Document Title

Tier 2 Summary

KIIA 6 of the Metabolism and Residues Data

for

Iprovalicarb

(Annex I Renewal)

Specification No.

102000006810-05

Data Requirements

EU Commission Regulation No. 1141/2010
on the renewal of the inclusion of AIR2 active substances
in conjunction with Directive 91/414/EEC and Regulation EC/1107/2009

Annex II
Document M
Section 4, Point 6

According to OECD format guidance for industry data submissions on plant protection products and their active substances

Date

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Bayer CropScience

OWNERSHIP STATEMENT

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IIA 6 Metabolism and Residues Data

Iprovalicarb (SZX 0722) is a fungicidal active substance. In early 1998, the original Annex II dossier was submitted to the Irish PCS. In that dossier, two uses were supported with residue trial data: grapes and potatoes.

In this Annex I Renewal ("AIR") dossier, only the "safe use" in grapes will be presented.

IIA 6.1 Stability of residues

IIA 6.1.1 Stability of residues during storage of samples

Original Annex II dossier

In the original Annex II dossier, the storage stability of iprovalicarb was described for grapes and grape juice (representing beverages made of grapes). The results of the respective studies indicated that the compound is stable in deep-frozen samples of the tested plant commodities for at least 1 year.

Studies submitted and evaluated for the first inclusion of iprovalicarb on Annex I (listed in grey typeface):

Report: **KIIA 6.1.1/01, [redacted] 1997**
Title: Deep freezer storage stability of residues of SZX 0722 in fortified samples of grapes
Report No: MR-590/97
Document No: M-000623-01-1
Guidelines: EPA.: Residue Chemistry Test Guidelines OPPTS 860.1380, Storage Stability Data
EU.: Directive 91/414/EEC, Residues in or on treated products, food, or feed
GLP: yes

Report: **KIIA 6.1.1/02, [redacted] 1997**
Title: Deep freezer storage stability of residues of SZX 0722 in fortified samples of grape juice
Report No: CR-591/97
Document No: M-000628-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1380, Storage Stability Data
EU: Directive 91/414/EEC, Residues in or on treated products, food, or feed
GLP: yes

Report: **KIIA 6.1.1/03, [redacted] 1997**
Title: Deep freezer storage stability of residues of SZX 0722 in fortified samples of potatoes
Report No: MR-436/97
Document No: M-000626-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1380, Storage Stability Data
EU: Directive 91/414/EEC, Residues in or on treated products, food, or feed
GLP: yes

"AIR2" process

The storage period from the original studies sufficiently covers the longest period of time for which samples from new field residue trials presented in this AIR2 dossier were stored before analysis. Hence, the results of the storage stability studies validate the residue values obtained from these trials

(cf. chapter 6.3.1) with respect to the stability of iprovalicarb in deep-frozen samples. Therefore, no new data for the Annex I Renewal are presented regarding the storage stability of iprovalicarb in plant matrices, as none are required.

IIA 6.1.2 Stability of residues in sample extracts

The storage stability of residues of iprovalicarb in extracts is routinely tested during method development. Since the validity of the methods is based on and confirmed by factors such as reproducibility for interruption during the work-up process, it can be concluded that the stability of residues in extracts is always guaranteed. (For details, please refer to point KIIA 4.3 of this dossier.) In addition, when conducting analyses of "normal" samples, the entire analytical procedure is monitored by conducting concurrent recoveries with each sample set.

IIA 6.2 Metabolism, distribution and expression of residues

IIA 6.2.1 In plants, at least three crops from three different crop categories

Original Annex II dossier

In the original Annex II dossier, the behavior and metabolism of iprovalicarb was investigated in grapes, potatoes, and tomatoes using [phenyl-UL-^{14}C] -labeled active substance. The studies demonstrated that the metabolic pathway of iprovalicarb is similar in all crops investigated. The rate of degradation on plants is quite low and the parent compound was always the major component, with quantitatively relevant metabolites formed only in potatoes. The metabolism of iprovalicarb proceeded along three pathways, namely:

- hydroxylation/glycosylation of the parent compound at the 4-methyl group on the phenyl ring, followed by further conjugations,
- cleavage at the amide group between the L-valine and PMPA moieties, and
- hydroxylation/glycosylation of the parent compound at the phenyl-ring 3 position.

As the metabolic pathway in potatoes was also evident in rats, the respective potato metabolites were covered by the rat toxicology studies. Therefore, iprovalicarb parent compound is considered to be the only residue of concern.

In separate parallel translocation experiments, it was shown that iprovalicarb, when applied to foliar tissues, is not systemic.

Studies submitted and evaluated for the first inclusion of iprovalicarb on Annex I (listed in grey typeface):

Report: KIIA 6.1.1/01, [redacted] 1996
Title: Metabolism of SZX 0722 in grapes
Report No: PF4159
Document No: M-000041-01-1
Guidelines: EPA: 171-4 Nature of Residue (Metabolism) - Plants
GLP: yes

Report:	**KIIA 6.2.1/02, [redacted] 1997**
Title:	Metabolism of [phenyl-UL-14C]SZX 0722 in tomatoes
Report No:	PF4156
Document No:	M-000017-01-1
Guidelines:	EPA:171-4 Nature of Residue (Metabolism) - Plants
GLP:	yes

Report:	**KIIA 6.2.1/03, [redacted]; 1997**
Title:	Metabolism of [phenyl-UL-14C]SZX 0722 in potatoes
Report No:	PF4157
Document No:	M-000014-01-1
Guidelines:	EPA Guidelines OPPTS 860.1300: Nature of the Residue - Plant European Communities Council Directive 91/414/EEC
GLP:	yes

"AIR2" process

The data from the original submission are regarded as being sufficient. As no new uses of consequence has been developed subsequent to the first submission and as grapes – the AIR2 "safe use" – have already been tested, no new studies are presented for the Annex I Renewal.

However, as the iprovalicarb molecule has "chiral centers" leading to stereoisomerism, the potential impact of this issue with regard to residues of the compound in plants was evaluated in a position document, as follows.

Isomeric composition of iprovalicarb residues in tomato and potato plants:

Report:	**KIIA 6.2.1/04, [redacted] 2011**
Title:	Iprovalicarb - Common metabolism in plants and diastereomeric stability of the original isomeric mixture of the test substance
Report No. & Document No.:	MEF-11/319 M-406914-01-1
Guidelines:	none
GLP:	no (not relevant)

Justification for including this report in this "AIR" dossier: Data facilitates evaluation of dietary risk assessment of iprovalicarb in plant matrices.

Technical iprovalicarb is composed of the two diastereomers *(S,R)* and *(S,S)* at a ratio of approx. 1:1. As the metabolism is caused by enzymes formed of chiral L-amino acids, the metabolic transformations of an isomeric parent substance can, in principle, be impacted stereomerically and the original composition may change. In order to examine this potential influence on the metabolism of iprovalicarb, an analysis of the isomeric composition in plant metabolism studies with tomatoes and potatoes was carried out, based on the available data from those studies.

In tomatoes, evaluation of gas chromatographic data showed that the diastereomeric composition of the iprovalicarb isomers did not change either on the surface or within the tomato fruits. In potatoes, no significant change of the 1:1-diastereomeric composition was observed during a 14-day period

between the last application and the harvest of the potato vines, either for the parent substance or for a hydroxylated metabolite.

The results clearly demonstrate that a "shift" in the diastereomeric composition of iprovalicarb does not take place in plants. Consequently, a scenario in which a shift occurs does not have to be considered in consumer risk assessments.

IIA 6.2.2 Poultry

A metabolism study in laying hens was not considered necessary, as the uses of iprovalicarb did not result in significant residues arising in feed commodities. Also, the AIR2 "safe use" for iprovalicarb and thus the only crop of concern in this dossier – is grapes, which is not a feed item.

IIA 6.2.3 Lactating ruminants (goat or cow)

Original Annex II dossier

The metabolism of iprovalicarb in rats and lactating goats are described in the original Annex II dossier. The following results were presented:

The metabolism and biokinetics study on **rats** showed a high degree of absorption of radioactivity followed by fast elimination from the body. After oral administration of [phenyl-UL-^{14}C]SZX 0722, more than 97.8% of the totally recovered radioactivity was excreted within 48 hours. The major route of elimination was faecal for male rats, comprising approximately 76% of the recovered radioactivity (independent of the dose and frequency of dosings). Female rats excreted about equal amounts of radioactivity with urine and faeces.

Biotransformation to volatile metabolites including carbon dioxide was negligible, i.e. 0.01% of the administered dose.

The main pathway of biotransformation proceeded via oxidation of the methyl group located on the aromatic ring leading to the final carboxylic acid metabolite via the hydroxymethyl-derivative. Some minor metabolites originated from cleavage of the molecule.

According to chromatographic analysis of the excreta, iprovalicarb was metabolised extensively by the rats. Only a small percentage of the parent compound passed through the animal unchanged, accounting for less than 10% of the dose in the low-dose experiments and for 16-21% in the high-dose experiments. Twelve metabolites were identified. The main metabolite was identified as the diastereomer pair of SZX 0722-carboxylic acid (*M03*). This metabolite pair accounted for more than 58% of the administered dose in all tests. Small amounts of eight other metabolites were detected in urine. All of these minor metabolites accounted for less than 2% each and added up to 7% of the administered dose at the most. The radioactive components identified in the rat bile were SZX 0722-carboxylic acid (*M03*) and two conjugates thereof (SZX 0722-carbonylglycine and SZX 0722-carbonyltaurine = *M05* and *M06*, respectively).

The identification rate ranged from about 80% to as much as 90% of the administered radioactivity.

After administration of 10 mg/kg bw on three consecutive days to **lactating goats**, the total radioactive residue of iprovalicarb in tissues, organs and milk amounted to 3.4%; this low figure is a result of the fast elimination kinetics observed. The highest residues were observed in the kidney and liver, the

main excretory and/or metabolizing organs. Very low amounts were secreted with the milk. 69-96% of the TRR was identified in the organs/tissues sampled.

Absorption from the gastrointestinal tract was rapid and nearly complete. Plasma concentrations reached a peak at about 1.6 hours after dosage. The radioactivity was eliminated from the plasma in two phases, characterized by elimination half-lives of about 1 and 11 hours, respectively. The renal excretion rate was high, with a total of about 70.1% of the dose being excreted with the urine over the 54-hour test period. 15% of the dose was excreted with faeces. Only an extremely low amount of the total dose (0.06%) was secreted with the milk.

As in the rat study, the primary residue determined in almost all tissues, organs, or excreta was SZX 0722-carboxylic acid (*M03*), which was formed after hydroxylation and oxidation at the 4-methyl ring position.

Iprovalicarb parent compound was also present in all tissues in considerable amounts, and formed the major residue in fat. Other metabolites were only formed in minor quantities.

SZX 0722-carboxylic acid (*M03*) is thus quantitatively relevant in both the goat and the rat studies, but as it is obviously present in the wide array of rat toxicology tests, and as iprovalicarb itself is also present in all tissues of concern for human consumption in the goat study, the proposed residue definition is parent compound alone.

Studies submitted and evaluated for the first inclusion of iprovalicarb on Annex I (listed in grey typeface):

Report: **KIIA 6.2.3/01, [redacted], 1997**
Title: [Phenyl-UL-^{14}C]SZX 0722: Absorption, distribution, excretion, and metabolism in the lactating goat
Report No: BF 4258
Document No: M-000018-01-1
Guidelines: EPA Pesticide Assessment Guidelines Subdivision O, Residue Chemistry, Series 171-4: Nature of the Residue, Livestock (Ruminant)
EPA 540/9-82-023, October, 1982
GLP: yes

"AIR2" process

The data presented in the original dossier are regarded as being sufficient. Therefore, no new data on the metabolism of iprovalicarb in animals are presented in this AIR2 dossier, as none are required.

IIA 6.2.4 Pigs

Since the metabolism in the rat and in the goat was very similar, no pig metabolism study was conducted. The pattern of metabolites was in good agreement with the rat metabolism studies.

IIA 6.2.5 Nature of residue in fish

Not required by Directive 91/414/EEC.

IIA 6.2.6 Chemical identity

Not required by Directive 91/414/EEC.

IIA 6.3 Residue trials (supervised field trials)

Iprovalicarb (SZX 0722) is a fungicidal active substance. In the Annex II dossier submitted in 1998 for Annex I inclusion, the use of the compound was supported in grapes and in potatoes.

Numerous new studies have since been conducted with iprovalicarb-containing formulations for use in European grapes, which is the "safe use" crop supported in the AIR2 process.

IIA 6.3.1 Grapes

Original Annex II dossier

To clarify the residue behavior of iprovalicarb in grapes, trials were conducted in grapes with the 50 WG straight formulation.

The use pattern for grapes, as shown in chapter 6.3 of the original dossier, was as follows:

Table 6.3.1-1: Use patterns (GAPs) for the spray application of the 50 WG straight formulation in/on grapes in Europe (northern and southern residue regions), as described in the 1998 dossier

Formulation	Region	Application timing	Max. a.s. rate of application (kg/ha)	Max. Σ a.s. rate of application (kg/ha/season)	Max. no. of appls.	PHI (days)
SZX 0722 50 WG	EU-N	pre-flowering	0.18*	1.5	2	28
		post-flowering (10-14 d int.)	0.48*		3	
	EU-S	pre-flowering	0.30	1.5	2	28
		post-flowering (10-14 d int.)	0.30		3	

* Whereas the constant post-flowering product rates are foreseen as the worst case for the use of iprovalicarb in grapes in southern Europe, increasing rates are necessary in the north, particularly in Germany. Prior to bloom, 120-180 g/ha of the active substance will be applied, but 300-480 g/ha will be used after flowering. These rates are based on constant product concentrations and increasing volumes of water (400-600-1000-1400-1600 l/ha).

Over 3 growing seasons, 18 residue trials were conducted in both the northern and southern European residue regions on grapes. Two trials were not performed according to the typical agricultural practice; in the other 16 trials, iprovalicarb was applied in accordance both with the proposed use pattern and with the peculiarities of the cultivation practices used in the trial regions. The results from these 16 trials demonstrate that iprovalicarb residues decline with time, and that some regional differences in the residue levels are apparent.

In general, residue levels at day 28 (=labelled PHI) were somewhat higher in the north than in the south; in bunches, they ranged from 0.31-1.30 mg/kg (median 0.72 mg/kg) and 0.13-0.54 mg/kg (median 0.27 mg/kg), respectively. In grape (berry) samples from 3 northern and 2 southern trials, residue levels were 0.43-0.87 mg/kg (median 0.63 mg/kg) and 0.14-0.36 mg/kg (median 0.25 mg/kg), respectively, somewhat lower than in bunches. This was attributed to surface residues and the relatively high surface area of the stems and stalks which were removed from the grape samples. Based on this residue behaviour, an MRL proposal of 2.0 mg/kg was made.

An EU pMRL of 2 mg/kg was subsequently published in Commission Directive 2003/60/EC, dated 18 June 2003 and in Commission Directive 2004/112/EC, dated 15 December 2004. More recently, EU

temporary MRLs were published for iprovalicarb in the Regulation (EC) no. 149/2008 dated 29 January 2008; for grapes, these tMRLs are the same as the pMRLs published previously.

Studies submitted and evaluated for the first inclusion of iprovalicarb on Annex I (listed in grey typeface):

Report: **KIIA 6.3.1/01, [redacted] 1997**
Title: Determination of residues of SZX 0722 (50 WG) in/on grape following spray application in Spain and Italy
Report No: RA-2140/95
Document No(s): M-000065-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1500 Crop Field Trials
EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report: **KIIA 6.3.1/02;, [redacted] 1997**
Title: Determination of residues of SZX 0722 (50 WG) in/on grape following spray application in Germany and in France
Report No: RA-2139/95
Document No(s): M-000070-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1500 Crop Field Trials
EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report: **KIIA 6.3.1/03, [redacted] 1997**
Title: Determination of residues of SZX 0722 (50 WG) in/on grape following spray application in Portugal, Spain, Italy and France
Report No: RA-2141/96
Document No(s): M-000134-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1500 Crop Field Trials
EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report: **KIIA 6.3.1/04, [redacted] 1997**
Title: Determination of residues of SZX 0722 (50 WG) in/on grape following spray application in Germany and France
Report No: RA-2140/96
Document No(s): M-000127-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1500 Crop Field Trials
EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report: **KIIA 6.3.1/05, [redacted] 1997**
Title: Determination of residues of SZX 0722 (50 WG) in/on grape following spray application in Germany and France
Report No: RA-2127/97
Document No(s): M-000723-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1500 Crop Field Trials
EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report:	**KIIA 6.3.1/06, [redacted] 1997**
Title:	Determination of residues of SZX 0722 (50 WG) in/on grape following spray application in France and Italy
Report No:	RA-2128/97
Document No(s):	M-000717-01-1
Guidelines:	EPA: Residue Chemistry Test Guidelines OPPTS 860.1500 Crop Field Trials EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP:	yes

"AIR2" process

Since the Annex I inclusion, numerous Annex III dossiers have been prepared and submitted for additional combination formulations of iprovalicarb. In grapes grown in the northern and southern European residue regions, iprovalicarb was applied three to eight times as an SC, WP, or WG formulation at a.s. rates of 48-240 g/ha, based on "core" rates of 150 or 120 g a.s./ha. (In trials conducted in the northern European residue region, particularly in Germany, rates were generally adjusted to the typically higher height of the vines used there compared to those in the south.)

The a.s. rates were lower when used in combination than when used as a straight WG, thus it was expected that the resulting residues would be lower than the EU MRL as proposed in the original Annex II dossier and then adopted as a pMRL/tMRL in the EU; this was in fact always the case. Thus, the data were considered to form a "bridge" to the existing EU Annex II dossier.

However, in the meantime, it has been decided not to market the 50 WG. One of the reasons was the concern about possible resistance development. As the use patterns presented with the new combinations in Annex III dossiers differ considerably (>25%) from the one in the original Annex II dossier, the relevant residue data in grapes need to be re-evaluated.

In Table 6.3.1-2, the two standard "core" use patterns for the combination formulations are summarized in general terms.

Table 6.3.1-2: Use patterns (GAPs) for the spray application of iprovalicarb-containing formulations in/on grapes in Europe (northern and southern regions)

Use pattern "core rate"	Region**	Application timing	Max. a.s. rate of application (kg/ha)	Max. no. of appls.	PHI (days)
150 g/ha*	EU-N	pre-flowering	0.09	1	28
		post-flowering (10-14 d int.)	0.15†	4	
	EU-S	pre-flowering	0.09	1	28
		post-flowering (10-14 d int.)	0.15	3-4	
120 g/ha*	EU-N	pre-flowering (10-14 d int.)	0.072	2	28
		post-flowering (10-14 d int.)	0.12†	3	
	EU-S	pre-flowering (10-14 d int.)	0.12	2	28
		post-flowering (10-14 d int.)	0.12	2-3	

* The rate listed here is, in the northern residue region, based on one meter of vine foliage height.

** EU-N = northern EU residue region, EU-S = southern EU residue region

† Whereas the constant product rates are foreseen as the worst case for the use of the formulations in grapes in southern Europe, increased rates are necessary in the north, particularly in Germany. Thus, these rates are expressed as kg/(ha×m); the rate expressed as kg/ha rate is higher on higher vines.

The number of trials conducted for each use described above (incl. information on geographical "residue region" and vegetation period) is summarized below in Table 6.3.1-3.

