failure in performance can be identified, samples may be taken for testing as described above

Where resistance can be confirmed as the cause for loss of field performance this will be reported to the authorities on an annual basis or as required.

Containment plan

The above recommendations will be adjusted as needed depending on the success of the proposed strategy. In the event that practical field resistance should occur on any significant scale, Sharda's plan for

containing the further development or spread of resistance includes a number of possible actions on a temporary or permanent basis, including but not exclusively:

- Recommendations to use only fungicides from alternative mode of action groups for the remainder of the growing season
- Reduction in number of applications
- Recommendation to use only in a programme e.g. before or after an application of a fungicide from a different mode of action group.

Normally any action taken would be in consultation with the relevant authorities.

Comments of zRMS:	The agronomic risk for the CIAZ (product code: SHA 7216 A) which include boscalid and difenoconazole is estimated in generally as low to medium. However, in terms of agronomic practice, the selection pressure on the intended disease target for Boscalid 23.3% + Difenoconazole 6.6% SC may be low to high in annual cereal crops like wheat (depending on whether a successful crop rotation system is applied, or mono-cropping is carried out in the crop, respectively). The resistance management is coordinated by FRAC recommendations. Applying the anti-resistance use recommendations, development of resistance can be considerably decreased or avoided. Generally, it can be concluded, that the proposed management strategy for the prevention of fungicide resistance can be regarded as sufficient. ***Difenoconazole*** is a fungicide belonging to the group of SBI-Class I: Demethylation-Inhibitors (DMI) a subgroup of the Sterol Biosynthesis Inhibitors (SBI)-triazoles. The active ingredient is classified after the target site and code by FRAC to inhibition of biosynthesis in membrane G1: C14-demethylase in sterol biosynthese. Difenoconazole is intended to be used in cereals and sugar beets. Especially the substance is active against *Erysiphe graminis*, *Puccinia spp*., *Leptosphaeria nodorum*, *Mycosphaerella graminicola* and *Fusarium sp*. in cereals. The biochemical mode of action of the DMI is the inhibition of C14-demethylase in sterol biosynthesis. Based on the current evidence the resistance risk assessment for DMI, SBI-Class I, Triazoles will be medium. It is known a cross resistance between DMI fungicide active against the same fungus. DMI fungicides show no cross resistance to other SBI classes. For this group resistance is known in various fungus species. Several resistance mechanisms are known including target site mutations in cyp51 (erg 11) gene (Anonymous 2011a). The published use pattern for all SBI classes covered by the FRAC SBI Working Group guidelines for management strategy reflects the resistance risk assessment. Difenoconazole is a systemic active ingredient. It will be absorbed very fast by plant tissue and translocated acropetally in the transpiration stream. The active ingredient inhibits spore germination, mycelial growth, and the development of infection structures are thus prevented. Difenoconazole has a protective as well as an eradicative/curative effect. The active ingredient is selective on a wide range of dicotyledonous and monocotyledonous crop species. Difenoconazole will be used for foliar application and seed treatment. Difenoconazole is a candidate for substitution. ***Boscalid*** is a member of the fungicide group succinate dehydrogenase inhibitors (SDHI) and pyraclostrobin belongs to the group of QoI fungicides (Quinone outside inhibitors). Mutations in several plant pathogenic fungi have been identified causing resistance against active substances of both fungicide groups. Cross resistance between SDHI fungicides is known. Cross resistance between the two fungicide groups has not been observed so far. Concerning fungicide risk FRAC describes the SDHI fungicides in general as medium to high-risk compounds and the QoI fungicides in general as high-risk compounds

	Septoria tritici blotch (STB) caused by the fungal pathogen *Zymoseptoria tritici* is a global threat to sustainable wheat production. The use of fungicides against STB is considered the primary means of minimizing yield losses; however, fungicide resistance is developing, which greatly affects their effectiveness. Only a few classes of fungicides are available for STB control. DMI fungicides are seen as a major group but growing resistance problems are calling their use into question. Based on the current evidence the resistance risk assessment for DMI, SBI-Class I, Triazoles will be medium. It is known a cross resistance between DMI fungicide active against the same fungus. DMI fungicides show no cross resistance to other SBI classes. For this group resistance is known in various fungus species. Several resistance mechanisms are known including target site mutations in cyp51 (erg 11) gene (Anonymous 2011a). The published use pattern for all SBI classes covered by the FRAC SBI Working Group guidelines for management strategy reflects the resistance risk assessment. Laboratory studies using single generation exposures to different SDHIs have reported several target-site mutations conferring reduced sensitivity in mutants of *Z. tritici* and other plant pathogens (Fraaije et al., 2012; Scalliet et al., 2012; Sierotzki & Scalliet, 2013; Skinner et al., 1998). The SDHI sensitivity can be differentially affected by mutations. For example, SdhB-H267Y mutants of *Z. tritici* are insensitive to boscalid but hypersensitive to fluopyram. Since the agronomic factors influencing the risk of resistance development tend to vary between the member states, the individual and detailed assessment of the resistance risk (Evaluation of the Agronomic risk of resistance, Management of resistance, Use pattern, Proposed Risk Modifiers) has to be finalised on national level. It is critical to use an effective disease management program to delay the emergence of resistance, so it is necessary to keep as many fungicides belonging to different modes of action or different chemical groups on the market as possible. The resistance management strategy must include changing active substances from different MoA groups during the growing season but should also consider the possibility of using the best active substance from each group in a given situation. It is generally necessary to include all available MoA groups in the spray sequence and to avoid spraying products from the same group consecutively to minimize selection pressure on target diseases (and non-target diseases that may be present). Boscalid is classified by FRAC with medium to high impact on resistance, and difenoconazole with medium impact on resistance. Among the 278 PPPs, 115 can be found with high resistance, containing active ingredients such as azoxystrobin, dimoxystrobin, fluoxastrobin, kresoxim-methyl, pyraclostrobin, thiophanate-methyl, and trifloxystrobin. These substances, existing as single active substances, cannot be considered as better alternatives to CIAZ according to the resistance strategy. <u>zRMS considers that the following modifiers may be appropriate:</u> • Maximising efficacy by using the right dose at the right growth stage in the right conditions • Monitoring success and reporting any unexpected results to [distributor]‘ • As far as possible, vary the chemicals used on the crop and alternate or combine with products having different modes of action.

3.4 Adverse effects on treated crops (KCP 6.4)

Data from ~~27~~ 28 efficacy and 7 selectivity trials conducted in the Maritime EPPO zone (~~17~~ 18, i.e. Czech Republic (11), Germany (1), United Kingdom (1), N-France (~~4~~ 5)), the North-east EPPO zone (7; i.e. Poland), the South-east EPPO zone (4; i.e. Hungary (4)) and the Mediterranean EPPO zone (6, i.e. S-France (1) and Italy (5)) have been included in this biological assessment dossier to support the label claims and recommendations on efficacy in the EU Central Registration zone.

The ~~34~~ 35 trials were conducted in winter wheat.

Information on trials submitted (6.4 Adverse effects on treated crops)

Trials in this dossier were carried out by contractor companies and Official Research institutes, all of which follow the EPPO guidelines and are officially recognized by the competent authorities to carry out field registration trials in accordance with the principles of Good Experimental Practice (GEP). The GEP-requirement and the Uniform Principles are therefore taken care of.

On the basis of the EPPO guideline 1/241(1) "Guidance on comparable climates", the trials included in this dossier have been grouped and summarized by EPPO zones. EPPO zones have been defined by taking into account differences between the agro-climatic sub-areas of the EPPO region.

In general, the trials were conducted according to the respective EPPO guidelines.

