A14111B

Chlorothalonil 400 g/L + Azoxystrobin 80 g/L SC

NOTIFICATION OF AN ACTIVE SUBSTANCE UNDER COMMISSION REGULATION (EU) 844/2012

DOCUMENT M-CP, Section 7

TOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCT

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number
14/12/15	CP 7.2.3: Inclusion of new DFR data (all changes are highlighted in green).	21 March 2015 updated 14/12/15
27/07/16	CP 7.1.1: Inclusion of additional statistical analysis for acute oral study. CP 7.1.3: Inclusion of additional data to support classification proposal (all changes are highlighted in yellow)	21 March 2015, 14 December 2015 updated 27 July 2016

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

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CP 7 TOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCTS

Introduction

This document supports the application for renewal of the regulatory approval of chlorothalonil under Commission Implementing Regulation (EU) 844/2012 of 18 September 2012. This document reviews the toxicological studies forfor the product A14111B containing:

- 400 g/L chlorothalonil
- 80 g/L azoxystrobin

A14111B is a suspension concentrate (SC) containing 400 g/L chlorothalonil and 80 g/L azoxystrobin for use as a fungicide in cereals and other speciality crops. A14111B was not the representative formulation in the EU review of chlorothalonil; for further details refer to the confidential dossier of this submission (Document J).

Chlorothalonil was included in Annex I of Council Directive 91/414/EEC (Commission Directive 2005/53/EC of 15 September 2005). This active substance is an approved active substance under Regulation (EC) 1107/2009 (repealing Commission Directive 91/414/EEC) as specified in Commission Implementing Regulation (EU) No. 540/2011 of 25 May 2011.

Azoxystrobin which was included into Annex I of Council Directive 91/414/EEC (Commission Directive 1998/47/EC; 7 July 1998) and for which a renewal of this inclusion was voted by SCoFCAH on 9 July 2010 (Commission Directive 2010/55/EU; 20 August 2010). This active substance is an approved active substance under Regulation (EC) 1107/2009 (repealing Commission Directive 91/414/EEC) as specified in Commission Implementing Regulation (EU) No. 540/2011 of 25 May 2011.

In accordance with Commission Implementing Regulation (EU) 844/2012, this document summarises new information which are relevant for the renewal of the approval of chlorothalonil under Regulation (EC) 1107/2009.

- Where appropriate this document refers to the Commission Implementing Regulation (EU) No. 540/2011 for chlorothalonil and to the Review Report for chlorothalonil (SANCO/4343/2000 final (revised) 28 September 2006), and in particular the endpoints provided in Appendices I and II thereof.
- Where appropriate this document refers to the Commission Implementing Regulation (EU) No. 540/2011 for azoxystrobin and EFSA report for the renewal of the inclusion of azoxystrobin (**EFSA Journal (2010) 8(4), 1542**), and in particular Appendices I and II thereof.

This document covers data and risk assessments which were not part of the original dossier and which are necessary to reflect changes:

- In requirements under Commission Regulation (EU) No 284/2013, and the associated Annex, which repeals Commission Regulation (EU) No 545/2011 which, under Regulation (EC) 1107/2009, replaced the requirements of Annex III to Directive 91/414/EEC
- In scientific and technical knowledge since the approval or last renewal of the approval
- To representative uses

The proposed representative use pattern is included in Document D1.

Each section of this document provides the agreed EU endpoints and if relevant proposals for amended endpoints.

Where new guidance documents have been introduced since the EU review of chlorothalonil, an updated evaluation of chlorothalonil and A14111B has been included. To adequately assess A14111B to the new guidance documents, it may have been necessary to provide new data, if so these are also included. Where the report has been previously submitted, but an OECD summary has been provided for clarity reasons only, the original report has not been submitted again.

Information on the detailed composition of A14111B can be found in the confidential dossier of this submission (Document J).

Details of all relevant data from the scientific peer reviewed open literature on the active substance, metabolites and breakdown or reaction products and plant protection products containing the active substance have been provided in the **Document M-CA Section 9** and are discussed within the relevant data point of the associated dossier for the active substance, chlorothalonil. If the published literature is also relevant to A14111B, it has been discussed within the relevant data point in this document.

CP 7.1 Acute Toxicity

Summary of acute toxicity

A14111B, containing 80 g/L azoxystrobin and 400 g/L chlorothalonil, is of low toxicity by the oral and dermal route of administration and is considered harmful if inhaled. It is non-irritating to the skin but a severe irritant to the rabbit eye. No skin sensitisation study was conducted for this formulation as there is adequate information from animal studies and human experience to conclude that technical chlorothalonil has skin sensitisation potential in humans and the formulation should therefore be labelled accordingly.

The classification according to Regulation (EC) No 1272/2008, as amended, is given in the table below.

Table 7.1-1: Summary of acute toxicological data obtained with A14111B

Parameter [Reference]	Species	Result	Classification according to Regulation (EC) No 1272/2008 as amended
Acute oral LD50 (Kuhn J, 2004)	Rat	>3045 mg/kg	None
Acute dermal LD50 (Kuhn J, 2004a)	Rat	5050mg/kg	None
Acute inhalation (Rattray NJ, 2004)	Rat	> 1.06mg/l	H332
Acute skin irritation (Kuhn J, 2004b)	Rabbit	Non-irritating	None
Acute eye irritation (Kuhn J, 2004c)	Rabbit	Severe irritant	H318
Skin sensitisation*	Guinea Pigs	May cause skin sensitization	H317

* No skin sensitisation was conducted because for this formulation as there is adequate information from animal studies and human experience to conclude that technical chlorothalonil has skin sensitisation potential in humans.

CP 7.1.1 Oral toxicity

Report:	K-CP 7.1.1/01, Kuhn J. (2004). Azoxystrobin (80 g/l) and chlorothalonil (400 g/l) SC formulation (A14111B): Acute Oral Toxicity Study In Rats. Stillmeadow Inc, Sugar Land, TX 77478, US. Laboratory Report No. 8065-04. Issue date 15 April 2004. Unpublished. (Syngenta File No. ICI5504/2243)

GUIDELINES

OECD 425 (2008): OPPTS 870.1100 (2002). There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

GLP: Signed and dated GLP and Quality Assurance statements were provided.

TEST MATERIAL (PURITY): Azoxystrobin (80 g/l) and chlorothalonil (400 g/l) SC formulation (A14111B) (purity 6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil).

SPONSOR: Syngenta Crop Protection, Inc., 410 Swing Road, Post Office Box 18300, Greensboro, NC 27419, US.

EXECUTIVE SUMMARY

Young adult female Sprague-Dawley albino rats were given a single oral dose of azoxystrobin/chlorothalonil SC formulation (A14111B). An initial limit test at 5000 mg/kg resulted in the death of the dosed animal and a full test was initiated at doses of 175, 550, 1750 and 5000 mg/kg. The test substance was dosed as supplied, the dose volume ranged from 0.14 ml/kg at the 175 mg/kg level to 4.15 ml/kg at the 5000 mg/kg level. The rats were fasted overnight prior to dosing. They were assessed daily for the following 14 days for any signs of systemic toxicity and their bodyweights were recorded at intervals throughout the study. Animals found dead and those killed at the end of the study were subjected to a macroscopic examination *post mortem*.

Animals dosed with 175 and 550 mg/kg survived. One of three rats dosed at 1750 mg/kg died and two of three rats dosed at 5000 mg/kg died.

Clinical signs included decreased activity, crusted fur, diarrhoea, polyuria and sensitivity to touch. There was complete recovery by day 5.

Bodyweight gain in surviving animals was unaffected by the administration of azoxystrobin/chlorothalonil SC formulation (A14111B), with the exception of one animal that lost weight between days 0 and 7.

Macroscopic examination *post mortem* of the animals that were found dead revealed stained fur, fluid in the chest cavity, discoloured lungs, liver, spleen and contents of the gastrointestinal tract. There were no abnormalities seen in animals killed at study termination.

Based on the AOT 425 Stat Program the acute oral LD_{50} of azoxystrobin/chlorothalonil SC formulation (A14111B) was estimated to be in excess of 3045 mg/kg to female rats.

The acute oral toxicity was greater than 2000 mg/kg therefore no classification is required for acute oral toxicity of A14111B according to Regulation (EC) No 1272/2008 as amended.

MATERIALS AND METHODS
Materials:

Test Material:	Azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B)
Description:	Formulation, cream coloured aqueous suspension
Lot/Batch number:	J7518/024
Purity:	6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil
CAS#:	
Stability of test compound:	Stable (stored at room temperature)

Vehicle and/or positive control: None

Test Animals:

Species	Rat
Strain	Sprague-Dawley
Age/weight at dosing	Young adult / 162-192g (fasted weight)
Source	Texas Animal Specialities, Humble, TX, US.
Housing	Individually in suspended, wire bottom, stainless steel cages
Acclimatisation period	5 days
Diet	PMI Feeds Inc.™ Formulab #5008 *ad libitum*, except for approximately 16 hours prior to dosing.
Water	Muncical water *ad libitum*
Environmental conditions	Temperature: 22 ± 3°C Humidity: 30-70 % Air changes: 10-12 per hour Photoperiod: 12 hour light / dark cycle

Study Design and Methods:

In-life dates: Start: 22 January 2004 End: 25 February 2004

Animal assignment and treatment: Rats were assigned to the test groups noted in Table 1. Following an overnight fast, they were given a single oral dose of azoxystrobin/chlorothalonil SC formulation (A14111B). An initial limit test at 5000 mg/kg resulted in the death of the dosed animal and a full test was initiated at doses of 175, 550, 1750 and 5000 mg/kg. The test substance was dosed as supplied, the dose volume ranged from 0.14 ml/kg at the 175 mg/kg level to 4.15 ml/kg at the 5000 mg/kg level. The rats were fasted overnight prior to dosing. They were assessed daily for the following 14 days for any signs of systemic toxicity and their bodyweights were recorded at intervals throughout the study. Animals found dead and those killed at the end of the study were subjected to a macroscopic examination *post mortem*.

Table 7.1.1-1 : Doses, mortality/animals treated

Step	Dose Regime/Mortality		
	Animal numbers	Dose level (mg/kg)	Comment
1	2	175	Survived
2	3	550	Survived
3	4	1750	Survived
4	5	5000	Survived
5	6	5000	Died
6	7	1750	Survived
7	8	5000	Died
8	9	1750	Died

Statistics: The LD_{50} value with 95% confidence interval was calculated using the AOT425 Stat Program supplied by the EPA.

RESULTS AND DISCUSSION

Mortality: Mortality is given in Table 1. Animals dosed with 175 and 550 mg/kg survived. One of three rats dosed at 1750 mg/kg died and two of three rats dosed at 5000 mg/kg died.

Clinical observations: Clinical signs included decreased activity, crusted fur, diarrhoea, polyuria and sensitivity to touch. There was complete recovery by day 5.

Body Weight: Bodyweight gain in surviving animals was unaffected by the administration of azoxystrobin/chlorothalonil SC formulation (A14111B), with the exception of one animal that lost weight between days 0 and 7.

Necropsy: Macroscopic examination *post mortem* of the animals that were found dead revealed stained fur, fluid in the chest cavity, discoloured lungs, liver, spleen and contents of the gastrointestinal tract. There were no abnormalities seen in animals killed at study termination.

CONCLUSION: The acute oral LD_{50} of azoxystrobin/chlorothalonil SC formulation (A14111B) was estimated to be in excess of 3045 mg/kg to female rats.

The acute oral toxicity was greater than 2000 mg/kg therefore no classification is required for acute oral toxicity of A14111B according to Regulation (EC) No 1272/2008 as amended.

(Kuhn J, 2004)

RMS Comment in draft RAR

The OECD test guideline indicates that testing stops when: a) 3 consecutive animals survive at the upper bound; b) 5 reversals occur in any 6 consecutive animals tested; c) at least 4 animals have followed the first reversal and the specified likelihood-ratios exceed the critical value. The applicant should indicate why testing was stopped when only 3 animals followed the first reversal animal number 6.

Syngenta Response

Table 3 of the acute oral study report (Syngenta File No. ICI5504/2243, Page 12) provides details of the output from the LD50 analysis using AOT425statpgm (Version 1) Test results and recommendations Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program indicating the likelihood-ratio stopping criterion has been met and gives an estimated MLD of 3045mg/kg.

In order to further substantiate this MLD value, the reported mortality data have also been evaluated using probit analysis and gave an MLD estimate of 2722mg/kg (see OECD summary below) which is in good agreement with the study report. An additional comment was made that these data are considered scientifically valid for classification purposes taking into account the requirement not to use excessive numbers of animals in LD5O testing.

Given the majority of the formulation constituents in A14111B do not trigger classification for acute oral toxicity and only a very small proportion (6% by weight) would be considered harmful, this provides further support to the conclusion that the MLD for A14111B is greater than 2000mg/kg and should not therefore be classified.

Report:	K-CP 7.1.1/02, Esdaile D. (2016). Concerning: Mortality Data Provided by Syngenta For Probit Analysis to Estimate the LD50 of Azoxystrobin (80 g/L) and Chlorothalonil (400 g/L) SC (A14111B). CiToxLAB, 8200 Veszprem, Szabadsagpuszta, Hungary. Laboratory Reference TK008321-03. Issue date 23 May 2016. Unpublished. (Syngenta File No. A14111B_11617)

GUIDELINES : Probit analysis from mortality data obtained from an Acute Oral Toxicity (rat) OECD 425 (2001): OPPTS 870.1100 (2002)

GLP : Signed and dated GLP and Quality Assurance statements were not provided.

SPONSOR: Syngenta Ltd, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, United Kingdom

EXECUTIVE SUMMARY

Based on the data provided, the LD50 for the test item Azoxystrobin (80 g/L) and Chlorothalonil (400 g/L) SC (A14111B) was estimated to be 2722.8 mg/kg bw. The confidence interval was too wide to calculate.

It was considered that the LD50 estimate is scientifically valid for classification purposes, taking into account the requirement not to use excessive numbers of animals in LD50 testing.

Oral LD_{50} = 2722.8 mg/kg bw (C.I. too wide to calculate)

MATERIALS AND METHODS

Data included in the Probit analysis were based upon mortality data and dose levels reported by Kuhn 2004. The data was processed in the 'SPSS/PC+ V4.0' validated software package at CiToxLAB Hungary. The data was tabulated into an Excel sheet, the data and results are displayed overleaf.

RESULTS AND DISCUSSION

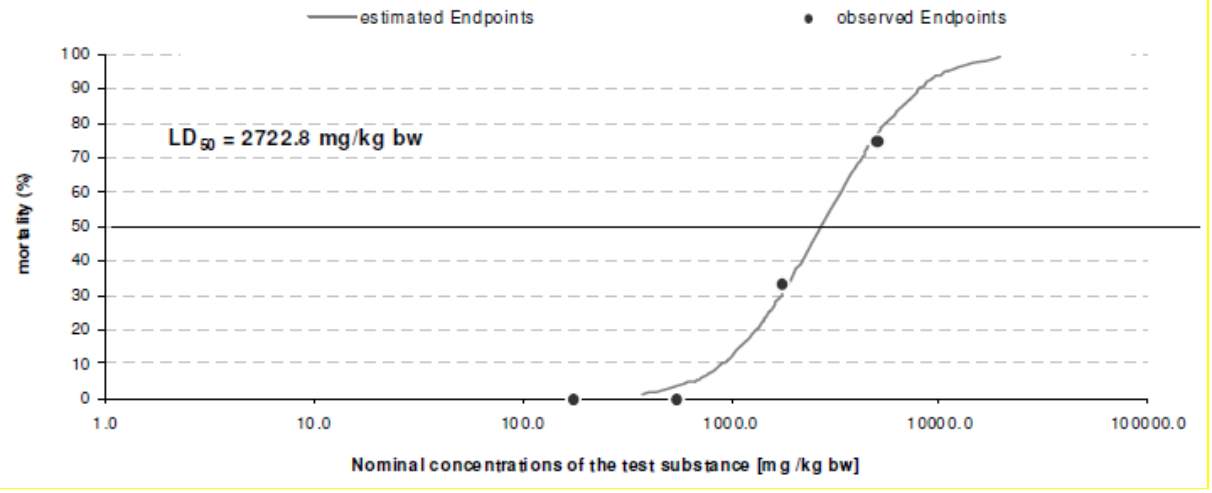
Mortality and the LD50

GROUPS	Dose (mg/kg bodyweight)	Number of animals treated	Dead animals No.	Dead animals %
1	175	1	0	0
2	550	1	0	0
3	1750	3	1	33
4	5000	4	3	75

PROBIT A + B*LOG C
Where;

A = -4.28150 **B = 2.70203 ± 1.83658**
CHI2 = 0.049 **P = 0.976**

%	LD50 (mg/kg bodyweight)	95% Confidence Limits	
		Lower	Upper
1	375.0169	-	-
5	670.2961	-	-
10	913.5284	-	-
25	1329.0368	-	-
20	1532.4669	-	-
30	1741.5583	-	-
40	2194.0820	-	-
50	2722.7936	-	-
60	3378.9097	-	-
70	4256.8803	-	-
75	4837.6933	-	-
80	5578.1790	-	-
90	8115.3525	-	-
95	11060.1939	-	-
99	19768.7251	-	-



Remark : 95% confidence limits were not calculated because their range is too wide

CONCLUSION: Based on the data provided, the LD50 for the test item Azoxystrobin (80 g/L) and Chlorothalonil (400 g/L) SC (A14111B) was estimated to be 2722.8 mg/kg bw. The confidence interval was too wide to calculate. It was considered that the LD50 estimate is scientifically valid for classification purposes, taking into account the requirement not to use excessive numbers of animals in LD50 testing.

References:

Kuhn J (2004). Azoxystrobin (80g/L) and Chlorothalonil (400 g/L) SC (A14111B). Acute Oral Toxicity Study in Rats. Stillmeadow, Inc, 12852 Park One Drive, Sugar Land, TX 77478, US. Report number 8065-04

(D.J. Esdail, 2016)

CP 7.1.2 Dermal toxicity

Report:	K-CP 7.1.2/01, Kuhn J. (2004a). Azoxystrobin (80 g/l) and Chlorothalonil (400 g/l) SC (A14111B): Acute Dermal Toxicity Study In Rats. Stillmeadow Inc, Sugar Land, TX 77478, US. Laboratory Report No. 8066-04. Issue date 15 April 2004. Unpublished. (Syngenta File No. ICI5504/2244)

GUIDELINES
OECD 402 (1987): OPPTS 870.1200 (1998): EC 440/2008 (2008). There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

GLP: Signed and dated GLP and Quality Assurance statements were provided.

TEST MATERIAL (PURITY): Azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) (purity 6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil).

SPONSOR: Syngenta Crop Protection, Inc., 410 Swing Road, Post Office Box 18300, Greensboro, NC 27419, US.

EXECUTIVE SUMMARY

A group of five male and five female Sprague-Dawley rats were dermally exposed to 5050 mg (4.19 ml/kg) azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B)/kg bodyweight. The test substance was tested as supplied. Test sites (not less than 10% of total body surface) were covered with an occlusive dressing for approximately 24 hours, after which the dressing was removed and the skin cleansed using clean warm water. The animals were assessed daily for the following 14 days for any signs of systemic toxicity and their bodyweights were recorded at intervals throughout the study. At the end of the study the animals were killed and subjected to a macroscopic examination *post mortem*.

None of the animals died and there were no signs of systemic toxicity. Four males and four females showed signs of slight skin irritation (very slight to well-defined erythema and desquamation), which was still present in one male on day 11, but had disappeared by day 14. One male and two females lost bodyweight, and one male failed to gain bodyweight, between days 7 and 14. There were no macroscopic abnormalities at examination *post mortem*.

The acute dermal LD_{50} of azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) is in excess of 5050 mg/kg (limit test, no mortalities).

The acute dermal toxicity was greater than 2000 mg/kg therefore no classification is required for acute dermal toxicity of A14111B according to Regulation (EC) No 1272/2008 as amended.