Table 6.3.1-3: Overview of European residue trials conducted in grapes per geographical region and vegetation period

Formulation	Region	No. of trials Vegetation period 1995	1996	1997	1998	1999	2000	2003	2004	Σ	Report No.: *RA-...*	Dossier ref.: *IIA 6.3.1...*
150 g/ha *"CORE RATE"*												
43.5 WP (& folpet)	EU-N			5						10	2129/97	07
	EU-S			5							2130/97	08
325 SC (& azoxystrobin)	EU-N			5	5					15	2140/97, 2123/98	09, 10
	EU-S			5							2135/97	11
120 g/ha *"CORE RATE"*												
66 WG (& mancozeb)	EU-N	2								4	2141/95	12
	EU-S	2									2142/95	13
66 WP (& mancozeb)	EU-N			3						7	2133/97	14
	EU-S		2	2							2145/96, 2134/97	15, 16
66 WP (& fosetyl-AL& mancozeb)	EU-S				5					5	2122/98	17
43.5 WG (& tolylfluanid)	EU-N		2	3						9	2146/96, 2136/97	18, 19
	EU-S						4				2113/01	20
79 WG (& folpet & fosetyl-AL)	EU-N								2	4	2330/04	21
	EU-SC								2		2331/04	22
24.5 WP (& copper)	EU-N		2	3						13	2142/96, 2131/97	23, 24
	EU-S		4	4							2143/96, 2132/97	25, 26
66 WP (& fenamidone)	EU-S				2	1				3	2186/98, 2186/99	27, 28
44 SC (& fluopicolide)	EU-N							4		8	2429/03	29
	EU-S							4			2430/03	30

EU-N = northern EU residue region, EU-S = southern EU residue region

General remarks:

- *In the this section of the AIR2 dossier, only the residues relevant to iprovalicarb will be described in detail. As the products applied also contained other active substances, residues of those compounds were also determined, but these results are not considered relevant to this dossier. For details on the results for the other compounds, see the study reports or the Tier 1 summary forms.*

► **"SAFE USE" – "150 g core-rate" use pattern**

Iprovalicarb & Folpet WP 43.5 (=SZX 0722 & Folpet 43.5 WP)

Table 6.3.1-4: Use patterns (GAPs) for the spray application of SZX 0722 & Folpet 43.5 WP in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s.* rate of application (kg/ha)	Max. no. of appls.	PHI (days)
SZX 0722 & Folpet 43.5 WP (6.0% iprovalicarb and 37.5% folpet)	EU-N	pre-flowering	1.5	0.09	1	28
		post-flowering (10-14 d int.)	2.5**	0.15**	4	
	EU-S	pre-flowering	1.5	0.09	1	28
		post-flowering (10-14 d int.)	2.5	0.15	4	

EU-N = northern EU residue region, EU-S = southern EU residue region

* This rate refers to iprovalicarb only

** These rates are expressed as "kg/ha per meter foliage ('leaf wall' or leafy surface) height". The maximum absolute amounts to be applied refer to vines with 1.6 m "leafy surface", resulting in post-bloom a.s. rates of 0.24 kg/ha iprovalicarb.

New studies submitted for Annex I Renewal ("AIR2")

Report:	**KIIA 6.3.1/07, [redacted] 1998a**
Title:	Determination of residues of SZX 0722 & Folpet (43.5 WP) in/on grape following spray application in France and Germany
Report No. & Document No.:	RA-2129/97 M-002068-01-1

Report:	**KIIA 6.3.1/08, [redacted] 1998b**
Title:	Determination of residues of SZX 0722 & Folpet (43.5 WP) in/on grape following spray application in France, Portugal and Spain
Report No. & Document No.:	RA-2130/97 M-002066-01-1

Guidelines *(applies to both studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to both studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and to support uses in grapes in the EU.

I. Materials and Methods

Northern European residue region

In northern Europe, a total of 5 trials on grapes were conducted in 1997 (KIIA 6.3.1/07), using SZX 0722 & Folpet 43.5 WP, containing 6.0% iprovalicarb and 37.5% folpet. The trials were

performed in Germany (2) and in France (3). The use pattern as defined for this residue region was based on a set product concentration and water rates of approx. 600 L/ha prior to bloom (1 appl.) and then 1000 L/(ha × m leaf wall height) post-flowering (4 appl.); thus, vines were treated at a worst-case concentration (0.25% in high-volume sprays) and at water rates applicable to the practices common in the countries in which the trials were performed. In this system, while the post-flowering rate per hectare and meter vine height remains constant, the actual amount of product applied in a given trial can vary based on the height of the vines on the test plot, so that varying absolute amounts of product are directly comparable with one another.

Post-blossom sprays were at expected product rates of 4.0 kg/ha in Germany (1.6 m "leaf wall" height) and 2.0-2.5 kg/ha in France (0.8-1.0 m leaf wall), corresponding to 0.24 and 0.12-0.15 kg iprovalicarb/ha, respectively. Spray intervals were 10-14 days in post-blossom spraying. In all trials, vines were treated a total of 6 times (1 pre-/5 post-blossom) instead of 5 (1/4), but this deviation from the nominal worst-case use pattern is within the EU's tolerances for residue trials. (Besides the extra post-blossom spray was at a very early interval, thus having little effect on the final residue levels.) All applications in all studies were at the required rates.

Southern European residue region

In southern Europe, a total of 5 trials on grapes were conducted in 1997 (RA-2130/97). The trials were conducted in Portugal (1), Spain (2), and France (2). SZX 0722 & Folpet 43.5 WP was applied 5 times (1 pre-bloom/4 post-bloom) at rates of 1.5 kg/ha prior to and 2.5 kg/ha subsequent to flowering, equivalent to 0.09 kg/ha (pre-fl.) or 0.15 kg/ha (post-fl.) iprovalicarb a.s. Spray intervals were generally 10-14 days in post-blossom spraying. Water rates were about 600 L/ha (pre-blossom) and 1000 L/ha (post-blossom sprays). All applications in all studies were at the required rates.

All trials

In all trials in the northern and southern European residue regions, bunches of grapes were sampled at days 0 and 28 (PHI) after the last application. At harvest time, additional samples of destemmed grapes (berries) were taken.

The samples were analyzed for iprovalicarb according to method 00442/M003, with a limit of quantitation of 0.05 mg/kg.

II. Findings

Concurrent recoveries of iprovalicarb were obtained from grapes (berries) fortified at levels between 0.05 mg/kg and 2 mg/kg. The sample material was chosen to represent all relevant sample materials collected in these trials. Mean recoveries were all within acceptable ranges (85-95%, RSDs 5.5-8.0%, n=2-8). Details of recovery data are shown in Table 6.3.1-7.

All trials are summarized below in Tables 6.3.1-5 and 6.3.1-6 and in greater detail in the Tier 1 summary forms.

Northern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.26-1.6 mg/kg (median value 1.4 mg/kg). These residues declined to levels of 0.10-1.2 mg/kg (median 0.47) by day 28.

Samples of destemmed grapes (berries) were also taken in the trials. The residues were slightly lower in day-28 samples of grapes alone than those in bunches (0.07-1.1 mg/kg in destemmed grapes [median = 0.38 mg/kg]).

Southern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.13-1.3 mg/kg (median value 0.33 mg/kg). These residues declined to levels of <0.05-0.76 mg/kg (median 0.17) by day 28.

Samples of grapes themselves (destemmed berries) were also taken in the trials. The residues were slightly lower in day-28 samples of grapes alone than in bunches (<0.05-0.66 mg/kg in grapes alone [median 0.13 mg/kg]).

III. Conclusions

Ten residue trials were conducted with SZX 0722 & Folpet 43.5 WP, containing 6.0% iprovalicarb and 37.5% folpet, on grapes, five each in the northern and southern European residue regions. The product was applied in accordance with the proposed use patterns (slight deviations in the northern trials were within EU tolerances), and the tests were carried out according to GLP principles.

The results of trials presented above demonstrate that:

- residue levels of iprovalicarb in grape bunches decline with time, from values of 0.26-1.6 mg/kg (north) or 0.13-1.3 mg/kg (south) on day 0 to 0.10-1.2 mg/kg (north) or <0.05-0.76 mg/kg (south) on day 28. The respective median values were 1.4 and 0.33 mg/kg on day 0, and 0.47 and 0.17 mg/kg on day 28.
- residue values of iprovalicarb in destemmed grapes (berries) on day 28 were slightly lower than those in bunches, with median values of 0.38 and 0.13 mg/kg in the samples from the northern and southern European trials, respectively.
- all residue values for iprovalicarb on day 28 were well below the existing EU MRL for iprovalicarb in grapes (2 mg/kg).

Table 6.3.1-5: Residues of iprovalicarb in/on grapes following applications of SZX 0722 & Folpet (43.5 WP) in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2129/97 70238/2 0238-97 GLP: yes 1997	Grape Sauvignon	France F-[redacted] EU-N	43.5 WP[1]	6	0.090-0.120	0.015	83	bunch	0	0.26
									28	0.10
								berry	**28**	0.07
RA-2129/97 70701/5 0701-97 GLP: yes 1997	Grape Müller-Thurgau	Germany D-[redacted] EU-N	43.5 WP[1]	6	0.090-0.240	0.015	80	bunch	0	1.6
									28	1.2
								berry	**28**	1.1
RA-2129/97 70702/3 0702-97 GLP: yes 1997	Grape Chardon-nay	France F-[redacted] EU-N	43.5 WP[1]	6	0.090-0.150	0.015	83	bunch	0	1.4
									28	0.47
								berry	**28**	0.38
RA-2129/97 70703/1 0703-97 GLP: yes 1997	Grape Portugieser	Germany D-[redacted] EU-N	43.5 WP[1]	6	0.090-0.240	0.015	80	bunch	0	1.4
									28	0.92
								berry	**28**	0.42
RA-2129/97 70705/8 0705-97 GLP: yes 1997	Grape Gamay	France F-[redacted] EU-N	43.5 WP[1]	6	0.090-0.150	0.015	85	bunch	0	1.3
									29	0.45
								berry	29	0.38

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = SZX 0722 & Folpet (43.5 WP), containing 6.0% iprovalicarb and 37.5% folpet

Table 6.3.1-6: Residues of iprovalicarb in/on grapes following applications of SZX 0722 & Folpet (43.5 WP) in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2130/97 70237/4 0237-97 GLP: yes 1997	Grape Periquita	Portugal P-[redacted] EU-S	43.5 WP[1]	5	0.090-0.150	0.015	89	bunch	0	1.3
									28	0.76
								berry	**28**	0.66
RA-2130/97 70644/2 0644-97 GLP: yes 1997	Grape Grenache	France F-[redacted] EU-S	43.5 WP[1]	5	0.090-0.150	0.015	85	bunch	0	0.13
									28	0.05
								berry	**28**	<0.05
RA-2130/97 70645/0 0645-97 GLP: yes 1997	Grape Cabernet Sauvignon	Spain E-[redacted] EU-S	43.5 WP[1]	5	0.090-0.150	0.015	85	bunch	0	0.33
									28	0.17
								berry	**28**	0.13
RA-2130/97 70646/9 0646-97 GLP: yes 1997	Grape Grenache blanc	France F-[redacted] EU-S	43.5 WP[1]	5	0.090-0.150	0.015	85	bunch	0	0.17
									28	<0.05
								berry	**28**	0.05
RA-2130/97 70647/7 0647-97 GLP: yes 1997	Grape Macabeo	Spain E-[redacted] EU-S	43.5 WP[1]	5	0.090-0.150	0.015	84	bunch	0	0.37
									28	0.23
								berry	**28**	0.16

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = SZX 0722 & Folpet (43.5 WP), containing 6.9% iprovalicarb and 37.5% folpet

Table 6.3.1-7: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2129/97	Grape	berry*	iprovalicarb	5	0.05	76	95	85	8.0
70238/2 (0238-97)				8	1.0	85	99	95	5.5
70701/5 (0701-97)				2	2.0	89	91	90	
70702/3 (0702-97)				15	overall	76	99	91	7.6
70703/1 (0703-97)									
70705/8 (0705-97)									
RA-2130/97									
70237/4 (0237-97)									
70644/2 (0644-97)									
70645/0 (0645-97)									
70646/9 (0646-97)									
70647/7 (0647-97)									
GLP: yes									
1997									

* *berry* recoveries also valid for sample material *bunch of grapes*.

Iprovalicarb & Azoxystrobin SC 325 (SZX 0722 & Azoxystrobin 325 SC)

The formulation SZX 0722 & Azoxystrobin 325 SC was applied using the same use pattern with regard to iprovalicarb as SZX 0722 & Folpet 43.5 WP. (The use of SZX 0722 & Azoxystrobin 325 SC has not been registered, but nevertheless the trials were conducted in order to support a prospective registration.)

Table 6.3.1-8: Use patterns (GAPs) for the spray application of SZX 0722 & Azoxystrobin 325 SC in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s.* rate of application (kg/ha)	Max. no. of appls.	PHI (days)
SZX 0722 & Azoxystrobin 325 SC (150 g/L iprovalicarb and 175 g/L azoxystrobin)	EU-N	pre-flowering	0.6	0.09	1	28
		post-flowering (10-14 d int.)	1.0**	0.15**	4	
	EU-S	pre-flowering	0.6	0.09	1	28
		post-flowering (10-14 d int.)	1.0	0.15	3	

EU-N = northern EU residue region; EU-S = southern EU residue region

* This rate refers to iprovalicarb only

** These rates are expressed as "kg/ha per meter foliage ('leaf wall' or leafy surface) height". The maximum absolute amounts to be applied refer to vines with 1.6 m "leafy surface", resulting in post-bloom a.s. rates of 0.24 kg/ha iprovalicarb.

In addition to the uses described in the table above, a second use pattern was also tested in the north based on a specific request by the German authorities to simulate a situation in which a single product is used over an entire growing season. This called for 8 applications per season (3 before, 5 post-bloom) at intervals of 10-14 days (with a single longer interval during flowering), though the intended use of any iprovalicarb-containing product would specify a maximum of 5 applications per season.

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/09, [redacted]1998c**
Title: Determination of residues of SZX 0722 & Azoxystrobin (325 SC) on grape following spray application in Germany and France
Report No. & Document No.: RA-2141/97, M-004869-01-2

Report: **KIIA 6.3.1/10, [redacted]1999a**
Title: Determination of residues of SZX 0722 & Azoxystrobin (325 SC) on grape following spray application in Germany and France
Report No. & Document No.: RA-2123/98, M-018554-01-1

Report: **KIIA 6.3.1/11, [redacted] 1998d**
Title: Determination of residues of SZX 0722 & Azoxystrobin (325 SC) on grape following spray application in France, Spain, Italy, and Portugal
Report No. & Document No.: RA-2135/97, M-004870-01-2

Guidelines *(applies to all studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to all studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and to support uses in grapes in the EU.

I. Materials and Methods

Northern European residue region

Northern European trials were performed in Germany (3) and in France (2) (KIIA 6.3.1/09), using SZX 0722 & Azoxystrobin 325 SC, containing 150 g/L iprovalicarb and 175 g/L azoxystrobin. The use pattern as defined for this residue region was based on a set product concentration and water rates of approx. 600 L/ha prior to bloom (1 appl.) and then 1000 L/(ha × m foliage height) post-flowering (4 appl.); thus, vines were treated at a worst-case concentration (0.1% in high-volume sprays) and at water rates applicable to the practices common in the countries in which the trials were performed. In this system, while the post-flowering rate per hectare and meter vine height remains constant, the actual amount of product applied in a given trial can vary based on the height of the vines on the test plot, so that varying absolute amounts of product are directly comparable with one another.

Post-blossom sprays of SZX 0722 & Azoxystrobin 325 SC amounted to 1.6 L/ha in Germany (1.6 m "leaf wall" height) and 0.9-1.25 L/ha in France (0.9-1.25 m leafy surface), which is equivalent to 0.24 kg iprovalicarb/ha (Germany) and 0.135-0.19 kg iprovalicarb/ha (France). Spray intervals were 10-14 days in post-blossom spraying in the German trials. In the French studies, the interval between the 4th and 5th applications was 41 or 43 days, as a mistake was made in the treatment sequencing. Nevertheless, the final (critical) application was made 28 days before harvest in all tests. All applications in all studies were at the required rates.

Because of a specific request by the German authorities to simulate a situation in which a single product is used over an entire growing season, five further trials were conducted in Germany (3) and France (2) (KIIA 6.3.1/10) in which SZX 0722 & Azoxystrobin 325 SC was applied 8 times at the standard rates described above (0.6 L/ha prior to bloom and 1.0 L/(ha per m foliage height) thereafter). Two of the three additional applications were in the pre-flowering stages, whereas the third was very shortly after flowering. Spray intervals were 10-14 days, except for between the 3rd and 4th treatments (flowering), where they were 23-38 days. Water rates were about 600 L/ha pre-bloom and 1000 L/(ha × m foliage height) post-bloom in high-volume spraying. In the French trials, post-bloom applications were performed with low-volume techniques at a water rate of 100 L/(ha × m foliage height). All applications in all studies were at the required rates, except for the first two in German trial 815349 (=1534-98), which were overdosed by 5.4 and 6.8%, respectively; however, these deviations are well within the EU's acceptance criteria for residue studies, thus the trials are valid.

Southern European residue region

In southern Europe, trials were conducted in Portugal (1), Spain (2), Italy (1), and France (1) (KIIA 6.3.1/11). SZX 0722 & Azoxystrobin 325 SC was applied 5 times (1 pre-bloom/4 post-bloom) at rates of 0.6 L/ha prior to and 1.0 L/ha subsequent to flowering, equivalent to 0.09 kg/ha (pre-fl.) or 0.15 kg/ha (post-fl.) iprovalicarb a.s. Spray intervals were generally 10-13 days in post-blossom spraying. Water rates were about 600 L/ha (pre-blossom) and 1000 L/ha (post-blossom sprays), except in French trial 704164 (=0416-97), in which the post-bloom treatments were made using low-volume techniques (100 L/ha). All applications in all studies were at the required rates.

All trials

In all trials in both residue regions, samples of bunches of grapes were taken on day 0 after the last treatment (0 DALT), and 28 DALT. Samples of destemmed grapes (berries) were also taken 28 DALT. Samples were analyzed for iprovalicarb according to methods 00442/M003 or 00562. The limit of quantitation (LOQ) was always 0.05 mg/kg for iprovalicarb.

II. Findings

Recoveries of iprovalicarb were obtained from bunch of grapes fortified at levels between 0.05 mg/kg and 1.0 mg/kg. The sample materials chosen served to represent all relevant sample materials collected in these trials. Mean recoveries were all within acceptable ranges (78-97%, RSDs 4.4-7.4%, n=1-10). Details of recovery data are shown in Table 6.3.1-11.

All trials are summarized below in Tables 6.3.1-9 and 6.3.1-10 and in greater detail in the Tier 1 summary forms.

Northern European residue region

Immediately following the final application in the studies performed according to the standard worst-case use pattern (5 treatments), samples of grape bunches yielded iprovalicarb residues ranging from 0.09-2.4 mg/kg (median value 1.7 mg/kg). These residues declined to levels of 0.05-1.7 mg/kg (median 1.1 mg/kg) by day 28 (=PHI).

Samples of destemmed grapes (berries) were also taken in the trials. The residues were very slightly lower in day-28 samples of grapes alone than those in bunches (<0.05-1.3 mg/kg in destemmed grapes [median 0.93 mg/kg]).

As mentioned previously, tests were also carried out with an 8-treatment use pattern based on a request by the German authorities. (The additional applications were conducted at relatively early stages in the growing season.) No elevation of the residue levels could be seen following eight applications; residues on bunches dropped from 0.68-1.1 mg/kg on day 0 (median 0.90 mg/kg) to 0.31-0.60 mg/kg on day 28 (median 0.38 mg/kg). Day-28 residues on destemmed fruit were also very similar to those in bunches, ranging from 0.26-0.65 mg/kg (median value 0.41 mg/kg).

Southern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.22-1.0 mg/kg (median value 0.26 mg/kg). These residues declined to levels of 0.09-0.62 mg/kg (median 0.14 mg/kg) by day 28 (=PHI).

Samples of grapes themselves (destemmed berries) were also taken in the trials. The residues were essentially the same in day-28 samples of grapes alone as in bunches (0.09-0.44 mg/kg in grapes alone [median 0.18 mg/kg]).

III. Conclusion

A total of fifteen residue trials were conducted with SZX 0722 & Azoxystrobin 325 SC, containing 150 g/L iprovalicarb and 175 g/L azoxystrobin on grapes, five in the southern European residue region and ten in the north (five each with two different use patterns). The product was applied in accordance with the scheduled use patterns (slight deviations in one northern trial were within EU tolerances), and the tests were carried out according to GLP principles. The purpose was to evaluate the residue behavior of the combination product, in the form of a "bridge" from existing EU submissions for each of the substances (although, finally, the trials were never submitted for registration). The results presented here demonstrate that:

- following five applications, residue levels of iprovalicarb in grape bunches decline with time, from values of 0.09-2.4 mg/kg (north) or 0.22-1.0 mg/kg (south) on day 0 to 0.05-1.7 mg/kg (north) or 0.09-0.62 mg/kg (south) on day 28. The respective median values were 1.7 and 0.26 mg/kg on day 0, and 1.1 and 0.14 mg/kg on day 28.
- residue values of iprovalicarb in destemmed grapes (berries) on day 28 were very similar to those in bunches, with median values of 0.93 and 0.18 mg/kg in the samples from the northern and southern European trials, respectively.
- when using an "expanded" use pattern (8 applications instead of 5) in the northern residue region, residue levels remained unaffected by the extra applications, with day-28 residue values of 0.31-0.60 mg/kg were determined in bunches (median 0.38 mg/kg). Day-28 residues on destemmed fruit were also very similar to those in bunches, ranging from 0.26-0.65 mg/kg (median value 0.41 mg/kg).
- all residue values for iprovalicarb on day 28 were well below the current EU MRL for iprovalicarb in grapes (2 mg/kg), regardless of the use pattern tested.