In support of the current application for registration of Boscalid 23.3% + Difenoconazole 6.6% SC, ~~27~~ 28 efficacy and 7 selectivity trials were conducted in the Maritime, the North-east, the South-east and the Mediterranean EPPO zones:

Table 3.4-1: Presentation of selectivity trials

Crop*	Country	Type of trial**	Number of trials				Years	GEP, non-GEP, official***	Comments (any other relevant information)
			EPPO zone						
			MAR	MED	S-E	N-E			
TRZAW	Italy	S + Y + Q	-	1 (1)	-	-	2017	GEP	
	France	S + Y + Q	1 (1)	-	-	-	2017	GEP	
	Czech Rep.	S + Y + Q	1 (1)	-	-	-	2016	GEP	
	UK	S + Y + Q	1 (1)	-	-	-	2016	GEP	
	Poland	S + Y + Q	-	-	-	2	2017	GEP	
		S + Y + Q	-	-	-	1	2016	GEP	
	Total, Winter wheat (sel.)		3 (3)	1 (1)	-	3 (3)			

Table 3.4-2: Details on efficacy trial methodology

Guidelines	General guidelines	EPPO PP 1/152(4), PP 1/181(4), PP 1/135(4), PP 1/225(2), PP 1/226(2), PP 1/239(2)
Experimental design	Plot design	RCBD (7)
	Plot size	10-24 m²
	Number of replications	4 (7)
Crop	Trials per crop	Winter wheat (7)
	Varieties per crop	Winter wheat: Palesio, Moisson, Cordiale, Svitava, Arkadia, Memory, Sailor
	Sowing period	Winter wheat: September 16th to December 19th

Application	Crop stage (BBCH)* at application	Winter wheat: BBCH 37-51 (1st appl.) and BBCH 47-69 (2nd appl.)
	Timing Pest stage at appl. (1)	Please refer to detailed summary tables in Appendix 5.
	Number of appl. Intervals between appl.	1 (2); 2 (5) n.r.; 10-15 days
	Spray volumes	150-400 L/ha
Assessment	Assessment types	- Visual estimation of Pest severity, compared to 'untreated' ('untreated' = 0 % control); total control = 100 % control) – based on the assessment of attacked plant area, as compared to the untreated check. - Visual estimation of Pest incidence, compared to 'untreated' ('untreated' = 0 % control); total control = 100 % control) – based on the percentage of attacked plants or plant parts on a sample of a defined number of plants/plant parts per plot, as compared to the untreated check. - Visual estimation of crop injury and crop stand reduction (thinning) compared to 'untreated' ('untreated' = 0% crop injury; 100% crop injury = total crop destruction). Where appropriate this overall score was substituted or supplemented by assessments of individual symptoms. - Crop yield was assessed in 18 efficacy and 4 selectivity trials conducted on TRZAW. Yield assessments included grain yield [T/ha] as well as different quality parameters (i.e. TGW and HLW).
	Assessment dates	Please refer to the summary tables in the following section
Other relevant information	Soil type	Light to heavy soils
	Natural / artificial innoculation…	Natural
	Field / Greenhouse...	Field

The reference products used in the trials are listed in Table 3.4-3.

Table 3.4-3: Presentation of test- and reference standards used in trials (selectivity trials, transformation trials...)

Trade name	Formulation	Composition	Rates	Country	N° of Trials
National reference product					
PROLINE STAR	EC	125 g/L prothioconazole + 125 g/L tebuconazole	1.0 2.0	IT CZ	1 1
BELL STAR	EC	140 g/L boscalid + 50 g/L epoxiconazole	2.5 5.0	FR	1
TRACKER	EC	233 g/L boscalid + 67 g/L epoxiconazole	1.5 3.0	UK	1
VENTUR 300	SC	233 g/L boscalid + 67 g/L epoxiconazole	1.5 3.0	PL	3

3.4.1 Phytotoxicity to host crop (KCP 6.4.1)

As Boscalid 23.3% + Difenoconazole 6.6% SC is a fungicide, no specific studies are required as long as in the efficacy trials no negative effects are observed. The crop safety of applying Boscalid 23.3% + Difenoconazole 6.6% SC at a dose rate similar to the recommended rates in winter wheat was evaluated in ~~27~~ 28 efficacy and 7 selectivity trials (~~17~~ 18 MAR, 7 N-E, 4 S-E and 6 MED). In the efficacy trials, Boscalid 23.3% + Difenoconazole 6.6% SC was applied at 1.0 to 3.0 L/ha in winter wheat.

The trials were conducted in the Maritime EPPO zone (~~17~~ 18, i.e. Czech Republic (11), Germany (1), United Kingdom (1), N-France (~~4~~ 5)), the North-east EPPO zone (7; i.e. Poland), the South-east EPPO zone (4; i.e. Hungary (4)) and the Mediterranean EPPO zone (6, i.e. S-France (1) and Italy (5)) in 2016, 2017 and 2019 to evaluate the crop safetyness of Boscalid 23.3% + Difenoconazole 6.6% SC in winter wheat.

3.4.1.1 Winter wheat (TRZAW)

Crop phytotoxicity was evaluated in efficacy and selectivity trials where Boscalid 23.3% + Difenoconazole 6.6% SC was applied at one or two applications, when the crop was at growth stages ranging from BBCH 31 to BBCH 65, at the rate of 0.8 to 3.0 L/ha in winter wheat. The 1.5 L/ha dose rate corresponds to 100% of the proposed dose rate. Crop phytotoxicity was assessed in all trials at various intervals from application and up to harvest.

Phytotoxicity in winter wheat trials, Maritime EPPO zone

A total of ~~14~~ 15 efficacy and three selectivity trials were conducted in the Maritime EPPO zone to assess the crop safety of Boscalid 23.3% + Difenoconazole 6.6% SC when applied as recommended in winter wheat. The trials were conducted on commercially available varieties.

No adverse effects in regards to phytotoxicity and vigour were observed in any efficacy and selectivity trials treated with Boscalid 23.3% + Difenoconazole 6.6% SC.

Furthermore, harvest results from the Maritime winter wheat trials demonstrated that the applied treatments did not have any detrimental effects on yield or quality of yield either

Phytotoxicity in winter wheat trials, North-east EPPO zone

Seven trials (4 efficacy and 3 selectivity) trials were conducted in the North-east EPPO zone to assess the crop safety of Boscalid 23.3% + Difenoconazole 6.6% SC when applied as recommended in winter wheat. The trials were conducted on commercially available varieties.

No adverse effects in regards to phytotoxicity and vigour were observed in any efficacy trials treated with Boscalid 23.3% + Difenoconazole 6.6% SC.

Furthermore, harvest results from the winter wheat trials demonstrated that the applied treatments did not have any detrimental effects on yield or quality of yield either.

Phytotoxicity in winter wheat trials, South-east EPPO zone

Four efficacy trials were conducted in the South-east EPPO zone to assess the crop safety of Boscalid 23.3% + Difenoconazole 6.6% SC when applied as recommended in winter wheat. The trials were conducted on commercially available varieties.

No adverse effects in regards to phytotoxicity and vigour were observed in any efficacy trials treated with Boscalid 23.3% + Difenoconazole 6.6% SC.

Furthermore, harvest results from the winter wheat trials demonstrated that the applied treatments did not have any detrimental effects on yield or quality of yield either.

Phytotoxicity in winter wheat trials, Mediterranean EPPO zone

A total of 5 efficacy and 1 selectivity trials were conducted in the Mediterranean EPPO zone to assess the crop safety of Boscalid 23.3% + Difenoconazole 6.6% SC when applied as recommended in winter wheat. The trials were conducted on commercially available varieties.

No adverse effects in regards to phytotoxicity and vigour were observed in any efficacy trials treated with Boscalid 23.3% + Difenoconazole 6.6% SC.

Furthermore, harvest results from the Mediterranean winter wheat trials demonstrated that the applied treatments did not have any detrimental effects on yield or quality of yield either.

3.4.1.2 Overall conclusion

Winter wheat is claimed on the label. The claims of crop safety on winter wheat are supported with a total of ~~34~~ 35 trials conducted in Italy, Poland, United Kingdom, France, Germany, Czech Republic and Hungary in 2016, 2017 and 2019 in winter wheat. In all trials, Boscalid 23.3% + Difenoconazole 6.6% SC proved to be crop safe and in the vast majority of the trials did not significantly affect the crop adversely when applied at a range of growth stages within and occasionally beyond the label recommended range, at the maximum proposed label recommended rates of 1.5 L/ha in winter wheat. The same was observed in the treatments where Boscalid 23.3% + Difenoconazole 6.6% SC was applied at twice the recommended rates or more, representative of sprayer overlap.

As the data on winter wheat show, the crop safety and efficacy of Boscalid 23.3% + Difenoconazole 6.6% SC is equivalent to that of the boscalid + difenoconazole co-formulated reference products tested in the trials. As comparability between the formulations has been demonstrated, the applicant therefore wishes to cite the original registrant's data on boscalid and difenoconazole now out of protection in support of those recommendations on the draft label that are not adequately supported by the applicant's data and requests that the Zonal Evaluator extrapolate from those data.