MATERIALS AND METHODS

Materials:

Test Material:	Azoxystrobin (80 g/l) and chlorothalonil (400 g/l) SC formulation (A14111B)
Description:	Formulation, cream coloured aqueous suspension
Lot/Batch number:	J7518/024
Purity:	6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil
CAS#:	
Stability of test compound:	Stable (stored at room temperature)

Vehicle and/or positive control: None

Test Animals:

Species	Rat
Strain	Sprague-Dawley
Age/weight at dosing	Young adult / males 280-327g, females 187-226g
Source	Texas Animal Specialities, Humble, TX, US.
Housing	Individually in suspended, wire bottom, stainless steel cages
Acclimatisation period	5 days
Diet	Purina Formulab Chow #5008 *ad libitum.*
Water	Municipal water *ad libitum*
Environmental conditions	Temperature: 22 ± 3°C Humidity: 30-70 % Air changes: 10-12 per hour Photoperiod: 12 hour light / dark cycle

Study Design and Methods:

In-life dates: Start: 29 January 2004 End: 12 February 2004

Animal assignment and treatment: A group of five male and five female rats were dermally exposed to 5050 mg (4.19 ml/kg) azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B)/kg bodyweight. The test substance was applied, as supplied, to the previously-clipped dorsal surface of the trunk (not less than 10% of total body surface). The test sites were covered with an occlusive dressing for approximately 24 hours, after which the dressing was removed and the skin cleansed using clean warm water. The animals were assessed daily for the following 14 days for any signs of systemic toxicity and their bodyweights were recorded at intervals throughout the study. At the end of the study the animals were killed and subjected to a macroscopic examination *post mortem*.

Statistics: The acute dermal LD_{50} was estimated.

RESULTS AND DISCUSSION

Mortality: There were no mortalities.

The acute dermal LD_{50} for males and females is in excess of 5050 mg/kg bodyweight (limit test, no mortalities).

Clinical observations: There were no signs of systemic toxicity. Four males and four females showed signs of slight skin irritation (very slight to well-defined erythema and desquamation), which was still present in one male on day 11, but had disappeared by day 14.

Body Weight: One male and two females lost bodyweight, and one male failed to gain bodyweight, between days 7 and 14.

Necropsy: There were no macroscopic abnormalities at examination *post mortem*.

CONCLUSION: The acute dermal LD_{50} of azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) is in excess of 5050 mg/kg.

The acute dermal toxicity was greater than 2000 mg/kg therefore no classification is required for acute dermal toxicity of A14111B according to Regulation (EC) No 1272/2008 as amended.

(Kuhn J, 2004a)

CP 7.1.3 Inhalation toxicity

Report:	K-CP 7.1.3/01, Rattray NJ. (2004). Azoxystrobin/Chlorothalonil 80/400 g/l SC Formulation (A14111B) 4-Hour Acute Inhalation Toxicity Study In Rats. Syngenta Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, UK. Laboratory Report No. CTL/HR2464/REGULATORY/REPORT. Issue date 25 March 2004. Unpublished. (Syngenta File No. ICI5504/2229)

GUIDELINES
Acute Inhalation (rat) OECD 403 (1981): OPPTS 870.1300 (1998): 92/69/EEC (1992) + amendment 93/21/EEC (1993). There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

GLP: Signed and dated GLP and Quality Assurance statements were provided.

TEST MATERIAL (PURITY): Azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) (purity 6.6% w/w, 80 g/l azoxystrobin, 34.6% w/w, 419 g/l chlorothalonil).

SPONSOR: Syngenta Limited, Alderley Park, Macclesfield, Cheshire, SK10 4TJ

EXECUTIVE SUMMARY

A group of five male and five female Alpk:AP_fSD (Wistar-derived) rats was exposed nose-only for a single four-hour period to azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) at a target formulation concentration of 1 mg/l. Test atmospheres were analysed for total particulate concentration and chlorothalonil. The particle size distribution of the test atmosphere was analysed twice during the exposure period. Following exposure, the animals were retained without treatment for 14 days. Clinical observations and bodyweights were recorded throughout the study and at the end of the scheduled period, the animals were killed and subjected to a gross examination *post mortem*.

The achieved test atmosphere had the following characteristics:

Target Total Formulation Concentration mg/l	Achieved Total Formulation Concentration mg/l	MMAD* µm	GSD+
1	1.06±0.1	5.52 6.56	1.85 1.78

* Mass Median Aerodynamic Diameter (µm)
+ Geometric Standard Deviation

There was one death on day 2 of the study. The surviving animals had transient clinical signs indicative of mild respiratory tract irritation. Macroscopic examination showed stained nares in the dead animal.

Nose-only exposure for 4 hours to a total formulation concentration of 1.06 mg/l resulted in one death. Evidence of transitory mild respiratory irritation was seen in the surviving animals. It is concluded that the acute LC_{50} of this azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) exceeds 1.06 mg/l.

The inhalation toxicity was less than 5 mg/L threshold defined in Regulation (EC) No 1272/2008 as amended. Therefore, H332 classification is required for inhalation properties of A14111B.

MATERIALS AND METHODS

Materials:

Test Material:	Azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B)
Description:	Formulation, cream opaque liquid
Lot/Batch number:	J7518/024
Purity:	6.6% w/w, 80 g/l azoxystrobin, 34.6% w/w, 419 g/l chlorothalonil
CAS#:	
Stability of test compound:	Stable (stored at ambient temperature in the dark)

Vehicle and/or positive control: Deionised water

Test Animals:

Species	Rat
Strain	Alpk:AP_fSD
Age/weight at dosing	7-8 weeks / males 386.8 ± 31.2g, females 271.8 ± 21.0g
Source	Rodent breeding unit, Alderley Park, Macclesfield, Cheshire, UK
Housing	5 per cage, sexes separately, in multiple rat racks suitable for animals of this strain and the weight range expected during the study.
Acclimatisation period	At least 5 days
Diet	RMI diet *ad libitum*, .except during exposure.
Water	Mains water *ad libitum*
Environmental conditions	Temperature: 22 ± 3°C Humidity: 30-70 % Air changes: at least 15 per hour Photoperiod: 12 hour light / dark cycle

Study Design and Methods:

In-life dates: Start: 22 October 2003 End: 5 November 2003

Exposure conditions: Trial generations were carried out prior to the start of the study in order to:

- determine the appropriate generation system and conditions
- determine that the appropriate target concentration could be achieved, or, if not, what was the maximum stable attainable concentration
- obtain data on the aerodynamic particle size of the atmosphere generated
- determine an appropriate method of analysis of chlorothalonil in the particulate phase of the test atmosphere.

Exposure conditions during the main study are summarised later in a test atmosphere characteristics table.

Animal assignment and treatment: A group of five male and five female Alpk:AP_fSD (Wistar-derived) rats was exposed nose-only for a single four-hour period to azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) at a target formulation concentration of 1 mg/l. Prior to the start of the study, all rats were examined to ensure that they were physically normal and exhibited normal activity. During exposure, they were observed frequently and, at the end of the 4-hour exposure period, each rat was given a detailed clinical examination. The animals were also subjected to detailed clinical observations, included the finding of no abnormalities detected, daily during the 14 day observation period. The bodyweight of each animal was recorded on day -1, 1, 8 and prior to termination on day 15. All animals were subjected to a gross examination *post mortem.* This included an external observation and a careful examination of all thoracic and abdominal viscera. Any rats found dead were subjected to a gross examination *post mortem* as soon as possible after death.

Generation of the test atmosphere / chamber description: Before exposure of the test animals, the atmosphere was shown to have been acceptable stable for approximately 30 minutes. The test atmosphere was generated using a glass concentric - jet atomiser. The test substance was pumped to the atomiser using a peristaltic pum. Clean, dry air was passed through the atomiser at a nominal flow rate of 38 l/minute (at normal temperature and pressure) and carried the atmosphere to the exposure chamber, having an internal volume of 27.6 litres, in order to achieve a minimum of 12 air changes per hour. Since diluting air was not employed, the flow rate through the exposure chamber was the same as that employed in the generation of the test atmosphere. Air flows were monitored continuously and recorded 7 times using variable area flowmeters and were altered as necessary to maintain the target concentration. Animals were exposed nose-only to the test atmosphere. They were restrained in polycarbonate tubes which were inserted into a Perspex® exposure chamber. The chamber was covered with an aluminium cone and stood on an aluminium base.

Nominal atmosphere concentration: The nominal atmosphere concentration is a concentration based on the total weight of test substance used during the exposure period. This represents the maximum concentration to which the animals could be exposed, assuming no losses within the generation or exposure systems. The nominal concentration of the test substance during the exposure generation period was calculated from the following formula:

$$\text{Concentration (mg/l)} = \frac{\text{weight loss (mg)}}{\text{time (minutes)} \times \text{airflow (l/minute)}}$$

Particulate concentration: The particulate concentration of the test atmosphere, close to the animals' breathing zone, was measured gravimetrically 8 times during exposure. This was done by drawing the test atmosphere, at a known flow rate, for a known time, through a 25mm diameter, polyvinyl chloride (PVC) GLA 5000 filter housed in a Delrin open-faced filter holder. The filter was weighed before and after the sample was taken. The concentration was calculated as follows:

$$\text{Concentration (mg/l)} = \frac{\text{post wt (mg) - pre wt (mg)}}{\text{time (minutes) x airflow (l/minute)}}$$

pre wt = weight of filter prior to sampling
post wt = weight of filter after sampling

Aerodynamic particle size determination: The aerodynamic particle size distribution was measured twice during the exposure period, using a Marple Cascade Impactor which aerodynamically separated airborne particles into pre-determined size ranges. The amount of aerosol, by weight, in each size range, was then used to calculate the aerodynamic particle size distribution of the aerosol. The data were transformed using a log/probit transform and a linear regression derived from the cumulative data. Using this regression line, the mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were calculated.

Analysed atmospheric concentration: The atmospheric concentration of chlorothalonil was determined by analysis of the chlorothalonil content of the material collected on the GLA 5000 filter and the stages of the cascade impactors.

Total formulation concentration: The total formulation concentration represents the total in the atmosphere to which the rats were exposed, based on the chemical analysis of chlorothalonil in the particulate phase, and compensates for the initial dilution and subsequent volatilisation of solvent components. The total formulation concentration was calculated and derived from the analysed chlorothalonil concentration in the particulate phase of the test atmosphere and the actual concentration of chlorothalonil in the formulation:

$$\text{Total formulation concentration (mg/l)} = \text{Analysed chlorothalonil concentration} \times \frac{100}{A}$$

where A = % chlorothalonil in the formulation

Table 7.1.3-1: Summary of acute study test atmosphere characteristics of azoxystrobin/ chlorothalonil 80/400 g/l SC formulation (A14111B)

Test atmosphere characteristics		
Parameter	**Target concentration 1 mg/ml**	
Gravimetric particulate concentration	0.58 ± 0.05 mg/l (n=8)	
Analysed total formulation concentration (mg/l)	1.06 ± 0.10 (n=8)	
Analysed concentration of chlorothalonil (mg/l)	0.37 ± 0.04 (% total particulate 63.1± 1.4)	
Nominal concentration	24.9 mg/l	
Particle size MMAD; GSD (60 and 270 minutes into exposure)	5.52, 6.56 µm; 1.85, 1.78	
Particle size distribution	1 hour / 2 hours 50 mins into exposure	
	Analysed	Gravimetric
Particles >9.8µm (% w/w)	28.4 / 26.3	19.2 / 24.8
Particles 9.8-6.0 µm (% w/w)	32.3 / 35.3	32.3 / 33.2
Particles 6.0-3.5 µm (% w/w)	22.3 / 26.3	23.2 / 27.7
Particles 3.5-1.55 µm (% w/w)	11.3 / 10.8	20.2 / 12.9
Particles 1.55-0.93 µm (% w/w)	1.3 / 0.7	4.0 / 1.0
Particles 0.93-0.52 µm (% w/w)	0.6 / 0.0	1.0 / 0.5
Particles <0.52 µm (% w/w)	3.9 / 0.7	0.0 / 0.0
Flow rate (whole system)	38 l/min	
Temperature	22.1-22.4 °C ± (n=7)	
Humidity	56-60 % ± (n=7)	

Statistics: The acute inhalation LC_{50} was estimated. No statistical analyses were performed.

RESULTS AND DISCUSSION

Mortality: One male was found dead on day 2.

The acute inhalation LC_{50} for males and females is in excess of 1.06 mg/l.

Clinical observations: Abnormalities generally associated with restraint (wet fur and salivation all animals, and chromodacryorrhoea, some animals) were observed during exposure. All animals had test substance around the snout.

Immediately following exposure, abnormalities generally associated with restraint (wet fur and salivation, all animals, and chromodacryorrhoea, some animals) were observed and all animals had test substance around the snout. Changes indicative of mild toxicity (decreased activity was seen in 1 female) and irritation of the respiratory tract (reduced breathing rate, increased breathing depth, abnormal respiratory noise and stains around the nose,) were observed in all animals.

The clinical condition of the surviving animals had greatly improved by day 5 of the study and all animals had fully recovered by day 11 of the study.

Body Weight: Of the surviving animals, 2 males and 2 females had gained weight by day 8 of the study and all surviving animals had gained weight by the end of the study.

Necropsy: Stained nares were observed in the male rat, found dead, on day 2 of the study. This finding is considered to be related to treatment.

CONCLUSION: Nose-only exposure for 4 hours to a total formulation concentration of 1.06 mg/l resulted in 1 death. Evidence of transitory mild respiratory irritation was seen in the surviving animals. It is concluded that the acute LC_{50} of this azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) exceeds 1.06 mg/l.

The inhalation toxicity was less than 5 mg/L threshold defined in Regulation (EC) No 1272/2008 as amended. Therefore, H332 classification is required for inhalation properties of A14111B.

(Rattray NJ, 2004)

RMS Comment in draft RAR

The MMAD is exceeding the recommended MMAD of 1-4 µm. The acceptability of the test should be explained in more detail; if the MMAD was lower, the rats might have inhaled more test substance and mortality might have been higher.

Syngenta Response

Justification for classification as Harmful by inhalation (H332 Harmful if inhaled)

While chlorothalonil technical material meets the criteria for classification H330 Fatal if inhaled, Syngenta believe that the available data support a classification of H332 Harmful if inhaled for the AZ/CTN 480g/L SC formulation A14111B.

Data are available that clearly show liquid formulations containing chlorothalonil are not respirable in their native state, and hence that hazard classification for inhalation toxicity is therefore not merited. Furthermore, Syngenta have conducted studies in which it was attempted to generate respirable aerosols from liquid SC formulations and these have demonstrated that:

- respirable aerosols could not be generated from the neat formulations
- the AZ/CTN 480g/l SC formulation A14111B, required dilution in water (75:25 respectively) in order to make the generation of a respirable aerosol possible. The resulting inhalation LC_{50} value was >1.06mg/l.
- A higher strength 500 g chlorothalonil/l SC formulation A7867A, also required dilution in water (75:25 respectively) in order to make the generation of a respirable aerosol possible, The resulting inhalation LC_{50} value was >1.96 mg/l.

Respirability of the formulations

Chlorothalonil is not volatile. Inhalation exposure can only arise from the inhalation of suspended particulate material or liquid aerosols of a particular particle size. Data on the potential for liquid formulations to form suspended particulate material or liquid aerosols are available (A14111B, Rattray 2004 B.6 (CP) Section B.6.1.3 reported above and a higher strength 500g/L SC formulation A7867A OECD summary given below for a study previously reviewed in DAR Addendum March 2001 (Kilgour 1999).

Chlorothalonil is of low acute toxicity by the oral route. Studies showing high inhalation toxicity of the technical material (powder) have only been conducted using particles which, by virtue of their very small size, can access the deep lung and alveoli. Such small particles (<15 μm in diameter in man) are termed respirable. Larger chlorothalonil particles (i.e. between 15 and 100 μm) will deposit on the upper airways and will be transported to the gut by the mucocillary escalator, in effect becoming an oral dose. These larger particles are termed inhalable. Respirable chlorothalonil particles are likely to present an acute respiratory hazard whereas those that are merely inhalable are likely to be of lower acute toxicity.

The available studies demonstrate that because of the inherently high viscosity of chlorothalonil liquid formulations, they will not form respirable aerosols in their neat (undiluted) state. Indeed, it is not possible to generate respirable aerosols using the SC formulations of chlorothalonil in the form in which they are supplied. Field use rate "spray dilutions" are typically less than 1% w/v in water for supported chlorothalonil uses in Europe, and typical spray droplets are sufficiently large as to be non-respirable.

Inhalation Toxicity Data on Chlorothalonil Preparations

Inhalation toxicity studies on two liquid formulations of chlorothalonil (A14111B and A7867A) are described below. The purpose of the studies was to determine whether it was technically feasible to generate respirable aerosols from the formulations when tested in the form in which they are supplied.

Chlorothalonil 500g/l SC formulation (A7867A) - Syngenta succeeded in generating a stable atmosphere of 1.96 mg preparation/l, but only following dilution of the formulation in water (75:25). The LC_{50} obtained in the study was >1.96 mg preparation/l.

Azoxystrobin/Chlorothalonil 480g/l SC formulation (A14111B) - Syngenta succeeded in generating a stable atmosphere of 1.06 mg preparation/l, but again only by diluting the formulation in water (75:25). The LC_{50} obtained in the study was >1.06 mg preparation/l.

Comparison of the detailed composition for A7867A and A14111B (Document J, confidential information. Syngenta file No. R044686_11071) indicates substantial similarity, with the majority of co-formulants being identical and found at similar or higher levels in A7867A. The main difference was the chlorothalonil concentration, where A7867A contains 40.4% w/w chlorothalonil versus 33% w/w in A14111B.

The acute toxicity of chlorothalonil containing formulations is well understood and principally driven by the amount of technical chlorothalonil present. This is well illustrated when comparing the toxicity of A7867A and A14111B against the similar composition for each product. Both formulations have been shown to be of low toxicity by the oral and dermal route of administration, moderately toxic by inhalation, irritating to eyes but non-irritant to the skin and are both are skin sensitisers.

Parameter	A7867A BRAVO 500 SC	A14111B 480 SC
Acute oral (Rat)	MLD 4200 mg/kg	MLD >3045 mg/kg bw
Acute dermal (Rabbit)	MLD >20000 mg/kg	MLD 5050 mg/kg bw
Acute inhalation (Rat)	MLC > 1.96 mg/l	MLC > 1.06mg/l
Skin irritation (Rabbit)	Not classifiable for skin irritancy	Not classifiable for skin irritancy
Eye irritation (Rabbit and/or Monkey)	Irritant	Irritant

Parameter	A7867A BRAVO 500 SC	A14111B 480 SC
Skin sensitisation (Guinea Pig)	Skin sensitiser	Skin Sensitiser

As described earlier, because of the inherently high viscosity of chlorothalonil liquid formulations, they will not form respirable aerosols in their neat (undiluted) state. Indeed, it is only possible to generate respirable aerosols using the SC formulations of chlorothalonil when the formulations are diluted with water, and even then, it was not possible to generate aerosols with an MMAD in the range 1-4µm as required by current test guidelines. It should be noted that both studies described here were conducted prior to the introduction of the 1-4µm MMAD guideline requirement, however, both studies satisfied the "respirable aerosol" criterion specified in contemporary guidelines at the time the studies were conducted.

Formulation	Chlorothalonil content	MLC	MMAD (µm)	GSD	Mortaility
A7867A	40% w/w	>1.96mg/L	6.40, 5.40	2.35, 1.97	0/5 males 1/5 females
A14111B	33% w/w	>1.06mg/L	5.52, 6.56	1.85, 1.78	1/5 males 0/5 females

As shown in the summary table above, the MLC for A7867A containing a higher percentage chlorothalonil than A14111B was >1.96mg/L. The MMAD values obtained in this study were 6.4µm and 5.4µm and GSD values of 2.35 and 1.97 respectively. Using both sets of MMAD and GSD data from this study, the **particle size adjusted test atmosphere concentration** having an MMAD less than 4µm has been calculated and shown to be "greater than" the concentration range 1.14 – 1.29mg/l (see below for details on how these values were derived).

Conclusion

Exposure to preparations of chlorothalonil by the inhalation route have been shown to be essentially impossible. The neat preparations do not form aerosols under the stringent conditions of acute inhalation toxicity testing. Respirable aerosols are not generated by the systems used for fungicidal spray applications. Only by dilution in water can respirable test aerosols be generated.