Table 6.3.1-9: Residues of iprovalicarb in/on grapes following applications of with SZX 0722 & Azoxystrobin SC 325 in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2141/97 70776/7 0776-97 GLP: yes 1997	Grape Müller-Thurgau	Germany D-[redacted] EU-N	325 SC[1]	5	0.090-0.240	0.015	81	bunch s	0 **28**	2.4 1.1
								berry	**28**	0.2
RA-2141/97 70775/9 0775-97 GLP: yes 1997	Grape Portugieser	Germany D-[redacted] EU-N	325 SC[1]	5	0.090-0.240	0.015	81	bunch	0 **28**	1.7 1.5
								berry	**28**	0.93
RA-2141/97 70777/5 0777-97 GLP: yes 1997	Grape Riesling	Germany D-[redacted] EU-N	325 SC[1]	5	0.090-0.240	0.015	80	bunch	0 **28**	1.8 1.7
								berry	**28**	1.3
RA-2141/97 70779/1 0779-97 GLP: yes 1997	Grape Chenin	France F-[redacted] EU-N	325 SC[1]	5	0.090-0.150	0.015	76	bunch	0 **28**	0.09 0.05
								berry	**28**	<0.05
RA-2141/97 70778/3 0778-97 GLP: yes 1997	Grape Cabernet Franc	France F-[redacted] EU-N	325 SC[1]	5	0.090-0.188	0.015	77	bunch	0 **28**	0.34 0.13
								berry	**28**	0.10

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = with SZX 0722 & Azoxystrobin 325 SC, containing 150 g/L iprovalicarb and 175 g/L azoxystrobin

Table continued on next page...

Table 6.3.1-9 (cont'd): Residues of iprovalicarb in/on grapes following applications of with SZX 0722 & Azoxystrobin SC 325 in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2123/98 R 1998 1533/0 1533-98 GLP: yes 1998	Grape Chardonnay; weiße Sorte	France F-[redacted] EU-N	325 SC[1]	8	0.090-0.180	0.015-0.150	81	bunch	0	1.1
									28	0.31
								berry	**28**	0.26
RA-2123/98 R 1998 1065/7 1065-98 GLP: yes 1998	Grape Portugieser; rote Traube	Germany D-[redacted] EU-N	325 SC[1]	8	0.090-0.240	0.015	81	bunch of grapes	0	1.0
									28	0.38
								berry	**28**	0.41
RA-2123/98 R 1998 1534/9 1534-98 GLP: yes 1998	Grape Kerner-Rebe; weiße Traube	Germany D-[redacted] EU-N	325 SC[1]	8	0.090-0.240	0.015	81	bunch	0	0.82
									28	0.34
								berry	**28**	0.48
RA-2123/98 R 1998 1532/2 1532-98 GLP: yes 1998	Grape Riesling; weiße Traube	Germany D-[redacted] EU-N	325 SC[1]	8	0.090-0.240	0.015	81	bunch	0	0.68
									28	0.60
								berry	**28**	0.65
RA-2123/98 R 1998 1531/4 1531-98 GLP: yes 1998	Grape Pinot Noir; Rote Sorte	France F-[redacted] EU-N	325 SC[1]	8	0.090-0.180	0.015-0.150	81	bunch	0	0.90
									28	0.38
								berry	**28**	0.31

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = with SZX 0722 & Azoxystrobin 325 SC, containing 150 g/L iprovalicarb and 175 g/L azoxystrobin

Table 6.3.1-10: Residues of iprovalicarb in/on grapes following applications of with SZX 0722 & Azoxystrobin SC 325 in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2135/97 70707/4 0707-97 GLP: yes 1997	Grape Carinena	Spain E-[redacted] EU-S	325 SC[1]	5	0.090-0.150	0.015	85	bunch	0	0.22
									28	0.09
								berry	**28**	0.09
RA-2135/97 70706/6 0706-97 GLP: yes 1997	Grape Cortese	Italy I-[redacted] EU-S	325 SC[1]	5	0.090-0.150	0.015	85	bunch	0	0.93
									28	0.33
								berry	**28**	0.44
RA-2135/97 70708/2 0708-97 GLP: yes 1997	Grape Agua Santa	Portugal P-[redacted] EU-S	325 SC[1]	5	0.090-0.150	0.015	81	bunch	0	1.0
									28	0.62
								berry	**28**	0.43
RA-2135/97 70662/0 0662-97 GLP: yes 1997	Grape Cabernet Sauvignon	Spain E-[redacted] EU-S	325 SC[1]	5	0.090-0.150	0.015	85	bunch	0	0.26
									28	0.14
								berry	**28**	0.18
RA-2135/97 70416/4 0416-97 GLP: yes 1997	Grape Grenache blanc	France F-[redacted] EU-S	325 SC[1]	5	0.090-0.150	0.015-0.150	85	bunch	0	0.26
									28	0.10
								berry	**28**	0.12

FL = formulation GS = growth stage at last application DALT = days after last treatment

* prior to last treatment

Formulations used in trials:
1 = with SZX 0722 & Azoxystrobin SC 325, containing 150 g/L iprovalicarb and 175 g/L azoxystrobin

Table 6.3.1-11: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2141/97 70775/9 (0775-97) 70777/5 (0777-97) 70778/3 (0778-97) 70776/7 (0776-97) 70779/1 (0779-97) GLP: yes 1997 *RA-2135/97* 70707/4 (0707-97) 70706/6 (0706-97) 70416/4 (0416-97) 70708/2 (0708-97) 70662/0 (0662-97) GLP: yes 1997	Grape	bunch	iprovalicarb	3 10 13	0.05 1.0 overall	78 89 78	89 104 104	82 97 93	7.4 4.7 8.6
RA-2123/98 R 1998 1065/7 (1065-98) R 1998 1531/4 (1531-98) R 1998 1532/2 (1532-98) R 1998 1533/0 (1533-98) R 1998 1534/9 (1534-98) GLP: yes 1998	Grape	bunch	iprovalicarb	4 10 1 15	0.05 0.5 1.0 overall	78 74 88 74	90 86 88 90	82 78 88 79	7.0 4.4 - 6.1

* *bunch* recoveries also valid for sample material *berry*.

► **"120 g core-rate" use pattern**

Iprovalicarb & Mancozeb WG/WP 66 (SZX 0722 & Mancozeb 66 WG/WP)

Table 6.3.1-12: Use patterns (GAPs) for the spray application of SZX 0722 & Mancozeb 66 WG/WP in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s.* rate of application (kg/ha)	Max. no. of appls.	PHI (days)
SZX 0722 & Mancozeb 66 WG/WP (6% iprovalicarb and 60% mancozeb)	EU-N	pre-flowering (10-14 d int.)	1.2	0.072	2	28
		post-flowering (10-14 d int.)	2.0**	0.120**	3	
	EU-S	pre-flowering (10-14 d int.)	2.0	0.120	2	28
		post-flowering (10-14 d int.)	2.0	0.120	3	

EU-N = northern EU residue region; EU-S = southern EU residue region

* This rate refers to iprovalicarb only.

** These rates are expressed as "kg/ha per meter foliage ("leaf wall" or leafy surface) height". The maximum absolute amounts to be applied refer to vines with 1.6 m "leafy surface", resulting in post-bloom a.s. rates of 0.192 kg/ha iprovalicarb.

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/12, [redacted] 1997a**
Title: Determination of residues of SZX 0722 & Mancozeb 66 WG in/on grape following spray application in France
Report No. & Document No.: RA-2141/95, M-000263-02-1

Report: **KIIA 6.3.1/13, [redacted] 1997b**
Title: Determination of residues of SZX 0722 & Mancozeb 66 WP in/on grape following spray application in France and Germany
Report No. & Document No.: RA-2133/97, M-000721-01-1

Report: **KIIA 6.3.1/14, [redacted] 1997c**
Title: Determination of residues of SZX 0722 & Mancozeb 66 WG on grape following spray application in Italy
Report No. & Document No.: RA-2142/95, M-000259-02-1

Report: **KIIA 6.3.1/15, [redacted] 1997d**
Title: Determination of residues of SZX 0722 & Mancozeb 66 WP on grape following spray application in Greece and Spain
Report No. & Document No.: RA-2145/96, M-000254-02-1

Report:	**KIIA 6.3.1/16, [redacted] 1997e**
Title:	Determination of residues of SZX 0722 & Mancozeb 66 WP in/on table grape following spray application in Italy
Report No. & Document No.:	RA-2134/97 M-000629-01-1

Guidelines *(applies to all studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to all studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and support uses in grapes in the EU.

I. Materials and Methods

Northern European residue region

Northern European trials with wine grapes were performed in Germany (1) and in France (4) using SZX 0722 & Mancozeb 66 WP or WG, containing 6% iprovalicarb and 60% mancozeb (KIIA 6.3.1/12; KIIA 6.3.1/13). Trial use patterns in the 1995 French trials (RA-2141/95) were adjusted to adapt the product rates to the ones theoretically expected for high German vines, i.e. despite the fact that post-flowering water rates remained constant, the product rate was increased based on a theoretical vine foliage height of 1.6 m. However, due to incorrect application timing by the field technician, an additional application was made in both trials at a rate of 2.8 kg/ha. The product rates corresponded to 0.048 to 0.192 kg a.s./ha iprovalicarb and 0.48 to 1.92 kg a.s./ha mancozeb.

In the 1997 trials in Germany and France (KIIA 6.3.1/13), SZX 0722 & Mancozeb 66 WP was applied at product concentrations of 0.2% in high-volume and 2% in low-volume sprays at water rates applicable to the practices common in the countries in which the trials were performed. Post-blossom sprays were adjusted to 2 kg/ha of product applied to each meter of vine foliage ("leaf wall") height. Thus, varying absolute amounts of product are directly comparable with one another; post-bloom sprays were at 3.2 kg/ha in Germany (1.6 m "leaf wall" height) and approx. 1.6 kg/ha in France (0.8 m "leaf wall").

All applications were at the required rate, or, in the case of three individual treatments in two French trials (4th/5th applications in trial 702013 [=0201-97], 4th application in trial 702021 [=0202-97]), within ±17% of the required rates. These deviations are well within the EU´s tolerances for residue trials. The product rates corresponded to 0.048 to 0.192 kg a.s./ha iprovalicarb.

Spray intervals were generally 12-14 days in wine grape trials (both in pre-blossom and post-blossom spraying). Samples of bunches of grapes were taken immediately before and/or after the last treatment (day 0), and 28 DALT. The grapes themselves (destemmed fruit) were also sampled 28 DALT in three trials. Samples were analyzed for iprovalicarb according to method 00442 or 00442/M003.

Southern European residue region

In southern Europe, trials were conducted in Greece (1), Spain (1), and Italy (4) with SZX 0722 & Mancozeb 66 WP or WG, containing 6% iprovalicarb and 60% mancozeb (KIIA 6.3.1/14; KIIA 6.3.1/15; KIIA 6.3.1/16). The grapes used were wine grape varieties (4 trials) in the 1995-96 trials and table grape varieties in 1997 (2 trials).

SZX 0722 & Mancozeb 66 WP or WG was applied five times to vines at a product rate of 2 kg/ha and a water rate of about 600-1000 L/ha (pre-blossom) and 1000 L/ha (post-blossom sprays). The product amount corresponds to 0.12 kg iprovalicarb/ha. In some trials, the final applications were made at growth stages of up to BBCH 88.

Spray intervals were generally 10-14 days in wine grape trials (both in pre-blossom and post-blossom spraying), and 10-12 d in the table grape trials. Samples of bunches of grapes were taken immediately before and/or after the last treatment (day 0), and 28 DALT. Grapes themselves (destemmed berries) were sampled 28 DALT in two trials. Samples were analyzed for iprovalicarb according to method 00442 or 00442/M003. The limit of quantitation (LOQ) was 0.05 mg/kg for iprovalicarb.

H. Findings

Method validation recoveries were conducted with bunches of grapes and grapes (berries) at fortification levels of 0.05 mg/kg (LOQ) to 1.0 mg/kg iprovalicarb. All recoveries were within guideline requirements (mean 81-105%, RSD 1.1-15.5%, n=2-5). Details of recovery data are shown in Table 6.3.1-15.

All trials are summarized below in Tables 6.3.1-13 and 6.3.1-14 and in greater detail in the Tier 1 summary forms.

Northern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.13-0.89 mg/kg (median value 0.24 mg/kg). By day 28, residues had declined to levels of <0.05-0.42 mg/kg (median 0.10 mg/kg).

Samples of grapes (berries) were also taken in the 1997 trials. The residues were similar in day-28 samples of grapes alone and of bunches (<0.05-0.44 mg/kg in grapes [median 0.15], <0.05-0.42 mg/kg in the corresponding bunches [median 0.14 mg/kg]).

Southern European residue region

Immediately following the final application, samples of grape bunches yielded residues of iprovalicarb ranging from 0.26-1.5 mg/kg (median value 0.70 mg/kg). By day 28, the residues had declined to levels of <0.05-0.38 mg/kg (median 0.24 mg/kg).

Samples of the grapes (berries) were taken in the two 1997 trials. The residues were slightly lower in day-28 samples of grapes alone than in bunches (0.12-0.16 mg/kg in grapes [median 0.14 mg/kg], 0.17-0.37 mg/kg in the corresponding bunches [median 0.27 mg/kg]).

III. Conclusion

Eleven residue trials were conducted with SZX 0722 & Mancozeb 66 WP or WG, containing 6% iprovalicarb and 60% mancozeb, on grapes, five in the northern European residue region and six in the south. The product was applied in accordance with the proposed use patterns (slight deviations in the southern trials were within EU tolerances). The PHI was 28 days in all trials. The final applications were made at growth stages of up to BBCH 88. The tests were carried out according to GLP principles.

The purpose was to evaluate the residue behavior of the combination product, in the form of a "bridge" from existing EU submissions.

The results presented here demonstrate that:

- Residue levels of iprovalicarb in grape bunches from northern and southern European trials declined with time, from values of 0.13-0.89 mg/kg (north; median 0.24 mg/kg) and 0.26-1.5 mg/kg (south; median 0.70 mg/kg) on day 0 to ~0.05-0.42 mg/kg (north) and ~0.05-0.38 mg/kg (south) on day 28 (=PHI). The respective day-28 median values were 0.10 and 0.24 mg/kg.
- Residue values of iprovalicarb in grapes (berries) were similar to those in bunches, with median values in the similar or virtually identical to those in the corresponding bunch samples.
- All residue values for iprovalicarb in grapes taken at harvest (28 DALT) were well below the established EU MRL for iprovalicarb in grapes (2.0 mg/kg).

Table 6.3.1-13: Residues of iprovalicarb in/on grapes following applications of SZX 0722 & Mancozeb WG/WP 66 in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2141/95 50344/4 0344-95 GLP: yes 1995	Grape Sauvignon	France [redacted] EU-N	66 WG[1]	6	0.048-0.192	0.012-0.019	83	bunch	0* 0 **28**	<0.05 0.18 0.08
RA-2141/95 50696/6 0696-95 GLP: yes 1995	Grape Pinot meunier	France [redacted] EU-N	66 WG[1]	6	0.048-0.192	0.012-0.019	83	bunch	0* 0 **28**	0.11 0.62 0.10
RA-2133/97 70201/3 0201-97 GLP: yes 1997	Grape Pinot Meunier	France F-[redacted] EU-N	66 WP[2]	5	0.048-0.112	0.012-0.120	83	berry bunch	**28** 0 **28**	0.15 0.24 0.14
RA-2133/97 70202/1 0202-97 GLP: yes 1997	Grape Sauvignon	France F-[redacted] EU-N	66 WP[2]	5	0.048-0.106	0.012-0.120	83	berry bunch	**28** 0 **28**	<0.05 0.13 <0.05
RA-2133/97 70648/5 0648-97 GLP: yes 1997	Grape Dornfelder	Germany D-[redacted] EU-N	66 WP[2]	5	0.048-0.192	0.036	80	berry bunch	**28** 0 **28**	0.44 0.89 0.42

FL = formulation GS = growth stage at last application DALT = days after last treatment
* prior to last treatment

Formulations used in trials:
1 = SZX 0722 & Mancozeb WG 66, containing 6% iprovalicarb and 60% mancozeb
2 = SZX 0722 & Mancozeb WP 66, containing 6% iprovalicarb and 60% mancozeb

Table 6.3.1-14: Residues of iprovalicarb in/on grapes following applications of SZX 0722 & Mancozeb WG/WP 66 in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2142/95 50697/4 0697-95 GLP: yes 1995	Grape Pinot bianco	Italy [redacted] EU-S	66 WG[1]	5	0.120	0.012	83	bunch	0* 0 **28**	0.81 1.5 0.38
RA-2142/95 50343/6 0343-95 GLP: yes 1995	Grape Barbera	Italy [redacted] EU-S	66 WG[1]	5	0.120-0.126	0.012-0.020	85	bunch	0* 0 **28**	0.13 0.43 0.10
RA-2145/96 60652/9 0652-96 GLP: yes 1996	Grape Carinena	Spain E-[redacted] EU-S	66 WP[2]	5	0.120	0.013-0.020	84	bunch	0 **28**	0.26 0.05
RA-2145/96 60175/6 0175-96 GLP: yes 1996	Grape Sultanina	Greece [redacted] EU-S	66 WP[2]	5	0.120	0.012-0.020	81	bunch	0 **28**	0.65 0.30
RA-2134/97 70709/0 0709-97 GLP: yes 1997	Table grape Italia	Italy I-[redacted] EU-S	66 WP[2]	5	0.120	0.012-0.020	79	berry bunch	**28** 0 **28**	0.12 0.74 0.17
RA-2134/97 70710/4 0710-97 GLP: yes 1997	Table grape Cardinal	Italy I-[redacted] EU-S	66 WP[2]	5	0.120	0.012-0.020	75	berry bunch	**28** 0 **28**	0.16 1.0 0.37

FL = formulation GS = growth stage at last application DALT = days after last treatment
* prior to last treatment

Formulations used in trials:
1 = SZX 0722 & Mancozeb WG 66, containing 6% iprovalicarb and 60% mancozeb
2 = SZX 0722 & Mancozeb WP 66, containing 6% iprovalicarb and 60% mancozeb

Table 6.3.1-15: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2141/95 50344/4 (0344-95) 50696/6 (0696-95) GLP: yes 1995	Grape	bunch	iprovalicarb	3 4 7	0.05 0.50 overall	86 84 84	88 92 92	87 90 88	1.1 4.2 3.4
RA-2142/95 50343/6 (0343-95) 50697/4 (0697-95) GLP: yes 1995	Grape	bunch	iprovalicarb	3 4 7	0.05 0.50 overall	86 84 84	88 92 92	87 90 88	1.1 4.2 3.4
RA-2145/96 60175/6 (0175-96) 60652/9 (0652-96) GLP: yes 1996	Grape	bunch	iprovalicarb	3 2 5	0.05 1.0 overall	80 71 71	104 91 104	94 81 89	13.1 - 14.8
RA-2133/97 70201/3 (0201-97) 70202/1 (0202-97) 70648/5 (0648-97) GLP: yes 1997	Grape	berry*	iprovalicarb	3 5 8	0.05 1.0 overall	103 65 65	109 99 109	105 89 95	3.1 15.5 14.3
RA-2134/97 70709/0 (0709-97) 70710/4 (0710-97) GLP: yes 1997	Table grape	berry*	iprovalicarb	3 5 8	0.05 1.0 overall	103 65 65	109 99 109	105 89 95	3.1 15.5 14.3

* *berry* recoveries also valid for sample material *bunch of grapes*

SZX 0722 & Fosetyl-Al & Mancozeb 69.1 WP

Table 6.3.1-16: Use patterns (GAPs) for the spray application of SZX 0722 & Fosetyl Al & Mancozeb 69.1 WP in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s. rate of application (kg/ha)	Max. no. of appls.	PHI (days)
SZX 0722 & Fosetyl Al & Mancozeb 69.1 WP (3.4% iprovalicarb, 28.6% mancozeb and 37.1% fosetyl-Al)	EU-S	pre-flowering (10-14 d int.)	2.1	0.07	2	28
		post-flowering (10-14 d int.)	3.5	0.12	2	

EU-S = southern EU residue region

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/17 [redacted]1999b**
Title: Determination of residues of SZX 0722 & Fosetyl Al & Mancozeb (69.1 WP) on grape following spray application in France, Spain and Italy
Report No. & Document No.: RA-2122/98, M-017631-03-1
Guidelines: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP: yes (certified laboratory). Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and support uses in grapes in the EU.