Table 3.4-4: Phytotoxicity of product

Number of trials with…		Efficacy trials (27 trials) and Selectivity trials (7 trials)	
		Test product	Standard
		1.5 L/ha	1N
Maximum of phytotoxicity recorded during the trials	0% to 5%	~~34~~ 35	~~34~~ 35
	>5% to 10%	0	0
	>10% to 15%	0	0
	>15 %	0	0
Level of symptoms at the last assessments	0% to 5%	~~34~~ 35	~~34~~ 35
	>5% to 10%	0	0
	>10% to 15%	0	0
	>15 %	0	0

Comments of zRMS:	The phytotoxicity trials about tested plant protection product have been carried out in accordance with EPPO Guidelines. The conduct of the field work is principally compliant with "Good Agricultural Practice" and in accordance with EPPO Guidelines PP 1/135. The trials were performed with the use of different agricultural practice. The trials were performed with the use of cultivars, differing in growth strength as well as soil and water requirements. The appropriate experimental design was applied. In all trials studied product was compared to the standard reference products. Statistical analysis of the data was performed. Also, quality of yield was evaluated in some trials. 28 phytotoxicity studies were performed on winter wheat: - *MAR*: 15 trials (DE-1, FR-4, CZ-10) - *N-E*: 4 trials (PL)

	- *S-E*: 4 trials (HU) - *MED :* 5 trials (IT-4, FR-1) No adverse effects regarding to phytotoxicity were observed in any of the 28 efficacy trials. Trials were carried out on different winter wheat varieties. Only dose N was studied. According to EPPO standards, dose 2N is not required for fungicides. All results were compared to standard reference products. Also, Applicant submitted 7 selectivity trials performed in Maritime EPPO zone (3 trials: UK, CZ, FR), MED EPPO zone (1 trial: IT) and N-E EPPO zone (3 trials: PL). Trials were carried out on different winter wheat varieties. Only dose N was studied. According to EPPO standards, dose 2N is not required for fungicides. All results were compared to standard reference products. In conclusion, the test product CIAZ (product code: SHA 7216 A) is regarded safe for the target crop when used according to the label recommendations.

3.4.2 Effect on the yield of treated plants or plant product (KCP 6.4.2)

~~Twenty-seven~~ Twenty-eight efficacy trials were conducted with the same formulation currently under registration, i.e. Boscalid 23.3% + Difenoconazole 6.6% SC, in the Maritime EPPO zone (18, i.e. Czech Republic (11), Germany (1), United Kingdom (1), N-France (5)), the North-east EPPO zone (~~4~~ 7; i.e. Poland), the South-east EPPO zone (4; i.e. Hungary (4)) and the Mediterranean EPPO zone (6, i.e. S-France (1) and Italy (5)) to evaluate the effect of Boscalid 23.3% + Difenoconazole 6.6% SC on the quality of the harvested crop of winter wheat (TRZAW). The results obtained in the twenty-three trials are presented in the section below.

3.4.2.1 Materials and methods

Plot yields, as fresh weight and dry weight of wheat grains per plot, were measured at harvest and converted to t/ha. The data of the treated plots are presented as relative values in relation to the weight of wheat grains harvested from the untreated plots. For further information on materials and methods please refer to section 3.4.

3.4.2.2 Summary and evaluation of the field trials conducted in winter wheat, treated with two applications

A summary of the mean yield assessments, expressed as %-relative of the untreated, are presented in Table 3.4-5 for results obtained in winter wheat trials harvested in the Maritime, North-east, South-east and Mediterranean EPPO zone.

Winter wheat

A total of twenty-eight efficacy and selectivity trials in winter wheat were harvested. The trials were conducted in Germany (1), Italy (1), S-France (1), N-France (5), United Kingdom (5), Czech Republic (5) and Hungary (4) in 2016, 2017 and 2019. In the efficacy trials, Boscalid 23.3% + Difenoconazole 6.6% SC was applied at 1.0 to 3.0 L/ha. The trials were sprayed at crop growth stages ranging between BBCH 30 and BBCH 65. In Table 3.4-5, the results obtained in the efficacy trials when treated with 1.0 and 1.5 L/ha and in the

Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:	Ref. prod. at:
		Mean (min-max)	% relative, compared to untreated (min-max, no. of trials)	

		t/ha	1.0 L/ha	1.5 L/ha	1 N
Winter wheat – Efficacy trials, all reference products					
Maritime EPPO zone	12	6.98 (3.1-9.9)	112 (103-133)	112 (100-136)	115 (100-139)
North-east EPPO zone	4	6.79 (5.28-7.48)	107 (104-112)	109 (104-11)	108 (102-116)
South-east EPPO zone	4	5.16 (4.25-6.11)	106 (104-109)	105 (102-109)	106 (100-112)
Mediterranean EPPO zone	1	6.78	102	107	121

Table 3.4-6 the results obtained in the selectivity trials when treated with 1.5 and 3.0 L/ha, are presented. Not in all trials the yield was recorded.

Table 3.4-5: Yield – Maritime, North-east, South-east and Mediterranean: Crop yield of winter wheat treated with Boscalid 23.3% + Difenoconazole 6.6% SC two applications, as % of untreated (Untreated = 100%), efficacy trials

Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
		Mean (min-max)	% relative, compared to untreated (min-max, no. of trials)		
		t/ha	1.0 L/ha	1.5 L/ha	1 N
Winter wheat – Efficacy trials, all reference products					
Maritime EPPO zone	12	6.98 (3.1-9.9)	112 (103-133)	112 (100-136)	115 (100-139)
North-east EPPO zone	4	6.79 (5.28-7.48)	107 (104-112)	109 (104-11)	108 (102-116)
South-east EPPO zone	4	5.16 (4.25-6.11)	106 (104-109)	105 (102-109)	106 (100-112)
Mediterranean EPPO zone	1	6.78	102	107	121

Table 3.4-6: Yield – Maritime, North-east and Mediterranean: Crop yield of winter wheat treated with Boscalid 23.3% + Difenoconazole 6.6% SC two applications, as % of untreated (Untreated = 100%), selectivity trials

Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:	
		Mean (min-max)	% relative, compared to untreated (min-max, no. of trials)			
		t/ha	1.5 L/ha	3.0 L/ha	1 N	2 N
Winter wheat – Selectivity trials, all reference products						
Maritime EPPO zone	2	8.37 (8.34-8.4)	102 (100-104)	102 (101-102)	98 (94-102)	105 (104-106)
North-east EPPO zone	3	8.19 (7.35-8.9)	103 (95.6-107)	104 (99.7-109)	106 (92.5-120)	114 (110-117)
Mediterranean EPPO zone	1	9.08	115	118	122	123

Neither Boscalid 23.3% + Difenoconazole 6.6% SC nor the boscalid + difenoconazole co-formulated reference product significantly affected the yield when applied at a dose rate similar to the proposed dose rate (1.5 L/ha) in any of the ~~27~~ 28 trials. Rather, overall Boscalid 23.3% + Difenoconazole 6.6% SC provided an increase in the yielded mass of the treated crop which is most likely as a consequence of the disease control in the efficacy and selectivity trials as presented in Section 3.2.3. The results obtained in the trials supports the label claim that Boscalid 23.3% + Difenoconazole 6.6% SC is safe to be applied at the recommended dose rate to winter wheat at the recommended number of applications.

3.4.2.3 Conclusion

Boscalid 23.3% + Difenoconazole 6.6% SC applied at the proposed dose rate, at a range of growth stages within or occasionally beyond the label recommended range, in winter wheat did not affect crop yield nor the quality of the crop yield significantly in any of the ~~27~~ 28 trials harvested. In all efficacy trials, Boscalid 23.3% + Difenoconazole 6.6% SC applied at dose rates higher than the recommended rate did not significantly affect the crop yield.

Furthermore, the data obtained in trials harvested demonstrate that Boscalid 23.3% + Difenoconazole 6.6% SC is as safe to the crop as the reference products used in the trials.

For recommendations on the label not sufficiently supported with trials harvested, the applicant wishes to bridge to the trials conducted in winter wheat where harvest data demonstrated the safe use following application of Boscalid 23.3% + Difenoconazole 6.6% SC as recommended. Furthermore, the data presented in this BAD also clearly demonstrates that the efficacy and crop safety of Boscalid 23.3% + Difenoconazole 6.6% SC is equivalent to the standard boscalid + difenoconazole co-formulated product to which it was compared. The applicant therefore wishes to cite the original registrant's data on boscalid

and difenoconazole now out of protection in support of those recommendations on the draft label that are not adequately supported by the applicant's data and requests that the Zonal Evaluator extrapolate from those data.

Comments of zRMS:	The data obtained in trials harvested demonstrate that CIAZ (product code: SHA 7216A) is as safe to the crop as the reference products used in the trials. Based on this submitted data and on the expert knowledge about boscalid and difenoconazole it can be concluded to accept the data provided by the Applicant.

3.4.2.4 Relationship between phytotoxicity and yield

No adverse effects were observed in ~~27~~ 28 efficacy and 7 selectivity trials in which crop yields were assessed. The adverse effects were observed in winter wheat.