Inhalation toxicity of the liquid formulations described above is principally driven by chlorothalonil content and based on the 500g/l SC formulation A7867 the calculated MLC was >1.96mg/l and when adjusted to take account of the proportion of the atmosphere with an MMAD of less than 4µM, the MLC was > 1.14mg/l.

Given the similarity in composition between the liquid formulations A14111B and A7867A and that A7867A contains a significantly higher percentage chlorothalonil, Syngenta propose that A14111B should be classified as Harmful if inhaled (H332) based on the weight of evidence presented above.

Summary of acute inhalation study for A7867A.

Report:	*KIIA 5.2.3/03, Kilgour JD (1999). Chlorothalonil 500g/l SC: 4-Hour Acute Inhalation Toxicity Study in Rats. Central Toxicology Laboratory; Syngenta unpublished report no: CTL/P/6317. Study dates: 27 April 1999 to 8 June 1999. Syngenta File No. R44686/0081*

Guidelines: None.

Deviations: 92/69/EEC B.2 ≅ OECD 403 (1981) ≅ FIFRA § 81-3

GLP: Yes (laboratory certified by the UK authority)

Materials and methods: BRAVO 500®, nominally a 500 g/l SC formulation of chlorothalonil; Batch No. YF10934 Ref. 882; analysed purity 41.2% w/w chlorothalonil.

A group of five male and five female rats were exposed, nose-only, for a single four-hour period to a 500 g/l SC formulation of chlorothalonil at a target gravimetric concentration of 1.0 mg/l chlorothalonil (due to the high viscosity of the test substance, dilution with water was necessary to facilitate generation and this was shown to be the maximum stable concentration attainable).
Test atmospheres were analysed for particulate concentration and the formulated product. The particle size distribution of the test atmosphere was analysed twice during the exposure period. Following exposure, the animals were retained without treatment for 14 days. Clinical observations and bodyweights were recorded throughout the study and at the end of the scheduled period. The animals were then killed and subjected to a gross examination *post mortem*.

Findings: The achieved test atmosphere, generated from the test substance as supplied, had the characteristics shown below.

Atmosphere Analyses

Target Concentration (mg/l)	**Analysed Chlorothalonil Concentration (mg/l)**	**Particulate Concentration (mg/ml)**	**Total Formulation Concentration (mg/l)**	**MMAD (D50 µm)**	**GSD**
1.0	0.81 ± 0.15	1.29 ± 0.24	1.96 ± 0.37	6.40, 5.40	2.35, 1.97

MMAD: Mass Median Aerodynamic Diameter
GSD: Geometric Standard Deviation

There were no deaths in males and one female was killed *in extremis* on day 2 following exposure to 1.96 mg/l of formulation. Clinical signs indicative of toxicity were seen in the female that was killed, including gasping, abnormal respiratory noise, reduced rate and increased depth of breathing, decreased activity, reduced reflexes and cold to touch.

Clinical abnormalities generally associated with restraint were seen during and immediately after exposure. Clinical symptoms consistent with the formulation being an eye irritant (eyelids closed, reddened, swollen, discharge) and a respiratory tract irritant (abnormal respiratory noise) were seen in most animals. The general condition of the animals had improved after the first week but signs of respiratory tract irritation were still evident in 3 males at day 13 and in one female at day 14. Signs of ocular irritation had resolved by day 8, with the exception of one female, which had reddened eyes until day 12 and corneal opacity from day 7 until the end of the study.

Acute Inhalation Toxicity of a 500 g/l SC Formulation of Chlorothalonil in the Rat

Exposure (mg/l)	Time after Dosing (Days)	Number of Deaths	
		Male	Female
1.96	2	0/5	1/5
	14 (total)	0/5	1/5

None of the animals had gained weight by day 8 of the study, but all exceeded their starting weight by the end of the study.

Mean Bodyweights (g)

Day	**Exposure (mg/l)**	
	1.96	**1.96**
	Male	**Female**
1	337	234
8	316	225
15	361	250

Treatment related macroscopic findings at *post mortem* were seen in the female killed *in extremis* (discharge from the eyes and stained nares) and in one terminal female (opaque eye).

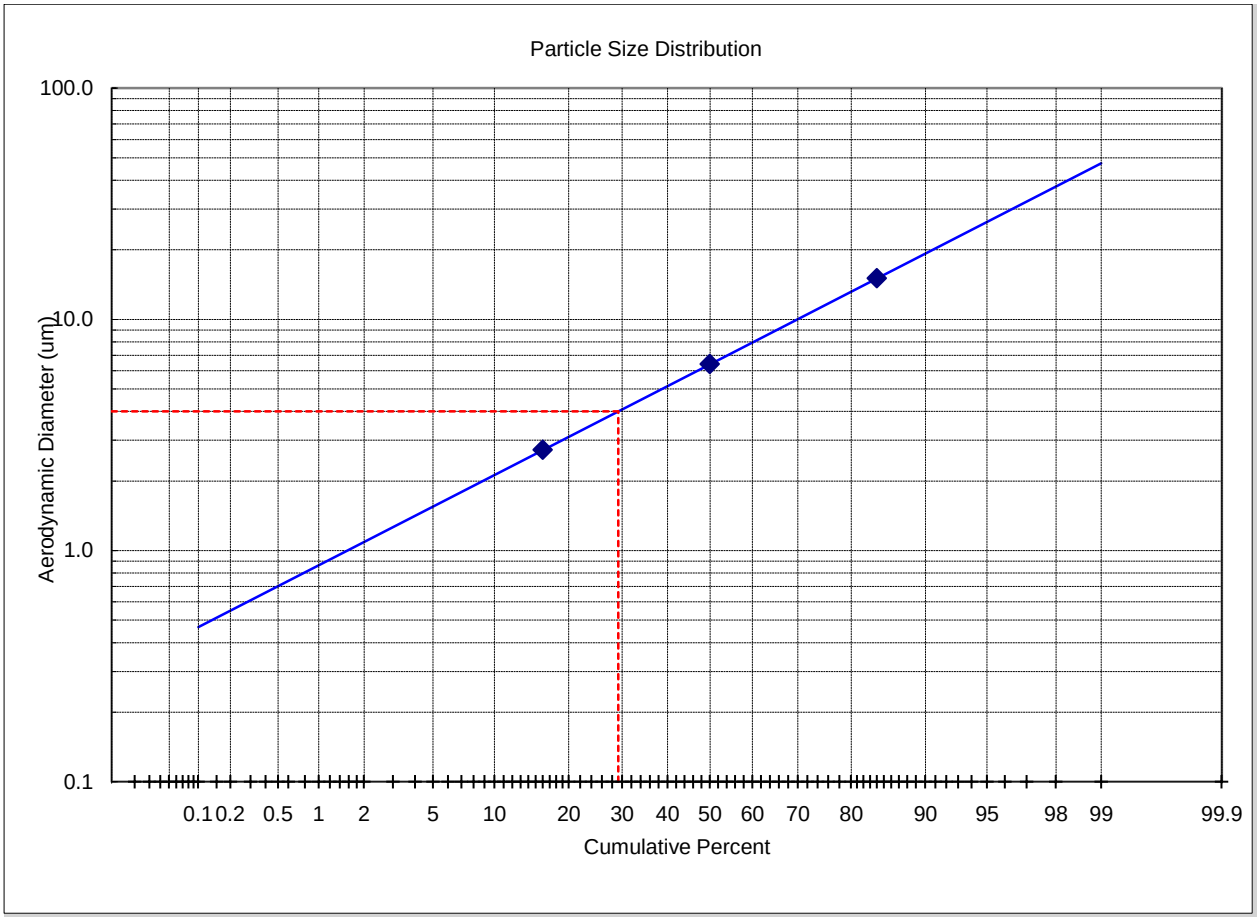
Conclusion: Nose-only exposure for 4 hours to a 500 g/l SC formulation of chlorothalonil at 1.96 mg/l resulted in the death of a single female animal. Clinical symptoms were consistent with the formulation being a marked eye irritant and a respiratory tract irritant.

It is concluded that the median lethal concentration of a 500g/l SC formulation of chlorothalonil exceeds 1.96mg/ml. The formulation should be classified as Harmful by inhalation (H332).

Calculation of adjusted test atmosphere concentration having an MMAD less than 4µm.

A7867A : Log-Probability plot using MMAD/GSD to determine % < 4µm (1st aerosol measurement)

Using the MMAD and GSD values calculated in the study, the mean size distribution of the aerosol can be plotted as a linear plot on log-probability paper. From this, any proportion of the aerosol that is less than any given aerodynamic size can be interpolated from the graph. The MMAD is always the 50% point on the probability scale and one geometric standard deviation from the mean lies at either the 15.9 % or 84.1 % points (usually referred to as the D_{16} and D_{84}).



MMAD	6.4
GSD	2.35
D16	2.72
D84	15.04
% < 4µm	**29.1%**

Since the MMAD represents the size that divides the distribution of an aerosol in half when measured by mass, there must always be a proportion that can be described by an MMAD which has a different value to that for the overall aerosol, but which clearly represents a lower mass than the total. Therefore, within the aerosol tested in this study, a proportion of the total can be described by an MMAD of 4 µm and hence this proportion conforms to the current testing guideline requirements.

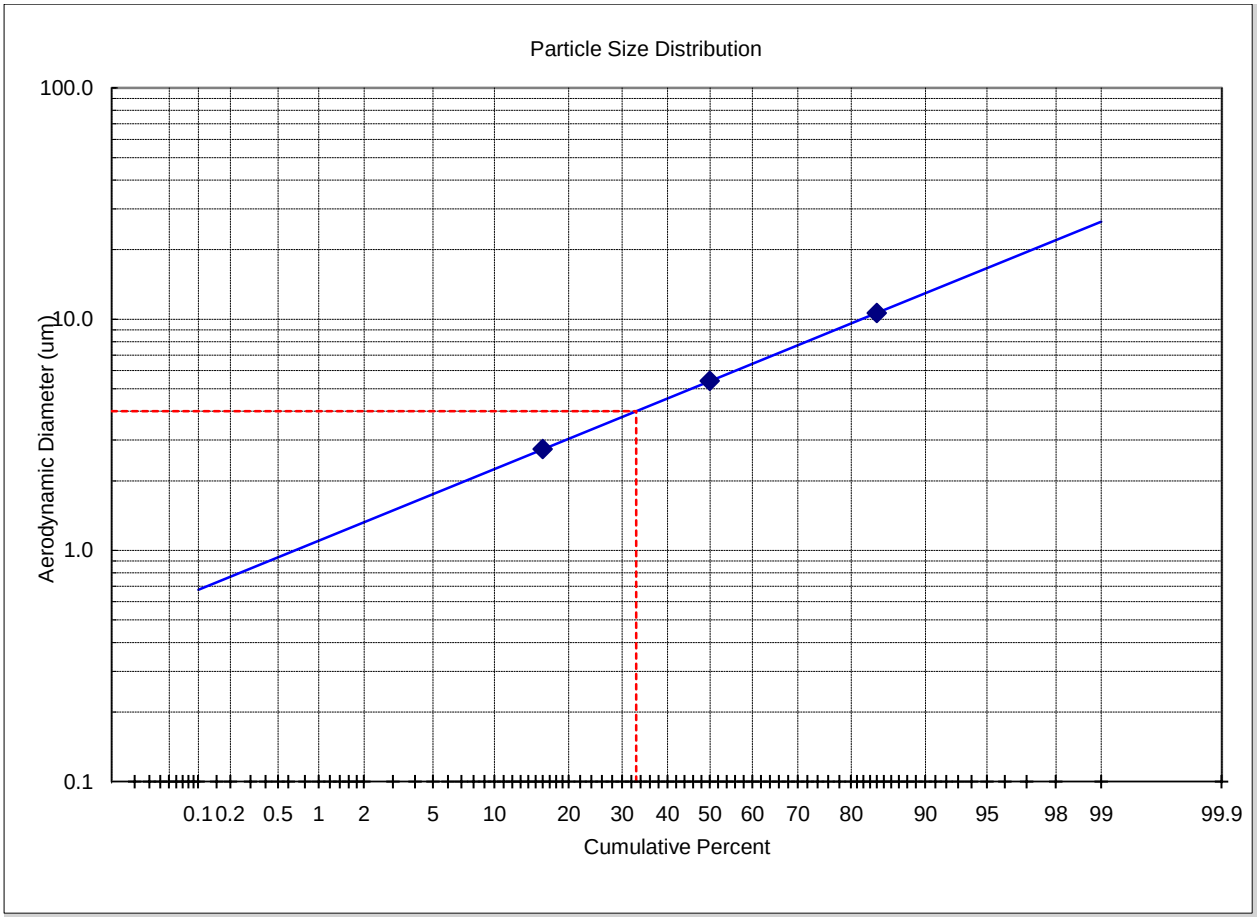
For this first aerosol measurement, the proportion less than 4 µm was 29.1%, representing a concentration of 0.57 mg/l.

If 0.57mg/l is the concentration, by weight, of all particles having aerodynamic diameters of < 4µm, then twice this, i.e. 1.14mg/l, represents the proportion of the whole aerosol which can be described by an MMAD of 4 µm, since the MMAD is defined as the value that divides the size distribution of an aerosol in half when measured by mass.

Therefore, a concentration of 1.14 mg/l of the total formulation tested had a particle size distribution that can be described by an MMAD of 4 µm.

A7867A : Log-Probability plot using MMAD/GSD to determine % < 4µm (2nd aerosol measurement)

Using the MMAD and GSD values calculated in the study, the mean size distribution of the aerosol can be plotted as a linear plot on log-probability paper. From this, any proportion of the aerosol that is less than any given aerodynamic size can be interpolated from the graph. The MMAD is always the 50% point on the probability scale and one geometric standard deviation from the mean lies at either the 15.9 % or 84.1 % points (usually referred to as the D_{16} and D_{84}).



MMAD	5.4
GSD	1.97
D16	2.74
D84	10.64
% < 4µm	**32.9%**

Since the MMAD represents the size that divides the distribution of an aerosol in half when measured by mass, there must always be a proportion that can be described by an MMAD which has a different value to that for the overall aerosol, but which clearly represents a lower mass than the total. Therefore, within the aerosol tested in this study, a proportion of the total can be described by an MMAD of 4 µm and hence this proportion conforms to the current testing guideline requirements.

For this second aerosol measurement, the proportion less than 4 µm was 32.9%, representing a concentration of 0.64 mg/l.

If 0.64mg/l is the concentration, by weight, of all particles having aerodynamic diameters of < 4µm, then twice this, i.e. 1.29mg/l, represents the proportion of the whole aerosol which can be described by an MMAD of 4 µm, since the MMAD is defined as the value that divides the size distribution of an aerosol in half when measured by mass.

Therefore, a concentration of 1.29 mg/l of the total formulation tested had a particle size distribution that can be described by an MMAD of 4 µm.

CP 7.1.4 Skin irritation

Report:	K-CP 7.1.4/01, Kuhn J. (2004b). Azoxystrobin (80g/l) and Chlorothalonil (400g/l) SC (A14111B): Acute Dermal Irritation Study In Rabbits. Stillmeadow Inc, Sugar Land, TX 77478, US. Laboratory Report No. 8068-04. Issue date 15 April 2004. Unpublished. (Syngenta File No. ICI5504/2245)

GUIDELINES
Primary Dermal Irritation (rabbit) OECD 404 (2002): OPPTS 870.2500 (1998): 2004/73/EC B.4 (2004). There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

GLP: Signed and dated GLP and Quality Assurance statements were provided.

TEST MATERIAL (PURITY): Azoxystrobin (80g/l) and chlorothalonil (400g/l) SC formulation (A14111B) (purity 6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil).

SPONSOR: Syngenta Crop Protection, Inc., 410 Swing Road, Post Office Box 18300, Greensboro, NC 27419, US.

EXECUTIVE SUMMARY

In a primary irritation study, three young adult New Zealand White albino rabbits (one male and two female) were dermally exposed to 0.5 ml of undiluted azoxystrobin/chlorothalonil 80/400 g/l SC formulation (A14111B) for 4 hours to an area (approximate size 2.5 cm x 2.5 cm) on the shorn flank under an occlusive dressing. The Draize scale was used to assess any irritation approximately 1 hour, 1, 2, 3 and 7 days after removal of the dressings. Mean erythema and oedema scores were calculated. Bodyweights were recorded at the start of the study.

Very slight to well-defined erythema was present up to and including day 3. Oedema was not observed. Desquamation was seen in one animal at the 48 hour reading.

The primary irritation index of 0.9 out of a possible 8.0 was used to give azoxystrobin (80g/l) and chlorothalonil (400 g/l) SC (A14111B) a descriptive rating of slightly irritating.

The mean irritation scores 24 to 72 hours after application were less than the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, no classification is required for skin irritating properties of A14111B.

MATERIALS AND METHODS

Materials:

Test Material:	Azoxystrobin (80 g/l) and chlorothalonil (400 g/l) SC formulation (A14111B)
Description:	Formulation, cream coloured aqueous suspension
Lot/Batch number:	J7518/024
Purity:	6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil
CAS#:	
Stability of test compound:	Stable (stored at room temperature)

Vehicle and/or positive control: None

Test Animals:	
Species	Rabbit
Strain	Albino, New Zealand White
Age/weight at dosing	Young adult / male 2.4 kg, females 2.0-2.4 kg
Source	Nichols Rabbitry Inc; Lumberton, TX., US.
Housing	Individually in suspended, wire bottom, stainless steel cages
Acclimatisation period	At least 5 days
Diet	PMI Feeds Rabbit Diet #5321 *ad libitum.*
Water	Municipal water *ad libitum*
Environmental conditions	Temperature: 20 ± 3°C Humidity: 30-70 % Air changes: 10-12 per hour Photoperiod: 12 hour light / dark cycle

Study Design and Methods:

In-life dates: Start: 10 February 2004 End: 17 February 2004

Animal assignment and treatment: Prior to starting the study, the pH of the test substance was determined to be 7.13. The hair was removed from the dorsal area of the trunk (at least 8cm x 8cm) the day before application. A single intact exposure site was selected as the test site and the contralateral intact site served as a control site. On the day of application, 0.5 ml of the undiluted formulation was applied to the test site and covered with a gauze patch (2.5 cm x 2.5 cm) which was held in place with a strip of non-irritating adhesive dressing. The entire trunk was loosely wrapped with a semi-permeable dressing secured with strips of tape. After 4 hours the dressings were removed and the test sites washed gently with tap water. The sites were observed for erythema and oedema and any other dermal defects or irritation 1, 24, 48 and 72 hours and on 7 days following the end of the application. The Draize scale was used to score the degree of erythema and oedema and the primary irritation index was calculated using the scores obtained.

RESULTS AND DISCUSSION

Very slight to well-defined erythema was present up to and including day 3. Oedema was not observed. Desquamation was seen in one animal at the 48 hour reading.

Table 7.1.4-1: Individual and mean skin irritation scores of azoxystrobin (80g/l) and chlorothalonil (400 g/l) SC (A14111B) according to the Draize scheme

Time	Erythema			Oedema		
Animal number	**6892**	**6847**	**6899**	**6892**	**6847**	**6899**
after 1 hour	1	2	2	0	0	0
after 24 hours	1	1	1	0	0	0
after 48 hours	0	1	1	0	0	0
after 72 hours	0	1	0	0	0	0
mean score 24-72 h	0.3	1.0	0.7	0	0	0
after 7 days	0	0	0	0	0	0

CONCLUSION: The primary irritation index of 0.9 out of a possible 8.0 was used to give azoxystrobin (80g/l) and chlorothalonil (400 g/l) SC (A14111B) a descriptive rating of slightly irritating.

The mean irritation scores 24 to 72 hours after application were less than the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, no classification is required for skin irritating properties of A14111B.

(Kuhn J, 2004b)

CP 7.1.5 Eye irritation

Report:	K-CP 7.1.5/01, Kuhn J. (2004c). Azoxystrobin (80g/l) and Chlorothalonil (400g/l) SC (A14111B): Acute Eye Irritation Study In Rabbits. Stillmeadow Inc, Sugar Land, TX 77478, US. Laboratory Report No. 8067-04. Issue date 15 April 2004. Unpublished. (Syngenta File No. ICI5504/2242)

GUIDELINES
Primary Eye Irritation (rabbit) OECD 405 (2002): OPPTS 870.2400 (1998): 2004/73/EC B.5 (2004). There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

GLP: Signed and dated GLP and Quality Assurance statements were provided.