I. Materials and Methods

Southern European residue region

Five trials were conducted in southern European vineyards, in Spain (2), Italy (2), and France (1) with the combination product Fosetyl-Al & Iprovalicarb & Mancozeb WP 69.1, containing 3.4% iprovalicarb, 28.6% mancozeb, and 37.1% fosetyl-Al (KIIA 6.3.1/17).

The product was applied 4 times (2 pre-bloom, 2 post-bloom) at rates of 2.1 kg/ha prior to and 3.5 kg/ha subsequent to flowering, equivalent to 0.071 kg iprovalicarb /ha (pre-fl.) or 0.12 kg iprovalicarb /ha (post-fl.). Spray intervals were generally 10-14 days, both in pre- and post-blossom spraying. Water rates were about 600 L/ha (pre-flowering) and 1000 L/ha (post-flowering, high-volume spray). In the French trial, water rates were 100 L/ha post-flowering (low-volume spraying).

All applications in all studies were at the required rates, or, in the case of two individual treatments (1st appl. in trial 816086 [=1608-98] and the 3rd in trial 816094 [=1609-98]), within ±11% of the required rates, i.e. well within the EU´s tolerances for study acceptability. Samples of bunches of

grapes were taken on days 0 and 28 days after the last treatment (DALT), and samples of destemmed grapes (berries) 28 DALT.

Samples were analyzed for iprovalicarb according to method 00562. The limit of quantitation (LOQ) was 0.05 mg/kg for iprovalicarb.

II. Findings

Method validation recoveries were conducted at fortification levels of 0.05 mg/kg (LOQ) to 1.0 mg/kg iprovalicarb. Recoveries were within guideline requirements (means 78-88%, RSD 4.4-7.0%, n=1-10). Details are given in Table 6.3.1-18.

All trials are summarized below in Table 6.3.1-17 and in greater detail in the Tier 1 summary forms.

Southern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.11-0.44 mg/kg (median value 0.20 mg/kg). These residues declined to levels of <0.05-0.21 mg/kg (median 0.07 mg/kg) by day 28 (=PHI).

Samples of grapes themselves (destemmed berries) were also taken in the trials. The residues were virtually the same in day-28 samples of grapes alone as in bunches (<0.05-0.20 mg/kg in grapes alone; median 0.05 mg/kg).

III. Conclusion

Five residue trials were conducted in southern Europe with Fosetyl-Al & Iprovalicarb & Mancozeb WP 69.1 on grapes. The product was applied in accordance with the proposed use patterns (two slight deviations were within EU tolerances), and the tests were carried out according to GLP principles. The purpose was to evaluate the residue behavior of the combination product, in the form of a "bridge" from existing EU submissions (Annex II for each of the compounds) and national registrations.

The results presented here demonstrate that:

- Residue levels of iprovalicarb in grape bunches declined with time, from values of 0.11-0.44 mg/kg on day 0 to <0.05-0.21 mg/kg on day 28. The respective median values were 0.20 and 0.07 mg/kg.
- Residue values of iprovalicarb in destemmed grapes (berries) on day 28 were virtually the same as those in bunches, ranging from <0.05-0.20 mg/kg, with a median value of 0.05 mg/kg.
- All residue values for iprovalicarb on day 28 were well below the EU MRL for iprovalicarb in grapes (2 mg/kg).

Table 6.3.1-17: Residues of iprovalicarb in/on grapes following applications of Fosetyl-Al & Iprovalicarb & Mancozeb WP 69.1 in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2122/98 R 1998 1607/8 1607-98 GLP: yes 1998	Grape Grenache noir; red variety	France F-[redacted] EU-S	69.1 WP[1]	4	0.071-0.119	0.012-0.119	81	bunch	0	0.20
									28	0.07
								berry	**28**	<0.05
RA-2122/98 R 1998 1608/6 1608-98 GLP: yes 1998	Grape Carinena; red variety	Spain E-[redacted] EU-S	69.1 WP[1]	4	0.071-0.119	0.012	86	bunch	0	0.20
									28	0.07
								berry	**28**	0.07
RA-2122/98 R 1998 1609/4 1609-98 GLP: yes 1998	Grape Xarelo; white variety	Spain E-[redacted] EU-S	69.1 WP[1]	4	0.071-0.125	0.012	84	bunch	0	0.11
									28	<0.05
								berry	**28**	<0.05
RA-2122/98 R 1998 1610/8 1610-98 GLP: yes 1998	Grape Trebbiano; white variety	Italy I-[redacted] EU-S	69.1 WP[1]	4	0.071-0.119	0.012	81	bunch	0	0.37
									28	0.06
								berry	**28**	0.05
RA-2122/98 R 1998 1698/1 1698-98 GLP: yes 1998	Grape Barbera; red variety	Italy I-[redacted] EU-S	69.1 WP[1]	4	0.071-0.119	0.012	83	bunch	0	0.44
									28	0.21
								berry	**28**	0.20

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = with Fosetyl-Al & Iprovalicarb & Mancozeb WP 69.1, containing 3.4% iprovalicarb, 28.6% mancozeb, and 37.1% fosetyl-Al

Table 6.3.1-18: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2122/98	Grape	bunch*	iprovalicarb	4	0.05	78	90	82	7.0
R 1998 1607/8 (1607-98)				10	0.5	74	86	78	4.4
R 1998 1608/6 (1608-98)				1	1.0	88	88	88	
R 1998 1609/4 (1609-98)				15	overall	74	90	79	6.1
R 1998 1610/8 (1610-98)									
R 1998 1698/1 (1698-98)									
GLP: yes									
1998									

* recoveries for *bunch* also valid for sample material *berry*

Iprovalicarb & Tolylfluanid WG 43.5 (SZX 0722 & Tolylfluanid 43.5 WG)

Table 6.3.1-19: Use patterns (GAPs) for the spray application of SZX 0722 & Tolylfluanid 43.5 WG in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s.* rate of application (kg/ha)	Max. no. of appls.	PHI (days)
SZX 0722 & Tolylfluanid 43.5 WG (6% iprovalicarb and 37.5% tolylfluanid)	EU-N	pre-flowering	0.8	0.048	1	28
		post-flowering (10-14 d int.)	2.0**	0.120**	3	
	EU-S	pre-flowering	0.8	0.048	1	21
		post-flowering (10-14 d int.)	2.0	0.120	3	

EU-N = northern EU residue region; EU-S = southern EU residue region

* This rate refers to iprovalicarb only

** These rates are expressed as "kg/ha per meter foliage ('leaf wall' or leafy surface) height". The maximum absolute amounts to be applied refer to vines with 1.6 m "leafy surface", resulting in post-bloom a.s. rates of 0.192 kg/ha iprovalicarb.

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/18, [redacted]; 1997f**
Title: Determination of residues of SZX 0722 & Tolylfluanid 43.5 WG on grape following spray application in Germany
Report No. & Document No.: RA-2146/96, M-000221-01-1

Report: **KIIA 6.3.1/19, [redacted]; 1998a**
Title: Determination of residues of SZX 0722 & Tolylfluanid 43.5 WG in/on grapes following spray application in France and Germany
Report No. & Document No.: RA-2136/97, M-000805-01-1

Report: **KIIA 6.3.1/20, [redacted] 2002**
Title: Determination of residues of SZX 0722 & Tolylfluanid 43.5 WG in/on grape after spray application in southern France, Greece, Spain and Italy
Report No. & Document No.: RA-2113/01, M-053787-01-1

Guidelines *(applies to all studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to all studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and support uses in grapes in the EU.

I. Materials and Methods

Northern European residue region

In northern Europe, a total of five trials were performed in Germany (4) and in France (1) using SZX 0722 & Tolylfluanid 43.5 WG, containing 6% iprovalicarb and 37.5% tolylfluanid.

In 1996 (KIIA 6.3.1/18) four applications with a set product concentration of 0.2% were conducted at increasing water rates, 400 L/ha prior to bloom and 1000-1400-1600 L/ha post-flowering, which equates to product rates of 0.8 and 2.0-2.8-3.2 kg/ha, respectively. (Alternatively, the product is applied in low-volume spray programs, e.g. with a third of the respective water volumes and at 3× concentration.). The product rates corresponded to 0.048 to 0.192 kg iprovalicarb/ha.

In the 1997 trials in Germany and France (KIIA 6.3.1/19), SZX 0722 & Tolylfluanid 43.5 WG was applied six times at increasing product rates, once prior to bloom (0.8 kg/ha) and 5× post-flowering (2.0-2.4-2.8-3.2-3.2 kg/ha), in order to test a 2nd proposed use pattern. Whereas a constant product concentration of 0.6% was applied in Germany (low-volume spraying, increasing water rates), increasing concentrations were used in the French trial in order to achieve the worst-case German product amounts at a constant post-blossom water rate of 100 L/ha. The product rates corresponded to 0.048 to 0.192 kg iprovalicarb/ha. All applications were at the required rate, or, in the case of two individual treatments in the two German trials (the 1st application in both trials), within ±10% of the required rates. These deviations are well within the EU´s tolerances for residue trials.

The PHI was 28 days. Samples of grape bunches were taken on day 0 and at harvest (day 28), and samples of berries (destemmed grapes) were taken at harvest.

Southern European residue region

In southern Europe (southern France, Greece, Spain and Italy), a total of four trials were conducted in 2001 on grapes (KIIA 6.3.1/20). SZX 0722 & Tolylfluanid 43.5 WG, containing 6% iprovalicarb and 37.5% tolylfluanid, was applied 3 times at constant rates (2.5 kg/ha, equivalent to 0.15 kg/ha iprovalicarb).

The product was applied according to proposed used pattern, simulating the worst-case situation. Spray intervals were 10-11 days at BBCH growth stages 77-83, 79-85 and 82-87. The PHI was 21 (20) days. Water rates were 1000 L/ha, except in the French trial 0251-01 (=2001 0251/8), for which 100 L/ha water was applied as a low-volume spray. All applications in all studies were at the required rates.

All trials

Analytical samples were analyzed for iprovalicarb parent compound (residue definition for iprovalicarb) according to method 00562. The limit of quantitation (LOQ) was 0.05 mg/kg for iprovalicarb.

II. Findings

Recoveries of iprovalicarb were obtained from bunches and the destemmed fruit (berries) fortified at levels between 0.05 mg/kg and 5 mg/kg. The sample materials chosen served to represent all relevant

sample materials collected in these trials. Mean recoveries were all within acceptable ranges (85-100%, RSDs 3.0-8.0%, n=2-5). Details of recovery data are shown in Table 6.3.1-22.

All trials are summarized below in Tables 6.3.1-20 and 6.3.1-21 and in greater detail in the Tier 1 summary forms.

Northern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.35-1.0 mg/kg (median value 0.47 mg/kg). The residues declined with time and, by day 28, had reached levels of 0.22-0.72 mg/kg (median 0.39 mg/kg).

Samples of destemmed grapes (berries) were also taken in the 1997 trials. The residues were similar in day-28 samples of grapes alone and of bunches (0.16-0.62 mg/kg in grapes [median 0.43 mg/kg], 0.29-0.72 mg/kg in the corresponding bunches [median 0.45 mg/kg]).

Southern European residue region

Immediately following the final application (day 0), samples of grape bunches yielded iprovalicarb residues ranging from 0.24-0.56 mg/kg (median value 0.44 mg/kg). These residues declined with time, and by day 20/21 (=designated PHI), had reached levels of 0.12-0.31 mg/kg (median 0.29 mg/kg) in bunches. Similar levels were found in the destemmed fruit (=berries; range 0.17-0.31 mg/kg, median 0.27 mg/kg).

III. Conclusion

Over 3 growing seasons, 9 residue trials were conducted with SZX 0722 & Tolylfluanid 43.5 WG on grapes in both the northern (5) and southern (4) European residue regions. The product was applied in accordance with the proposed use patterns, and the tests were carried out according to GLP principles. The purpose was to evaluate the residue behavior of the combination product, in the form of a "bridge" from existing national and EU submissions. The results presented here demonstrate that:

- in the northern European trials, residue levels of iprovalicarb in grape bunches declined with time, from values of 0.35-1.0 mg/kg on day 0 to 0.22-0.72 mg/kg on day 28. The respective median values were 0.47 mg/kg on day 0 and 0.39 mg/kg on day 28.
- in the south, residue levels of iprovalicarb in grapes also declined with time, from values of up to 0.56 mg/kg on day 0 to a maximum of 0.31 mg/kg in bunches and the grapes themselves at the proposed PHI (day 20/21). The respective median values were 0.44 mg/kg on day 0, and 0.29 and 0.27 mg/kg on day 20/21 in bunches and the destemmed fruit (berries), respectively.
- Residue values of iprovalicarb in destemmed grapes (berries) were similar to those in bunches, with median values in the 1997 and 2001 trials similar or virtually identical to those in the corresponding bunch samples.
- All residue values for iprovalicarb at harvest (PHI 21 or 28 days) were well below the current EU MRL for iprovalicarb in grapes (2 mg/kg), irrespective of the use pattern tested.

Table 6.3.1-20: Residues of iprovalicarb in/on grapes following applications of with SZX 0722 & Tolylfluanid 43.5 WG in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2146/96 60008/3 0008-96 GLP: yes 1996	Grape Portugieser	Germany D-[redacted] EU-N	43.5 WG[1]	4	0.048-0.192	0.012	81	bunch	0 **28**	0.47 0.22
RA-2146/96 60009/1 0009-96 GLP: yes 1996	Grape Müller-Thurgau	Germany D-[redacted] EU-N	43.5 WG[1]	4	0.048-0.192	0.012	81	bunch	0 **28**	0.35 0.23
RA-2136/97 70199/8 0199-97 GLP: yes 1997	Grape Müller-Thurgau	Germany D-[redacted] EU-N	43.5 WG[1]	6	0.051-0.192	0.036	81	bunch berry	0 **28** **28**	1.0 0.72 0.62
RA-2136/97 70200/5 0200-97 GLP: yes 1997	Grape Portugieser	Germany D-[redacted] EU-N	43.5 WG[1]	6	0.053-0.192	0.036	81	bunch berry	0 **28** **28**	0.55 0.45 0.43
RA-2136/97 70649/3 0649-97 GLP: yes 1997	Grape Sauvignon	France F-[redacted] EU-N	43.5 WG[1]	6	0.048-0.192	0.048-0.192	83	bunch berry	0 **28** **28**	0.37 0.29 0.16

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = with SZX 0722 & Tolylfluanid 43.5 WG, containing 6% iprovalicarb and 37.5% tolylfluanid

Table 6.3.1-21: Residues of iprovalicarb in/on grapes following applications of SZX 0722 & Tolylfluanid 43.5 WG in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2113/01 R 2001 0251/8 0251-01 GLP: yes 2001	Grape Syrah; red variety	France F-[redacted] EU-S	43.5 WG[1]	3	0.150	0.150	86	bunch	0	0.32
									21	0.30
								berry	**21**	0.31
RA-2113/01 R 2001 0532/0 0532-01 GLP: yes 2001	Grape Xarelo; white variety	Spain E-[redacted] EU-S	43.5 WG[1]	3	0.150	0.015	85	bunch	0	0.24
									20	0.12
								berry	20	0.17
RA-2113/01 R 2001 0533/9 0533-01 GLP: yes 2001	Grape Cesanese; red variety	Italy I-[redacted] EU-S	43.5 WG[1]	3	0.150	0.015	87	bunch	0	0.55
									21	0.27
								berry	**21**	0.29
RA-2113/01 R 2001 0531/2 0531-01 GLP: yes 2001	Grape Soultanina; White variety	Greece GR-[redacted] EU-S	43.5 WG[1]	3	0.150	0.015	82	bunch	0	0.56
									21	0.31
								berry	**21**	0.25

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = SZX 0722 & Tolylfluanid 43.5 WG, containing 6% iprovalicarb and 37.5% tolylfluanid

Table 6.3.1-22: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2146/96 60008/3 (0008-96) 60009/1 (0009-96) GLP: yes 1996	Grape	bunch	iprovalicarb	3	0.05	84	94	89	5.6
				2	1.0	89	95	92	4.3
				5	overall	84	95	90	4.9
RA-2136/97 70199/8 (0199-97) 70200/5 (0200-97) 70649/3 (0649-97) GLP: yes 1997	Grape	berry*	iprovalicarb	5	0.05	76	95	85	8.0
				5	0.50	78	92	85	7.0
				3	1.0	89	97	92	4.5
				3	5.0	88	96	92	4.4
				16	overall	76	97	88	7.0
RA-2113/01 R 2001 0251/8 (0251-01), R 2001 0531/2 (0531-01), R 2001 0532/0 (0532-01), R 2001 0533/9 (0533-01) GLP: yes 2001	Grape	bunch**	iprovalicarb	3	0.05	97	103	100	3.0
				4	0.5	88	97	94	4.7
				7	overall	88	103	96	5.1

* recoveries also valid for sample material *bunch of grapes*
** recoveries also valid for sample material *berry*

Folpet & Fosetyl-Al & Iprovalicarb WG 79

Table 6.3.1-23: Use patterns (GAPs) for the spray application of Folpet & Fosetyl-Al & Iprovalicarb WG 79 in/on grapes

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s. rate of application (kg/ha)	Max. no. of appls.	PHI (days)
Folpet & Fosetyl-Al & Iprovalicarb 79 WG (25% folpet, 50% fosetyl Al, and 4% iprovalicarb)	EU-S EU-N	post-flowering (12-14 d int.)	3.0	0.12	4	28

EU-S = southern EU residue region; EU-N = northern EU residue region

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/21, [redacted] 2005a**
Title: Determination of the residues of SZX 0722, fosetyl-Al and folpet in/on grape after low-volume spraying and spraying of SZX0722 & Fosetyl-Al & Folpet (79 WG) in the field in northern France and Germany
Amendment No. 1 to Report
Report No. & Document No.: RA-2330/04, M-257508-02-1

Report: **KIIA 6.3.1/22, [redacted] 2005b**
Title: Determination of the residues of SZX 0722, fosetyl-Al and folpet in/on grape after low-volume spraying and spraying of SZX0722 & Fosetyl-Al & Folpet (79 WG) in the field in southern France and Italy
Amendment No. 1 to Report
Report No. & Document No.: RA-2331/04, M-257534-02-1

Guidelines *(applies to both studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to both studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and support uses in grapes in the EU.

I. Materials and Methods

Northern European residue region

In the 2004 growing season, two trials were performed in Germany (1) and in France (1) (KIIA 6.3.1/21) with the combination product Folpet & Fosetyl-Al & Iprovalicarb WG 79, containing 25% folpet, 50% fosetyl-Al, and 4% iprovalicarb. The product was applied 3 times (post-bloom) at

nominal product rates of 3.0 kg/(ha × m crop height), at spray intervals of 10 days for all applications. Water rates were 130 L/ha for low-volume applications (in the French trial) and, for high-volume applications, 1000 L/(ha × m) in Germany.

The product was applied at actual (2-dimensional) rates of 3.9 kg/ha in France, and 4.5 kg/ha in Germany, corresponding to 0.156-0.180 kg iprovalicarb/ha.

Southern European residue region

In southern Europe, two trials were conducted in France (1), and Italy (1) (KIIA 6.3.1/22) with the combination product Folpet & Fosetyl-Al & Iprovalicarb WG 79, containing 25% folpet, 50% fosetyl-Al, and 4% iprovalicarb. The product was applied 3 times (post-bloom) at nominal product rates of 3.0 kg/ha at intervals of 10 days. Water rates were 145-167 L/ha for low-volume applications (in the French trial) and, for high-volume applications, 1000 L/ha in the Italian trial.

The product was applied at actual (2-dimensional) rates of 3 kg/ha in Italy and 2.8-3.3 kg/ha in France, corresponding to 0.112-0.133 kg iprovalicarb/ha.

All trials

In all trials in both European residue regions, samples of bunches were taken on days 0 and 28 (PHI) after the last application. Samples of destemmed grapes (berries) were also taken at harvest. Samples were analyzed for iprovalicarb according to method 00562/M001. The limit of quantitation (LOQ) was 0.05 mg/kg for iprovalicarb

II. Findings

Method validation recoveries were conducted on grape bunches or the destemmed berries at fortification levels of 0.05 mg/kg (LOQ) to 5.0 mg/kg iprovalicarb. Recoveries were within guideline requirements (means 78-97%, RSD 6.0-13.3%, n=9-16). Details of recovery data are shown in Table 6.3.1-26.