No significant reductions in crop yield were recorded in any of the plots treated with Boscalid 23.3% + Difenoconazole 6.6% SC at dose rates representative of the recommended dose rate.

Comments of zRMS:	ZRMs agree with Applicant. CIAZ (product code: SHA 7216A) applied at dose recommended did not significantly affect the crop yield Also, no phytotoxic symptoms were present in trials. Based on this submitted data and on the expert knowledge about boscalid and difenoconazole it can be concluded to accept the data provided by the Applicant.

3.4.3 Effects on the quality of plants or plant products (KCP 6.4.3)

~~Twenty-seven~~ Twenty-eight efficacy trials treated with Boscalid 23.3% + Difenoconazole 6.6% SC were harvested and yields recorded. Besides recording yield, assessments were also carried out on the potential impact of treatment on a range of quality parameters including moisture content, hectolitre weight and thousand grain weight.

Winter wheat

The results obtained from assessments on the quality of the harvested winter wheat grains are presented in Table 3.4-7 and

Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, Mediterranean EPPO zone					
Moisture content (%)	1	12.9	97.7	101	103
HectoLitre weight (kg)	1	77.9	101	101	102
Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, Maritime EPPO zone					
Moisture content (%)	13	12.6 (11.5-15.3)	102.2 (99-105)	102.7 (99.8-107)	101.5 (95-108)
HectoLitre weight (kg)	13	77.4 (70.9-82.7)	101.5 (99.7-104)	101.7 (100-103)	101.8 (100-104)
Thousand grain weight (g)	10	43.2 (34.4-50.0)	104.7 (100-110.7)	105.2 (100-111.4)	107.0 (100-112)

Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, South-east EPPO zone					
Moisture content (%)	4	14.1 (13.8-14.3)	98 (97-99)	99 (98-101)	99 (97-100)
HectoLitre weight (kg)	4	75.3 (69.9-79.4)	100 (99.0-101)	101 (100-101)	100 (99-101)
Thousand grain weight (g)	4	34.5 (26.5-38.4)	102 (100-104)	102 (100-103)	102 (100-104)
Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, North-east EPPO zone					
HectoLitre weight (kg)	4	78.1 (76.7-79.4)	101 (101-101)	101 (101-101)	101 (100-101)
Thousand grain weight (g)	4	45.57 (42.66-48.83)	103 (101-104)	104 (103-106)	103 (101-106)

Table 3.4-8.

Table 3.4-7: Quality of Yield – Maritime, North-east, South-east and Mediterranean zone: Quality of harvested winter wheat grains – crop treated with Boscalid 23.3% + Difenoconazole 6.6% SC with one or two applications in efficacy trials, as % of untreated (Untreated = 100%)

Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, Mediterranean EPPO zone					
Moisture content (%)	1	12.9	97.7	101	103
HectoLitre weight (kg)	1	77.9	101	101	102
Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, Maritime EPPO zone					
Moisture content (%)	13	12.6 (11.5-15.3)	102.2 (99-105)	102.7 (99.8-107)	101.5 (95-108)
HectoLitre weight (kg)	13	77.4 (70.9-82.7)	101.5 (99.7-104)	101.7 (100-103)	101.8 (100-104)
Thousand grain weight (g)	10	43.2 (34.4-50.0)	104.7 (100-110.7)	105.2 (100-111.4)	107.0 (100-112)
Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, South-east EPPO zone					
Moisture content (%)	4	14.1 (13.8-14.3)	98 (97-99)	99 (98-101)	99 (97-100)
HectoLitre weight (kg)	4	75.3 (69.9-79.4)	100 (99.0-101)	101 (100-101)	100 (99-101)
Thousand grain weight (g)	4	34.5 (26.5-38.4)	102 (100-104)	102 (100-103)	102 (100-104)
Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:
			% relative, compared to untreated (min-max, no. of trials)		
		Mean (min-max)	1.0 L/ha	1.5 L/ha	1.0 L/ha
Winter wheat – Efficacy trials, North-east EPPO zone					
HectoLitre weight (kg)	4	78.1 (76.7-79.4)	101 (101-101)	101 (101-101)	101 (100-101)
Thousand grain weight (g)	4	45.57 (42.66-48.83)	103 (101-104)	104 (103-106)	103 (101-106)

Table 3.4-8: Quality of Yield – Maritime, North-east and Mediterranean zone: Quality of harvested winter wheat grains – crop treated with Boscalid 23.3% + Difenoconazole 6.6% SC with one or two applications in selectivity trials, as % of untreated (Untreated = 100%)

	No. of	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:	Ref. prod. at:

Crop, trial type	trials		% relative, compared to untreated (min-max, no. of trials)			
		Mean (min-max)	1.5 L/ha	3.0 L/ha	1 N	2 N
Winter wheat – Efficacy trials, Mediterranean EPPO zone						
Moisture content (%)	1	15.4	99.3	98.7	100	100
Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:	
			% relative, compared to untreated (min-max, no. of trials)			
		Mean (min-max)	1.5 L/ha	3.0 L/ha	1 N	2 N
Winter wheat – Efficacy trials, Maritime EPPO zone						
Moisture content (%)	2	12.8 (12.0-13.5)	102 (101-102)	102 (102-103)	102 (102-102)	102 (100-104)
HectoLitre weight (kg)	3	65.9 (58.1-77.8)	102 (95.9-110)	102 (97.5-108)	100 (95.0-106)	103 (97.0-112)
Thousand grain weight (g)	2	34.9 (26.5-43.2)	106 (102-110)	108 (103-113)	111 (105-117)	112 (105-118)
Crop, trial type	No. of trials	Untreated	Boscalid 23.3% + Difenoconazole 6.6% SC at:		Ref. prod. at:	
			% relative, compared to untreated (min-max, no. of trials)			
		Mean (min-max)	1.5 L/ha	3.0 L/ha	1 N	2 N
Winter wheat – Efficacy trials, North-east EPPO zone						
HectoLitre weight (kg)	3	76.5 (75.6-77.9)	101 (99.7-101)	101 (101-102)	102 (101-102)	103 (101-104)
Thousand grain weight (g)	3	42.6 (38.48-47.1)	104 (101-102)	105 (101-103)	109 (102-102)	115 (100-104)

In the trials evaluated, Boscalid 23.3% + Difenoconazole 6.6% SC had no detrimental effect on the quality parameters assessed on the harvested winter wheat grains. When comparing the results obtained with Boscalid 23.3% + Difenoconazole 6.6% SC against the results obtained with the reference product at comparable dose rates, both products performed statistically similar on all quality parameters assessed.

3.4.3.1 Conclusion

Boscalid 23.3% + Difenoconazole 6.6% SC applied at the proposed dose rate, at a range of growth stages within or occasionally beyond the label recommended range, did not affect the quality of the harvested crop significantly in the any of the ~~27~~ 28 trials taken to harvest. In all efficacy and selectivity trials, Boscalid 23.3% + Difenoconazole 6.6% SC applied at the recommended dose rate did not significantly affect the quality of the harvested crop either.

As this document clearly demonstrates, the efficacy and crop safety of Boscalid 23.3% + Difenoconazole 6.6% SC is equivalent to the standard reference product to which it was compared. The applicant therefore wishes to cite the original registrant's data on boscalid and difenoconazole now out of protection in support of those recommendations on the draft label that are not adequately supported by the applicant's data and requests that the Zonal Evaluator extrapolate from those data.

Comments of zRMS:	ZRMs agree with Applicant. CIAZ (product code: SHA 7216 A) applied at dose recommended did not significantly affect the quality of crop yield Also, no phytotoxic symptoms were present in trials. Based on this submitted data and on the expert knowledge about boscalid and difenoconazole it can be concluded to accept the data provided by the Applicant.

3.4.4 Effects on transformation processes (KCP 6.4.4)

Processing can include physical processing such as milling of cereals. It has already been shown in section**Błąd! Nie można odnaleźć źródła odwołania.** that the application of Boscalid 23.3% + Difenoconazole 6.6% SC at the proposed label rate and rates above this rate has no negative effect on the quality parameters assessed in efficacy trials harvested.

Other processes depend on biological activity and are referred to as 'transformation'. These include e.g. brewing and baking and are potentially sensitive to plant protection products. Fungicides are usually only considered with regards to their potential effect on transformation processes if applied close to harvest (EPPO standard PP 1/243(1) *Effects of plant protection products on transformation processes*). It is also

the case that if residues cannot be detected at harvest (dRR Part B Section 4) then it is reasonable to assume that the likelihood of an effect on transformation processes is greatly reduced.

Finally, it should be noted that currently, boscalid as well as difenconazole containing products do not have any label restrictions concerning their use on crops destined for processing. In addition, both actives are part of many products which have been used for a long time as fungicide in e.g. cereals. Since the market introduction, no effects on transformation processes have been recorded for any of these products.