TEST MATERIAL (PURITY): Azoxystrobin (80g/l) and chlorothalonil (400g/l) SC formulation (A14111B) (purity 6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil).

SPONSOR: Syngenta Crop Protection, Inc., 410 Swing Road, Post Office Box 18300, Greensboro, NC 27419, US.

EXECUTIVE SUMMARY

In a primary eye irritation study, 0.1 ml of azoxystrobin (80g/l) and chlorothalonil (400 g/l) SC formulation (A14111B) was instilled into the conjunctival sac of the right eye of a group of three young adult (two male and one female) New Zealand White albino rabbits. The eyes were examined and the grade of ocular reaction was assessed approximately 1 hour and 1, 2, 3, 4, 7, 10, 14, 17, 21, 24 and 28 days after instillation. All treated eyes were rinsed for 1 minute with deionised water immediately following the 24 hour reading. A modified form of the Kay and Calandra system (***Kay and Calandra,1962***) was used to interpret and classify the numerical scores.

Signs of severe eye irritation were seen following application of azoxystrobin (80g/l) and chlorothalonil (400 g/l) SC formulation (A14111B) into the rabbit eye. Fluorescein staining was observed in all animals after treatment and evidence of irritation persisted in all animals up to day 28 (study termination) and included: corneal opacity (scores of 1-2 on a 0-4 scale) covering more than 75% of the cornea after one hour and 25% or less at all other readings; conjunctival redness (scores of 1-3 on a 0-3 scale); conjunctival chemosis (scores of 1-4 on a 0-4 scale) and conjunctival discharge (scores of 1-3 on a 0-3 scale). In addition, constricted pupils were seen in all 3 rabbits, necrosis of the conjunctivae was seen in all three rabbits, blisters on the nictitating membrane/eyelid were seen in 2 rabbits and invasion of the cornea by blood vessels was seen in one animal.

Under the conditions of this study, azoxystrobin (80 g/l) and chlorothalonil (400 g/l) SC formulation (A14111B) is considered to be severely irritating to the rabbit eye according to a modified form of the Kay and Calandra system.

The mean irritation scores 24 to 72 hours after application were greater the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, H319 classification is required for eye irritating properties of A14111B.

MATERIALS AND METHODS

Materials:

Test Material:	Azoxystrobin (80 g/l) and chlorothalonil (400 g/l) SC formulation (A14111B)
Description:	Formulation, cream coloured aqueous suspension
Lot/Batch number:	J7518/024
Purity:	6.6% w/w azoxystrobin, 34.6% w/w chlorothalonil
CAS#:	
Stability of test compound:	Stable (stored at room temperature)

Vehicle and/or positive control: None

Test Animals:

Species	Rabbit
Strain	Albino, New Zealand White
Age/weight at dosing	Young adult / males 2.0 – 2.025 kg, female 2.0 kg
Source	Nichols Rabbitry Inc; Lumberton, TX., US.
Housing	Individually in suspended, wire bottom, stainless steel cages
Acclimatisation period	At least 5 days
Diet	PMI Feeds Rabbit Diet #5321 in measured amounts
Water	Municipal water *ad libitum*
Environmental conditions	Temperature: 20 ± 3°C Humidity: 30-70 % Air changes: 10-12 per hour Photoperiod: 12 hour light / dark cycle

Study Design and Methods:

In-life dates: Start: 26 January 2004 End: 23 February 2004

Animal assignment and treatment: Prior to starting the study, the pH of the formulation was determined to be 7.13. On day 0, a dose of 0.1 ml of undiluted azoxystrobin (80g/l) and chlorothalonil

(400 g/l) SC formulation (A14111B) was instilled into the conjunctival sac of the right eye of a group of three young adult (two male and one female) New Zealand White albino rabbits. The eyes were examined and the grade of ocular reaction was assessed approximately 1 hour and 1, 2, 3, 4, 7, 10, 14, 17, 21, 24 and 28 days after instillation. The corneas of all treated eyes were examined immediately after the 24 hour reading using fluorescein and any corneas exhibiting flourescein staining at this time were re-examined using flourescein at each consecutive observation until flourescein staining of the cornea no longer occurred. All treated eyes were rinsed for 1 minute with deionised water immediately following the 24 hour reading. A modified form of the Kay and Calandra system (***Kay and Calandra,1962***) was used to interpret and classify the numerical scores.

RESULTS AND DISCUSSION

Signs of severe eye irritation were seen following application of azoxystrobin (80g/l) and chlorothalonil (400 g/l) SC formulation (A14111B) into the rabbit eye. Fluorescein staining was observed in all animals after treatment and evidence of irritation persisted in all animals up to day 28 (study termination) and included: corneal opacity (scores of 1-2 on a 0-4 scale) covering more than 75% of the cornea after one hour and 25% or less at all other readings; conjunctival redness (scores of 1-3 on a 0-3 scale); conjunctival chemosis (scores of 1-4 on a 0-4 scale) and conjunctival discharge (scores of 1-3 on a 0-3 scale). In addition, constricted pupils were seen in all 3 rabbits, necrosis of the conjunctivae was seen in all three rabbits, blisters on the nictitating membrane/eyelid were seen in 3 rabbits and invasion of the cornea by blood vessels was seen in one animal.

Table 7.1.5-1: Eye irritation scores

Time	Cornea			Iris			Conjunctiva								
							Redness			Chemosis			Discharge		
Animal number	**6864**	**6868**	**6865**	**6864**	**6868**	**6865**	**6864**	**6868**	**6865**	**6864**	**6868**	**6865**	**6864**	**6868**	**6865**
1 hour	1	1	1	0	0	0	1	1	1	1 d	1 d	1 d	3	2	3
24 hours	2	a	2	0 c	a	0 c	3	3	3	3	4	3	3	3	3
48 hours	2	a	2	0 c	a	0	3	3	3	3	4	3 d	3	3	3
72 hours	2	2	2	0 c	0 c	0 c	3	3	3	3	3	3	3	3	3
Mean: 24-72h	2	a	2	0	a	0	3	3	3	3	3.7	3	3	3	3
4 days	2	2	2	0 c	0 c	0 c	3	3	3	3	3	3	3	3	3
7 days	2	2	2	0 c	0 c	0 c	3	3	3	2	3	2	2	3	2
10 days	2	1	2	0 c	0	0 c	3	2	3	2	1	1	3	1	2
14 days	2	1	1	0	0	0	3	1	1	1	0	1	1	0	0
17 days	2	1	2 b	0	0	0	2	2	3	1	0	2	0	0	2
21 days	2	1	2 b	0	0	0	0	0	3	0	0	2	0	0	2

a – unable to score due to severity of chemosis b – invasion of cornea by blood vessels c – constricted pupil
d – blister on nictating membrane/eyelid

CONCLUSION: Under the conditions of this study, azoxystrobin (80 g/l) and chlorothalonil (400 g/l) SC formulation (A14111B) is considered to be severely irritating to the rabbit eye according to a modified form of the Kay and Calandra system.

The mean irritation scores 24 to 72 hours after application were greater the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, H319 classification is required for eye irritating properties of A14111B.

REFERENCE

Kay J H and Calandra J C (1962). Interpretation of eye irritation tests. J Soc Cosmet Chem 13, 281-289.

(Kuhn J, 2004c)

CP 7.1.6 Skin sensitization

No skin sensitisation study was conducted for this formulation as there is adequate information from animal studies and human experience to conclude that technical chlorothalonil has skin sensitisation potential in humans. A default classification of H317 'may cause sensitisation following skin contact' should be applied to the formulation.

CP 7.1.7 Supplementary studies on the plant protection product

No additional studies have been conducted. A14111B is an azoxystrobin/chlorothalonil solo formulation and its potential acute toxicity has been fully addressed as presented in Sections CP 7.1.1-7.1.6. No additional studies to address potential health effects are considered to be unnecessary.

CP 7.1.8 Supplementary studies for combinations of plant protection product

This product does not contain recommendations for combinations of plant protection products therefore supplementary studies are not required.

CP 7.2 Data on Exposure

CP 7.2.1 Operator exposure

Azoxystrobin

Table 7.2.1-1: EU Conclusions - Toxicological endpoints of azoxystrobin required for evaluation of operator, worker, bystander and residential risk

Endpoint	EU agreed/Pre-EU inclusion proposed endpoint ((EFSA Journal (2010) 8(4), 1542)	Proposed endpoint*
AOEL (mg/kg bw/day)	0.2 mg/kg bw/day	0.2
Dermal absorption of concentrate	0.3% (azoxystrobin 250 g/L SC)	25%
Dermal absorption of in-use dilution	0.5% (azoxystrobin 250 g/L SC)	75%
Oral absorption	>80%	>80%

* Dermal absorption values are default values in accordance with EFSA guidance.

Chlorothalonil

Table 7.2.1-2: EU Conclusions - Toxicological endpoints of chlorothalonil required for evaluation of operator, worker, bystander and residential risk

Endpoint	EU agreed endpoint (SANCO/4343/2000 final (revised) (2006))	Proposed endpoint*
AOEL (mg/kg bw/day)	0.009	0.009
Dermal absorption of concentrate	0.02% (chlorothalonil 720 g/L SC)	0.05%
Dermal absorption of in-use dilution	0.34% (chlorothalonil 720 g/L SC)	0.7% (100 L/ha water volume) 3% (400 L/ha water volume) 7% (1500 L/ha water volume)
Oral Absorption	26-30%	26-30%

* Since Annex I inclusion new study on the active substance has been performed and as a result there are new proposed endpoints, for dermal absorption refer to Point CP 7.3.

Summary

Operator exposure to A14111B has not been evaluated as part of an EU review for the proposed critical use rate/crops. Therefore all relevant data and risk assessments are provided and are considered adequate.

Risk assessment for operator

Operator exposure was assessed against the AOELs agreed in the EU reviews of azoxystrobin and chlorothalonil. No data on dermal absorption of the active substance azoxystrobin in A14111B was provided and therefore default values for the concentrate and in-use dilution have been assumed in accordance with the EFSA Guidance on dermal absorption. Data on dermal absorption of A14111B was provided for chlorothalonil and considered acceptable. Operator exposure was modelled using the German BBA[1] and UK POEM[2] exposure models.

According to the German model calculations for azoxystrobin, it can be concluded that the risk for the operator applying A14111B in the manner proposed is acceptable without the use of personal protective equipment. Levels of exposure predicted using UK POEM are within the AOEL where PPE are worn.

According to the German model calculations for chlorothalonil, estimates of exposure are within the AOEL with the use of PPE. Levels of exposure predicted using the UK POEM exceed the AOEL for chlorothalonil for tractor boom and hand-held application with the use of PPE.

A higher tier exposure assessment for chlorothalonil (field crop boom and hand-held sprayers), which is based on representative exposure studies conducted to modern standards, confirms that the risk for the operator applying A14111B to the proposed crops is acceptable with the use of personal protective equipment.

The following personal protective equipment is recommended: suitable protective clothing (coverall) and suitable protective gloves should be worn when handling the concentrate. Gloves should also be used for

[1] Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protection), Mitteilungen aus der Biologischen Bundesanstalt für Land-und Forstwirtschaft, Berlin-Dahlem, Heft 277, 1992. ("German Model").

[2] Estimation of Exposure and Absorption of Pesticides by Spray Operators, Scientific subcommittee on Pesticides and British Agrochemical association Joint Medical Panel Report (UK MAFF), 1986 and the Predictive Operator Exposure Model (POEM) V 1.0, (UK MAFF), 1992, 2007 version. ("UK POEM").

the maintenance of the sprayer during application with tractor mounted/trailed equipment or when applying the spray solution with hand-held equipment.

Evaluation

The formulation is a suspension concentrate (SC) formulation containing 80 g/L azoxystrobin and 400 g/L chlorothalonil. Estimations of operator exposure have been undertaken for A14111B using the critical uses (Table 7.2.1-3) and the following predictive models: German BBA and UK POEM.

Table 7.2.1-3: Summary of critical use patterns (i.e. worst case) for use of A14111B

Application equipment	Representative Crop (field)	Application rate (g/ha) azoxystrobin/ha chlorothalonil/ha	Spray dilution (L/ha)	Number applications	Application Interval (days)
Tractor-mounted, low crop	Wheat, barley	150 750	100 - 400	2	14
Tractor-mounted, low crop & hand-held equipment	Tomato	200 1000	500 – 1500	1	-

According to UK POEM, taking into account application rate, water volumes and corresponding dermal absorption values, use on cereals (1.875 L product/ha) presents a worst case for tractor-mounted boom sprayer application.

According to German model, taking into account application rate, water volumes and corresponding dermal absorption values, use on tomato (2.5 L product/ha) presents a worst case for tractor-mounted boom sprayer application.

The German model does not contain data for knapsack application to low crops therefore hand held application to tomato has been presented using the UK POEM.

Azoxystrobin

A summary of the estimated operator exposure to azoxystrobin is presented in Table 7.2.1-4.

In Table 7.2.1-4, the estimations were compared to the proposed EU endpoints for azoxystrobin given in Table 7.2.1-1.

Table 7.2.1-4: Summary of estimated operator exposure to azoxystrobin

Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of AOEL (0.2 mg/kg bw/day)
Tractor-mounted boom sprayer application outdoors to low crops (cereals) Application rate = 0.15 kg azoxystrobin/ha (1.875 L A14111B/ha)			
UK POEM 50 ha/day, 6 h/day 100 L/ha 60 kg operator	No PPE	0.947	474
	Gloves when mixing/loading & application	0.131	66
German Model 20 ha/day 70 kg operator	No PPE	0.091	46

Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of AOEL (0.2 mg/kg bw/day)
Tractor-mounted boom sprayer application outdoors to low crops (tomato) Application rate = 0.2 kg azoxystrobin/ha (2.5 L A14111B/ha)			
UK POEM 50 ha/day, 6 h/day 500 L/ha 60 kg operator	No PPE	0.423	212
	Gloves when mixing/loading & application	0.043	22
German Model 20 ha/day 70 kg operator	No PPE	0.122	61.0
Hand-held (Knapsack) sprayer application outdoors to low crops (tomato) Application rate = 0.2 kg azoxystrobin/ha (2.5 L A14111B/ha)			
UK POEM 0.8 ha/day, 6 h/day 500 L/ha 60 kg operator	No PPE	0.601	300
	Gloves when mixing/loading & application; impermeable coverall during application	0.099	50.0

No PPE German Model: Operator wearing T-shirt and shorts.
UK POEM: Operator wearing long-sleeved shirt, long trousers ("permeable") but no gloves.

According to the German model calculations, it can be concluded that the risk of exposure to azoxystrobin for the operator during tractor-mounted boom sprayer application using A14111B for the proposed uses is acceptable without the use of personal protective equipment.

According to the UK-POEM calculations, it can be concluded that the risk of exposure to azoxystrobin for the operator during tractor-mounted boom sprayer application using A14111B for the proposed uses is acceptable with the use of personal protective equipment: gloves during mixing/loading and application.

The risk of exposure to azoxystrobin for the operator during hand-held (knapsack) sprayer low level application using A14111B for the proposed uses is acceptable with the use of personal protective equipment: gloves during mixing/loading and application; coverall during application.

Chlorothalonil

A summary of the estimated operator exposure to chlorothalonil is presented in Table 7.2.1-5.

In Table 7.2.1-5, the estimations were compared to the proposed EU endpoints for chlorothalonil given in Table 7.2.1-2.

Table 7.2.1-5: Summary of estimated operator exposure to chlorothalonil

Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of AOEL (0.009 mg/kg bw/day)
Tractor-mounted boom sprayer application outdoors to low crops (cereals) Application rate = 0.75 kg chlorothalonil/ha (1.875 L A14111B/ha)			
UK POEM 50 ha/day, 6 h/day 100 L/ha 60 kg operator	No PPE	0.0455	506
	Gloves when mixing/loading & application	0.0132	147

Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of AOEL (0.009 mg/kg bw/day)
German Model 20 ha/day 70 kg operator	No PPE	0.0137	152
	Gloves when mixing/loading & application; coverall and sturdy footwear during application	0.0013	14
Tractor-mounted boom sprayer application outdoors to low crops (tomato) Application rate = 1.0 kg chlorothalonil/ha (2.5 L A14111B/ha)			
UK POEM 50 ha/day, 6 h/day 500 L/ha 60 kg operator	No PPE	0.0457	508
	Gloves when mixing/loading & application	0.0086	95
German Model 20 ha/day 70 kg operator	No PPE	0.0416	462
	Gloves when mixing/loading & application; coverall and sturdy footwear during application	0.0033	37
Hand-held (Knapsack) sprayer application outdoors to low crops (tomato) Application rate = 1.0 kg chlorothalonil/ha (2.5 L A14111B/ha)			
UK POEM 0.8 ha/day, 6 h/day 500 L/ha 60 kg operator	No PPE	0.107	1188
	Gloves when mixing/loading & application; impermeable coverall during application	0.023	253

No PPE German Model: Operator wearing T-shirt and shorts.
UK POEM: Operator wearing long-sleeved shirt, long trousers ("permeable") but no gloves.

According to the German model calculations, it can be concluded that the risk of exposure to chlorothalonil for the operator during tractor-mounted boom sprayer application using A14111B for the proposed uses is acceptable with one layer of work clothing and with the use of gloves during mixing/loading and application.

According to the UK POEM calculations, it can be concluded that the risk of exposure to chlorothalonil for the operator during tractor-mounted boom sprayer application in cereals and hand-held (knapsack) sprayer low level application in tomato using A14111B is not acceptable even with the use of personal protective equipment.

A further refinement of the exposure assessment for chlorothalonil is given using higher tier data. This addresses both boom sprayers and hand-held equipment. A summary of the higher tier exposure assessments are provided below. Further details are given in CP 7.2.1.2.

Table 7.2.1-6: Summary of estimated operator exposure to chlorothalonil using higher tier data for applications made using a field crop (boom) sprayer

	Arith mean	Geomean	75th percentile	95th percentile	Maximum value
Actual dermal exposure (µg/operator)	402.56	238.57	482.38	1107.43	1387.54
*Inhalation exposure ((µg/operator)	1.10	0.37	1.32	2.98	3.84
$Total systemic exposure (mg/kg bw/day)	1.5×10^{-4}	9.4×10^{-5}	1.4×10^{-4}	4.3×10^{-4}	5.3×10^{-4}
% of AOEL (0.009 mg/kg bw/day)	2	1	2	5	6

*assumes a breathing rate of 16.7 L/day.
$Assumes 3% absorption by the dermal route and 100% absorption by inhalation. Actual operator bodyweights used for exposure values.

Assuming the 75th percentile value for repeated exposure, the predicted exposure is 2% of the systemic AOEL. As a worse case, i.e. as an acute exposure, the maximum predicted exposure is 6% of the systemic AOEL.

Table 7.2.1-7: Summary of estimated operator exposure to chlorothalonil using higher tier data for applications made using a hand-held (knapsack) sprayer

	Arith mean	Geomean	75th percentile	95th percentile	Maximum value
Actual dermal exposure (µg/operator)	1375	848.25	2737	3378.9	3657.0
*Inhalation exposure (µg/operator)	Value taken from UK POEM (75th percentile) is 240 µg/person				
$Total systemic exposure (mg/kg bw/day)	0.0045	0.0043	0.0050	0.0053	0.0054
% of AOEL (0.009 mg/kg bw/day)	50	48	56	59	60

*Inhalation exposure value taken from UK POEM (see Appendix 1)
$Assumes 7% absorption by the dermal route and 100% absorption by inhalation. Actual operator bodyweights used for dermal exposure values. UK-POEM default (60 kg) for inhalation exposure.

Assuming the 75th percentile value for repeated exposure, the predicted exposure is 56% of the systemic AOEL. As a worse case, i.e. as an acute exposure, the maximum predicted exposure is 60% of the systemic AOEL.

Overall Assessment

According to the model calculations for azoxystrobin, it can be concluded that the risk for the operator using A14111B for the proposed uses is acceptable with the use of personal protective equipment.

Predicted levels of exposure for chlorothalonil, based on higher tier data for applications made using field crop (boom) sprayers and hand-held (knapsack) sprayers are within the AOEL for operators wearing personal protective equipment.