All trials are summarized below in Tables 6.3.1-24 and 6.3.1-25 and in greater detail in the Tier 1 summary forms.

Northern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.45-0.87 mg/kg (median 0.66 mg/kg). These residues declined to levels of 0.29-0.63 mg/kg (median 0.46 mg/kg) by day 28 (=PHI).

Samples of destemmed grapes (berries) were also taken in the trials. The residues were very slightly higher in day-28 samples of grapes alone than those in bunches (0.31-0.71 mg/kg in destemmed grapes [median 0.51 mg/kg]).

Southern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.30-0.85 mg/kg (median 0.58 mg/kg). These residues declined to levels of 0.18-0.21 mg/kg (median 0.20 mg/kg) by day 28 (=PHI).

Samples of grapes themselves (destemmed berries) were also taken in the trials. The residues were essentially the same in day-28 samples of grapes alone as in bunches (0.19-0.25 mg/kg in grapes alone [median 0.22 mg/kg]).

III. Conclusion

Four trials were conducted with Folpet & Fosetyl-Al & Iprovalicarb WG 79, containing 25% folpet, 50% fosetyl-Al, and 4% iprovalicarb, in/on grapes; two each in the northern and southern European residue regions. The product was applied in accordance with the scheduled use patterns (slight deviations in one northern trial were within EU tolerances), and the tests were carried out according to GLP principles. The purpose was to evaluate the residue behaviar of the combination product, in the form of a "bridge" from existing EU submissions.

The results of trials presented above demonstrate that:

- Residue levels of iprovalicarb in grape bunches (in all trials) declined with time, from values of 0.30-0.87 mg/kg (median 0.65 mg/kg) on day 0 to 0.18-0.63 mg/kg (median 0.25 mg/kg) by day 28.
- Residues appeared to be lower in the southern trials, with day-28 bunch values of 0.18 and 0.21 mg/kg, as opposed to 0.29 and 0.63 mg/kg in the northern trials.
- All residue values for iprovalicarb on day 28 were below the EU MRL for iprovalicarb in grapes (2 mg/kg).

Table 6.3.1-24: Residues of iprovalicarb in/on grapes following applications SZX 0722 & Fosetyl-AL & Folpet (79 WG) in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2330/04 R 2004 1050/6 1050-04 GLP: yes 2004	Grape Riesling	Germany D-[redacted] (Rheinland-Pfalz) EU-N	79 WG[1]	3	0.180	0.012	85	bunch	0	0.82
									28	0.63
								berry	**28**	0.71
RA-2330/04 R 2004 1048/4 1048-04 GLP: yes 2004	Grape Cabernet Franc	France F-[redacted] EU-N	79 WG[1]	3	0.156	0.120	85	bunch	0	0.45
									28	0.29
								berry	**28**	0.31

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = Folpet & Fosetyl-Al & Iprovalicarb WG 79 containing 25% folpet, 50% fosetyl Al, and 4% iprovalicarb

Table 6.3.1-25: Residues of iprovalicarb in/on grapes following applications SZX 0722 & Fosetyl-AL & Folpet (79 WG) in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2331/04 R 2004 1052/2 1052-04 GLP: yes 2004	Grape Chardonnay; white	Italy I-[redacted] EU-S	79 WG[1]	3	0.120	0.012	79	bunch	0	0.85
									28	0.18
								berry	**28**	0.25
RA-2331/04 R 2004 1051/4 1051-04 GLP: yes 2004	Grape Gamay	France F-[redacted] EU-S	79 WG[1]	3	0.112-0.123	0.077-0.080	81	bunch	0	0.30
									28	0.21
								berry	**28**	0.19

FL = formulation GS = growth stage at last application DALT = days after last treatment

* prior to last treatment

Formulations used in trials:
1 = SZX 0722 &Fosetyl-AL & Folpet (79 WG), containing 25% folpet, 50% fosetyl-Al, and 4% iprovalicarb

Table 6.3.1-26: Procedural recoveries for iprovalicarb in grape matrices

Study Trial No. (Trial SubID) GLP Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg) min	Fortification level (mg/kg) max	Recovery (%) min	Recovery (%) max	Recovery (%) mean	Recovery (%) RSD
RA-2330/04 R 2004 1048 4 (1048-04) R 2004 1050 6 (1050-04) *RA-2331/04* R 2004 1051 4 (1051-04) R 2004 1052 2 (1052-04) GLP: yes 2004	grape	bunch*	iprovalicarb	9	0.05	5.0	83	99	91	6.9

* *bunch* recoveries also valid for sample material *berry*

Iprovalicarb & Copper WP 24.5 (SZX 0722 & Copper 24.5 WP)

The formulation SZX 0722 & Copper 24.5 WP was applied using the same use pattern with regard to iprovalicarb as Folpet & Fosetyl-Al & Iprovalicarb WG 79 (described above), except that the PHI to be labelled was designated as being 20 days.

Table 6.3.1-27: Use patterns (GAPs) for the spray application of SZX 0722 & Copper 24.5 WP in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s.* rate of application (kg/ha)	Max. no. of appls.	PHI (days)
SZX 0722 & Copper 24.5 WP (4.2% iprovalicarb and 20.3% copper (as 34.1% copper oxychloride))	EU-N	post-flowering (10-14 d int.)	2.5**	0.105**	4	20
	EU-S	post-flowering (10-14 d int.†)	3.0	0.126	4	20

EU-N = northern EU residue region; EU-S = southern EU residue region

* This rate refers to iprovalicarb only

** These rates are expressed as "kg/ha per meter foliage ('leaf wall' or leafy surface) height". The maximum absolute amounts to be applied refer to vines with 1.6 m "leafy surface") resulting in post-bloom a.s. rates of 0.168 kg/ha iprovalicarb

† The first interval can be shortened to 7 d in table grapes (EU-S only)

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/23,** [redacted] **1997g**
Title: Determination of residues of SZX 0722 & copper 24.5 WP on grape following spray application in Germany
Report No. & Document No.: RA-2142/96, M-000234-01-1

Report: **KIIA 6.3.1/24,** [redacted] **1998b**
Title: Determination of residues of SZX 0722 & copper 24.5 WP in/on grapes following spray application in France and Germany
Report No. & Document No.: RA-2131/97, M-000813-01-1

Report: **KIIA 6.3.1/25,** [redacted] **1997h**
Title: Determination of residues of SZX 0722 & copper 24.5 WP on grape following spray application in Italy and France
Report No. & Document No.: RA-2143/96, M-000228-01-1

Report: **KIIA 6.3.1/26, [redacted]1998c**
Title: Determination of residues of SZX 0722 & copper 24.5 WP in/on tablegrapes following spray application in Greece, Italy and France
Report No. & Document No.: RA-2132/97, M-000801-01-1

Guidelines *(applies to all studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to all studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and support uses in grapes in the EU.

I. Materials and Methods

Northern European residue region

Northern European trials were performed in Germany (3) and in France (2) (KIIA 6.3.1/23, KIIA 6.3.1/24), using SZX 0722 & Copper 24.5 WP, containing 4.2% iprovalicarb and 20.3% copper (as 34.1% copper oxychloride). The product was applied four times at product concentrations of 0.25% at increasing water rates, 1000, 1200, 1400 and 1600 L/ha post-flowering, which equates to product rates of 2.5, 3.0, 3.5 and 4.0 kg/ha, respectively, and corresponds to 0.105-0.168 kg iprovalicarb/ha. Alternatively, the product is applied in low-volume spray programs, e.g. with a third of the respective water volumes and at triple concentration. All applications were at the required rate, or, in the case of one individual treatment (2nd application in French trial 701947 [=0194-97]), within ±6% of the required rates.

Southern European residue region

In southern Europe, trials were conducted in Greece (1), France (3), and Italy (4) (KIIA 6.3.1/25, KIIA 6.3.1/26), using SZX 0722 & Copper 24.5 WP, containing 4.2% iprovalicarb and 20.3% copper (as 34.1% copper oxychloride). The grapes used were wine grape varieties in 1996 (4 trials) and table grape varieties in 1997 (4 trials). SZX 0722 & Copper 24.5 WP was applied four times post-bloom at constant rates of 3.0 kg/ha, equivalent to 126 g iprovalicarb/ha. Spray intervals were generally 12-15 days in wine grape trials (7 d in the 2nd interval in French trials), and 6-7 d (first interval) or 10-16 d (later intervals) in the table grape trials. Water rates were 1000 L/ha (high-volume spraying) or 100 L/ha (low volume). All applications in all studies were at the required rates.

All trials

In all trials in both residue regions, bunches of grapes were sampled at days 0 and 20 (PHI) after the last application. In the trials conducted in table grapes, additional samples were taken directly before the last application and at days 7, 14 and 28 after the last application.

In 1996 and 1997, the samples were analyzed for iprovalicarb according to method 00442 and 00442/M003, respectively. The limit of quantitation in both methods was 0.05 mg/kg.

II. Findings

Recoveries of iprovalicarb were obtained from bunches and grapes (berries) fortified at levels between 0.05 mg/kg and 2 mg/kg. The sample materials chosen served to represent all relevant sample materials collected in these trials. Mean recoveries were all within acceptable ranges (82-101%, RSDs 9.7-4.3%, n=2-11). Details of recovery data are shown in Table 6.3.1-30.

All trials are summarized below in Tables 6.3.1-28 and 6.3.1-29 and in greater detail in the Tier 1 summary forms.

Northern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.23-0.54 mg/kg (median 0.37 mg/kg). These residues declined with time and, by day 20, had reached levels of 0.11-0.36 mg/kg (median 0.25 mg/kg).

Samples of destemmed grapes (berries) were also taken in the 1997 trials. The residues were similar in day-20 samples of grapes alone and of bunches (0.10-0.33 mg/kg in grapes [median 0.25 mg/kg], 0.11-0.36 mg/kg in the corresponding bunches [median 0.28 mg/kg]).

Southern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.11-1.8 mg/kg (median value 0.40 mg/kg). These residues declined with time and, by day 20, had reached levels of 0.08-0.44 mg/kg (median 0.19 mg/kg).

Samples of grapes themselves (destemmed berries) were also taken in the 1997 trials. The residues were similar in day-20 samples of grapes alone and of bunches (0.08-0.61 mg/kg in grapes [median 0.21 mg/kg], 0.09-0.44 mg/kg in the corresponding bunches [median 0.25 mg/kg]).

III. Conclusion

Over 2 growing seasons, eight residue trials were conducted with SZX 0722 & Copper 24.5 WP, containing 4.2% iprovalicarb and 20.3% copper (as 34.1% copper oxychloride), on grapes in the southern European residue region, and five in the north. The product was applied in accordance with the proposed use pattern, and the tests were carried out according to GLP principles. The purpose was to evaluate the residue behavior of the combination product, in the form of a "bridge" from an existing EU submission (iprovalicarb) or national registrations (copper).

The results of trials presented above demonstrate that:

- residue levels of iprovalicarb in grape bunches decline with time, with levels declining from 0.11-1.8 mg/kg (south) or 0.23-0.54 mg/kg (north) on day 0 to 0.08-0.44 mg/kg (south) or 0.11-0.36 mg/kg (north) on day 20. The respective median values were 0.40 and 0.37 mg/kg on day 0, and 0.19 and 0.25 mg/kg on day 20.
- residue values of iprovalicarb in grapes (berries) were similar to those in bunches, with median values in the 1997 trials virtually identical to those in the corresponding bunch samples.

– all residue values for iprovalicarb on day 20 were well below the EU MRL for iprovalicarb in grapes (2 mg/kg).

Table 6.3.1-28: Residues of iprovalicarb in/on grapes following applications of SZX 0722 & Copper 24.5 WP in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Portion analyzed	Residues DALT (days)	Residues iprovalicarb (mg/kg)
RA-2142/96 60730/4 0730-96 GLP: yes 1996	Grape Müller-Thurgau	Germany D-[redacted] EU-N	24.5 WP[1]	4	0.105-0.168	0.0105-0.168	81	bunch*	0 **20**	0.37 0.28
RA-2142/96 60731/2 0731-96 GLP: yes 1996	Grape Portugieser	Germany D-[redacted] EU-N	24.5 WP[1]	4	0.105-0.168	0.0105-0.168	81	bunch*	0 **20**	0.44 0.22
RA-2131/97 70194/7 0194-97 GLP: yes 1997	Grape Pinot Meunier	France F-[redacted] EU-N	24.5 WP[1]	4	0.105-0.168	0.105-0.168	85	bunch berry	0 **20** **20**	0.31 0.28 0.25
RA-2131/97 70195/5 0195-97 GLP: yes 1997	Grape Sauvignon	France F-[redacted] EU-N	24.5 WP[1]	4	0.105-0.168	0.105-0.168	85	bunch berry	0 **20** **20**	0.23 0.11 0.10
RA-2131/97 70666/3 0666-97 GLP: yes 1997	Grape Müller-Thurgau	Germany D-[redacted] EU-N	24.5 WP[1]	4	0.105-0.168	0.031-0.032	81	bunch berry	0 **20** **20**	0.54 0.36 0.33

FL = formulation GS = growth stage at last application DALT = days after last treatment
* sample material was called "segment of a bunch of grapes" in this study report

Formulations used in trials:
1 = SZX 0722 & Copper (24.5 WP) containing 4.2% iprovalicarb and 20.3% copper (as 34.1% copper oxychloride)

Table 6.3.1-29: Residues of iprovalicarb in/on grapes following applications of SZX 0722 & copper (24.5 WP) in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2143/96 60623/5 0623-96 GLP: yes 1996	Grape Pinot Blanc	Italy I-[redacted] EU-S	24.5 WP[1]	4	0.126	0.0126	83	bunch**	0 **20**	0.61 0.37
RA-2143/96 60733/9 0733-96 GLP: yes 1996	Grape Grenache noir	France F-[redacted] EU-S	24.5 WP[1]	4	0.126	0.126	86	bunch**	0 **20**	0.11 0.15
RA-2143/96 60732/0 0732-96 GLP: yes 1996	Grape Grenache noir	France F-[redacted] EU-S	24.5 WP[1]	4	0.126	0.126	86	bunch**	0 **20**	0.14 0.08
RA-2143/96 60622/7 0622-96 GLP: yes 1996	Grape Barbera	Italy I-[redacted] EU-S	24.5 WP[1]	4	0.126	0.0126	89	bunch**	0 **20**	0.42 0.14
RA-2132/97 70714/7 0714-97 GLP: yes 1997	Table grape Cardinal	France F-[redacted] EU-S	24.5 WP[1]	4	0.126	0.126	81	bunch berry	0* 0 7 14 **20** 28 **20**	0.29 0.38 0.38 0.36 0.27 0.21 0.16
RA-2132/97 70712/0 0712-97 GLP: yes 1997	Table grape Italia	Italy I-[redacted] EU-S	24.5 WP[1]	4	0.126	0.0126	81	bunch berry	0* 0 7 14 **20** 28 **20**	0.44 0.68 0.48 0.39 0.22 0.26 0.25

FL = formulation GS = growth stage at last application DALT = days after last treatment
* prior to last treatment
** sample material was called "segment of a bunch of grapes" in this study report

Formulations used in trials:
1 = SZX 0722 & Copper (24.5 WP), containing 4.2% iprovalicarb and 20.3% copper (as 34.1% copper oxychloride)

Table continued on next page...

Table 6.3.1-29 (cont'd): Residues of iprovalicarb in/on grapes following applications of SZX 0722 & Copper 24.5 WP in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2132/97 70711/2 0711-97 GLP: yes 1997	Table grape Soultanina	Greece GR-[redacted] EU-S	24.5 WP[1]	4	0.126	0.0126	83	bunch	0*	0.09
									0	0.31
									7	0.18
									14	0.11
									20	0.09
									28	0.09
								berry	**20**	0.08
RA-2132/97 70713/9 0713-97 GLP: yes 1997	Table grape Cardinal	Italy I-[redacted] EU-S	24.5 WP[1]	4	0.126	0.0126	77	bunch	0*	0.73
									0	1.8
									7	1.1
									14	0.57
									20	0.44
									28	0.16
								berry	**20**	0.61

FL = formulation GS = growth stage at last application DALT = days after last treatment

* prior to last treatment

Formulations used in trials:
1 = SZX 0722 & Copper (24.5 WP), containing 4.2% iprovalicarb and 20.3% copper (as 34.1% copper oxychloride)

Table 6.3.1-30: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2142/96 60730/4 (0730-96) 60731/2 (0731-96) *RA-2143/96* 60622/7 (0622-96) 60623/5 (0623-96) 60732/0 (0732-96) 60733/9 (0733-96) GLP: yes 1996	Grape	bunch*	iprovalicarb	6 3 2 11	0.05 1.0 2.0 overall	80 90 94 80	104 98 96 104	91 94 95 93	9.7 4.3 7.2
RA-2131/97 70194/7 (0194-97) 70195/5 (0195-97) 70666/3 (0666-97 *RA-2132/97* 70712/0 (0712-97) 70711/2 (0711-97) 70713/9 (0713-97) 70714/7 (0714-97) GLP: yes 1997	Grape	berry**	iprovalicarb	3 11 14	0.05 1.0 overall	78 89 78	89 119 119	82 101 97	7.4 9.6 12.4

* sample material called "segments of bunches of grapes" in these trials

** *berry* recoveries also valid for sample material *bunch*

Iprovalicarb & Fenamidone WP 44 (SZX 0722 & Fenamidone 44 WP)

The formulation SZX 0722 & Fenamidone 44 WP was applied using essentially the same use pattern with regard to iprovalicarb as SZX 0722 & Copper 24.5 WP. (The use of SZX 0722 & Fenamidone 44 WP has not been registered, but nevertheless the trials were conducted in order to support a prospective registration.)

Table 6.3.1-31: Use patterns (GAPs) for the spray application of SZX 0722 & Fenamidone 44 WP in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s. rate of application (kg/ha)	Max. no. of appls.	PHI (days)
SZX 0722 & Fenamidone 44 WP (240 g/kg iprovalicarb, 200 g/kg fenamidone)	EU-S	post-flowering (7-10 d int.)	0.5	0.12	5	21

EU-S = southern EU residue region

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/27, [redacted] 1999c**
Title: Determination of residues of SZX 0722 & RPA 407213 (44 WP) on grape following spray application in Italy
Report No. & Document No.: RA-2186/98, M-016234-01-1

Report: **KIIA 6.3.1/28, [redacted] 2001**
Title: Determination of residues of SZX 0722 & RPA 407213 in/on grape after spray application of SZX 0722 & RPA 407213 44 WP in the field in Italy
Report No. & Document No.: RA-2186/99, M-078120-01-1

Guidelines *(applies to both studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to both studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and support uses in grapes in the EU.

I. Materials and Methods

Southern European residue region

In Italy, a total of three trials were conducted in 1998/1999 on grapes (KIIA 6.3.1/27; KIIA 6.3.1/28). SZX 0722 & Fenamidone WP 44, containing 240 g/kg iprovalicarb and 200 g/kg fenamidone (RPA 407213), was applied 5 times at constant rates of 0.5 kg/ha (equivalent to 0.120 kg iprovalicarb/ha) with water rates of 1000 L/ha.

The product was applied according to proposed used pattern, simulating the worst-case situation. Spray intervals were 7-10 days at BBCH growth stages from 79 to 89. The PHI was 21 days. All applications in all studies were at the required rates. In 1998, samples of grape bunches were taken at days 0, 7, 14, 21 (PHI), and 28 after the last application. At days 14 and 21, samples of the grapes themselves (berries) were taken as well. In 1999, samples of grape bunches were taken at days 0, 21, and 28 after the last application; samples taken at days 21 and 28 were divided in bunch and berries (the destemmed grapes themselves).

Analytical samples were analyzed for iprovalicarb parent compound (residue definition for iprovalicarb) according to method 00562. The limit of quantitation in both methods was 0.05 mg/kg.

II. Findings

Recoveries of iprovalicarb were obtained from bunches and berries fortified at levels between 0.05 mg/kg and 1 mg/kg. The sample materials chosen served to represent all relevant sample materials collected in these trials. Mean recoveries were all within acceptable ranges (78-98%, RSDs 4.4-7.4%, n=1-10). Details of recovery data are shown in Table 6.3.1-33.

All trials are summarized below in Table 6.3.1-32 and in greater detail in the Tier 1 summary forms.

Southern European residue region

One trial showed irregular and inexplicable residue behavior, no. R 1998 1728/7 (=1728/98). Residue levels of 0.53 mg/kg were determined immediately subsequent to the last application, but these increased on day 7 and again on day 14 to a maximum of 0.67 mg/kg before beginning to decline. It is technically possible that the samples from this trial were mixed up, but because this could not be proven, one additional trial was planned and conducted in the next year. (The general level of residues was, nevertheless, similar in this trial to the other 1998 trial.)