Comments of zRMS:	Evaluator agrees with Applicant. Argumentation on impact on "transformation procedure" is deemed sufficient. Data should be submitted according to the requirements of the EPPO Standard PP 1/243(2). No studies were submitted by the applicant. Due to this fact the restriction may be considered to be put on the label. e.g. Effects on transformation processes should be consulted with the authorization holder. However, in the opinion of Evaluator on the basis on information's that no cases of negative influences on parameters influencing the processing procedure were reported, so lack of special studies is accepted. In addition, as CIAZ (product code: SHA 7216 A) is not applied close to harvest, in line with the EPPO guideline PP 1/135, no further data are required in the opinion of Evaluator.

3.4.5 Impact on treated plants or plant products to be used for propagation (KCP 6.4.5)

Boscalid 23.3% + Difenoconazole 6.6% SC is composed of boscalid and difenoconazole, which both have been widely used for several years on e.g. cereals, without identifying any issues in regard to ability of grains of treated plants to germinate.

Thus, negative effects of the two active ingredients on parts of plant used for propagating purposes can be excluded due to the fungicidal nature of the product. Furthermore, phytotoxicity assessments in the performed trials demonstrated the crop safetyness of the product and the absence of any negative effect on the plants or plant products in the vast majority of the trials.

The product complies with the Uniform Principles.

Comments of zRMS:	Submission of data is not considered to be required due to the fungicidal nature of the product (EPPO guideline PP 1/135(3)). Data on plant parts used for propagating purposes are not considered to be required in terms of fungicides being applied to crops that are propagated by cuttings, runners and bulbs or corms. **In conclusion, no negative influence of the product CIAZ (product code: SHA 7216 A) on propagating purposes is to be expected when applied at the intended dose rate and used according to the label recommendations.**

3.5 Observations on other undesirable or unintended side-effects (KCP 6.5)

3.5.1 Impact on succeeding crops (KCP 6.5.1)

Not relevant.

The impact on succeeding crops is determined in accordance with guidance provided by EPPO standard PP 1/207(2) *'Effect on succeeding crops'*.

3.5.1.1 Boscalid

The EU requirements on plant protection products requires, that sufficient data must be reported to permit an evaluation of possible adverse effects of a treatment with the plant protection product on succeeding crops if studies and evaluations presented in the other part of the dossier, show that significant residues of the active substance, its metabolites or degradation products, which have or may have biological activity on succeeding crops, remain in soil or in plant materials up to sowing or planting time of possible succeeding crops.

Results according to Additional Report to DAR of Boscalid, point B.7.9., Published on November 08, 2002, shows the results of the report made by Hamm RT, Veit P. 2001 in Germany for Boscalid residues levels in succeeding crops.

Material and methods

The test compound was applied, as an acetonic solution to the surface of a bare, loamy sand soil at an application rate equivalent to 2100 g as/ha. After application, the soil was aged for 30 days (simulating an emergency plant back; 30 DAT), 120 days, 270 days and 365 days. After 30 days, ploughing was simulated by mixing the treated and untreated soil layers (about 20 cm). Afterwards, the crops: radish, lettuce and wheat were sowed or planted and grown either in growth chambers, where natural climatic conditions were simulated, or in a vegetation hall or in a green house.

After each harvest, the top layer of 20 cm was digged up again and the next plants were sowed or planted correspondent to the ageing periods. The roots of wheat and lettuce remained in the soil after harvest.

Food and feed items of mature crops were harvested, processed and analysed by combustion and subsequent radioactivity measurement for the determination of the total radioactive residues in the raw agricultural commodities (RAC's). In addition soil samples were taken after application, ploughing and after each harvest of mature crops.

The total radioactive residues (TRR) of each sample were determined by combustion analysis. All samples were extracted with methanol and in some cases an additional aqueous ammonia extraction was added. The remaining post extraction solids from the wheat matrices: forage, straw and grain and in addition from radish leaf and root (diphenyl label, 120 DAT) were treat-ed with sodium hydroxide or DMSO to release part of the remaining radioactivity. Methanol extracts of all samples under investigation were analysed by HPLC.

Soil

The total radioactive residues in soil (see Table 3.5-1) after ageing and ploughing decreased at longer ageing intervals. After the 1st ageing period (30 DAT), the TRR level in the diphenyl treated soil was higher than in the pyridine treated soil (1.112 to 0.716 mg/kg) but the levels were close after an ageing interval of 365 days (0.429 to 0.356 mg/kg).

The TRR levels in soils after harvest varied within the crops and the plant back intervals. A tendency could not be detected. Soils after harvest were extracted with methanol and analysed by HPLC. Only parent was detected.

Table 3.5-1: Total radioactive residues in soil samples after treatment with ^{14}C-boscalid (pyridine and diphenyl label)

Soil Samples	**Pyridine label** TRR [mg/kg]	**Diphenyl label** TRR [mg/kg]
After application		
Plant back intervals (after soil ageing, ploughing)		
30 DAT	0.716	1.112
120 DAT	0.648	0.813
270 DAT	0.647	n.d.
365 DAT	0.356	0.429
After harvest of ripe crops		
Plant back interval: 30 DAT		
Radish	n.d.	0.731
Lettuce	0.545	0.747
Wheat	0.379	0.393
Plant back interval: 120 DAT		
Radish	0.548	0.585
Lettuce	0.484	0.409
Wheat	0.386	0.506
Plant back interval: 270 DAT		
Radish	0.377	0.521
Lettuce	0.321	0.436
Wheat	0.537	0.551
Plant back interval: 365 DAT		
Radish	n.d.	0.460
Lettuce	n.d.	0.434
Wheat	0.125	0.343

n.d. = not determined

Metabolism

The methanol extractable ^{14}C-residues were characterised by different HPLC methods. In all extracts, the most prominent peak was ^{14}C-boscalid.

In *lettuce*, the ^{14}C-boscalid concentration ranged from 0.014 – 0.072 mg/kg/ 55.6 – 94.1 % TRR for the both labels. One higher value was detected after 120 days of soil ageing for the pyridine label at 0.146 mg/kg. One polar peak at low concentrations was detected in both labels.

In *radish root*, the concentration of ^{14}C-boscalid varied between 0.009 - 0.091 mg/kg (52.6 – 92.8 % TRR) for both labels. In addition, the metabolite M510F61, a sugar conjugate of the parent compound, was detected in a concentration of ≤ 0.006 mg/kg (diphenyl label) after a soil ageing period of 120 and 365 days and a polar peak was detected.

In *radish leaves* the concentration of ^{14}C-boscalid varied between 0.088 to 0.304 mg/kg for both labels. The metabolite M510F61 was found in most of the radish leave samples (0.004 – 0.032 mg/kg; with the highest values for the diphenyl label). Additionally, in the sample at 120 DAT of the diphenyl label a polar peak in a concentration of 0.039 mg/kg / 13.2% TRR was found.

In *wheat straw*, the concentration of ^{14}C-boscalid varied between 0.808 to 3.156 mg/kg (50.0 – 87.5 % TRR) for the pyridine label and between 1.088 – 7.991 mg/kg (70.8 – 84.6 % TRR) for the diphenyl label. In addition, the metabolite M510F61 was detected in a concentration of ≤ 0.117 mg/kg for the pyridine label and with a concentration of 0.025 – 0.423 mg/kg for the diphenyl label. At plant back intervals of 270 DAT and 365 DAT two peaks were detected in concentrations of ≤ 0.032 mg/kg / 2.0 % TRR (pyridine label) and 0.140 – 0.174 mg/kg / 5.4 –10.0 % TRR (diphenyl label).

In *wheat grain*, the concentration of ^{14}C-boscalid ranged from 0.005 to 0.015 mg/kg for the pyridine label and from 0.008 – 0.028 mg/kg for the diphenyl label. The metabolite M510F61 was not detected in grain. A polar peak amounted to ≤ 0.010 mg/kg (≤ 3.8% TRR) for both labels.