The following personal protective equipment is recommended: suitable protective clothing (coverall) and suitable protective gloves should be worn when handling the concentrate. Gloves should also be used for the maintenance of the sprayer during application with tractor mounted/trailed equipment or when applying the spray solution with hand-held equipment.

CP 7.2.1.1 Estimation of operator exposure

The following parameters were used in the operator exposure assessment:

UK POEM:

Application method:	**Tractor-mounted boom sprayer**
Treated area:	50 ha/day
Max. dose rate:	Cereal - 0.15 kg azoxystrobin/ha; 0.75 kg chlorothalonil/ha (1.875 L product/ha) Tomato - 0.2 kg azoxystrobin/ha; 1.0 kg chlorothalonil/ha (2.5 L product/ha)
Pack size:	10 L with 63 mm closure
Application volume:	Cereal: 100 L/ha; Tomato: 500 L/ha
Dermal absorption:	Cereal: Azoxystrobin: 25% for concentrate; 75% for in-use dilution; Chlorothalonil: 0.05% for concentrate; 0.7% for in-use dilution Tomato: Azoxystrobin: 25% for concentrate; 75% for in-use dilution; Chlorothalonil: 0.05% for concentrate; 3% for in-use dilution
Operator body weight:	60 kg
No PPE:	Operator wearing long sleeved shirt, long trousers ("permeable") but no gloves
PPE:	Gloves during mixing/loading and application.

Application method:	**Hand-held (knapsack), low level sprayer (tomato)**
Treated area:	0.8 ha/day (relevant to 500 L/ha spray application)
Max. dose rate:	0.2 kg azoxystrobin/ha; 1.0 kg chlorothalonil/ha (2.5 L product/ha)
Pack size:	5 L wide neck closure
Application volume:	500 L/ha
Dermal absorption:	Azoxystrobin: 25% for concentrate; 75% for in-use dilution; Chlorothalonil: 0.05% for concentrate; 3% for in-use dilution
Operator body weight:	60 kg
No PPE:	Operator wearing long sleeved shirt, long trousers ("permeable") but no gloves
PPE:	Gloves during mixing/loading and application; impermeable coveralls during application.

German Model:

Application method:	**Tractor-mounted boom sprayer**
Treated area:	20 ha/day
Max. dose rate:	Cereal: 0.15 kg azoxystrobin/ha; 0.75 kg chlorothalonil/ha (1.875 L product/ha) Tomato: 0.2 kg azoxystrobin/ha; 1.0 kg chlorothalonil/ha (2.5 L product/ha)
Dermal absorption:	Cereal: Azoxystrobin: 25% for concentrate; 75% for in-use dilution; Chlorothalonil: 0.05% for concentrate; 3% for in-use dilution Tomato: Azoxystrobin: 25% for concentrate; 75% for in-use dilution; Chlorothalonil: 0.05% for concentrate; 7% for in-use dilution
Operator body weight:	70 kg
No PPE:	Operator wearing T-shirt and shorts
PPE:	Gloves during mixing/loading and application; coverall and sturdy footwear during application.

The detailed estimations of exposure are provided in in Appendix 1.1 – 1.18. A summary is provided in CP 7.2.1.

CP 7.2.1.2 Measurement of operator exposure

Further refinement of the exposure assessment for chlorothalonil is given using higher tier data.

FIELD CROP SPRAYER APPLICATION

The following report is used to support the assessment.

Report:	K-CP 7.2.1.2/01, Wilson A. (2012). Diquat - Determination of Operator Exposure (Passive Dosimetry) during Typical Activities Associated with Mixing/Loading and Application of Reglone® (Soluble Concentrate Containing 200 g/L Diquat cation) as a Desiccant to Ware Potatoes in The Netherlands, 2011. AgroChemex International Ltd, Aldhams Farm Research Station, Lawford, Essex, UK. Report No. ACI11-003, Issue date 12 February 2012. Unpublished. (Syngenta File No. A1412A_10300)

Guidelines: OECD/GD (97)148 Series on Testing and Assessment No. 9, Guidance Document for the Conduct of Studies of Occupational Exposure to Pesticides During Agricultural Application, Organisation for Economic Cooperation and Development, Paris.

Deviations: None

GLP: Yes

Executive Summary

In 2011, a Good Laboratory Practice (GLP) operator exposure study was conducted with thirteen operators in The Netherlands. The study was performed to determine the dermal and inhalation exposure to diquat during typical activities associated with a ground boom application of Reglone® as a desiccant to ware potatoes.

Reglone® was mixed and sprayed as closely as possible to normal practices using commercial tractor mounted (self-propelled) or trailed boom sprayers. Cabin equipped tractors were used in this study and all the windows were kept closed during the crop treatment.

Reglone® was applied at a target rate of 4.0 L/ha (800 g diquat cation/ha). The actual application rate was 706 to 803 g diquat cation/ha. The application volume was in the range of 250 to 483 L/ha, depending on crop canopy and the typical practices of each operator.

The duration of each application was 5.38 to 8.82 hours (from the start of mixing/loading to completion of spraying, excluding scheduled breaks). The area actually treated was 21.6 to 63.3 ha. The total amount of formulated product and corresponding active substance handled by each operator was between 81 and 252 L of formulation and 16.2 to 50.4 kg of corresponding diquat cation.

Materials

Test Material:	Reglone®
Description:	Soluble concentrate (SL)
Lot/Batch Number:	BSN1G1438, BSN1F1050, BSN1H0432, BSN1G1429, BSN1G0437, BSN1H0827
Purity:	Nominal 200 g/L diquat cation
Stability of test compound:	Stable for the duration of the study

Study Design and Methods

Field Phase dates: 23rd August 2011 to 15th September 2011

Experimental dates: 29th September 2011 to 20th December 2011

Study Description:

13 operators were monitored between 23rd August 2011 and 15th September 2011.

The purpose of the study was to determine the dermal and inhalation exposure to diquat during typical activities associated with the mixing and loading and ground boom application of Reglone® as a desiccant to ware potatoes.

Dermal exposure to diquat cation was measured by operators wearing standardised whole-body outer and inner dosimeters. The outer dosimeter consisted of a 35/65% cotton/polyester coverall. The inner dosimeter, representing the skin, consisted of a full-length cotton undergarment covering arms, legs and torso.

Head exposure was measured by face/neck wipes.

Actual hand exposure was measured by the handwash procedure. Protective gloves, worn in accordance with label recommendations (one pair for mixing and loading tasks and one pair for maintenance tasks), were analysed for the determination of potential hand exposure.

Inhalation exposure was measured by means of personal air sampling pumps connected to an IOM sampling cassette with cellulose ester fibre filter located in the operator's breathing zone.

All samples collected were analysed for residues of diquat cation.

Inner and outer dosimeters, face/neck wipes and nitrile gloves were extracted with ammonium formate/acetonitrile by shaking. Extracts were analysed by high performance liquid chromatography using triple quadrupole mass spectrometry LC-MS/MS.

Hand wash solutions were directly analysed by LC-MS/MS.

Air sampling filters were extracted with ammonium formate/acetonitrile in an ultrasonic bath and aliquots analysed by GC-MS.

Results

Since all mean field fortification recoveries were greater than 91% operator exposure results have not been corrected. Where a residue below the limit of quantification (LOQ) or limit of detection (LOD) has been found a value of 0.5 x LOQ has been reported and used in summary calculations.

The following table gives a summary of the residues of test item on each dosimeter for each operator.

Potential dermal exposure is calculated by summing all dermal exposure residues. Actual dermal exposure is calculated by summing residues from inner dosimeters, hand wash and face/neck wipe specimens. Potential inhalation exposure is the residues measured in the breathing zone based upon a ventilation rate of 16.7 L/min for tasks.

All field fortified recovery samples, gave recoveries greater than 91%.

Table 7.2.1.2-1: Determined Residues of diquat cation (all values in µg/sample)

Operator Number	1	2	3	4	5	6	7	8	9	10	11	12	13
Body Weight (kg)	134.0	90.4	89.4	95.8	83.2	71.0	81.1	101.0	74.5	115.1	80.9	93.0	102.5
Work Duration (mins)	451.0	504.0	406.0	475.0	510.0	494.0	406.0	370.0	323.0	323.0	391.0	529.0	380.0
Diquat cation mixed (kg)	34.0	36.8	26.8	24.5	38.4	16.2	26.8	36.0	32.4	39.2	43.2	50.4	28.0
Area Sprayed (ha)	42.4	48.8	34.8	34.3	47.8	21.6	35.0	46.0	41.0	54.0	55.8	63.3	35.0
Volume of air samples (L)	856.9	982.8	812.0	950.0	1020	963.3	791.7	721.5	646.0	646.0	782.0	1058	760.0
Outer Dosimeter – cotton/polyester coverall													
lower arms	26.25	379.88	523.13	61.38	1267.89	394.54	436.95	245.93	650.02	3251.03	453.25	122.41	527.41
upper arms	3.13	109.69	212.23	17.73	113.92	80.10	44.60	20.14	96.29	121.35	135.44	50.20	129.03
lower legs	944.46	8273.99	1479.36	203.32	1000.75	1731.92	473.46	107.52	126.60	5106.59	296.07	153.86	419.58
upper legs	440.30	144.55	151.57	38.47	265.95	543.27	1611.44	419.96	492.36	2611.38	241.99	369.29	211.03
front torso	725.24	240.54	328.07	88.91	590.90	243.75	4469.49	22.01	108.89	4515.13	700.38	91.86	1946.83
rear torso	5.01	150.68	77.17	11.65	106.28	151.44	73.12	25.28	57.77	226.20	67.89	51.02	174.10
TOTAL	2144.39	9299.33	2771.53	421.45	3345.69	3145.03	7109.06	840.84	1531.93	15831.67	1895.02	838.63	3407.98
Inner dosimeter (representing the skin)													
lower arms	2.261	14.768	7.421	1.446	31.889	87.928	17.001	6.502	7.847	12.551	21.849	4.948	14.753
upper arms	*0.050*	1.954	5.100	*0.500*	16.892	*0.500*	1.113	1.189	1.044	2.117	4.219	*0.500*	1.440
lower legs	1.512	2.455	2.235	*0.500*	1.351	3.081	1.467	4.282	1.087	2.519	4.755	2.294	*0.500*
upper legs	1.407	2.025	2.483	1.081	1.575	1.662	7.073	2.022	*0.500*	5.704	5.653	9.410	*0.500*
torso	2.458	9.702	11.971	1.564	5.493	1.546	4.922	5.111	2.044	18.901	15.241	3.480	4.050
TOTAL	7.688	30.903	29.210	5.092	57.200	94.716	31.575	19.106	12.521	41.792	51.717	20.632	21.243
Handwash													
Measured	*10.0*	547.2	239.4	109.4	842.0	25.9	1350.6	427.0	218.9	429.4	159.5	366.1	13.0
TOTAL	*10.0*	547.2	239.4	109.4	842.0	25.9	1350.6	427.0	218.9	429.4	159.5	366.1	13.0
Face/neck wipes													
Measured	*0.500*	5.698	2.455	*0.500*	21.440	1.921	5.384	3.453	1.505	11.220	9.998	5.940	1.453
TOTAL	*0.500*	5.698	2.455	*0.500*	21.440	1.921	5.384	3.453	1.505	11.220	9.998	5.940	1.453
Nitrile Gloves													
mixing	2218.6	7668.1	10642.7	187.0	1457.3	3964.9	3745.6	229.0	1322.7	8396.8	1389.6	1101.2	201.0
application		12.4	107.8	27.3	3833.1	1121.0	8091.5			17685.4	2830.3		243.3
TOTAL	2218.6	7680.5	10750.5	214.4	5290.4	5085.9	11837.0	229.0	1322.7	26082.2	4219.8	1101.2	444.2
Residues in air sampling tubes													
Measured	*0.003*	0.084	0.077	*0.003*	0.289	0.448	0.116	*0.003*	*0.003*	0.159	0.095	0.144	0.273
TOTAL	*0.003*	0.084	0.077	*0.003*	0.289	0.448	0.116	*0.003*	*0.003*	0.159	0.095	0.144	0.273

Values in italics are <LOQ. Half the LOQ is taken for the calculations

Table 7.2.1.2-2: Summary of Field Results

Operator Number	1	2	3	4	5	6	7	8	9	10	11	12	13
Potential Dermal Exposure (µg/operator)	4381	17564	13793	751	9557	8353	20334	1519	3088	42396	6336	2333	3888
Actual Dermal Exposure (µg/operator)	18.19	583.84	271.11	115.01	920.69	122.49	1387.54	449.51	232.94	482.38	221.24	392.69	35.66
Potential Inhalation Exposure (µg/operator)	0.022	0.715	0.645	0.021	2.416	3.838	0.990	0.021	0.021	1.324	0.795	1.198	2.280

Potential Dermal Exposure (PDE) = Sum of residues on outer clothing (coverall), inner dosimeter representing the skin, face/neck wipes, protective gloves (nitrile – if worn) and handwash solutions.
Actual Dermal Exposure (ADE) = Sum of residues on inner dosimeter representing the skin, face/neck wipes and hand wash solutions.
Potential Inhalation Exposure (PIE) = Residues measured in the breathing zone expressed as µg diquat cation/operator based on an inhalation rate of 16.7 L/min.

Conclusions

The study is considered to provide suitable exposure data for the estimation of operator exposure for the tasks of mixing/loading and ground boom application. The exposure results for the dermal dosimeters show that whilst some spray operators received high levels of contamination to their outer clothing and gloves, the protective coverall and gloves worn by the spray operators provided an effective barrier, as levels of actual dermal exposure were significantly lower than corresponding levels of potential dermal exposure. For this dataset the mean penetration of the outer dosimeter is 1% and the mean penetration/contamination of hands through protective gloves is 6%.

Chlorothalonil

A justification for the use of the study to refine the exposure assessment for chlorothalonil is given below.

Table 7.2.1.2-3: Comparison of proposed use of A14111B with diquat exposure study

	Proposed use of A14111B chlorothalonil	**Application parameters for Diquat exposure study**
Application method	Field crop boom sprayer	Field crop boom sprayer
Formulation	400 g/L SC	200 g/L SC
Application rate (g a.s./ha)	750	706 - 803
Water volume (L/ha)	100 - 400	250 - 483
Area treated (ha)	Cereals, so assume full working day – German model assumes 20 ha, UK POEM 50 ha	21.6 to 63.3
Duration of spraying	Cereals, so assume full working day – UK POEM assumes 6 hours for application of spray solution plus 2 hours for mix/loading and travelling to field(s)	5.38 to 8.82

In summary, the formulation and application parameters used for the diquat exposure study are similar to the use of chlorothalonil proposed for A14111B. It is noteworthy that all of the spray tasks exceeded 20 ha and some exceeded 50 ha (the default parameters for the German model and UK POEM

respectively) although the operator handling and applying the highest amount of active substance did not have the highest dermal or inhalation exposure. Overall, this GLP study, performed to modern standards, is a representative study for operators using field crop (boom) sprayers to treat large areas and provides a precautionary basis to refine the Tier 1 assessment, made using the German model and UK POEM.

The exposure assessment is performed using the diquat exposure study values for (actual) dermal and inhalation exposure as reported in the study, i.e. these values have not been adjusted for differences in the application rate between chlorothalonil (750 g a.s./ha) and diquat (706 g a.s./ha to 803 g a.s./ha). As the diquat study measured dermal exposure as a single task (mixing/loading and application) it is necessary to assume a dermal absorption value of 3%, (derived for a spray solution of chlorothalonil, 1/213 dilution) to calculate the absorbed dose for operators via the dermal route. As the dermal absorption value for undiluted chlorothalonil in A14111B is significantly lower than this value (i.e. 0.05%) this will significantly over predict systemic exposure from the mixing/loading operations and therefore provides a precautionary exposure assessment for chlorothalonil.

Table 7.2.1.2-4: Summary of estimated operator exposure to chlorothalonil using higher tier data

	Arith mean	Geomean	75th percentile	95th percentile	Maximum value
Actual dermal exposure (µg/operator)	402.56	238.57	482.38	1107.43	1387.54
*Inhalation exposure ((µg/operator)	1.10	0.37	1.32	2.98	3.84
$Total systemic exposure (mg/kg bw/day)	1.5×10^{-4}	9.4×10^{-5}	1.4×10^{-4}	4.3×10^{-4}	5.3×10^{-4}
% of AOEL (0.009 mg/kg bw/day)	2	1	2	5	6

*assumes a breathing rate of 16.7 L/day.
$Assumes 3% absorption by the dermal route and 100% absorption by inhalation. Actual operator bodyweights used for exposure values.

Assuming the 75th percentile value for repeated exposure, the predicted exposure is 2% of the systemic AOEL. As a worse case, i.e. as an acute exposure, the maximum predicted exposure is 6% of the systemic AOEL.

HAND-HELD (KNAPSACK) SPRAYER APPLICATION

The following report is used to support the assessment.

Report:	K-CP 7.2.1.2/02, Tack T.J. (1995). Operator Exposure Study – To assess the exposure of GESATOP 500SC to farm operators when applied through a knapsack sprayer. Ciba Agriculture, Whittlesford, Cambridge, UK. Residue Report No. CSTR 39:3. Issue date 07 December 1995. Unpublished. (Syngenta File No. G27692/1897)

Guidelines: Procedures and Principles of GLP (OECD Paris 1981 and Switzerland, Bern 1986), UK Principles of GLP, The UK Compliance Programme, Department of Health, London, 1989.

Deviations: None

GLP: Yes

Executive Summary

The exposure of 10 experienced spray operators was monitored during the application of GESATOP® 500 SC (A3796J) in stubble fields using knapsack sprayers. Each operator mixed/loaded and applied the spray solution. The use rate was 1.5 kg a.s./ha, with a spray volume of 200 L/ha. The daily work rate was 0.8 to 1 ha per operator. The operators followed label recommendations using all safety precautions specified. Passive dosimetry was used to obtain measurements of dermal exposure. Each operator was

dressed in a long sleeved and long legged cotton undergarment to represent the skin, a cotton coverall to represent a single layer of work clothing, a dust/mist mask to trap inhalable particles, a cotton hat, rubber boots, cotton liner gloves and nitrile protective gloves during mixing/loading and spraying. Due to heavy contamination after a spillage incident during filling the results of one operator are excluded.

Field Phase dates: 04 to 06.09 1994.

Experimental dates: 11.05 1994

Study Design and Methods

Table 7.2.1.2-5: Application conditions of the performed operator exposure study

Formulation	GESATOP 500 SC (500 g/L simazine)
Crop	stubble
Use rate	1.5 kg a.s./ha
Spray liquid/ha	200 litres
Number of replicates	9 (10) 1 operator was excluded due to heavy spillage which made change of clothing necessary
Spraying equipment	knapsack
Protective clothing	cotton coverall, rubber boots, cap nitrile rubber gloves and breathing mask
Treated surface per working day	about 0.8 to 1 ha/person/day, totally 9 ha

Conclusions

The study is considered to provide suitable exposure data for the estimation of operator exposure for the tasks of mixing/loading and hand-held (knapsack) sprayer application. The exposure results for the dermal dosimeters show a range of exposures, with some potential dermal exposures (PDE) being an order of magnitude higher than others. The results for the inner dosimeters show the outer clothing and protective gloves provided an effective barrier to contamination during the spray task (mean actual dermal exposure is 6% of PDE). There was a gross contamination event for one of the study subjects, which resulted in significant spillage of mixed spray solution onto their clothing. This subject's exposure is not representative of a repeat exposure scenario and is not therefore included in the analysis of the study results.

Results

Table 7.2.1.2-6: Results of the Performed Exposure Study (µg) (measured exposure to simazine)

Type of exposure	**Range of individuals values**	**75th %tile**	**Average**	**Mean geometric value**
TUDX µg/person	5129 to 40008	30555.0	21777	17436.5
TUDX (µg/kg bw) based on actual bw	69.3 to 763	416.5	354.01	284.62
DX (µg/person)	234.5 to 3657.0	2737.0	1375	848.2
DX (µg/kg bw) based on actual bw	2.5 to 46.3	33.8	17.5	10.71
REX (µg/person)	7.5 to 11	8.70	8.22	8.149
REX (µg/kg bw) based on actual bw	0.08 to 1.22	0.100	0.224	0.131
TUDX: total unprotected dermal exposure (coverall, outer gloves, glove wash, cap) DX: dermal exposure (whole undergarment, inner gloves, hand wash) REX: inhalation exposure – measured on surface of mask worn by operator.				