Regarding the "normal" trials, immediately following the final application (day 0), samples of grape bunches yielded iprovalicarb residues ranging of 0.30 and 0.59 mg/kg. These residues initially declined with time, and by day 21 (=PHI) had reached levels of 0.11 and 0.35 mg/kg. Similar levels were found in the berries (range 0.14 and 0.27 mg/kg). However, day-28 sampling of bunches yielded residue values which were very slightly higher than those on day 21: 0.13 and 0.40 mg/kg.

III. Conclusion

Over 2 growing seasons, residue trials were conducted with SZX 0722 & Fenamidone 44 WP on grapes in southern Europe. (In total, three trials were conducted. Two were originally planned and conducted, but the residue behavior in one of them was irregular and inexplicable, so that an additional

trial was carried out in the following season.) The product was applied in accordance with the proposed use patterns, and the tests were carried out according to GLP principles. The original purpose was to evaluate the residue behavior of the combination product, in the form of a "bridge" from existing EU submissions (although the trials were never submitted for registration). The results presented here (excluding the "irregular" trial) demonstrate that:

- residue levels of iprovalicarb in grapes declined from values of up to 0.59 mg/kg on day 0 to a maximum of 0.35 mg/kg in bunches at the proposed PHI (day 21).
- day-21 residue values of iprovalicarb in destemmed grapes (berries) were similar to those in bunches, with a highest value of 0.27 mg/kg.
- all residue values for iprovalicarb at harvest (PHI 21 days) were well below the EU MRL for iprovalicarb in grapes (2 mg/kg).

Table 6.3.1-32: Residues of iprovalicarb in/on grapes following applications of with SZX 0722 & Fenamidone 44 WP in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2186/98 R 1998 1728/7 1728-98 GLP: yes 1998	Grape Barbera; red variety	Italy I-[redacted] EU-S	44 WP[1]	5	0.120	0.012	89	bunch	0*	0.41
									0	0.59
									7	0.59
									14	0.43
									21	0.35
									28	0.40
								berry	14	0.33
									21	0.27
RA-2186/98 R 1998 1729/5 1729-98 GLP: yes 1998	Grape Pampanuto; white variety	Italy I-[redacted] EU-S	44 WP[1]	5	0.120	0.012	85	bunch	0*	0.37
									0	0.83
									7	0.66
									14	0.67
									21	0.58
									28	0.54
								berry	14	0.55
									21	0.44
RA-2186/99 R 1999 0302/2 0302-99 GLP: yes 1999	Grape Contese; White variety	Italy I-[redacted] EU-S	44 WP[1]	5	0.120	0.012	85	bunch	0	0.30
									21	0.11
									28	0.13
									28	0.12
								berry	**21**	0.14
									28	0.12
									28	0.11

FL = formulation GS = growth stage at last application DALT = days after last treatment
* sampling prior to last sampling;

Formulations used in trials:
1 = with SZX 0722 & Fenamidone WP 44, containing 248 g/kg iprovalicarb and 200 g/kg fenamidone

Table 6.3.1-33: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2186/98	Grape	bunch*	iprovalicarb	4	0.05	78	90	82	7.0
R 1998 1728/7 (1728-98)				10	0.5	74	86	78	4.4
R 1998 1729/5 (1729-98)				1	1.0	88	88	88	-
GLP: yes				15	overall	74	90	79	6.1
1998									
RA-2186/99	Grape	berry**	iprovalicarb	2	0.05	97	99	98	-
R 1999 0302/2 (0302-99)				2	1.0	85	88	87	-
GLP: yes				4	overall	85	99	92	7.4
1999									

* recoveries for *bunch* also valid for sample material *berry*
** recoveries for *berry* also valid for sample material *bunch of grapes*

Fluopicolide & Iprovalicarb 440 SC (AE C638206 01 SC40 A1 440 SC)

Table 6.3.1-34: Use patterns (GAPs) for the spray application of Fluopicolide & Iprovalicarb 440 SC in/on grapes in Europe

Formulation	Region	Application timing	Max. rate of application (kg/ha [prod.])	Max. a.s. rate of application (kg/ha)	Max. no. of appls.	PHI (days)
Fluopicolide & Iprovalicarb 440 SC (200 g/L fluopicolide 240 g/L iprovalicarb)	EU-N	post-flowering (9-11 d int.)	0.5	0.12	4	21
	EU-S	post-flowering (9-11 d int.)	0.5	0.12	4	21

EU-N = northern EU residue region; EU-S = southern EU residue region

New studies submitted for Annex I Renewal ("AIR2")

Report: **KIIA 6.3.1/29, [redacted] 2004a**
Title: Determination of residues of AE C638206 and SZX 0722 in/on grape after spraying application of AE C638206 01 SC40 A1 (440 SC) in the field in Germany and northern France
Report No. & Document No.: RA-2429/03, M-122826-01-1

Report: **KIIA 6.3.1/30, [redacted] 2004b**
Title: Determination of residues of AE C638206 and SZX 0722 in/on grape following spray application of AE C638206 01 SC40 A1 440 SC in the field in Italy, Spain and southern France
Report No. & Document No.: RA-2430/03, M-123374-01-1

Guidelines *(applies to both studies)*: Directive 91/414/EEC, residues in or on treated products, food and feed
GLP *(applies to both studies)*: yes (certified laboratory); Deviations: none

Justification for including these studies in this "AIR" dossier: Data required to establish MRLs and to support uses in grapes in the EU.

A. Materials and Methods

Northern European residue region

In northern Europe, a total of four trials were conducted in 2003 on grapes (KIIA 6.3.1/29). The trials were conducted in northern France and Germany. Fluopicolide & Iprovalicarb SC 440, containing 200 g/L fluopicolide and 240 g/L iprovalicarb, was applied 4 times at constant rates (0.5 L/ha, equivalent to 0.12 kg iprovalicarb/ha).

The product was applied according to proposed used pattern. Spray intervals were 9-10 days at BBCH growth stages 81-85, 83-85, 85 and 85-89. The PHI was 21 days. Water rates ranged from 500 to 1000 L/ha, corresponding to a spray concentration of 0.05-0.1%.

Southern European residue region

In southern Europe, a total of four trials were conducted in 2003 on grapes (KIIA 6.3.1/30). The trials were conducted in southern France, Spain and Italy. Fluopicolide & Iprovalicarb SC 440, containing 200 g/L fluopicolide and 240 g/L iprovalicarb, was applied 4 times at constant rates (0.5 L/ha, equivalent to 0.12 kg iprovalicarb/ha and 0.10 kg fluopicolide/ha).

The product was applied according to proposed used pattern. Spray intervals were 10-11 days at BBCH growth stages 77-81, 79-83, 79-86 and 81-87. The PHI was 21 days. Water rates ranged from 500 to 1000 L/ha, corresponding to a spray concentration of 0.05-0.1%.

All trials

All applications in the study were at the required rates. In all trials samples of grape bunches were taken on day 0 and at harvest (day 21). Samples of berries (destemmed grapes) were also taken at harvest, except in one trial.

Analytical samples were analyzed for iprovalicarb parent compound (residue definition for iprovalicarb) according to method 00562. The limit of quantitation was 0.05 mg/kg.

II. Findings

Recoveries of iprovalicarb were obtained from bunches of grapes fortified at levels between 0.05 mg/kg and 0.5 mg/kg. The sample materials chosen served to represent all relevant sample materials collected in these trials. Mean recoveries were all within acceptable ranges (94-98%, RSDs 7.9-10.6%, n=4-6). Details of recovery data are shown in Table 6.3.1-38.

All trials are summarized below in Tables 6.3.1-36 and 6.3.1-37 and in greater detail in the Tier 1 summary forms.

Northern European residue region

Immediately following the final application, samples of grape bunches yielded iprovalicarb residues ranging from 0.36-0.62 mg/kg (median value 0.42 mg/kg). These residues generally declined with time and, by day 21, had reached levels of 0.25-0.58 mg/kg (median 0.27 mg/kg). (In one trial, R 2003 1002/1, residues on day 0 were lowest of all trials but increased considerably. It is likely that the day-0 sample was not representative.)

Samples of destemmed grapes (berries) were also taken in northern Europe. The residues were similar to day-21 samples of bunches of grapes (0.23-0.93 mg/kg [median 0.38 mg/kg]).

During the conduct of the German trial R 2003 0350/5, another iprovalicarb-containing formulation (SZX 0722 & Tolylfluanid 43.5 WG) was accidentally applied to both the treated and the untreated plots. Therefore the residue values were considerably higher in this trail. On day 0 after the last treatment the residue value was 2.0 mg/kg in/on bunches of grapes. It declined to 1.5 mg/kg in bunches and to 1.7 mg/kg in the grapes themselves (berries). If the residues determined in the control

samples are subtracted from the reported results, the day-28 values from this trial in bunches and in destemmed grapes are 0.70 and 1.1 mg/kg, respectively. The residue values and ranges are summarized below in Table 6.3.1-35.

Table 6.3.1-35: Summary of the results (ranges and median values, both in mg/kg) in for the use of Fluopicolide & Iprovalicarb 440 SC on grapes in the northern European residue region, at day 21 in all trials:
A) *excluding* trial with iprovalicarb "contamination" (R 2003 0350/5)
B) control values subtracted from result for R 2003 0350/5
C) as reported

Matrix	A: excluding "contaminated" trial			B: control values subtracted			C: as reported		
	n	range	med.	*n*	range	med.	*n*	range	med.
bunch	3	0.25-0.58	0.27	4	0.25-0.70	0.43	4	0.25-1.5	0.43
fruit ("berry")	3	0.23-0.93	0.31	4	0.23-1.13	0.62	4	0.23-1.7	0.62

In consideration of the events in trial R 2003 0350/5, constellations "A" or "B" in the table above both give more realistic impressions of the residue behavior than would using all values as reported (i.e. constellation "C").

Southern European residue region

Immediately following the final application (day 0), samples of grape bunches yielded iprovalicarb residues ranging from 0.14-0.42 mg/kg (median 0.26 mg/kg). These residues declined with time, and by day 21 (=PHI) had reached levels of <0.05-0.14 mg/kg (median 0.14 mg/kg) in bunches. Similar levels were found in the destemmed fruit (=berries, range 0.05-0.18 mg/kg, median 0.12 mg/kg).

III. Conclusion

Eight residue trials were conducted with Fluopicolide & Iprovalicarb SC 440 on grapes, four each in the northern and southern European residue regions. One northern trial was irregular, because an iprovalicarb-containing product was applied as a maintenance pesticide during the study; it was excluded from further evaluation. The product was applied in accordance with the proposed use patterns, and the tests were carried out according to GLP principles. The purpose was to evaluate the residue behavior of the combination product, in the form of a "bridge" from existing national and EU submissions. The results presented here demonstrate that:

- In the northern European residue region, levels of iprovalicarb in grape bunches generally declined with time, from values of 0.36-0.62 mg/kg on day 0 to 0.25-0.58 mg/kg on day 21. The respective median values were 0.42 mg/kg on day 0 and 0.27 mg/kg on day 21. (One irregular trial was excluded from this evaluation.)
- In the south, residue levels of iprovalicarb in grape bunches also declined with time, from values of up to 0.42 mg/kg on day 0 to a maximum of 0.18 mg/kg at the proposed PHI (day 21). The respective median values were 0.26 mg/kg on day 0, and 0.14 on day 21.

– Residue values of iprovalicarb in destemmed grapes (berries) were similar to those in bunches, with median values in the trials similar identical to those in the corresponding bunch samples.

– All residue values for iprovalicarb at harvest (PHI 21 days) were well below the established EU MRL for iprovalicarb in grapes (2 mg/kg).

Table 6.3.1-36: Residues of iprovalicarb in/on grapes following applications of Fluopicolide & Iprovalicarb 440 SC in the field in the northern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Portion analyzed	Residues DALT (days)	iprovalicarb (mg/kg)
RA-2429/03 R 2003 0350/5 0350-03 GLP: yes 2003	Grape Müller-Thurgau	Germany D-[redacted] EU-N	440 SC[1]	4	0.120	0.012-0.015	85	bunch berry	0 **21** **21**	2.0/0.72* 1.5/0.80* 1.7/0.57*
RA-2429/03 R 2003 1001/3 1001-03 GLP: yes 2003	Grape Pinot Gris	France F-[redacted] EU-N	440 SC[1]	4	0.120	0.024	85	bunch berry	0 **21** **21**	0.42 0.27 0.23
RA-2429/03 R 2003 1002/1 1002-03 GLP: yes 2003	Grape Spät-burgunder	Germany D-[redacted] EU-N	440 SC[1]	4	0.120	0.012	89	bunch berry	0 **21** **21**	0.36 0.58 0.93
RA-2429/03 R 2003 1004/8 1004-03 GLP: yes 2003	Grape Gamay	France F-[redacted] EU-N	440 SC[1]	4	0.120	0.024	85	bunch berry	0 **21** **21**	0.62 0.25 0.31

FL = formulation GS = growth stage at last application DALT = days after last treatment

* residues measured in control sample

Formulations used in trials:
1 = Fluopicolide & Iprovalicarb 440 SC containing 200 g/L fluopicolide and 240 g/L iprovalicarb

Table 6.3.1-37: Residues of iprovalicarb in/on grapes following applications of Fluopicolide & Iprovalicarb 440 SC in the field in the southern European residue region

Study No. Trial No. Plot No GLP Year	Crop Variety	Country	Application FL	No	kg/ha (a.s.)	kg/hL (a.s.)	GS	Residues Portion analyzed	DALT (days)	iprovalicarb (mg/kg)
RA-2430/03 R 2003 1007/2 1007-03 GLP: yes 2003	Grape Macabeo	Spain E-[redacted] EU-S	440 SC[1]	4	0.120	0.012	85	bunch	0	0.14
									21	<0.05
								berry	**21**	0.05
RA-2430/03 R 2003 1005/6 1005-03 GLP: yes 2003	Grape Tempranillo	Spain E-[redacted] EU-S	440 SC[1]	4	0.120	0.015	81	bunch	0	0.28
									21	0.13
								berry	**21**	0.16
RA-2430/03 R 2003 0351/3 0351-03 GLP: yes 2003	Grape Pinot Grigio	Italy I-[redacted] EU-S	440 SC[1]	4	0.120	0.012	83	bunch	0	0.42
									21	0.14
								berry	**21**	0.18
RA-2430/03 R 2003 1006/4 1006-03 GLP: yes 2003	Grape Syrah	France F-[redacted] EU-S	440 SC[1]	4	0.120	0.024	87	bunch	0	0.24
									21	0.14

FL = formulation GS = growth stage at last application DALT = days after last treatment

Formulations used in trials:
1 = Fluopicolide & Iprovalicarb 440 SC, containing 240 g/L fluopicolide and 240 g/L iprovalicarb

Table 6.3.1-38: Procedural recoveries for iprovalicarb in grape matrices

Study No., Trial No. (Trial SubID) GLP, Year	Crop	Portion analyzed	a.s./ metabolite	*n*	Fortification level (mg/kg)	Recovery (%) min	max	mean	RSD
RA-2429/03 R 2003 0350/5 (0350-03) R 2003 1001/3 (1001-03) R 2003 1002/1 (1002-03) R 2003 1004/8 (1004-03) GLP: yes 2003	Grape	bunch*	iprovalicarb	4	0.05	89	106	98	7.9
				6	0.5	76	102	94	10.6
				10	overall	76	106	96	9.4
RA-2430/03 R 2003 0351/3 (0351-03) R 2003 1005/6 (1005-03) R 2003 1006/4 (1006-03) R 2003 1007/2 (1007-03) GLP: yes 2003	Grape	bunch *	iprovalicarb	4	0.05	89	106	98	7.9
				6	0.5	76	102	94	10.6
				10	overall	76	106	96	9.4

* recoveries for *bunch* also valid for sample material *berry*

IIA 6.4 Livestock feeding studies

No livestock feeding studies were triggered for iprovalicarb because grapes are not feed items.

Iprovalicarb is not used on other primary animal feed crops such as cereals or rape silage, nor did the metabolism study indicate that significant residues are to be expected in animal tissues.

IIA 6.4.1 Poultry

No livestock feeding study in poultry was conducted. Please refer to IIA 6.4.

IIA 6.4.2 Lactating ruminants (goat or cow)

No livestock feeding study in lactating ruminants was conducted. Please refer to IIA 6.4.

IIA 6.4.3 Pigs

No livestock feeding study in pigs was conducted. Please refer to IIA 6.4.

IIA 6.4.4 Fish

Not required by Directive 91/414/EEC.

IIA 6.5 Effects of industrial processing and/or household preparation on...

IIA 6.5.1 The nature of residue

Original Annex II dossier (including evaluation process)

Experiments conducted to study the hydrolytic degradation of iprovalicarb at pH values 5, 7, and 9 showed that the parent compound is not affected by this process (chapter 7 of the original dossier). Subsequently, an additional hydrolysis study was conducted testing the effects of simulated processing

conditions on iprovalicarb. Iprovalicarb was added to drinking water, which was then incubated at three representative sets of conditions:
- 90°C at pH 4 for 20 min
- 100°C at pH 5 for 60 min
- 120°C at pH 6 for 20 min

Material balances were established at each sampling date, and, at >95% in all cases, demonstrated that no significant losses occurred. At test termination, parent compound accounted for 96.8-98.9% of the applied radioactivity, indicating that iprovalicarb does not degrade significantly in conditions relevant to processing. It is therefore unlikely that processing will affect the nature of iprovalicarb residues.

Studies submitted and evaluated for the first inclusion of iprovalicarb on Annex I (listed in grey typeface):

Report:	**KIIA 6.5.1/01, [redacted] 1999**
Title:	Aqueous hydrolysis of SZX 0722 under conditions of processing studies
Report No:	MR-223/99
Document No:	M-011633-01-1
Guidelines:	ECPA Residue Task Force, March 1993: Guidelines for the conduct of studies to investigate the nature of the potential residue in the product of industrial processing or household preparation
GLP:	yes

"AIR2" process

As this topic was sufficiently covered in the original Annex II dossier, no new are required.

IIA 6.5.2 Distribution of the residue in peel/pulp

Not relevant for grapes.

IIA 6.5.3 Residue levels - balance studies on set of representative processes

Original Annex II dossier (including evaluation process)

In the original Annex II dossier the effects of processing on iprovalicarb residues in grapes were investigated for juice, raisins, must and wine.

Since these commodities are not usually prepared at home, industrial processing procedures were used following treatment of grapevines at the standard recommended European rates. When comparing the residue levels determined in the RAC (grape bunches) and in processed products, the mean transfer factors were as follows: 0.7 in wine, 0.7 in must, 1.2 in raisins, and approx. 0.25 in juice. Therefore, whereas a slight concentration of residues is possible in raisins, no concentration – or even a reduction – would be anticipated in juice, must, or wine. In fact, quite a considerable reduction of residues is apparent in juice.

(Additional "balancing" data was submitted during the evaluation period, amending the original reports; the studies were accepted and considered to be valid.)

Studies submitted and evaluated for the first inclusion of iprovalicarb on Annex I (listed in grey typeface):

Report: **KIIA 6.5.3/01, [redacted] 1997**
Title: Determination of residues of SZX 0722 50 WG in/on processed commodities of grapes following spray application in Germany
Report No: RA-3139/95
Document No(s): M-000087-01-1
Guidelines: EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report: **KIIA 6.5.3/02, [redacted] 1997**
Title: Determination of residues of SZX 0722 (50 WG) in/on processed commodities of grapes following spray application in Italy
Report No: RA-3140/95
Document No(s): M-000106-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1520 Processed Food/Feed
EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report: **KIIA 6.5.3/03, [redacted] 1997**
Title: Determination of residues of SZX 0722 50 WG in/on processed commodities of grapes following spray application in Germany
Report No: RA-3140/96
Document No(s): M-000116-01-1
Guidelines: EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

Report: **KIIA 6.5.3/04, [redacted] 1997**
Title: Determination of residues of SZX 0722 (50 WG) in/on processed commodities of grape following spray application in Portugal and France
Report No: RA-3139/96
Document No(s): M-000137-01-1
Guidelines: EPA: Residue Chemistry Test Guidelines OPPTS 860.1520 Processed Food/Feed
EU: Directive 91/414/EEC, Residues in or on treated products, food and feed
GLP: yes

"AIR2" process

The presented data are regarded as being sufficient. No new data was generated re. processing of grapes, thus no new studies are presented in this AIR2 dossier on the effects of industrial processing on the residue level of iprovalicarb.