Table B.3.5-1: Investigation of the nature of the residues in rotational crops after treatment with pyridine labelled ^{14}C-boscalid

Crop parts	TRR	ERR	RRR	Boscalid	M510F61	Unidentified Metabolites		
	mg/kg	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)		mg/kg	% TRR
Plant back interval: 30 DAT								
lettuce leaf	0.035	0.028 (81.2)	0.007 (18.8)	0.020 (58.5)	-	1 peak	0.008	22.7%
radish leaf	0.343	0.317 (92.2)	0.027 (7.8)	0.301 (87.6)	0.016 (4.6)		-	
radish root	0.048	0.039 (80.7)	0.009 (19.3)	0.030 (62.7)	-	1 peak:	0.009	18.0%
wheat forage	0.690	0.643 (93.2)	0.047 (6.8)	0.619 (89.8)	0.024 (3.4)		-	
wheat straw	3.609	3.258 (90.3)	0.351 (9.7)	3.156 (87.5)	0.102 (2.8)		-	
wheat grain	0.147	0.017 (11.7)	0.130 (88.3)	0.009 (6.1)	-	2 peaks:	0.006 0.003	3.8% 1.8%
Plant back interval: 120 DAT								
lettuce leaf	0.161	0.146 (90.8)	0.015 (9.2)	0.146 (90.8)	-		-	
radish leaf	0.211	0.187 (88.8)	0.024 (11.2)	0.172 (81.8)	0.015 (7.0)		-	
radish root	0.038	0.031 (81.6)	0.007 (18.4)	0.023 (60.1)	-	1 peak:	0.008	21.5%
wheat forage	0.433	0.379 (87.5)	0.054 (12.5)	0.379 (87.5)	-		-	
wheat straw	4.008	2.715 (67.7)	1.293 (32.3)	2.598 (64.8)	0.117 (2.9)		-	
wheat grain	0.285	0.025 (8.9)	0.260 (91.1)	0.015 (5.3)	-	1 peak:	0.010	3.6%
Plant back interval: 270 DAT								
lettuce leaf	0.031	0.023 (74.5)	0.008 (25.5)	0.020 (65.1)	-	1 peak:	0.003	9.4%
radish leaf	0.125	0.108 (86.1)	0.017 (13.9)	0.104 (82.5)	0.004 (3.6)		-	
radish root	0.017	0.013 (77.1)	0.004 (22.9)	0.009 (52.6)	-	1 peak:	0.004	24.5%
wheat forage	0.230	0.224 (97.3)	0.006 (2.7)	0.214 (92.8)	0.005 (2.3)	1 peak	0.005	2.2%
wheat straw	1.614	0.911 (56.4)	0.703 (43.6)	0.808 (50.0)	0.071 (4.4)	1 peak:	0.032	2.0%
wheat grain	0.271	0.011 (4.0)	0.260 (96.0)	0.005 (1.9)	-	1 peak:	0.006	2.1%
Plant back interval: 365 DAT								
lettuce leaf	0.022	0.017 (76.1)	0.005 (23.9)	0.014 (61.6)	-	1 peak:	0.003	14.5%

Crop parts	TRR	ERR	RRR	Boscalid	M510F61	Unidentified Metabolites		
	mg/kg	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)		mg/kg	% TRR
radish leaf	0.113	0.103 (91.1)	0.010 (8.9)	0.088 (78.2)	0.013 (11.2)	1 peak:	0.002	1.7%
radish root	0.066	0.060 (91.0)	0.006 (9.0)	0.060 (91.0)	-		-	
wheat forage	0.255	0.213 (83.5)	0.042 (16.5)	0.191 (74.7)	0.008 (2.9)	2 peaks:	0.005 0.010	1.8% 4.0%
wheat straw	1.925	1.488 (77.3)	0.437 (22.7)	1.488 (77.3)	-		-	
wheat grain	0.148	0.010 (6.8)	0.138 (93.2)	0.006 (4.2)	-	1 peak:	0.004	2.6%

Table B.3.5-2: Investigation of the nature of the residues in rotational crops after treatment with diphenyl labelled ^{14}C-boscalid

Crop parts	TRR	ERR	RRR	Boscalid	M510F61	Unidentified Metabolites		
	mg/kg	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)		mg/kg	% TRR
Plant back interval: 30 DAT								
lettuce leaf	0.050	0.047 (93.8)	0.003 (6.2)	0.047 (93.8)	-		-	
radish leaf	0.337	0.324 (96.1)	0.013 (3.9)	0.304 (90.2)	0.020 (5.9)		-	
radish root	0.072	0.067 (93.1)	0.005 (6.9)	0.064 (89.6)	-	1 peak:	0.003	3.5%
wheat forage	1.575	1.504 (95.5)	0.071 (4.5)	1.472 (93.5)	0.032 (2.0)		-	
wheat straw	9.826	8.414 (85.6)	1.412 (14.4)	7.991 (81.3)	0.423 (4.3)		-	
wheat grain	0.166	0.031 (18.4)	0.135 (81.6)	0.028 (16.8)	-	1 peak:	0.003	1.6%
Plant back interval: 120 DAT								
lettuce leaf	0.084	0.075 (89.2)	0.009 (10.8)	0.072 (85.2)	-	1 peak:	0.003	4.0%
radish leaf	0.294	0.248 (84.4)	0.046 (15.6)	0.209 (71.2)	-	1 peak:	0.039	13.2%
radish root	0.052	0.041 (78.7)	0.011 (21.3)	0.035 (67.8)	0.006 (10.9)		-	
wheat forage	0.980	0.867 (88.5)	0.113 (11.5)	0.846 (86.4)	0.021 (2.1)		-	
wheat straw	3.912	3.498 (89.4)	0.414 (10.6)	3.311 (84.6)	0.187 (4.8)		-	
wheat grain	0.243	0.030 (12.3)	0.213 (87.8)	0.023 (9.6)	-	1 peak:	0.007	2.7%
Plant back interval: 270 DAT								
lettuce leaf	0.067	0.063 (94.1)	0.004 (5.9)	0.063 (94.1)	-		-	
radish leaf	0.150	0.141	0.009	0.109	0.032		-	

Crop parts	TRR	ERR	RRR	Boscalid	M510F61	Unidentified Metabolites		
	mg/kg	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)	mg/kg (% TRR)		mg/kg	% TRR
		(94.3)	(5.7)	(73.1)	(21.2)			
radish root	0.098	0.091 (92.8)	0.007 (7.2)	0.091 (92.8)	-		-	
wheat forage	0.562	0.496 (88.3)	0.066 (11.7)	0.352 (62.8)	0.102 (18.1)	2 peaks:	0.024 0.018	4.2% 3.3%
wheat straw	3.226	2.487 (77.1)	0.739 (22.9)	2.283 (70.8)	0.030 (0.9)	1 peak:	0.174	5.4%
wheat grain	0.023	0.008 (35.4)	0.015 (64.6)	0.008 (35.4)	-		-	
Plant back interval: 365 DAT								
lettuce leaf	0.028	0.018 (62.8)	0.010 (37.2)	0.016 (55.6)	-	1 peak:	0.002	7.2%
radish leaf	0.207	0.197 (95.2)	0.018 (4.8)	0.144 (69.4)	0.032 (15.5)	2 peaks:	0.018 0.004	8.5% 1.7%
radish root	0.030	0.027 (89.9)	0.003 (10.1)	0.024 (78.4)	0.001 (4.0)	1 peak:	0.002	7.5%
wheat forage	0.265	0.247 (93.1)	0.018 (6.9)	0.199 (75.0)	0.026 (9.8)	1 peak:	0.002	8.3%
wheat straw	1.404	1.253 (89.3)	0.151 (10.7)	1.088 (77.6)	0.025 (1.8)	1 peak:	0.140	10.0%
wheat grain	0.048	0.012 (25.1)	0.036 (74.9)	0.011 (23.6)	-	1 peak:	0.001	1.5%

Conclusion

This study was conducted with an application rate of 2.1 kg as/ha to bare soil. The application rate according to GAP is 2 x 500 g as/ha for beans and peas.

With the exception of wheat grain the major part of the residues in all other matrices was identified as parent. The concentrations of boscalid were relatively low in lettuce leaf (0.014 – 0.072 mg/kg, one sample = 0.146 mg/kg) and radish root (0.009 – 0.09 mg/kg). Higher residues were found in radish leaves (0.09 – 0.30 mg/kg) and wheat forage (0.19 – 1.47 mg/kg) and very high residues in wheat straw (0.81 – 7.99 mg/kg).

In wheat grain, the concentration of parent was low (≤ 0.028 mg/kg). The greater portion of the TRR were non extractable residues and part of these radioactive residues, especially for the pyridine label, could be detected in the starch fraction (36.2 – 48.4 % TRR for pyridine label, 0.6 – 4.3 % TRR for diphenyl label). Ammonia solubility of the residual residues in wheat grain was in the range of 12.9 – 22.9 % TRR.

Besides parent one metabolite (M510F61) could be identified in low concentrations in radish leaves/roots and in wheat straw/forage. This metabolite was a sugar conjugate of the parent compound.