Chlorothalonil

A justification for the use of the study to refine the exposure assessment for chlorothalonil is given below.

Table 7.2.1.2-7: Comparison of proposed use of A14111B with simazine exposure study

	Proposed use of A14111B chlorothalonil	Application parameters for Gesatop 500 SC exposure study
Application method	Hand-held sprayer	Hand-held sprayer
Formulation	400 g/L SC	500 g/L SC
Application rate (g a.s./ha)	1000	1500 g a.s/ha
Water volume (L/ha)	500 – 1500	200
Area treated (ha)	Assume full working day – UK POEM assumes 1 ha	0.8 to 1 ha

The exposure assessment is performed using the simazine exposure study values for (actual) dermal exposure as reported in the study, i.e. these values have not been adjusted for differences in the application rate between chlorothalonil (1000 g a.s./ha) and simazine (1500 g a.s./ha). As the simazine study measured dermal exposure as a single task (mixing/loading and application) it is necessary to assume a dermal absorption value of 7%, (derived for a spray solution of chlorothalonil, 1/600) to calculate the absorbed dose for operators via the dermal route. As the dermal absorption value for undiluted chlorothalonil in A14111B is significantly lower than this value (i.e. 0.05%) this will significantly over predict systemic exposure from the mixing/loading operations and therefore provides a precautionary exposure assessment for chlorothalonil.

Inhalation exposure was monitored in the exposure study using a dust/mist mask to trap inhalable particles. As this method for monitoring inhalation exposure does not meet modern standards, i.e. a personal air sampling pump fitted with suitable collection media, these data are not considered in the exposure assessment. Instead levels of inhalation exposure predicted by UK POEM are used, in combination with the dermal exposure results from the exposure study to provide a total systemic dose for operators.

Table 7.2.1.2-8: Summary of estimated operator exposure to chlorothalonil using higher tier data (dermal) and UK POEM (inhalation exposure) for applications made using a hand-held (knapsack) sprayer

	Arith mean	Geomean	75th percentile	95th percentile	Maximum value
Actual dermal exposure (µg/operator)	1375	848.25	2737	3378.9	3657.0
*Inhalation exposure (µg/operator)	Value taken from UK POEM (75th percentile) is 240 µg/person				
$Total systemic exposure (mg/kg bw/day)	0.0045	0.0043	0.0050	0.0053	0.0054
% of AOEL (0.009 mg/kg bw/day)	50	48	56	59	60

*Inhalation exposure value taken from UK POEM (see Appendix 1)
$Assumes 7% absorption by the dermal route and 100% absorption by inhalation. Actual operator bodyweights used for dermal exposure values. UK POEM default (60 kg) for inhalation exposure.

Assuming the 75th percentile value for repeated exposure, the predicted exposure is 56% of the systemic AOEL. As a worse case, i.e. as an acute exposure, the maximum predicted exposure is 60% of the systemic AOEL.

CP 7.2.2 Bystander and resident exposure

Risk assessment for bystander and resident

Summary

Bystander and residential exposure to A14111B has not been evaluated as part of an EU review for the proposed critical use rate/crops. Therefore all relevant data and risk assessments are provided and are considered adequate.

It is concluded that there is no undue risk to any bystander or resident during and following local application of A14111B. This has no labelling implications.

Evaluation

Estimations of bystander and residential exposure have been undertaken for A14111B using the critical uses (Table 7.2.1-3) and the German guidance paper[3]. All assumptions made in the following are quoted in this guidance paper. Tractor-mounted boom sprayer application has been presented as a worst case scenario.

Azoxystrobin

A summary of the estimated bystander/resident exposure to azoxystrobin is presented in Table 7.2.2-1.

Table 7.2.2-1: Estimated bystander/residential exposure to azoxystrobin and % of the AOEL

	Azoxystrobin (AOEL = 0.2 mg/kg bw/day)	
Bystander exposure	Adult	Child
Dermal exposure (mg/kg bw/day)	$7.25 * 10^{-4}$	$5.66 * 10^{-4}$
Inhalation exposure (mg/kg bw/day)	$9.00 * 10^{-7}$	$2.00 * 10^{-6}$
Total systemic exposure (mg/kg bw/day)	**$7.26 * 10^{-4}$**	**$5.68 * 10^{-4}$**
% of AOEL	**0.36**	**0.28**
Residential exposure		
Dermal exposure (mg/kg bw/day)	$5.29 * 10^{-5}$	$7.00 * 10^{-5}$
Inhalation exposure (mg/kg bw/day)	-	-
Hand to mouth transfer (mg/kg bw/day)	-	$7.2 * 10^{-6}$
Object to mouth transfer (mg/kg bw/day)	-	$1.80 * 10^{-6}$
Total systemic exposure (mg/kg bw/day)	**$5.29 * 10^{-5}$**	**$7.90 * 10^{-5}$**
% of AOEL	**0.03**	**0.04**

It is concluded that there is no undue risk to any bystander or resident from azoxystrobin during and following local application of A14111B. This has no labelling implications.

Chlorothalonil

A summary of the estimated bystander/resident exposure to chlorothalonil is presented in Table 7.2.2-2.

[3] Guidance for Exposure and Risk Evaluation for Bystanders and Residents exposed to Plant Protection Products during and after Application; S. Martin et al.; J. Verbr. Lebensm. 3 (2008): 272 – 281, 1661-5751/08/030272-10 DOI 10.1007/s00003-008-0361-5, ©Birkhäuser Verlag, Basel, 2008

Table 7.2.2-2: Estimated bystander/residential exposure to chlorothalonil and % of the AOEL

	Chlorothalonil (AOEL = 0.009 mg/kg bw/day)	
Bystander exposure	Adult	Child
Dermal exposure (mg/kg bw/day)	$3.38 * 10^{-4}$	$2.64 * 10^{-4}$
Inhalation exposure (mg/kg bw/day)	$4.63 * 10^{-6}$	$9.88 * 10^{-6}$
Total systemic exposure (mg/kg bw/day)	**$3.43 * 10^{-4}$**	**$2.74 * 10^{-4}$**
% of AOEL	**3.81**	**3.04**
Residential exposure		
Dermal exposure (mg/kg bw/day)	$2.47 * 10^{-5}$	$3.27 * 10^{-5}$
Inhalation exposure (mg/kg bw/day)	$2.76 * 10^{-4}$	$5.15 * 10^{-4}$
Hand to mouth transfer (mg/kg bw/day)	-	$1.08 * 10^{-5}$
Object to mouth transfer (mg/kg bw/day)	-	$2.70 * 10^{-6}$
Total systemic exposure (mg/kg bw/day)	**$3.01 * 10^{-4}$**	**$5.61 * 10^{-4}$**
% of AOEL	**3.34**	**6.23**

It is concluded that there is no undue risk to any bystander or resident from chlorothalonil during and following local application of A14111B. This has no labelling implications.

Overall Assessment

It is concluded that there is no undue risk to any bystander or resident during and following local application of A14111B. This has no labelling implications.

CP 7.2.2.1 Estimation of bystander and resident exposure

Bystander Assessment

According to this exposure model the worst case is given by the single treatment of 2.5 L product/ha.

The following parameters were used in the bystander assessment:

- Application method: Tractor-mounted boom sprayer
- Application rate: 0.2 kg azoxystrobin/ha; 1.0 kg chlorothalonil/ha (2.5 L product/ha)
- Drift deposition: 0.29% at 10 m
- Exposure duration: 5 minutes
- Exposed body surface: 1 m^2 for an adult and 0.21 m^2 for children
- Dermal absorption: 75% for azoxystrobin; 7% for chlorothalonil
- Body weights: 60 kg for adults and 16.15 kg for children.

Resident Assessment

According to this exposure model, taking into consideration the application rate and the worst case dermal absorption values, the worst case is given by the single treatment of 2.5 L product/ha.

The following parameters were used in the resident assessment:

- Application rate: 0.2 kg azoxystrobin/ha; 1.0 kg chlorothalonil/ha
- Drift deposition: 0.29% at 10 m
- The vapour pressure: 1.1 x 10^{-11} Pa @ 20°C for azoxystrobin, therefore considered as non – volatile by the exposure model and 7.62 x 10^{-5} Pa @ 25°C for chlorothalonil, therefore considered as semi-volatile by the exposure model
- Exposure duration: 2 hours for dermal exposure
- In the case of semi-volatile or volatile active substances, the inhalation exposure duration is 24 hours
- Dermal absorption: 75% for azoxystrobin; 7% for chlorothalonil
- Oral absorption: 100 % for azoxystrobin; 30% for chlorothalonil
- Body weights: 60 kg for adults and 16.15 kg for children.

The detailed estimation of exposure is provided in Appendix 1.19 – 1.22. A summary is provided in CP 7.2.2.

The estimated bystander and resident exposures are below the AOELs for azoxystrobin and chlorothalonil. Therefore, it is concluded that there is no undue risk to any bystander or resident during and following local application of A14111B.

CP 7.2.2.2 Measurement of bystander and resident exposure

Measurement of bystander exposure is not required since model estimations predict the systemic exposure to azoxystrobin and chlorothalonil to be within the AOELs.

CP 7.2.3 Worker exposure

Risk assessment for worker

Worker exposure to A14111B has not been evaluated as part of an EU review for the proposed critical use rate/crops. Therefore all relevant data and risk assessments are provided and are considered adequate.

For workers performing crop inspection activities it is concluded that there is no unacceptable risk anticipated for the worker wearing adequate work clothing when re-entering crops treated with A14111B. For workers hand harvesting tomatoes there is no unacceptable risk anticipated for the worker wearing adequate work clothing and PPE (i.e. gloves), when re-entering crops treated with A14111B.

Evaluation

Estimations of worker exposure have been undertaken for A14111B using the critical uses (Table 7.2.1-3) and the generic re-entry exposure approach approved for use in Germany[4] and default parameters from the EUROPOEM II re-entry report[5].

Two re-entry scenarios have been considered. The first is a crop inspection scenario for cereals where re-entry could potentially occur soon after application. Higher tier risk assessments are also included for this scenario based on the measured dislodgeable foliar residues for both azoxystrobin and chlorothalonil from a field study, and in addition, a refined TC value from the US database. As the EUROPOEM re-entry model has no TC values for crop inspection, ~~as a second tier refinement~~ the TC value for this activity is taken from the US EPA Policy Paper 2000[6]. This paper recommends a TC value of 1100 cm^2/hr derived from data on peas and corn which represents a more robust set of data compared to the default values available in the EUROPOEM II re-entry report. The US EPA apply this value to all cereal growth stage scenarios irrespective of crop height or foliage density.

The second re-entry scenario has been ~~is an assessment~~ given for workers hand-harvesting tomato crops. For tomato, the assessments for chlorothalonil incorporate actual measurements of chlorothalonil dislodgeable foliar residues derived from a field study and consider the dissipation of these DFR over time i.e. pre-harvest intervals.

Azoxystrobin

A summary of the estimated worker exposure to azoxystrobin is presented in Table 7.2.3-1.

[4] Krebs B. *et al*., (1998) Uniform Principles for Safeguarding the Health of Worker Re-entering Crop Growing Areas after Application of Plant Protection Products. (Bulletin of the German Plant Protection Service) Nachrichtenblatt des Deutschen Pflanzenschutzdienstes.10/98;Vol 50, Verlag Eugen Ulmer , Stuttgart, Germany

[5] Post-Application Exposure of Workers to Pesticides in Agriculture – Report of the Re-entry Working Group. EUROPOEM II Project, FAIR3-CT96-1406. December 2002.

[6] EPA, Science Advisory Council for Exposure; 2000b; Agricultural Default Transfer Coefficients, Policy 003/1, May 7 1998 revised 7 August 2000; BASF Doc ID 2000/1023421

Table 7.2.3-1: Estimated worker exposure to azoxystrobin

Exposure scenario	Worker exposure (AOEL = 0.2 mg/kg bw/day)	
	Absorbed dose [mg/kg bw/day]	% of AOEL
Crop inspection in cereals, Tier 1 assessment	0.05625[a]	28.1
	0.00923[b]	4.6
Crop inspection in cereals, with a refined DFR value	0.023501[a]	11.8
Crop inspection in cereals, refinement with TC from the US EPA Policy Paper	0.02475[a]	12.4
Crop inspection in cereals, with a refined DFR value and TC from the US EPA Policy Paper	0.010341[a]	5.2
Hand-harvesting tomato, Tier 1 assessment	0.15000[a]	75
	0.02460[b]	12.3

a) Worker wearing shoes, socks, long-sleeved shirt, and long trousers
b) Worker wearing shoes, socks, long-sleeved shirt, and long trousers. Protective gloves also worn when handling the treated crop

Chlorothalonil

A summary of the estimated worker exposure to chlorothalonil is presented in Table 7.2.3-2.

Table 7.2.3-2: Estimated worker exposure to chlorothalonil

Exposure scenario	Worker exposure (AOEL = 0.009 mg/kg bw/day)	
	Absorbed dose [mg/kg bw/day]	% of AOEL
Crop inspection in cereals, Tier 1 assessment	0.01125[a]	125
	0.00185[b]	20.5
Crop inspection in cereals, with a refined DFR value	0.003152[a]	35.0
Crop inspection in cereals, refinement with TC from the US EPA Policy Paper	0.00495[a]	55.0
Crop inspection in cereals, with a refined DFR value and TC from the US EPA Policy Paper	0.001387[a]	15.4
Hand-harvesting tomato, Tier 1 assessment	0.07000[a]	778
	0.01148[b]	128
Hand-harvesting tomato, including data on dislodgeable foliar residues	0.00961[a]	107
	0.00158[b]	17.5

a) Worker wearing shoes, socks, long-sleeved shirt, and long trousers
b) Worker wearing shoes, socks, long-sleeved shirt, and long trousers. Protective gloves also worn when handling the treated crop

Overall Assessment

For workers performing crop inspection activities it is concluded that there is no unacceptable risk anticipated for the worker wearing adequate work clothing when re-entering crops treated with A14111B.

For workers hand harvesting tomatoes there is no unacceptable risk anticipated for the worker wearing adequate work clothing and PPE (i.e. gloves), when re-entering crops treated with A14111B.

CP 7.2.3.1 Estimation of worker exposure

The following parameters were used in the re-entry worker assessment:

- Application rate: For crop inspection in cereals (maximum total dose of two treatments) is 0.3 kg/ha for azoxystrobin and 1.5 kg/ha for chlorothalonil. For hand harvesting tomatoes (maximum total dose of one treatment) is 0.2 kg/ha for azoxystrobin and 1 kg/ha for chlorothalonil

- Dermal absorption:
  - Inspection in cereals: 75% for azoxystrobin; 3% for chlorothalonil (worst-case)
  - Hand-harvesting tomatoes: 75% for azoxystrobin; 7% for chlorothalonil (worst-case)

- No PPE: Worker wearing shoes, socks, long-sleeved shirt, and long trousers

- PPE: Worker wearing shoes, socks, long-sleeved shirt, and long trousers. Protective gloves also worn when handling the treated crop (95% reduction in hand exposure)

- Body weight: 60 kg.

The following parameters from the EUROPOEM II re-entry report were used in the assessment:

DFR: 3 µg a.s./cm²/kg a.s. applied. The DFR values of 1.2534 µg/cm²/kg a.s. for azoxystrobin and 0.8405 µg/cm²/kg a.s. for chlorothalonil for inspection of cereals is applied as a refinement based on a field DFR study.
A DFR value of 0.4118 µg a.s./cm^2/kg a.s. for chlorothalonil for tomato harvesting is applied as a refinement based on a field DFR study.

- TC: 2500 cm^2/hr for hand-harvesting tomatoes. This is expected to provide a precautionary TC value for crop inspection in cereals as first tier as the frequency of crop contact will be much lower for crop inspection tasks.
  A refined TC value of 1100 cm^2/h for re-entry activities such as crop inspection (available from the US EPA policy paper as mentioned above) has been applied as a second tier.

- Working time: A daily working time of 2 hours is assumed for crop inspection and 8 hours for hand-harvesting vegetables.

A precautionary assessment is given as a Tier 1 assessment. This assumes that the maximum total dose from two treatments is applied in cereals and one treatment is applied in tomatoes, and that there is no decline in dislodgeable foliar residues from the two treatments in cereals at the time of re-entry. Similarly, for dermal absorption, the higher of the respective values for azoxystrobin and chlorothalonil assumed for the concentrate and spray dilution have been used to predict systemic exposure from contact with a dry surface residue.

The detailed estimation of exposure is provided in Appendix 1.23 – 1.2933. A summary is provided in CP 7.2.3.

Estimation of worker exposure using dislodgeable residues data

Data on the foliar decline of chlorothalonil are also available for tomato. These data allow a higher tier exposure assessment to be given for the exposure assessment described in CP 7.2.3.

(i) Hand Harvesting Tomato

The following report is used to support the assessment.

Report:	K-CP 7.2.3.1/01, Amato S.L. (1998). Determination of the effects of freezing tomato leaf discs for conducting dislodgeable foliar residue studies of chlorothalonil. Ricerca Inc., Department of Residue Analysis, Painesville OH, USA. Report No. 7254-97-0116-CR-001. Issue date 03 March 1998. Unpublished. (Syngenta File No. R44686/1245)

Guidelines: No specific test guidelines for conducting dislodgeable foliar residue studies are specified in study report

Objectives : To analyse for chlorothalonil in duplicate sets of tomato leaf discs, one fresh and one frozen to determine if there was any significant effect due to freezing.

GLP: Yes

Field Phase dates: 4 May, 1992 to August 25, 1992.

Study Design and Methods

The test plot consisted of two three-row plots of trellised tomato plants. The untreated control plot was isolated from the treated plot by a distance of 56 feet (17.1 meters). All tomato plants were maintained according to commercial practices.

Two applications of Bravo Weather Stik (720 g/L chlorothalonil) were applied at an interval of one week by tractor mounted boom sprayer. The plot, treated at the rate of 1.5 US pt/100 gal/8712 ft row received approximately 100 gallons of spray per acre per application (1.7538 L product/ha).

After the second application the leaves were sampled at intervals of 3 and 7 days. Tomato leaf discs were sampled using a Birkestrand leaf punch from the treated and control plots. All samples were collected when leaf discs were dry. Duplicate sets of tomato leaf discus were collected using a paired sampling procedure. One set was analysed immediately (within 2 and ½ hours of collection), the other was placed in a freezer for six weeks prior to analysis. Each sample was comprised of forty discs each with an area of 10 cm^2 (both sides) for a total leaf disc area of 400 cm^2. Six replicates were taken at each time interval.

Chlorothalonil residues were dislodged from the leaf disc surface by shaking with a detergent water solution (Aerosal OT 75%). Residues were extracted into methylene chloride and quantified by electron capture gas chromatography.

Results

Dislodgeable foliar residues (DFR) of chlorothalonil on fresh tomato leaves are given below.

Table 7.2.3.1-2: Dislodgeable residues of chlorothalonil from the leaves of treated tomato plants

Day 0		Day 3		Day 7	
Sample ID	Residue (µg/cm^2)	Sample ID	Residue (µg/cm^2)	Sample ID	Residue (µg/cm^2)
10B	0.49	30B	0.45	70B	0.37
10C	0.62	30C	0.52	70C	0.39
10D	0.65	30D	0.51	70D	0.41
10E	0.71	30E	0.58	70E	0.38
10F	1.08	30F	0.56	70F	0.46
10G	0.67	30G	0.51	70G	0.48
Mean	0.70		**0.52**		0.42
Std Dev	0.2		0.05		0.05

Exposure Assessment

The tomato DFR study was performed with two applications and a seven day interval between treatments. Samples were collected 3 days after the final treatment had been applied. As this GAP matches the GAP proposed for the use of A14111B on tomato these data are used to refine the exposure assessment for workers hand-harvesting tomatoes treated with A14111B.