IIA 6.5.4 Residue levels - follow-up studies: concentration or dilution factors

Original Annex II dossier

As stated above, in the original Annex II dossier the effects of processing on iprovalicarb residues in grapes were investigated for juice, raisins, must and wine. Information on processing factors (i.e. concentration or dilution) was elucidated as summarized above under point 6.5.3.

"AIR2" process

The presented data are regarded as being sufficient. No new data was generated re. processing of grapes, thus no new studies are presented in this AIR2 dossier on the effects of industrial processing on the residue level of iprovalicarb.

IIA 6.6 Residues in succeeding crops

IIA 6.6.1 Theoretical consideration of the nature and level of the residue

Within the scope of this AIR2 submission, the determination of iprovalicarb residues in succeeding crops is not necessary, since grapevines are a permanent crop. However, in the original Annex II dossier, data were presented nevertheless; cf. point 6.6.2.

IIA 6.6.2 Metabolism and distribution studies on representative crops

Original Annex II dossier

A confined rotational crop was presented in the original Annex II dossier. Wheat, Swiss chard and turnips were evaluated when grown in soil that was treated with iprovalicarb labeled in the phenyl ring. The crops were sown at intervals of 32, 168, and 363 days following the application of iprovalicarb to soil at a rate equivalent to 1.174 kg a.s./ha. Crops planted at 32 and 363 days following application were cultivated under glass, while the crops planted at 168 days post application were grown outdoors. The TRR was determined in the different crops; samples were taken at maturity, except in the case of wheat forage (sampled at day 70) and wheat hay (sampled at day 123).

The results of the rotational crop study indicate that the three crops studied will take up residues of iprovalicarb and its metabolites from treated soil. A higher level of uptake was generally determined for the crops planted closest to the time of soil treatment [exception wheat straw/grain]. Residues of parent iprovalicarb, the proposed residue definition for food of plant origin, are detected in all of the rotational crops. As the residues in mature crop portions used for human consumption were ≤ 0.03 mg/kg, it is estimated that the use of iprovalicarb will not give rise to residues in rotational crops which will result in the limit of quantitation (LOQ, 0.05 mg/kg) being exceeded.

The study should be considered to be very much a worst-case situation in that all of the iprovalicarb was applied as one application with 100% of the application reaching the soil, which is unlikely to occur in practice.

Studies submitted and evaluated for the first inclusion of iprovalicarb on Annex I (listed in grey typeface):

Report:	**KIIA 6.6.2/01, [redacted] 1998**
Title:	Confined rotational crop study with SZX 0722
Report No:	PF4344
Document No(s):	M-001188-01-1
Guidelines:	EPA Guidelines N, § 165-1 (OPPTS 860.1850)
GLP:	yes

"AIR2" process

As stated above under point 6.6.1, the determination of iprovalicarb residues in succeeding crops is not necessary within the scope of this AIR2 submission, since grapevines are a permanent crop. The topic was sufficiently covered in the orginal Annex II dossier, so that no new studies are required for this AIR2 dossier.

IIA 6.6.3 Field trials on representative crops

The determination of iprovalicarb residues in succeeding crops is not necessary, since grapevines are a permanent crop.

IIA 6.7 Proposed residue definition and maximum residue levels

IIA 6.7.1 Proposed residue definition

As presented in the original Annex II dossier for iprovalicarb, the proposed residue definition in plants and animals, both for data collection and enforcement, is the parent compound iprovalicarb itself.

IIA 6.7.2 Proposed maximum residue levels (MRLs) and justification

Original Annex II dossier

Based on the current residue definition in plant materials – iprovalicarb parent compound – EU pMRLs were set for grapes at 2.0 mg/kg as originally published in Commission Directive 2003/60/EC, dated 18 June 2003, and subsequently published as tMRLs (cf. Regulation [EC] no. 149/2008, dated 28 January 2008). This value was based on the evaluation of data packages submitted with the original Annex II dossier, consisting of trials conducted with the straight formulation of iprovalicarb (50 WG).

"AIR2" process

Based on studies presented in this AIR2 dossier, new MRL calculations are presented below. Calculations were made according to the statistical methods described in EU guideline 7039/VI/95 and the German BBA-Guideline, Part IV, 3-6 (1990), using methods I and II, as well as according to the OECD MRL calculation model.

● **Grapes**

Numerous field residue trials with various formulations of iprovalicarb and slightly different use patterns were conducted in grapes in both European residue regions. When comparing the results, it is evident that final residue levels are generally higher in the north, with considerably higher median residues. For example, residues of iprovalicarb a.s. in all bunches of grape samples taken at 28 days after the final application were 0.05-1.7 mg/kg in the north (median 0.45 mg/kg) and <0.05-0.76 mg/kg in the south (median 0.16 mg/kg). This trend is evident at every sampling interval. Thus the critical region for the calculation of the MRL can be defined.

Since residue values for bunch and for the grapes themselves (destemmed fruit, or berries) are virtually the same, the results for bunch can be used for the calculation.

Residue values from trials with the same use pattern with regard to application rate and PHI were combined and considered together for MRL calculations.

Northern European residue region

Application rate 150 g a.s./(ha × m foliage height) and a PHI of 28 days

In 15 trials, either the product SZX 0722 & Folpet 43.5 WP or the product SZX 0722 & Azoxystrobin 325 SC was applied to grapes. One to two applications were made in the pre-flowering stages at application rates of 0.09 kg iprovalicarb/ha, and four to six applications post-flowering at rates of 0.15 kg iprovalicarb/(ha × m foliage height).

While the post-flowering rate per hectare and meter vine height remains constant, the actual amount of active substance applied in a given trial (expressed in two dimensions, i.e. kg/ha) can vary based on the height of the vines on the test plot, so that varying absolute amounts of active substance are directly comparable with one another. Post-blossom sprays were at rates of 0.24 kg iprovalicarb/ha in Germany (1.6 m "leaf wall" height) and 0.12-0.15 kg iprovalicarb/ha in France (0.8-1.25 m leaf wall).

Iprovalicarb residues in bunches taken 28 days after the last application ranged from 0.05-1.7 mg/kg. A summary of the resulting MRL calculations is shown below in Table 6.7.2-1.

Table 6.7.2-1: Iprovalicarb/grapes – maximum residue values for a pre-harvest interval of 28 days (northern European residue region, core rate: 150 g/[ha×m])

Method I (all values)	1.97 mg/kg
Method II (75% quantile)	2.20 mg/kg
OECD	3.0 mg/kg

0.05;0.10;0.13;0.31;0.34;0.38;0.38;0.45;0.47;0.60;0.92;1.1;1.2;1.5;1.7 mg/kg
STMR: *0.45*
HR: 1.7

Application rate 120 g a.s./(ha × m foliage height) and a PHI of 28 days

In twelve trials, either the product Folpet & Fosetyl-Al & Iprovalicarb WG 79, SZX 0722 & Mancozeb 66 WP, or SZX 0722 & Tolylfluanid 43.5 WG was applied to grapes. One to two applications were made prior to flowering at application rates of 0.048-0.072 kg iprovalicarb/ha, and three applications in the post-flowering stages at rates of 0.12 kg iprovalicarb/(ha × m foliage height).

While the post-flowering rate per hectare and meter vine height remains constant, the actual amount of active substance applied in a given trial (expressed in two dimensions, i.e. kg/ha) can vary based on the height of the vines on the test plot, so that varying absolute amounts of active substance are directly comparable with one another. Post-blossom sprays were at rates of 0.12-0.192 kg iprovalicarb/ha (1.0-1.6 m leaf wall).

Iprovalicarb residues in bunches taken 28 days after the last application ranged from <0.05 to 0.72 mg/kg. A summary of the resulting MRL calculations is shown below in Table 6.7.2-2.

Table 6.7.2-2: Iprovalicarb/grapes – maximum residue values for a pre-harvest interval of 28 days (northern European residue region, core rate: 120 g/[ha×m])

Method I (all values)	0.89 mg/kg
Method II (75% quantile)	0.89 mg/kg
OECD	1.50 mg/kg

<0.05;0.08;0.10;0.14;0.22;0.23;0.29;0.29;0.42;0.45;0.63;0.72 mg/kg
STMR: 0.26
HR: 0.72

Application rate 105-120 g a.s./(ha × m foliage height) and a PHI of 20-21 days

In nine trials the product SZX 0722 & Copper 24.5 WP or Fluopicolide & Iprovalicarb 440 SC was applied to grapes. Four applications were made post flowering at application rates of 0.105-0.168 kg iprovalicarb/ha.

Iprovalicarb residues in bunches taken 20/21 days after the last application ranged from 0.11 to 1.5 mg/kg, when using all data as reported. However, in the trials with Fluopicolide & Iprovalicarb 440 SC, one trial was contaminated with iprovalicarb (cf. section 6.3.1). If the iprovalicarb levels from the control samples in that trial are subtracted, the highest residue value in this data set would be 0.70 mg/kg; if the trial is excluded completely, the HR is 0.58 mg/kg. A summary of all resulting MRL calculations is shown below in Table 6.7.2-3.

Table 6.7.2-3: Iprovalicarb/grapes — maximum residue values for a pre-harvest interval of 21 days (northern European residue region, core rate: 120 g/[ha×m])

data set used:*	*A*	*B*	*C*
Method I (all values)	0.73 mg/kg	0.90 mg/kg	1.71 mg/kg
Method II (75% quantile)	0.68 mg/kg	0.94 mg/kg	0.94 mg/kg
OECD	0.9 mg/kg	1.5 mg/kg	3.0 mg/kg

* sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. table 6.3.1-35 for explanation)

0.11; 0.22;0.25; 0.27;0.28;0.28;0.36;0.58;1.5 mg/kg
STMR: 0.28
HR: 1.5

Southern European residue region

Application rate 150 g a.s./ha and a PHI of 28 days

In ten trials either the product SZX 0722 & Folpet 43.5 WP or the product SZX 0722 & Azoxystrobin 325 SC was applied to grapes. One application was made in the pre-flowering stages at an application rate of 0.09 kg iprovalicarb/ha, followed by four applications post flowering at rates of 0.15 kg iprovalicarb/ha.

Iprovalicarb residues in bunches taken 28 days after the last application ranged from <0.05 to 0.76 mg/kg. A summary of the resulting MRL calculations is shown below in Table 6.7.2-4.

Table 6.7.2-4: Iprovalicarb/grapes — maximum residue values for a pre-harvest interval of 28 days (southern European residue region, core rate: 150 g/ha)

Method I (all values)	0.97 mg/kg
Method II (75% quantile)	0.81 mg/kg
OECD	1.50 mg/kg

<0.05;<0.05;0.09;0.10;0.14;0.17;0.23;0.33;0.62;0.76 mg/kg
STMR: 0.16
HR: 0.76

Application rate 120 g a.s./ha and a PHI of 28 days

In 13 trials, either the product Folpet & Fosetyl-Al & Iprovalicarb WG 79, SZX 0722 & Mancozeb 66 WP, or Fosetyl-Al & Iprovalicarb & Mancozeb WP 69.1 was applied to grapes. One to two applications were made prior to flowering at application rates of 0.071-0.12 kg iprovalicarb/ha, followed by three applications post-flowering at rates of 0.12 kg iprovalicarb/ha.

Iprovalicarb residues in bunches taken 28 days after the last application ranged from <0.05 to 0.38 mg/kg. A summary of the resulting MRL calculations is shown below in Table 6.7.2-5.

Table 6.7.2-5: Iprovalicarb/grapes — maximum residue values for a pre-harvest interval of 28 days (southern European residue region, core rate: 120 g/ha)

Method I (all values)	0.49 mg/kg
Method II (75% quantile)	0.51 mg/kg
OECD	0.70 mg/kg

<0.05;<0.05;0.06;0.07;0.07;0.10;0.17;0.18;0.21;0.21;0.30;0.37;0.38 mg/kg
STMR: 0.17
HR: 0.38

Application rate 150 g a.s./ha and a PHI of 20-21 days

In four trials, the product SZX 0722 & Tolylfluanid WG 43.5 was applied to grapes. Three applications were made in the post flowering stages with application rates of 0.15 kg iprovalicarb/ha.

Iprovalicarb residues in bunches taken 20/21 days after the last application ranged from 0.12 to 0.31 mg/kg. A summary of the resulting MRL calculations is shown below in Table 6.7.2-6.

Table 6.7.2-6: Iprovalicarb/grapes — maximum residue values for a pre-harvest interval of 21 days (southern European residue region, core rate: 150 g/ha)

Method I (all values)	0.70 mg/kg
Method II (75% quantile)	0.62 mg/kg
OECD	0.80 mg/kg

0.12; 0.27; 0.30; 0.31 mg/kg
STMR: 0.29
HR: 0.31

Application rate 120 to 126 g a.s./ha and a PHI of 20-21 days

In 15 trials, either the product SZX 0722 & Copper 24.5 WP, SZX 0722 & Fenamidone 44 WP, or Fluopicolide & Iprovalicarb 440 SC was applied to grapes. Four to five applications were made post flowering at application rates of 0.12-0.126 kg iprovalicarb/ha.

Iprovalicarb residues in bunches taken 20/21 days after the final application ranged from <0.05 to 0.58 mg/kg. A summary of the resulting MRL calculations is shown below in Table 6.7.2-7.

Table 6.7.2-7: Iprovalicarb/grapes — maximum residue values for a pre-harvest interval of 21 days (southern European residue region, core rate: 120 g/ha)

Method I (all values)	0.61 mg/kg
Method II (75% quantile)	0.70 mg/kg
OECD	0.90 mg/kg

<0.05;0.08;0.09;0.11;0.13;0.14;0.14;0.14;0.15;0.22;0.27;0.35;0.37;0.44;0.58 mg/kg
STMR: 0.14
HR: 0.58

As stated previously, the values reported above are based on the residue values reported in grape bunches. In Table 6.7.2-8 below, the results are summarized of all MRL calculations for each use pattern and, in addition, for both commodities (bunches and the grapes themselves).

Based on the European model for MRL calculation, in which the highest calculated level would be 2.2 mg/kg (150 g "core rate", northern trials, 28-day PHI), but also taking into account that the fact that the highest residue (HR) in these (and all) trials was 1.7 mg/kg, an MRL of 2.0 mg/kg can be proposed for grapes. This value is the same as the previously published pMRLs and tMRLs for iprovalicarb in grapes in the EU. Using the OECD calculator would technically lead to an MRL proposal of 3.0 mg/kg. However, since the values used for the calculations are all results of European trials to cover the European use, and since this is the only use of the product in grapes relevant to trade in Europe, it is proposed to set the MRL according the European principles.

Therefore, BCS proposes to confirm and maintain the EU MRL for iprovalicarb in **grapes** at its current level, **2.0 mg/kg**, as it has been since the initial evaluation.

Table 6.7.2-8: Summary of MRL calculations carried out for the different use patterns (with regard to *use rate* and *PHI*) for iprovalicarb in grape commodities

Region	No. of trials	Application (g a.s./ha)	Application no.	Portion analyzed	DALT*	STMR (mg/kg)	HR (mg/kg)	MRL (mg/kg) EU I	MRL (mg/kg) EU II	MRL (mg/kg) OECD	data set†	details in…
EU-N	15	*150***	5-8	Bunch	28	**0.45**	**1.70**	**1.97**	**2.20**	**3.0**		Table 6.7.2-9
	12	120**	3-6		28	0.26	0.72	0.89	0.89	1.5		
	9		4-5		21	0.28	0.58	0.73	0.68	0.9	A	Table 6.7.2-10
						0.28	0.70	0.90	0.94	1.5	B	
						0.28	1.50	1.71	0.94	3.0	C	
EU-S	10	*150*	5		28	0.16	0.76	0.97	0.81	1.5		
	4		3		21	0.29	0.31	0.70	0.62	0.8		
	13	120	4-5		28	0.17	0.38	0.49	0.51	0.7		
	15		4		21	0.14	0.58	0.61	0.70	0.9		
EU-N	15	*150***	5-8	Grapes (berries)	28	**0.41**	1.30	1.59	**1.86**	**3.0**		Table 6.7.2-11
	8	120**	3-6		28	0.37	0.71	1.11	1.15	1.5		
	7		4-5		21	0.28	0.93	1.44	0.96	1.5	A	Table 6.7.2-12
						0.31	1.13	1.81	1.86	2.0	B	
						0.31	1.70	2.50	1.86	3.0	C	
EU-S	10	*150*	5		28	0.15	0.66	0.83	0.87	1.5		
	4		3		21	0.27	0.31	0.57	0.61	0.8		
	9	120	4-5		28	0.12	0.25	0.36	0.39	0.5		
	10		4-5		21	0.17	0.61	0.74	0.63	1.0		

Portion		STMR	HR	EU I	EU II	OECD
Bunches	max	0.45	1.70	1.97	2.20	3.0
	min	0.12	0.25	0.49	0.51	0.7
Grapes (berries)	max	0.41	1.70	2.50	1.86	3.0
	min	0.12	0.25	0.36	0.39	0.5

EU-N = northern European residue region; EU-S = southern European residue region
Maximum values for any given parameter are shown in **bold** typeface.

* DALT = days after last treatment
** g a.s./(ha × m foliage height)
† sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. table 6.3.1-35 for explanation)

The detailed calculations are presented on the following pages for the two "worst cases" (use patterns which resulted in the highest calculated MRLs for bunches and for grapes), as well as for the two cases involving the exclusion/inclusion of data from "contaminated" trial R 2003 0350/5 (as explained in section 6.3.1), in Tables 6.7.2-9 to 6.7.2-12.

(Detailed calculations of all permutations can be provided upon request.)