Although only some of the lettuce leaf and radish root samples exceed the LOQ of the enforcement method (0.05 mg/kg) which could be assigned to an exaggerated application rate, significantly higher levels were found in radish leaves and wheat forage and very high levels in straw even after plant back intervals of 270 and 365 days. This indicates that residues of boscalid could occur above the LOQ of 0.05 mg/kg in edible parts of other crops than investigated.

3.5.1.2 Difenoconazole

As per the peer review for difenoconazole (EFSA Journal 2011; 9(1):1967), average DT_{50} in the laboratory is 130 days (range 53-456 days, n=10) and in the field, average DT_{50} is 92 days (range 20-265 days, n=9). In the same field trials, conducted in Germany and Switzerland, the geometric mean of DT_{90} was 305 days (range 68-879, n=9). Data from soil dissipation studies where difenoconazole was applied using spray application at ≤500 g/ha (conducted in Germany (4) and Switzerland (1)) demonstrated that the average DT_{50} in the field, when using the geometric mean, was 53 days (range 22-83 days, n=5). The persistence of the two principal metabolites (CGA 205375 and CGA 71019) are considered to be medium to high (DT_{50} range: 83-152) and low to moderate (DT_{50} range: 6-12 days), respectively.

Since field DT_{50} > 3 months and field DT_{90} > 1 year were observed, soil accumulation studies with annual applications were provided in the DAR (Section 8.1.7, Volume 3, Annex B.8, pp 163 (2006). One 3-year study on bare soil and winter wheat in the UK considered as supplementary, one 10-year study on plot with crop rotation in Switzerland, one 4-year study in apple orchard in northern Italy, and finally a 4-year study on sugarbeet in Italy. Based on the available data, difenoconazole or the two principal metabolites (CGA 205375 and CGA 71019) are not expected to accumulate in soil following normal agricultural practice. No indication of accumulation in soil was indicated by the study in the UK following application to wheat at 75 or 150 g ai/ha. After application to bare soil, low residues (up to 0.05 mg/kg) remaining from the previous season were found but the residues after the 3rd treatment were not different to the first year. However, measurements were limited to the 0-10 cm soil section in this study and the results are only used as support to other studies. The long-term study on field crops in Switzerland, usually with applications of 125 g ai/ha each year, gave no indication of accumulation of difenoconazole, CGA 205375 or CGA 71019 to a soil depth of 30 cm. In the last year, analyses were done on samples to a depth of 60 cm with no residues of these compounds above LOD. However, there was an indication of potential accumulation of total, including bound, 1,2,4-triazole residues since up to 0.009-0.010 mg/kg were found immediately before application of difenoconazole. Since the majority of the residues are likely to be bound to the soil matrix and hence expected to be bioavailable only to a limited degree, these residues are not considered as an area of concern. In the Italian study with annual applications of 2 x 62.5 g ai/ha to an apple orchard, residues remaining from the previous season were only measurable in the second out of four years, at 0.01 mg/kg in soil (inter as well as intra rows). Finally, the Italian study with applications of 3 x 75 g ai/ha to sugarbeets gave no indication of accumulation in soil.

In the DAR (Section 7.9, Volume 3, Annex B.7, pp 200 (2006)), the metabolism of difenoconazole in succeeding or rotational crops was evaluated in five studies. In the five available studies, total radioactive residues in rotational crops (wheat, sugarbeet, maize, lettuce, turnips and mustard) planted 62 to 488 days after one application of difenoconazole applied to bare ground at rates of 32.4, 125 and 750 g ai/ha ranged from <0.0001 to 0.34 mg difenoconazole equivalents/kg. Following application equivalent to twice the maximum recommended rate for control of Alternaria spp. in tomatoes (3 x 125 g ai/ha), residues of difenoconazole were below the LOD (<0.02 and <0.05 ng/kg). The exaggerated application rate of 750 g ai/ha represents a worst-case for residues of difenoconazole in rotational crops and in commercial practice, residues of difenoconazole will not be expected in succeeding crops.

In conclusion, considering the application rates proposed and taking into account that a part of the applied substance is intercepted by the treated crops, it is concluded that significant levels of difenoconazole are not expected in rotational crops provided that Boscalid 23.3% + Difenoconazole 6.6% SC is applied according to GAP.

Comments of zRMS:	The zRMS concluded that all presented findings including recommendations for label text are more or less only general and more detailed evaluations are necessary in cMS considering the specific environment conditions agronomic practice and also national requirements. Boscalid and difenoconazole did not cause any symptoms of phytotoxicity. It is not probable that this product would cause damage to succeeding crops at the rec-

	ommended rate. **Difenoconazole**: Half-life, DT_{50}: 26-178 days. The substance is not persistent in soil. Considering the application rates proposed and considering that a part of the applied substance is intercepted by the treated crops, it is concluded that significant levels of difenoconazole are not expected in rotational crops provided that Boscalid 23.3% + Difenoconazole 6.6% SC is applied according to GAP. **Boscalid:** Half-life, DT_{50}: 118 days. Only some of the lettuce leaf and radish root samples exceed the LOQ of the enforcement method (0.05 mg/kg) which could be assigned to an exaggerated application rate, significantly high-er levels were found in radish leaves and wheat forage and very high levels in straw even after plant back intervals of 270 and 365 days. This indicates that residues of boscalid could occur above the LOQ of 0.05 mg/kg in edible parts of other crops than investigated.

3.5.2 Impact on other plants including adjacent crops (KCP 6.5.2)

During the conduct of efficacy trials, no observations about negative or positive effects on other plants or neighbouring crops were reported. Furthermore, in efficacy trials, it was demonstrated that the co-formulation of boscalid and difenoconazole is not phytotoxic to the crop claimed in the GAP.

EPPO guidelines PP1/256(1) is intended to examine whether the active substance of a plant protection product can cause negative effects on crop which would be in contact with that product. Based on the actual drift value calculated with the Ganzelmeier model and on the bio assay results from the Vegetative vigour test, TER values are obtained.

- If the active substance has no activity against plants at the highest doses tested in the bio-assays. Then field trials are unnecessary.
- If the TER values are > 1. Then no further testing is necessary.
- If the TER values are ≤ 1. Damage to the relevant succeeding crop is possible and further field testing is necessary as described in the EPPO guideline.

The maximum individual proposed rate of Boscalid 23.3% + Difenoconazole 6.6% SC is 1.5 L/ha (equivalent to 350 g boscalid/ha and 100 g difenoconazole/ha) and the maximum cumulative application rate per season is 3.0 L/ha (2 x 1.5 L/ha, equivalent to 700 g boscalid/ha and 200 g difenoconazole/ha).

3.5.2.1 Boscalid

Table 3.5-2: PEC-values (mg/ha) (drift) in boscalid – field crops

Distance to adjacent crop (m)	% drift	MAF	Drift test product (mg a.s./ha)
1	2.38	1.7	16184

Table 3.5-3: PEC-values (mg/ha) (drift) in boscalid – fruiting vegetable crops

Distance to adjacent crop (m)	% drift	MAF	Drift test product (mg a.s./ha)
3	6.9	2.3	6348

Table 3.5-4: PEC-values (mg/ha) (drift) in boscalid – orchard crops

Distance to adjacent crop (m)	% drift	MAF	Drift test product (mg a.s./ha)
3	23.96	2.3	110216

Greenhouse studies on vegetative vigour were conducted with the representative formulation BAS 510 01 F, were submitted in DAR. These studies were applied in 3 mono and 3 dicotyledonous species. Applications were made post-emergence. The results obtained will be used to assess the TER and compare it to the trigger value of 1. The values of ER_{50} >3600 g a.s./ha from the 14d post-emergence study are chosen for this risk assessment.

Table 3.5-12: ED50-values (mg a.s./ha) of different test plants for boscaild

Test plant		**EPPO Code**	**ER_{50} Boscalid (mg a.s./ha)**
Common name	**Scientific name (lat.)**		
Carrot	*Daucus carota*	DAUCA	>3600000
Cabbage	*Brassica oleracea*	BRSOX	>3600000
Pea	*Pisum sativum*	PIBSX	>3600000
Corn	*Zea Mays*	ZEAMX	>3600000
Oats	*Avena sativa*	AVESA	>3600000
Onion	*Allium cepa*	ALLCE	>3600000

Greenhouse studies on vegetative vigour were conducted with the representative formulation BAS 500 00 F, were submitted in DAR. These studies were applied in 3 mono and 3 dicotyledonous species. Applications were made post-emergence. The results obtained will be used to assess the TER and compare it to the trigger value of 1. The values of ER_{50} >4800 g a.s./ha from the 14d post-emergence study are chosen for this risk assessment.

These values were used to assess the TER and to compare it to the trigger value of 1.