In the DFR study the application rate was 1.5 US pints / acre (1.7538 L/ha). Adjusting for the product concentration (720 g/L) gives an application rate of 1.26 kg a.s./ha. Taking the mean residue at the 3 day timepoint (PHI = 3 days) and correcting for the application rate gives a DFR Day 3 value of 0.4118 µg/kg a.s./ha. This value reflects one application of 1 kg chlorothalonil and a 3 day interval from the treatment to the time of re-entry.

The following parameters were used in the re-entry worker assessment:

- Application rate (maximum of 1 application): 1 kg/ha for chlorothalonil
- Dermal absorption: 7%
- Body weight: 60 kg
- DFR at time of re-entry, i.e. 3 days after the treatment = 0.4118 µg a.s./cm^2/kg a.s./ha.

The following parameters from the EUROPOEM II re-entry report were used in the assessment:

- TC: 2500 cm^2/hr for workers hand-harvesting vegetables
- Working time: A daily working time of 8 hours is assumed for hand-harvesting activities.

The detailed estimation of exposure is provided in Appendix 1.23. A summary is provided in CP 7.2.3.

(ii) Inspection of Cereals

Data on the foliar decline of azoxystrobin and chlorothalonil are available for wheat. These data allow a higher tier exposure assessment to be given for the exposure assessment described in CP 7.2.3.

The following report is used to support the assessment.

Report:	K-CP 7.2.3.1/01 Roussel, C. (2015). Chlorothalonil and Azoxystrobin - Determination of Dislodgeable Foliar Residues of Chlorothalonil and Azoxystrobin on wheat leaves after one application of A14111B in Northern Europe (UK and Northern France), 2014. Staphyt, 23 rue de Moeuvres, F-62860 Inchy en Artois, France Study Dates: 22 May 2014 – 03 September 2015. Report Number ChR-14-19410 (Syngenta file No. A14111B_11228)

For the full study summary please refer to Appendix 2.

Results

Residues of azoxystrobin and chlorothalonil in total leaf washing specimens from wheat leaves treated at 200 and 1000 g per hectare for azoxystrobin and chlorothalonil respectively at BBCH 69 are summarised in tables below.

Table 7.2.3.1-3: Summary of azoxystrobin residues from wheat leaves following application at 200 g AI/ha

Sampling interval (days)	Azoxystrobin residue (µg/cm^2) Mean Uncorrected			
	Trial 1	Trial 2	Trial 3	Trial 4
0 DAA (<1 HAA)	0.197274	0.1090112	0.256480	0.234057
0 DAA (8 HAA)	0.139074	0.130319	0.191454	0.167726
1 DAA	0.087667	0.128377	0.150748	0.063579
2 DAA	0.164798	0.135038	0.185798	0.078148
3 DAA	0.048267	0.163796	0.171044	0.049432
5 DAA	0.010200	0.114250	0.142064	0.048904
7 DAA	0.036558	0.097354	0.114390	0.051728
14 DAA	0.006727	0.079629	0.108389	0.047942
21 DAA	0.005076	0.014475	0.004549	0.009173

Table 7.2.3.1-4: Summary of chlorothalonil residues from wheat leaves following application at 1000 g AI/ha

Sampling interval (days)	Chlorothalonil residue (µg/cm^2) Mean Uncorrected			
	Trial 1	Trial 2	Trial 3	Trial 4
0 DAA (<1 HAA)	0.566384	0.467546	0.527439	0.653522
0 DAA (8 HAA)	0.446222	0.286406	0.447930	0.711402
1 DAA	0.706845	0.295515	0.397389	0.382758
2 DAA	0.644190	0.270775	0.466705	0.354731
3 DAA	0.492122	0.595452	0.348478	0.357628
5 DAA	0.383307	0.474213	0.333197	0.413468
7 DAA	0.498692	0.374266	0.277854	0.384168
14 DAA	0.192450	0.213949	0.368633	0.294651
21-22 DAA	0.134716	0.405253	0.192508	0.141877

Derivation of DFR value

The intended use for A14111B on cereals includes two applications with 1.875 L product/ha (0.15 kg azoxystrobin/ha; 0.75 kg chlorothalonil/ha). The interval between applications is at least 14 days. The results of the GLP study were generated after single application of A14111B on cereals. This is not fully in compliance with the intended number of applications. Using DT50 values of 5.2 days for azoxystrobin and 16.3 days for chlorothalonil, the predicted DFR values after two applications are 1.2534 µg/cm²/kg a.s. for azoxystrobin and 0.8405 µg/cm²/kg a.s. for chlorothalonil. The calculated DFRs following two applications of A14111B are presented in the table below.

Table 7.2.3.1-5: DFR levels for azoxystrobin and chlorothalonil after the application of A14111B

	Calculated DFR (after 2 applications with 14-day interval)
	Azoxystrobin[1]
Geometric mean	
- µg a.s./cm²	0.2507
*- µg a.s./cm²/kg a.s. applied**	***1.2534***
	Chlorothalonil[2]
Geometric mean	
- µg a.s./cm²	0.8405
*- µg a.s./cm²/kg a.s. applied**	***0.8405***

[1] Application rate: 0.2 kg a.s./ha
[2] Application rate: 1 kg a.s./ha
* DFR values normalised to the application rate of 1 kg a.s./ha

Derivation of DT50 value

Four DFR trials were provided to derive the DT50 value. A log-linear model (base e) was fitted to the data and the 1st half-life/DT50 value was calculated using the mean values of replicates of all trials.

All calculations were performed in the statistical programming language R (R Core Team, 2015, version 3.2.1).

The DT50 value was calculated according to the following formula $DT50 = \frac{\ln(2)}{\lambda}$; where λ is the exponential decay constant, i.e. here the slope of the linear regression line.

Together, the assessment of all four trials with a log-linear model (base e) gives a DT50 of 5.2 days for azoxystrobin and 16.3 days for chlorothalonil.

Exposure Assessment

The following parameters were used in the re-entry worker assessment:

- Application rate: Two applications of 0.15 kg/ha for azoxystrobin and 0.75 kg/ha for chlorothalonil
- Dermal absorption:
  - Inspection in cereals: 75% for azoxystrobin; 3% for chlorothalonil (worst-case)
- Body weight: 60 kg
- Calculated DFR at time of re-entry, i.e. 0 days after two applications treatment:
  - For azoxystrobin: 1.2534 µg a.s./cm^2/kg a.s./ha
  - For chlorothalonil: 0.8405 µg a.s./cm^2/kg a.s./ha
- DT50: 5.2 days for azoxystrobin; 16.3 days for chlorothalonil.

The following parameters from the EUROPOEM II re-entry report were used in the assessment:

- TC: 2500 cm^2/hr is expected to provide a precautionary TC value for crop inspection in cereals as first tier as the frequency of crop contact will be much lower for crop inspection tasks.
  A refined TC value of 1100 cm^2/h for re-entry activities such as crop inspection (available from the US EPA policy paper as mentioned above) has been applied as a second tier.
- Working time: A daily working time of 2 hours is assumed for crop inspection.

Azoxystrobin

The detailed estimation of exposure is provided in Appendix 1.24 and 1.26. A summary is provided in CP 7.2.3.

Chlorothalonil

The detailed estimation of exposure is provided in Appendix 1.29 and 1.31. A summary is provided in CP 7.2.3.

CP 7.2.3.2 Measurement of worker exposure

Not required since model calculations predict the systemic exposure to azoxystrobin and chlorothalonil to be within the AOELs with protective equipment.

CP 7.3 Dermal Absorption

Azoxystrobin

No *in vitro* data has been generated to determine the dermal absorption potential of azoxystrobin from formulation A14111B.

For azoxystrobin, dermal absorption default values can be used as described in the EFSA guidance document (EFSA Journal 2012; 10(4):2665). Therefore, all relevant data are provided and are considered adequate.

The percentage absorptions used in the operator exposure assessment are given in Table 7.3-1.

Table 7.3-1: Dermal absorption end-points for the risk assessment of azoxystrobin

End-Point	Azoxystrobin	
Dermal penetration	Concentrate:	25%
	Spray dilutions:	75%

Chlorothalonil

The dermal absorption of chlorothalonil from A14111B has been investigated in an *in vitro* study using human dermatomed skin.

For chlorothalonil the dermal absorption values have been derived according to the EFSA guidance on Dermal Absorption.

Tape strips 1 and 2 were excluded from the estimation of systemically absorbed material as material in these layers of the *stratum corneum* are considered not to be bioavailable due to desquamation. Dermal absorption was therefore calculated as follows:

Table 7.3-2: Summary of dermal absorption study for chlorothalonil in formulation A14111B

Test	% of applied dose				Reference
	Concentrate	Spray dilution 1 (1/40)	Spray dilution 2 (1/213)	Spray dilution 3 (1/600)	
***In vitro* (human)**	0.05	0.7	3	7	Noakes J, 2013

The percentage absorptions used in the operator exposure assessment are given in Table 7.3-3.

Table 7.3-3: Dermal absorption end-points for the risk assessment of chlorothalonil

End-Point	Chlorothalonil	
Dermal penetration	Concentrate:	0.05%
	Spray dilution 1 (1/40):	0.7%
	Spray dilution 2 (1/213):	3%
	Spray dilution 3 (1/600):	7%

Further details regarding the basis for derivation of the proposed dermal absorption values are given in ***Document J*** (Syngenta File No. R044686_11071).

Report:	K-CP 7.3/01, Noakes J. (2013). Chlorothalonil/Azoxystrobin SC (A14111B) - In Vitro Absorption through Dermatomed Human Skin Using [^{14}C]-Chlorothalonil. Dermal Technology Laboratory Ltd., Med IC4, Keele University Science and Business Park, Keele, Staffordshire, ST5 5NL, United Kingdom. Report No. JV2271/REG, 12 September 2013. Unpublished. (Syngenta File No. A14111B_10828)

STUDY TYPE: OECD 428; *In Vitro* Dermal Absorption (Human)

COMPLIANCE: Signed and dated GLP and Quality Assurance statements were provided. There were no deviations from the current regulatory guideline considered to compromise the scientific validity of the study.

TEST MATERIAL (PURITY): Chlorothalalonil 400g/L formulation (32.8% w/w Chlorothalalonil/6.6% w/w Azoxystrobin)

SPONSOR: Syngenta Ltd, Jealotts Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, United Kingdom.

EXECUTIVE SUMMARY

The absorption and distribution of chlorothalonil from a chlorothalonil/azoxystrobin suspension concentrate (SC) formulation (A14111B) was measured *in vitro* through human dermatomed skin conforming to the Regulatory Guidelines.

The doses were applied to the dermatomed human skin as the chlorothalonil/azoxystrobin SC (A14111B) formulation concentrate containing 400 g chlorothalonil/L and three aqueous spray strength dilutions: nominally containing 10 g, 1.875 g and 0.667 g chlorothalonil/L: equivalent to 1/40, 1/213.3 and 1/600 w/v, respectively. The formulation and the aqueous spray strength dilutions were applied at rates of 10 µL/cm^2 and left unoccluded for an exposure period of six hours and a total run time of 24 hours.

The absorption process was followed by taking samples of the receptor fluid (50% ethanol in water) at recorded intervals throughout the exposure period. The surface of the dermatomed skin was decontaminated after a six hour exposure period to investigate the amount of chlorothalonil absorbed by the end of a typical 'working day' period. After decontamination, the absorption of chlorothalonil was monitored for the remainder of the 24 hour observation period. At the end of the experiment, the distribution of chlorothalonil in the test system was assessed, which included a tape stripping technique to determine its distribution in the *stratum corneum* and in the remaining skin.

The results obtained in this study demonstrate that the absorption of chlorothalonil through human dermatomed skin following the application of chlorothalonil/azoxystrobin SC (A14111B) is slow and the vast majority of chlorothalonil can be washed off the skin by normal decontamination procedures.

These data predict that the dermal absorption of chlorothalonil from potential exposure to this formulation concentrate and its aqueous spray strength dilutions would be generally low.

MATERIALS AND METHODS

Materials:

Test Material:	Azoxystrobin
Description:	Technical, yellow solid (powder)
Lot/Batch number:	GRA9J1084
Purity:	99.2% w/w a.i
Stability of test compound:	Confirmed

Test Material:	Chlorothalonil
Description:	Technical, grey/brown solid (powder)
Lot/Batch number:	P5
Purity:	98.6% w/w a.i
Stability of test compound:	Confirmed

Radiolabelled Test Material:	[^{14}C]-Chlorothalonil
Radiochemical number:	RDR-XVI-66
Purity:	98.3% (chemical), 98.9% (radiochemical)
Stability of test compound:	Confirmed

Blank Formulation:	Blank of A14111B
Batch number:	JHU001-026-005

Study Design and Methods:
In-life dates: Start: 10 May 2013 End: 28 June 2013
Diffusion cell: Diffusion of chlorothalonil into and across the skin to a receptor fluid was measured using glass diffusion cells in which the epidermis formed a horizontal membrane and provided an application area of 2.54cm^2.

Receptor fluid: The receptor fluid (50% ethanol in water) was chosen to ensure that the chlorothalonil would freely partition into this from the skin membrane and never reach a concentration that would limit its diffusion.

Skin preparations: Skin membranes were cut from human whole skin at a thickness of 400µm using an electric dermatome.

Skin preparation integrity: The integrity of the membranes was checked by measurement of the electrical resistance across the skin. Only those membranes with an acceptable resistance, thereby showing that they were intact, were used on the study.

Test substance: The four doses were prepared to mimic the commercial 400g/L formulation and its aqueous spray dilutions 10 g/L (1/40 w/v), 1.875 g/L (1/213.3w/v) and 0.667 g/L (1/600 w/v) using the technical material, [^{14}C]-labelled chlorothalonil, formulation blank and diluted with water as appropriate. The doses were prepared as close to the time of application as was practicable and were analysed to confirm their suitability for use in the study.

Application to the skin: Each application was represented by eight replicates from at least four subjects at a dose of 10µL/cm² and left unoccluded for the exposure period.

Temperature: Throughout the experiment the receptor fluid was stirred and the epidermal membranes were maintained at a normal skin temperature of 32 ± 1°C in a water bath.

Duration of exposure and sampling: The skin was exposed to the test preparations for six hours after which an interim decontamination of the application site was performed by gently swabbing the application site with natural sponges pre-wetted with 3% Teepol® and with further sponges pre-wetted with water. During the experimental run time samples of receptor fluid were taken at suitable intervals (pre, 1, 2, 3, 4, 6, 8, 10, 12, 16, 20 and 24 hours) to allow adequate characterisation of the absorption profile.

Terminal procedures: The donor chamber was carefully removed and washed with acetone. The epidermal surface of the skin was decontaminated by gently swabbing the application site with natural sponges pre-wetted with 3% Teepol® and with further sponges pre-wetted with water. Decontamination was shown to be complete following assessment of residual radioactivity levels on the skin surface with a Geiger counter. The sponges were digested in Soluene 350® and made up to a recorded volume. The surface of the skin was allowed to dry naturally and to assess penetration through the *stratum corneum*, successive layers of the *stratum corneum* were removed by the repeated application of adhesive tape to a maximum of 5 strips. Each individual adhesive strip was sequentially numbered and digested with Soluene 350®. The remaining epidermal tissue was carefully removed from the receptor chamber and digested in Soluene 350® and analysed.

Analysis: All components of the test system (e.g. receptor fluid, skin wash, donor chamber, tape strips and epidermis) were analysed by LSC and the recovery determined.

Data: Results of the analysis of the samples of receptor fluid collected in the study were expressed as amounts of chlorothalonil in the receptor solution in terms of µg/cm^2, 'percentage of dose absorbed' and rates of absorption (µg/cm^2/h) (see Tables below).

Definition of absorbed test material: The absorbed (systemically available) dose is considered to be the test material detected in the receptor fluid. Material removed from the surface of the epidermis by the washing procedure is regarded as unabsorbed. The test material recovered from the skin at the end of the exposure is also considered to be unabsorbed, although it is recognised that a proportion of this material may be absorbed beyond the duration of the exposure investigated in this study. *In vivo*, the majority of the dose in the skin, especially that recovered from the *stratum corneum*, would eventually be lost by desquamation.

RESULTS AND DISCUSSION

Analysis of the [^{14}C]-Dose Preparations

Dose levels achieved and homogeneity of the dose preparations

LSC analysis of the dose preparations confirmed that the dose levels achieved were 397 g chlorothalonil/L, 10.1 g chlorothalonil/L, 1.95 g chlorothalonil/L and 0.705 g chlorothalonil/L.

The dose preparations were considered to be homogeneous and acceptable for use in these experiments, with percentage relative standard deviations of < 2.1 between replicates.

Stability of chlorothalonil in the Formulations

Radiochemical purities of greater than 98% were seen in all dose preparations both prior to application and post dose preparation at 24 hours.

Absorption, mass balance and distribution of chlorothalonil

400 g Chlorothalonil/L formulation concentrate
The mean absorption rate of chlorothalonil from the formulation concentrate through human dermatomed skin was 0.008 µg/cm²/h over 24 hours. The amounts of chlorothalonil absorbed at 6, 8, 12 and 24 hours were 0.049, 0.072, 0.096 and 0.206 µg/cm^2, respectively. These respective amounts, expressed as percentages of the applied dose, equated to 0.001, 0.002, 0.003 and 0.006%.

The vast majority of the applied Chlorothalonil (mean 105%) was washed off the skin at six hours, and an additional 0.238% was removed in the skin wash after 24 hours. A small proportion of the dose applied was recovered from the donor chamber (0.039%), tape strips 1-2 (0.009%), tape strips 3-5 (0.007%) and 0.401% was found in the remaining skin. The mean total recovery was 105% of the dose applied.

10 g chlorothalonil/L aqueous spray dilution 1 (1/40 w/v)
The mean absorption rate of chlorothalonil from the 10 g/L aqueous dilution through human dermatomed skin was 0.005 µg/cm²/h during the 24 hour exposure period. The amounts of chlorothalonil absorbed at 6, 8, 12 and 24 hours were 0.025, 0.038, 0.058 and 0.120 µg/cm^2, respectively. These respective amounts, expressed as percentages of the applied dose, equated to 0.025, 0.037, 0.057 and 0.119%.

The majority of the applied Chlorothalonil (mean 90.6%) was washed off the skin at six hours, and an additional 4.39% was removed in the skin wash after 24 hours. A small proportion of the dose applied was recovered from the donor chamber (0.299%), tape strips 1-2 (0.181%), tape strips 3-5 (0.165%) and 7.89% was found in the remaining skin. The mean total recovery was 104% of the dose applied.

1.875 g chlorothalonil/L aqueous spray dilution 2 (1/213.3 w/v)
The mean absorption rate of chlorothalonil from the 1.875 g/L aqueous dilution through human dermatomed skin was 0.002 µg/cm²/h during the 24 hour exposure period. The amounts of chlorothalonil absorbed at 6, 8, 12 and 24 hours were 0.019, 0.026, 0.034 and 0.056 µg/cm^2, respectively. These respective amounts, expressed as percentages of the applied dose, equated to 0.100, 0.131, 0.174 and 0.285%.

A mean of 99.7% of the applied chlorothalonil was washed off the skin after 6 hours, with a further 1.61% removed at 24 hours. Small proportions were recovered from the remaining study compartments. A mean of 0.076% of the dose applied was recovered from the donor chamber, tape strips 1-2 (0.119%), tape strips 3-5 (0.182%) and 6.31% was found in the remaining skin. The mean total recovery was 108% of the dose applied.

0.667 g chlorothalonil/L aqueous spray dilution 3 (1/600 w/v)
The mean absorption rate of chlorothalonil from the 0.667 g/L aqueous dilution through human dermatomed skin was 0.002 µg/cm²/h during the 24 hour exposure period. The amounts of chlorothalonil absorbed at 6, 8, 12 and 24 hours were 0.013, 0.018, 0.027 and 0.054 µg/cm^2, respectively. These respective amounts, expressed as percentages of the applied dose, equated to 0.189, 0.261, 0.390 and 0.765%.

A mean of 85.1% of the applied chlorothalonil was washed off the skin after 6 hours, with a further 4.69% removed at 24 hours. Small proportions were recovered from the remaining study compartments. A mean of 0.322% of the dose applied was recovered from the donor chamber, tape strips 1-2 (0.145%), tape strips 3-5 (0.412%) and 10.8% was found in the remaining skin. The mean total recovery was 102% of the dose applied.