Table 6.7.2-9a: Values used for calculation of MRL proposals for iprovalicarb in grape bunches after application of 150 g a.s./(ha×m) (5-8 times) and a PHI of 28 days in the northern European residue region

Active substance : *iprovalicarb* Crop group : *berries and small fruit*
Portion analyzed : ***bunch*** Commodity : *grape*
Target value : *MRL* PHI : *28 d*

No.	Crop	DALT	Residue value (mg/kg)	Plot No.[1]/ Study No.	No. of applic.	FL type	Product	Country	Area of applic.
1	Grape	28	0.10	0238-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	France	F
2	Grape	28	1.2	0701-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	Germany	F
3	Grape	28	0.47	0702-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	France	F
4	Grape	28	0.92	0703-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	Germany	F
5	Grape	29	0.45	0705-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	France	F
6	Grape	28	1.5	0775-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
7	Grape	28	1.1	0776-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
8	Grape	28	1.7	0777-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
9	Grape	28	0.13	0778-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
10	Grape	28	0.05	0779-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
11	Grape	28	0.38	1065-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
12	Grape	28	0.38	1531-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
13	Grape	28	0.60	1532-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
14	Grape	28	0.31	1533-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
15	Grape	28	0.34	1534-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F

[1] as shown in the Tier 1 summaries
DALT = days after last treatment FL = formulation F= field use

Results presented on the following page…

Table 6.7.2-9b: Calculation of MRL proposals according to BBA Guideline Part IV, 3-6, January 1990

Method I (Weinmann/Nolting) (all values)	R s k **Rmax=R+k*s**	0.642 0.519 2.566 **1.973**
Method II (Wilkening) (75 % quantile)	R (0.75) **Rber=2*R(0.75)**	1.100 **2.200**

Summary of results:

Maximum residue values for a pre-harvest interval of 28 days

Method I (all values) 1.97 mg/kg
Method II (75% quantile) 2.20 mg/kg
STMR: 0.05;0.10;0.13;0.31;0.34;0.38;0.38;**0.45**;0.47;0.60;0.92;1.1;1.2;1.5;1.7

Table 6.7.2-9c: Calculation of MRL proposals according to OECD Calculator

Total number of data (n)	15	Standard deviation (SD)	0.519
Lowest residue	0.05	Percentage of censored data	0
Highest residue	1.7	Number of non-censored data	15
Median residue	0.450	Correction factor for censoring (CF)	1.000
Mean	0.642		

Proposed MRL estimate

Highest residue 1.7 mg/kg
Mean + 4 SD 2.717 mg/kg
CF x 3 mean 1.926 mg/kg
Unrounded MRL 2.717 mg/kg
Rounded MRL 3 mg/kg

Table 6.7.2-10a: Values used for calculation of MRL proposals for iprovalicarb in grape bunches after application of 120 g a.s./(ha×m) (4 times) and a PHI of 21 days in the northern European residue region

Active substance :	*iprovalicarb*	Crop group :	*berries and small fruit*
Portion analyzed :	***bunch***	Commodity :	*grapes*
Target value :	*MRL*	PHI :	*21 d*

No.	Crop	DALT	Residue value (mg/kg)	Plot No.[1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Grape	20	0.28	0194-97 / RA-2131/97	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	France	F
2	Grape	20	0.11	0195-97 / RA-2131/97	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	France	F
3	Grape	20	0.36	0666-97 / RA-2131/97	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	Germany	F
4	Grape	20	0.28	0730-96 / RA-2142/96	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	Germany	F
5	Grape	20	0.22	0731-96 / RA-2142/96	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	Germany	F
6	Grape	21	C[2]: 1.5 B[3]: 0.70	0350-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	Germany	F
7	Grape	21	0.27	1001-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	France	F
8	Grape	21	0.58	1002-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	Germany	F
9	Grape	21	0.25	1004-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	France	F

DALT = days after last treatment FL = formulation F= field use

Footnotes:
1 - as shown in the Tier 1 summaries
2 – value "C" is the value as reported in this trial
3 – as this trial was "contaminated" by incorrectly applied iprovalicarb, value "B" reflects value "C" *minus* the residue level determined in the control sample

Results presented on the following page…

Table 6.7.2-10b: Calculation of MRL proposals according to BBA Guideline Part IV, 3-6, January 1990

	data set:*	*A*	*B*	*C*
Method I (Weinmann/Nolting)	R	0.294	0.339	0.428
(all values)	s	0.135	0.185	0.422
	k	3.188	3.032	3.032
	Rmax=R+k*s	**0.725**	**0.901**	**1.706**
Method II (Wilkening)	R (0.75)	0.340	0.470	0.470
(75 % quantile)	**Rber=2*R(0.75)**	**0.680**	**0.940**	**0.940**

* sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. tables 6.3.1-35 and 6.7.2-3 for explanation)

Summary of results:

Maximum residue values for a pre-harvest interval of: 21 days

data set:*	*A*	*B*	*C*
Method I (all values)	0.73 mg/kg	0.90 mg/kg	1.71 mg/kg
Method II (75% quantile)	0.68 mg/kg	0.94 mg/kg	0.73 mg/kg

STMR: 0.11;0.22;0.25;0.27;**0.28**;0.28;0.36;0.58;(B*: 0.70/C*: 1.5)

* sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. tables 6.3.1-35 and 6.7.2-3 for explanation)

Table 6.7.2-10c: Calculation of MRL proposals according to OECD Calculator (data set "C"*)

Total number of data (n)	9	Standard deviation (SD)	0.422
Lowest residue	0.11	Percentage of censored data	0
Highest residue	1.5	Number of non-censored data	9
Median residue	0.280	Correction factor for censoring (CF)	1.000
Mean	0.428		

Proposed MRL estimates

data set:*	*A*	*B*	*C*
Highest residue	0.58 mg/kg	0.70 mg/kg	1.5 mg/kg
Mean + 4 SD	0.835 mg/kg	1.081 mg/kg	2.114 mg/kg
CF x 3 mean	0.881 mg/kg	1.017 mg/kg	1.283 mg/kg
Unrounded MRL	0.881 mg/kg	1.081 mg/kg	2.114 mg/kg
Rounded MRL	0.9 mg/kg	1.5 mg/kg	3 mg/kg

* sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. tables 6.3.1-35 and 6.7.2-3 for explanation)

Table 6.7.2-11a: Values used for calculation of MRL proposals for iprovalicarb in grapes (destemmed fruit or "berries") after application of 150 g a.s./(ha×m) (5-8 times) and a PHI of 28 days in the northern European residue region

Active substance : *iprovalicarb* Crop group : *berries and small fruit*
Portion analyzed : ***berry*** Commodity : *grape*
Target value : *MRL* PHI : *28 d*

No.	Crop	DALT	Residue value (mg/kg)	Plot No.[1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Grape	28	0.07	0238-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	France	F
2	Grape	28	1.1	0701-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	Germany	F
3	Grape	28	0.38	0702-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	France	F
4	Grape	28	0.42	0703-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	Germany	F
5	Grape	29	0.38	0708-97 / RA-2129/97	6	WP 43.5	SZX 0722 & Folpet WP 43.5	France	F
6	Grape	28	0.93	0775-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
7	Grape	28	1.2	0776-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
8	Grape	28	1.3	0777-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
9	Grape	28	0.10	0778-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
10	Grape	28	<0.05	0779-97 / RA-2141/97	5	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
11	Grape	28	0.31	1531-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
12	Grape	28	0.65	1532-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
13	Grape	28	0.26	1533-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	France	F
14	Grape	28	0.48	1534-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F
15	Grape	28	0.41	1065-98 / RA-2123/98	8	SC 325	SZX 0722 & Azoxystrobin SC 325	Germany	F

[1] as shown in the Tier 1 summaries
DALT = days after last treatment FL = formulation F= field use

Results presented on the following page…

Table 6.7.2-11b: Calculation of MRL proposals according to BBA Guideline Part IV, 3-6, January 1990

Method I (Weinmann/Nolting) (all values)	R s k **Rmax=R+k*s**	0.536 0.411 2.566 **1.590**
Method II (Wilkening) (75 % quantile)	R (0.75) **Rber=2*R(0.75)**	0.930 **1.860**

Summary of results:

Maximum residue values for a pre-harvest interval of 28 days

Method I (all values) 1.59 mg/kg
Method II (75% quantile) 1.86 mg/kg
STMR: <0.05;0.07;0.10;0.26;0.31;0.38;0.38;**0.41**;0.42;0.48;0.65;0.93;1.1;1.2;1.3

Table 6.7.2-11c: Calculation of MRL proposals according to OECD Calculator

Total number of data (n)	15	Standard deviation (SD)	0.411
Lowest residue	0.05	Percentage of censored data	7
Highest residue	1.3	Number of non-censored data	14
Median residue	0.410	Correction factor for censoring (CF)	0.956
Mean	0.563		

Proposed MRL estimate

Highest residue 1.3 mg/kg
Mean + 4 SD 2.179 mg/kg
CF x 3 mean 1.537 mg/kg
Unrounded MRL 2.179 mg/kg
Rounded MRL 3 mg/kg

Table 6.7.2-12a: Values used for calculation of MRL proposals for iprovalicarb in grapes (destemmed fruit or "berries") after application of 120 g a.s./(ha×m) (4 times) and a PHI of 20/21 days in the northern European residue region

Active substance : *iprovalicarb* Crop group : *berries and small fruit*
Portion analyzed : ***berry*** Commodity : *grape*
Target value : *MRL* PHI : *21 d*

No.	Crop	DALT	Residue value (mg/kg)	Plot No.[1]/ Study No.	No. of applic.	FL-Type	Product	Country	Area of applic.
1	Grape	20	0.25	0194-97 / RA-2131/97	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	France	F
2	Grape	20	0.10	0195-97 / RA-2131/97	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	France	F
3	Grape	20	0.33	0606-97 / RA-2131/97	4	WP 24.5	SZX 0722 & Cu (as copper oxychloride) WP 24.5	Germany	F
4	Grape	21	C[2]: 1.1 B[3]: 1.13	0350-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	Germany	F
5	Grape	21	0.23	1001-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	France	F
6	Grape	21	0.93	1002-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	Germany	F
7	Grape	21	0.31	1004-03 / RA-2429/03	4	SC 440	AE C638206 01 SC40 A1	France	F

DALT = days after last treatment FL = formulation F= field use

Footnotes:
1 - as shown in the Tier 1 summaries
2 – value "C" is the value as reported in this trial
3 – as this trial was "contaminated" by incorrectly applied iprovalicarb, value "B" reflects value "C" *minus* the residue level determined in the control sample

Results presented on the following page…

Table 6.7.2-12b: Calculation of MRL proposals according to BBA Guideline Part IV, 3-6, January 1990

	data set:*	*A*	*B*	*C*
Method I (Weinmann/Nolting)	R	0.358	0.469	0.550
(all values)	s	0.292	0.395	0.573
	k	3.711	3.401	3.401
	Rmax=R+k*s	**1.440**	**1.811**	**2.498**
Method II (Wilkening)	R (0.75)	0.480	0.930	0.930
(75 % quantile)	**Rber=2*R(0.75)**	**0.960**	**1.860**	**1.860**

* sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. table 6.3.1-35 for explanation)

Summary of results:

Maximum residue values for a pre-harvest interval of: 21 days

data set:*	A	B	C
Method I (all values)	1.44 mg/kg	1.81 mg/kg	2.50 mg/kg
Method II (75% quantile)	0.96 mg/kg	1.86 mg/kg	1.86 mg/kg

STMR: 0.10;0.23;0.25;**0.31**;0.33;0.93;1.7

* sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. table 6.3.1-35 for explanation)

Table 6.7.2-12c: Calculation of MRL proposals according to OECD Calculator (data set "C"*)

Total number of data (n)	7	Standard deviation (SD)	0.573
Lowest residue	0.1	Percentage of censored data	0
Highest residue	1.7	Number of non-censored data	7
Median residue	0.310	Correction factor for censoring (CF)	1.000
Mean	0.550		

Proposed MRL estimate

data set:*	A	B	C
Highest residue	0.93 mg/kg	1.13 mg/kg	1.7 mg/kg
Mean + 4 SD	1.524 mg/kg	2.048 mg/kg	2.841 mg/kg
CF x 3 mean	1.075 mg/kg	1.406 mg/kg	1.650 mg/kg
Unrounded MRL	1.524 mg/kg	2.048 mg/kg	2.841 mg/kg
Rounded MRL	1.5 mg/kg	2.0 mg/kg	3.0 mg/kg

* sets "A", "B", and "C" refer to the inclusion/exclusion of data from trial R 2003 0350/5 (cf. table 6.3.1-35 for explanation)

IIA 6.8 Proposed pre-harvest intervals, re-entry or withholding periods

IIA 6.8.1 Pre-harvest interval (in days) for each relevant crop

The envisaged pre-harvest intervals are as described above in the field residue trials section of this chapter (point KIIA 6.3). For the "safe use" in grapes, the critical PHI is 28 days.

(However, similar uses exist for which a PHI of 20/21 days is stipulated on the label)

IIA 6.8.2 Re-entry period (in days) for livestock, to areas to be grazed

Iprovalicarb-containing products are not intended for use in areas to be grazed by livestock. Therefore, a re-entry period does not need to be established.

IIA 6.8.3 Re-entry period for man to crops, buildings or treated spaces

a) Crops

Under practical conditions there is no reason to enter a field crop shortly after treatment. Even if done, one would wait until the spray solution has dried on the plant surface, at least. Under these circumstances, no unacceptable risk is anticipated for workers entering the treated crop.

In grapes, activities such as harvesting, pruning, or tying may usually be done by workers throughout the growing season. Re-entry exposure was evaluated from a cumulative foliar deposit based on a maximum number of applications made at the maximum dose and 8 hours contact with foliage per day. Exposure of operators entering treated areas is within acceptable levels (when considering iprovalicarb) when standard work clothing is worn by workers (shoes, socks, long pants, and long sleeves).

Therefore, setting a specific re-entry period is principally not indicated after an application of iprovalicarb-containing products in vineyards.

b) Buildings

Not relevant.

c) Spaces

On account of the relatively short chemical lifetime of iprovalicarb in the air, it is not to be expected that the active substance can be transported in the gaseous phase over large distances, or that it can accumulate in the air (see Annex II, points 2.10 and 7.10).

IIA 6.8.4 Withholding period (in days) for animals feedingstuffs

Not relevant for grapes since they are not used as animal feedstuffs.

IIA 6.8.5 Waiting period between last application and sowing or planting

Not relevant for the use on grapes.

IIA 6.8.6 Waiting period between application and handling treated products

The use of iprovalicarb-containing products is intended in grapevines prior to harvest. The proposed pre-harvest interval is 28 days for grapes ("safe use"). There is no need to handle treated crops before harvest.

IIA 6.8.7 Waiting period before sowing/planting succeeding crops

Not relevant, because grapevines are a permanent crop.

IIA 6.9 Estimation of exposure through diet and other means

IIA 6.9.1 TMDI calculations

The Acceptable Daily Intake (ADI) of 0.015 mg/kg body weight was established based on the NOEL in the chronic dog study (see Annex II, section 3, point 5.11).

In order to evaluate the potential chronic exposure to iprovalicarb residues through the diet, the Theoretical Maximum Dietary Intakes (TMDI) were estimated using the EFSA/PRAPeR model (revision 2). This model was initially developed for the evaluation of the harmonized EU MRLs and includes chronic and acute consumption data for adults and children. For the evaluation of the chronic exposure, the model uses 5 WHO diets relevant to the EU and 22 national diets from 13 different EU Member States.

As a worst-case scenario for the chronic exposure assessment, the TMDI calculations were based on all existing tMRLs as established in Regulation (EC) No 396/2005 amended by Regulation No. 149/2008 (1/9/2008), including the established tMRL – and, as discussed in this AIR2 dossier, proposed future MRL – for grapes, 2.0 mg/kg.

The total TMDI in all tested populations ranged from 8-65% with the maximum total calculated intake accounting for 65% of the ADI (WHO Cluster Diet B). As shown in Table 6.9.1-1 below, the chronic risk assessment calculation for iprovalicarb yields no chronic intake concerns for any of the European diets. No further refinement of the assessment (e.g. NEDI/IEDI) is necessary.

Table 6.9.1-1: Details of TMDI calculation for iprovalicarb according to the EFSA/PRAPeR model (rev. 2)

TMDI in % of ADI	MS Diet	Highest contributor to MS diet		2nd contributor to MS diet		3rd contributor to MS diet	
		% of ADI	Commodity / group of commodities	% of ADI	Commodity / group of commodities	% of ADI	Commodity / group of commodities
64.9	WHO Cluster diet B	28.6	Table and wine grapes	20.6	Tomatoes	4.0	CEREALS
63.4	FR all population	54.8	Table and wine grapes	2.9	Tomatoes	2.1	Lettuce and other salad plants
48.8	PT General population	36.9	Table and wine grapes	6.0	Tomatoes	1.8	CEREALS
36.6	WHO cluster diet E	23.9	Table and wine grapes	3.5	Tomatoes	2.0	CEREALS
36.1	DE child	16.9	Table and wine grapes	6.4	Tomatoes	4.2	Pome fruit
28.7	IE adult	15.5	Table and wine grapes	2.7	Tomatoes	2.2	CEREALS
27.2	NL child	10.1	Table and wine grapes	4.2	Tomatoes	3.3	Pome fruit
26.1	DK adult	19.6	Table and wine grapes	2.8	Tomatoes	1.0	CEREALS
23.3	UK Adult	15.1	Table and wine grapes	2.9	Tomatoes	1.3	SUGAR PLANTS
23.2	UK Toddler	7.6	SUGAR PLANTS	3.9	Tomatoes	3.7	Table and wine grapes
22.6	WHO Cluster diet F	9.8	Table and wine grapes	4.5	Tomatoes	2.0	Lettuce and other salad plants
22.1	WHO cluster diet D	7.4	Table and wine grapes	6.7	Tomatoes	2.8	CEREALS
21.3	UK vegetarian	11.9	Table and wine grapes	4.1	Tomatoes	1.3	SUGAR PLANTS
21.2	WHO regional European diet	7.3	Tomatoes	5.1	Table and wine grapes	2.7	Lettuce and other salad plants
20.3	NL general	6.3	Table and wine grapes	2.8	Tomatoes	1.6	Lettuce and other salad plants
18.8	ES adult	6.1	Table and wine grapes	5.2	Tomatoes	3.6	Lettuce and other salad plants
18.8	IT kids/toddler	9.5	Tomatoes	2.8	CEREALS	2.7	Lettuce and other salad plants
17.8	SE general population 90th percentile	6.1	Tomatoes	3.1	Table and wine grapes	2.7	Lettuce and other salad plants
17.0	IT adult	7.8	Tomatoes	3.7	Lettuce and other salad plants	1.7	Table and wine grapes
16.4	FR toddler	5.2	Tomatoes	2.8	Table and wine grapes	2.7	Root and tuber vegetables
16.0	ES child	6.5	Tomatoes	2.8	Lettuce and other salad plants	1.7	CEREALS
15.2	DK child	3.5	Tomatoes	3.5	CEREALS	2.4	Table and wine grapes
13.3	PL general population	5.8	Tomatoes	4.3	Table and wine grapes	1.4	Root and tuber vegetables
12.9	UK Infant	3.4	SUGAR PLANTS	2.9	Tomatoes	1.6	Root and tuber vegetables
10.1	FI adult	4.3	Table and wine grapes	2.8	Tomatoes	0.6	CEREALS
8.1	LT adult	4.1	Tomatoes	1.2	Root and tuber vegetables	0.9	CEREALS
8.0	FR infant	2.4	Root and tuber vegetables	1.1	Table and wine grapes	1.0	Tomatoes

IIA 6.9.2 NEDI calculations

As presented under point 6.9.1 above, TMDI calculations for iprovalicarb according to the EFSA/PRAPeR model (rev 2.0) yielded maximum ADI usage values of 65%.

Since the TMDI calculation demonstrate a margin of safety, it was not necessary to perform NEDI calculations in order to refine the dietary risk assessment.

IIA 6.9.3 NESTI calculations

No Acute Reference Dose (ARfD) was set for iprovalicarb, as it is not acutely toxic. Thus no NESTI/IESTI calculations are required.

IIA 6.10 Other/special studies

None.

IIA 6.11 Summary and evaluation of residue behavior and reasonable grounds

IIA 6.11.1 Summary and evaluation of residue behaviour

Original Annex II dossier

In early 1998, the original Annex II dossier was submitted to the Irish PCS. In that dossier, two uses were supported with residue trial data, grapes and potatoes. In this Annex I Renewal ("AIR2") dossier, only the "safe use" in grapes will be presented. With regard to the summary and evaluation of the residue behavior, all aspects of the original dossier but of relevance to to the AIR2 "safe use" are summarized briefly in their respective chapters and subchapters above. For all further information pertaining to the original dossier, please refer directly to it.

"AIR2" process

New residue data were presented in chapter 6.3.1 of this AIR2 dossier to describe the use of iprovalicarb in grapes in Europe. Numerous trials were conducted with various combination formulations, many of which have been used (in Annex III dossiers) to establish national registrations in the EU member states, some of which however are provided to make a more complete evaluation of the substance possible.

78 **field residue trials** conducted in both EU residue regions over eight growing seasons with over 10 different iprovalicarb-containing products were presented above, based on two basic use patterns with "core application rates" of 150 or 120 g/ha. In trials conducted in the northern European residue region, these rates were generally expressed as, e.g., 150 g/(ha×m vine foliage height), leading to higher "g/ha" rates in trials with higher vines, as is typical in Germany.

Residue levels were generally higher in the northern trials than in the south. Northern residue trials with the "150-g core rate" and a 28-day PHI were the most critical ones, with day-28 values in bunches ranging from 0.5-1.7 mg/kg.

MRL calculations were conducted based on the new data, using various permutations of the new trial data. It is proposed to maintain the current MRL for iprovalicarb in grapes, 2.0 mg/kg.

Based on the data presented, new **dietary risk assessments** were conducted, updating the previous data by using the EFSA/PRAPeR model (rev. 2). In the first tier of the chronic risk assessment (TMDI), the maximum ADI usage amounted to 65%. Thus, no further refinements (e.g. NEDI) were necessary. As the substance is not acutely toxic, no ARfD exists or was proposed, and no acute dietary risk assessment was conducted. Iprovalicarb will not present a risk to the consumer if used in grapes as currently registered in the EU.

No further new data has been generated or was considered to be required. For all other aspects regarding the metabolism and residue behavior of iprovalicarb (SZX 0722), please refer to the original Annex II dossier.

IIA 6.11.2 Reasonable grounds in support of the petition

Bayer CropScience is requesting Annex I Renewal of iprovalicarb as a fungicide for use in grapes. In this "AIR2" dossier, only the so-called "safe use" is described.

To support this registration, Bayer CropScience has evaluated the risk associated with registration on grapes (and other crops for which MRLs exist). Exposure to iprovalicarb residues was evaluated by the conduct of plant (primary and confined rotational crops) and animal metabolism studies to define the residues of concern followed by the conduct of field residue studies on grapes to define the magnitude of residue in food and feed items. Acute and chronic dietary exposure assessments according to the EFSA PRAPeR model (revision 2) have shown that total human dietary exposure to iprovalicarb represents only a small portion of the chronic reference dose (ADI) even when calculating with the most conservative approaches. Occupational exposure assessments have shown acceptable Margins of Exposure for all use practices.

Therefore, there is reasonable certainty that no harm will result from the use of iprovalicarb when it is used according to the label.

Adequate MRLs have been proposed for all crops and Bayer CropScience requests establishment of these MRLs.