The risk assessment is based on the "Guidance Document on Terrestrial Ecotoxicology", (SANCO/10329/2002 rev.2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group fruiting vegetables also covers the risk for non-target terrestrial plants from all other intended uses like tomato, artichoke and eggplant.

Table 3.5-13: Assessment of the risk for non-target plants due to the use of boscalid in fruiting vegetables

Intended use	Fruting vegetables			
Active substance/product	Boscalid			
Application rate (g/ha)	3 × 400			
MAF	2.3			
Test species	**ER_{50} (g/ha)**	**Drift rate**	**$PER_{off\text{-}field}$ (g/ha)**	**TER criterion: TER ≥ 1**
Daucus carota *Brassica oleracea* *Pisum sativum* *Zea mays* *Avena sativa* *Allium cepa*	>3600	0.069	63.48	>56.71

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group orchards also covers the risk for non-target terrestrial plants from all other intended uses like stone fruits.

Table 3.5-14: Assessment of the risk for non-target plants due to the use of boscalid in orchards

Intended use	Orchards			
Active substance/product	Boscalid			
Application rate (g/ha)	3 × 200			
MAF	2.3			
Test species	**ER_{50} (g/ha)**	**Drift rate**	**$PER_{off\text{-}field}$ (g/ha)**	**TER criterion: TER ≥ 1**
Daucus carota *Brassica oleracea* *Pisum sativum* *Zea mays* *Avena sativa* *Allium cepa*	>3600	0.2396	110.22	>32.66

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The calculated TER values are higher than trigger of 1 for all crop groups. Therefore, no risk mitigation measures are required.

3.5.2.2 Difenoconazole

In the seedling emergence study and the vegetative vigor study summarized in the DAR (Section 9.9.2, Volume 3, Annex B, part 5/B, B.9, pp. 188 (2006)), 6 representative species (3 dicotyledonous species (sugarbeet, oilseed rape and soybean) and 3 monocotyledonous species (maize, onion and oat)) were tested. In the seedling emergence study, Score 250EC, with 250 g/L difenoconazole, was applied pre-emergence (seedling emergence study) or post-emergence (vegetative vigour study) at four dose rates, i.e. 12.5, 25, 50, 100, 200 and 400 g difenoconazole per hectare. Visual assessments of phytotoxicity, at a scale of 1-9 were carried out after 14 days (seedling emergence study) or 21 days (vegetative vigour study).

The results obtained in these studies are presented in the tables below.

Table 3.5-5: Effects of difenoconazole on seedling emergence assessed 14 days after treatment (DAR B.9.9.2)

Species	Application rate (g formulation/ha)					
	400	200	100	50	25	12.5
Brassica napus	9	9	9	9	9	9
Avena fatua	9	9	9	9	9	9
Beta vulgaris	9	9	9	9	9	9
Zea mays	8	9	9	9	9	9
Glycine max	5	7.5	8	8	8	9
Allium cepa	9	9	9	9	9	9

Table 3.5-6: Effects of difenoconazole on vegetative vigour, assessed 21 days after treatment (DAR B.9.9.2)

Species	Application rate (g formulation/ha)					
	400	200	100	50	25	12.5
Brassica napus	9	9	9	9	9	9
Avena fatua	9	9	9	9	9	9
Beta vulgaris	9	9	9	9	9	9
Zea mays	7.5	8	8	8	8	9
Glycine max	7	8	8.5	8.5	8.5	9
Allium cepa	9	9	9	9	9	9

In the vegetative vigour test, Score 25EC concentrations up to 400 mL/ha caused <50% effect on the growth of those species tested. In the seedling emergence test, five of the six species tested showed less than 50% reduction in emergence/vigour at concentrations up to 400 mL/ha. In the case of *Glycine max*, effects of more than 50% decrease were seen at 400 mL/ha, but <25% effect was seen at 200 mL/ha. With the exception of seedling emergence of *Glycine max*, the EC_{50} is considered to be approximately 400 mL formulation/ha (100 g ai/ha). NOEC could be set to 12.5 mL formulation/ha (3.1 g ai/ha).

The maximum dose rates tested in the two studies is slightly lower than the recommended dose rate, when Azoxystrobin 20% + Difenoconazole 12.5% SC is applied at the max recommended dose rate.

Conclusion

Based on the results of the study cited above, the EC_{50} for *Glycine max* is 100 g ai/ha and for the remaining plant species, the EC_{50} is >100 g difenoconazole/ha.

The recommended use pattern of Azoxystrobin 20% + Difenoconazole 12.5% SC includes a maximum of three applications/season in tomato and leek with a maximum single application rate of 1.0 L/ha, corresponding to 125 g difenoconazole/ha. For the following risk assessment, the potential risk for plants based on the scenarios in off-crop areas has to be discussed.

The maximum off-crop exposure of plants has to be assumed as approx. 3.46 g difenoconazole/ha (2.77% of the maximum individual applied dose at a drift distance of 1m, according to the Ganzelmeier model). Thus, the exposure is more than 28 times less than the lowest EC_{50} for all plant species tested.

Conclusively, any risk to terrestrial non-target plants due to application of the difenoconazole part of Azoxystrobin 20% + Difenoconazole 12.5% SC according to good agricultural practices can be excluded. Precautions to reduce the environmental concentrations resulting from Azoxystrobin 20% + Difenoconazole 12.5% SC applications are not required for the protection of non-target plants.
For further information and guidance on the agronomic risk following an application of difenoconazole at a field rate of 125 g difenoconazole/ha, please refer to Registration Report Part B Section 6: Ecotoxicological studies.

Comments of zRMS:	Statement accepted, an acceptable risk is indicated for terrestrial non-target plants, without any risk mitigation measures, as the respective TER values is >1, as requested in EPPO guideline PP 1/256 for boscalid and any risk to terrestrial non-target plants due to application of the difenoconazole. No further testing required. The zRMS concluded that all presented findings including recommendations for label text are more or less only general and more detailed evaluations are necessary in cMS considering the specific environment conditions agronomic practice and also national requirements. The applicant claims that no impact on other plants including adjacent crops have been reported in the efficacy trials and the risk to non-target plants following the use of boscalid and difenoconazole are considered acceptable. Based on this submitted data and expert knowledge about boscalid and difenoconazole it can be concluded to accept the data provided by the applicant.

3.5.3 Effects on beneficial and other non-target organisms (KCP 6.5.3)

From the experimentation carried out with Boscalid 23.3% + Difenoconazole 6.6% EC in 2016, 2017 and 2019, no problems regarding adverse effects on beneficial organisms were reported.

Special tests to investigate this purpose are not required.

For more information, see the results of the standard ecotoxicological tests being presented in dRR Part B section 6.

The product complies with the Uniform Principles.

Compatibility with current management practices including IPM

This is not an EC data requirement/ not required by Directive 91/414/EEC.

Comments of zRMS:	For detailed consideration of risks to beneficial organisms please see the eco-toxicology section B section 6.

3.6 Other/special studies

No other studies were conducted.

Comments of zRMS:	ZRMs agree

3.7 List of test facilities including the corresponding certificates

The following table gives information about the testing facilities where trials mentioned in this document were conducted. All facilities are certified and the trials were conducted according to GEP guidelines.

Table 3.7-1: List of test facilities

			Year and trial type					
			2016		2017		2019	
Testing facility	**Zone**	**Country**	**Efficacy**	**Selectivity**	**Efficacy**	**Selectivity**	**Efficacy**	**Selectivity**
Winter wheat								
Biofarm s.r.l.	MED	IT	-	-	4	1		
Crop trials Gmbh	MAR	DE	1	-	-	-		
Agrostation	MED	FR	-	-	1	-		
Agrostation	MAR	FR	-	-	4	1		
SGS	MAR	UK	-	-	-	1		
Zkusebni Stanice Trutnov	MAR	CZ	4	1	-	-	1	
Zkusebni Stanice Domaninek	MAR	CZ	-	-	-	-	2	-
Zkusebni Stanice Rymarov	MAR	CZ	-	-	-	-	3	-
Plant-Art	S-E	HU	4	-	-	-		
Institute of plant protection product	N-E	PL	2	1	2	2		
Total, Winter wheat			**11**	**2**	**11**	**5**	**6**	**-**

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	**Title** **Company Report No.** **Source (where different from company)** **GLP or GEP status** **Published or not**	**Vertebrate study Y/N**	Owner
CP 6.0-001	Anonymous	2019	Biological Assessment Dossier: Boscalid 23.3% + Difenoconazole 6.6% SC (233 g/L boscalid + 66 g/L difenoconazole SC) – EU Central zone Sharda Cropchem España -, - Unpublished	N	SHA