Table 7.3-4: Summary of chlorothalonil absorption through human skin

Application of Test Materials	Mean Absorption Rates		Mean Amount and Percentage of Dose Absorbed		
	Time period (h)	Absorption rate (µg/cm^2/h ± SEM)	Time (h)	Amount (µg/cm^2)	Percentage absorbed
Formulation concentrate (nominally 400 g chlorothalonil/L)	0-6	0.008 ± 0.004#	6	0.049#	0.001#
397 g chlorothalonil/L	6-24	0.009 ± 0.005	8	0.072#	0.002#
10 µL/cm^2 (4000 µg AI/cm^2)*	0-24	0.008 ± 0.004	12	0.096	0.003
Unoccluded, n = 8			24	0.206	0.006
Duration of exposure: 24h					
10 g chlorothalonil/L Aqueous spray dilution 1					
(equivalent to 1/40 w/v)	0-6	0.004 ± 0.003	6	0.025	0.025
10.1 g chlorothalonil/L	6-24	0.005 ± 0.004	8	0.038	0.037
10 µL/cm^2 (100 µg AI/cm^2)*	0-24	0.005 ± 0.004	12	0.058	0.057
Unoccluded, n = 8			24	0.120	0.119
Duration of exposure: 24h					
1.875 g chlorothalonil/L Aqueous spray dilution 2					
(equivalent to 1/213.3 w/v)	0-6	0.003 ± 0.002	6	0.019	0.100
1.951 g chlorothalonil/L	6-24	0.002 ± 0.001	8	0.026	0.131
10 µL/cm^2 (18.75 µg AI/cm^2)*	0-24	0.002 ± 0.001	12	0.034	0.174
Unoccluded, n = 8			24	0.056	0.285
Duration of exposure: 24h					
0.667 g chlorothalonil/L Aqueous spray dilution 3					
(equivalent to 1/600 w/v)	0-6	0.002 ± 0.0004	6	0.013	0.189
0.705 g chlorothalonil/L	6-24	0.002 ± 0.001	8	0.018	0.261
10 µL/cm^2 (6.67 µg AI/cm^2)*	0-24	0.002 ± 0.001	12	0.027	0.390
Unoccluded, n = 8			24	0.054	0.765
Duration of exposure: 24h					

Table 7.3-5: Summary of chlorothalonil distribution from the 400 g/L concentrate formulation

Test Compartment	Percentage of Dose Recovered (%):								Mean % Recovered	SD
	Cell 36	Cell 49	Cell 51	Cell 56	Cell 58	Cell 62	Cell 67	Cell 69		
Donor chamber	0.032	0.012	0.067	0.022	0.007	0.015	0.137	0.018	0.039	0.044
Skin wash at 6 hours	108	105	105	103	102	106	106	103	105	1.79
Skin wash at 24 hours	0.104	0.127	0.452	0.149	0.118	0.097	0.501	0.361	0.238	0.170
Tape strips 1-2	0.007	0.016	0.020	0.002*	0.001*	0.001*	0.019	0.005	0.009	0.008
Tape strips 3-5	0.004	0.015	0.007	0.002*	0.001*	0.002*	0.013	0.014	0.007	0.006
Remaining skin	0.142	0.280	0.717	0.528	0.299	0.347	0.677	0.216	0.401	0.214
Receptor fluid	0.007	0.006	0.004	0.005	0.004	0.006	0.014	0.004	0.006	0.003
Total recovered	108	105	107	104	103	107	107	104	105	1.851

Stratum corneum = amount in tape strips; Remaining skin = skin tissue remaining after tape stripping; Absorbed = amount in receptor fluid

Table 7.3-6: Summary of chlorothalonil distribution from the 10 g/L (1/40 w/v) aqueous spray dilution 1

Test Compartment	Percentage of Dose Recovered (%):								Mean % Recovered	SD
	Cell 41	Cell 50	Cell 53	Cell 57	Cell 60	Cell 66	Cell 68	Cell 71		
Donor chamber	0.026	0.098	0.802	0.177	0.252	0.527	0.245	0.267	0.299	0.251
Skin wash at 6 hours	92.6	97.1	83.1	85.4	91.1	86.8	93.8	94.8	90.6	4.96
Skin wash at 24 hours	1.95	1.76	4.18	10.46	6.62	4.91	2.49	2.76	4.39	2.96
Tape strips 1-2	0.109	0.183	0.442	0.017	0.075	0.126	0.288	0.204	0.181	0.134
Tape strips 3-5	0.076	0.145	0.314	0.016	0.064	0.169	0.322	0.211	0.165	0.113
Remaining skin	6.26	3.46	15.14	7.36	5.15	10.27	7.54	7.93	7.89	3.55
Receptor fluid	0.286	0.047	0.079	0.062	0.228	0.150	0.047	0.050	0.119	0.093
Total recovered	101	103	104	103	103	103	105	106	104	1.43

Table 7.3-7: Summary of chlorothalonil distribution from the 1.875 g/L (1/213.3 w/v) aqueous spray dilution 2

Test Compartment	Percentage of Dose Recovered (%):								Mean % Recovered	SD
	Cell 29	Cell 36A	Cell 41A	Cell 46A	*Cell 48A*	Cell 51A	Cell 54A	Cell 63A		
Donor chamber	0.023	0.050	0.082	0.135	*0.328*	0.059	0.075	0.106	0.076	0.037
Skin wash at 6 hours	97.5	82.1	95.4	102	*140*	106	114	101	99.7	9.86
Skin wash at 24 hours	0.827	3.62	2.06	2.25	*1.33*	0.364	0.928	1.19	1.61	1.116
Tape strips 1-2	0.073	0.116	0.375	0.175	*0.112*	0.029	0.050	0.016	0.119	0.125
Tape strips 3-5	0.169	0.058	0.796	0.142	*0.053*	0.025	0.061	0.025	0.182	0.276
Remaining skin	4.50	15.9	10.7	2.67	*2.73*	2.78	4.36	3.20	6.31	5.07
Receptor fluid	0.099	0.624	0.460	0.217	*0.230*	0.199	0.232	0.218	0.293	0.182
Total recovered	103	102	110	108	*144*	109	120	106	108	5.75

Cell 48A excluded from mean due to anomalous mass balance result.

Table 7.3-8: Summary of chlorothalonil distribution from the 0.667 g/L (1/600 w/v) aqueous spray dilution 3

Test Compartment	Percentage of Dose Recovered (%):								Mean % Recovered	SD
	Cell 33	Cell 40A	Cell 45A	Cell 47A	Cell 50A	Cell 53A	Cell 58A	Cell 67A		
Donor chamber	0.023	0.307	1.535	0.190	0.072	0.072	0.194	0.179	0.322	0.499
Skin wash at 6 hours	82.2	65.2	84.2	92.3	82.9	93.0	89.3	91.4	85.1	9.10
Skin wash at 24 hours	3.21	14.1	7.66	2.31	2.89	1.81	2.35	3.11	4.69	4.24
Tape strips 1-2	0.146	0.038	0.071	0.452	0.321	0.026	0.065	0.038	0.145	0.158
Tape strips 3-5	0.119	0.095	0.360	0.092	0.353	0.138	0.950	1.187	0.412	0.424
Remaining skin	10.3	18.1	6.76	4.17	14.9	9.07	11.5	11.7	10.8	4.38
Receptor fluid	0.696	0.988	1.319	0.499	0.989	0.575	0.552	0.503	0.765	0.301
Total recovered	96.7	98.8	102	100	102	105	105	108	102	3.66

Stratum corneum = amount in tape strips; Remaining skin = skin tissue remaining after tape stripping; Absorbed = amount in receptor fluid

CONCLUSION: The results obtained in this study demonstrate that the absorption of chlorothalonil through human dermatomed skin following the application of chlorothalonil/azoxystrobin SC (A14111B) is slow and the vast majority of chlorothalonil can be washed off the skin by normal decontamination procedures.

These data predict that the dermal absorption of chlorothalonil from potential exposure to this formulation concentrate and its aqueous spray strength dilutions would be generally low.

(Noakes J, 2013)

CP 7.4 Available Toxicological Data Relating to Co-Formulants

CONFIDENTIAL information - data provided separately (Document J)

Appendix 1: Detailed Exposure Calculations

Appendix 1.1 UK POEM – Estimated operator exposure to azoxystrobin during mixing/loading and application using tractor-mounted/trailed boom sprayer to cereals – no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**A14111B**	Active substance	**azoxystrobin**
Formulation type	water-based	a.s. concentration	**80** mg/ml
Dermal absorption from product	**25** %	Dermal absorption from spray	**75** %
Container	10 litres 63 mm closure		
PPE during mix/loading	None	PPE during application	None
Dose	**1.875** l/ha	Work rate/day	**50** ha
Application volume	**100** l/ha	Duration of spraying	**6** h

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	1.875	litres product/ha
Work rate	50	ha/day
Number of operations	10	/day
Hand contamination	0.5	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0.5	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	100	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	None	Permeable	Permeable	
Penetration	100%	5%	15%	
Dermal exposure	6.5	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	41.55	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.5	ml/day	41.55	ml/day
Concen. of a.s. product or spray	80	mg/ml	1.5	mg/ml
Dermal exposure to a.s.	40	mg/day	62.325	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	10	mg/day	46.74375	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	1.5	mg/ml
Inhalation exposure to a.s.	0.09	mg/day
Percent absorbed	100	%
Absorbed dose	0.09	mg/day

PREDICTED EXPOSURE

Total absorbed dose	56.83375	mg/day
Operator body weight	60	kg
Operator exposure	0.947	mg/kg bw/day
AOEL	0.2	mg/kg bw/day
Percentage of AOEL	**473.5**	

Appendix 1.2 German model – Estimated operator exposure to azoxystrobin during mixing/loading and application using tractor-mounted/trailed boom sprayer to cereals – no PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles					
Product	**A14111B**			Active substance		**azoxystrobin**
Formulation type	Liquid			a.s. concentration		**80** g/l
Dermal absorption from product		**25** %		Dermal absorption from spray		**75** %
RPE during mix/loading	None			RPE during application		None
PPE during mix/loading	None					
PPE during application: Head	None	Hands	None	Body	None	
Dose		**1.875** l product/ha		Work rate/day		**20** ha
AOEL		**0.2** mg/kg bw/day		Percent AOEL		**45.7** % AOEL

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2.4	mg/kg a.s.
Hand contamination/day	7.2	mg/day
Protective clothing	none	
Transmission to skin	100	%
Dermal exposure to a.s.	7.2	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0.0006	mg/kg a.s.
Inhalation exposure/day	0.0018	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.0018	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique: Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body	
Dermal contamination/kg a.s.	0.06	0.38	1.6	
Dermal contamination/day	0.18	1.14	4.8	
Protective clothing	none	none	none	
Transmission to skin	100	100	100	%
Total dermal exposure to a.s.	6.12	mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0.001	mg/kg a.s.
Inhalation exposure/day	0.003	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.003	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	7.2	mg/day	6.12	mg/day
Percent absorbed	25	%	75	%
Absorbed dose (dermal route)	1.8	mg/day	4.59	mg/day
Inhalation exposure to a.s.	0.0018	mg/day	0.003	mg/day
Total systemic exposure	1.8018	mg/day	4.593	mg/day

PREDICTED EXPOSURE

Total systemic exposure	6.3948	mg/day
Operator body weight	70	kg
Operator exposure	0.091354286	mg/kg bw/day
AOEL	0.2	mg/kg bw/day
Percent AOEL	45.67714286	% AOEL

Appendix 1.3 UK POEM – Estimated operator exposure to azoxystrobin during mixing/loading and application using tractor-mounted/trailed boom sprayer to tomato – no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**A14111B**	Active substance	**azoxystrobin**
Formulation type	water-based	a.s. concentration	**80** mg/ml
Dermal absorption from product	**25** %	Dermal absorption from spray	**75** %
Container	10 litres 63 mm closure		
PPE during mix/loading	None	PPE during application	None
Dose	**2.5** l/ha	Work rate/day	**50** ha
Application volume	**500** l/ha	Duration of spraying	**6** h
AOEL	**0.2** mg/kg bw/day	%AOEL	**212**

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	2.5	litres product/ha
Work rate	50	ha/day
Number of operations	13	/day
Hand contamination	0.65	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0.65	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	500	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	None	Permeable	Permeable	
Penetration	100%	5%	15%	
Dermal exposure	6.5	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	41.55	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.65	ml/day	41.55	ml/day
Concen. of a.s. product or spray	80	mg/ml	0.4	mg/ml
Dermal exposure to a.s.	52	mg/day	16.62	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	13	mg/day	12.465	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	0.4	mg/ml
Inhalation exposure to a.s.	0.024	mg/day
Percent absorbed	100	%
Absorbed dose	0.024	mg/day

PREDICTED EXPOSURE

Total absorbed dose	25.489	mg/day
Operator body weight	60	kg
Operator exposure	0.424816667	mg/kg bw/day

%AOEL 212.4083333

Appendix 1.4 German model – Estimated operator exposure to azoxystrobin during mixing/loading and application using tractor-mounted/trailed boom sprayer to tomato – no PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles					
Product	**A14111B**			Active substance		**azoxystrobin**
Formulation type	Liquid			a.s. concentration		**80** g/l
Dermal absorption from product		**25** %		Dermal absorption from spray		**75** %
RPE during mix/loading	None			RPE during application		None
PPE during mix/loading	None					
PPE during application: Head	None		Hands	None	Body	None
Dose		**2.5** l product/ha		Work rate/day		**20** ha

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2.4	mg/kg a.s.
Hand contamination/day	9.6	mg/day
Protective clothing	none	
Transmission to skin	100	%
Dermal exposure to a.s.	9.6	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0.0006	mg/kg a.s.
Inhalation exposure/day	0.0024	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.0024	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique: Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body	
Dermal contamination/kg a.s.	0.06	0.38	1.6	
Dermal contamination/day	0.24	1.52	6.4	
Protective clothing	none	none	none	
Transmission to skin	100	100	100	%
Total dermal exposure to a.s.	8.16	mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0.001	mg/kg a.s.
Inhalation exposure/day	0.004	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.004	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	9.6	mg/day	8.16	mg/day
Percent absorbed	25	%	75	%
Absorbed dose (dermal route)	2.4	mg/day	6.12	mg/day
Inhalation exposure to a.s.	0.0024	mg/day	0.004	mg/day
Total systemic exposure	2.4024	mg/day	6.124	mg/day

PREDICTED EXPOSURE

Total systemic exposure	8.5264	mg/day
Operator body weight	70	kg
Operator exposure	0.122	mg/kg bw/day
AOEL	0.2	mg/kg bw/day
Percentage of AOEL	**61**	

Appendix 1.5 UK POEM – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to cereals – no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**A14111B**	Active substance	**chlorothalonil**
Formulation type	water-based	a.s. concentration	**400** mg/ml
Dermal absorption from product	**0.05** %	Dermal absorption from spray	**0.7** %
Container	10 litres 63 mm closure		
PPE during mix/loading	None	PPE during application	None
Dose	**1.875** l/ha	Work rate/day	**50** ha
Application volume	**100** l/ha	Duration of spraying	**6** h

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	1.875	litres product/ha
Work rate	50	ha/day
Number of operations	10	/day
Hand contamination	0.5	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0.5	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	100	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	None	Permeable	Permeable	
Penetration	100%	5%	15%	
Dermal exposure	6.5	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	41.55	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.5	ml/day	41.55	ml/day
Concen. of a.s. product or spray	400	mg/ml	7.5	mg/ml
Dermal exposure to a.s.	200	mg/day	311.625	mg/day
Percent absorbed	0.05	%	0.7	%
Absorbed dose	0.1	mg/day	2.181375	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	7.5	mg/ml
Inhalation exposure to a.s.	0.45	mg/day
Percent absorbed	100	%
Absorbed dose	0.45	mg/day

PREDICTED EXPOSURE

Total absorbed dose	2.731375	mg/day
Operator body weight	60	kg
Operator exposure	0.0455	mg/kg bw/day
AOEL	0.009	mg/kg bw/day
Percentage of AOEL	**505.6**	

Appendix 1.6 German model – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to cereals – no PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles					
Product	**A14111B**		Active substance		**chlorothalonil**	
Formulation type	Liquid		a.s. concentration		**400** g/l	
Dermal absorption from product	**0.05** %		Dermal absorption from spray		**3** %	
RPE during mix/loading	None		RPE during application		None	
PPE during mix/loading	None					
PPE during application: Head	None	Hands	None	Body	None	
Dose	**1.875** l product/ha		Work rate/day		**20** ha	
AOEL	**0.009** mg/kg bw/day		Percent AOEL		**152** % AOEL	

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2.4	mg/kg a.s.
Hand contamination/day	36	mg/day
Protective clothing	none	
Transmission to skin	100	%
Dermal exposure to a.s.	36	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0.0006	mg/kg a.s.
Inhalation exposure/day	0.009	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.009	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body	
Dermal contamination/kg a.s.	0.06	0.38	1.6	
Dermal contamination/day	0.9	5.7	24	
Protective clothing	none	none	none	
Transmission to skin	100	100	100	%
Total dermal exposure to a.s.	30.6	mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0.001	mg/kg a.s.
Inhalation exposure/day	0.015	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.015	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	36	mg/day	30.6	mg/day
Percent absorbed	0.05	%	3	%
Absorbed dose (dermal route)	0.018	mg/day	0.918	mg/day
Inhalation exposure to a.s.	0.009	mg/day	0.015	mg/day
Total systemic exposure	0.027	mg/day	0.933	mg/day

PREDICTED EXPOSURE

Total systemic exposure	0.96	mg/day
Operator body weight	70	kg
Operator exposure	0.013714286	mg/kg bw/day
AOEL	0.009	mg/kg bw/day
Percent AOEL	152.3809524	% AOEL

Appendix 1.7 UK POEM – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to tomato – no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**A14111B**	Active substance	**chlorothalonil**
Formulation type	water-based	a.s. concentration	**400** mg/ml
Dermal absorption from product	**0.05** %	Dermal absorption from spray	**3** %
Container	10 litres 63 mm closure		
PPE during mix/loading	None	PPE during application	None
Dose	**2.5** l/ha	Work rate/day	**50** ha
Application volume	**500** l/ha	Duration of spraying	**6** h
AOEL	**0.009** mg/kg bw/day	%AOEL	**508**

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	2.5	litres product/ha
Work rate	50	ha/day
Number of operations	13	/day
Hand contamination	0.65	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0.65	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	500	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	None	Permeable	Permeable	
Penetration	100%	5%	15%	
Dermal exposure	6.5	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	41.55	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.65	ml/day	41.55	ml/day
Concen. of a.s. product or spray	400	mg/ml	2	mg/ml
Dermal exposure to a.s.	260	mg/day	83.1	mg/day
Percent absorbed	0.05	%	3	%
Absorbed dose	0.13	mg/day	2.493	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	2	mg/ml
Inhalation exposure to a.s.	0.12	mg/day
Percent absorbed	100	%
Absorbed dose	0.12	mg/day

PREDICTED EXPOSURE

Total absorbed dose	2.743	mg/day
Operator body weight	60	kg
Operator exposure	0.045716667	mg/kg bw/day

%AOEL 507.962963

Appendix 1.8 German model – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to tomato – no PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles				
Product	**A14111B**		Active substance		**chlorothalonil**
Formulation type	Liquid		a.s. concentration		**400** g/l
Dermal absorption from product	**0.05** %		Dermal absorption from spray		**7** %
RPE during mix/loading	None		RPE during application		None
PPE during mix/loading	None				
PPE during application: Head	None	Hands	None	Body	None
Dose	**2.5** l product/ha		Work rate/day		**20** ha

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2.4	mg/kg a.s.
Hand contamination/day	48	mg/day
Protective clothing	none	
Transmission to skin	100	%
Dermal exposure to a.s.	48	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0.0006	mg/kg a.s.
Inhalation exposure/day	0.012	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.012	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique: Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body	
Dermal contamination/kg a.s.	0.06	0.38	1.6	
Dermal contamination/day	1.2	7.6	32	
Protective clothing	none	none	none	
Transmission to skin	100	100	100	%
Total dermal exposure to a.s.	40.8	mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0.001	mg/kg a.s.
Inhalation exposure/day	0.02	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.02	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	48	mg/day	40.8	mg/day
Percent absorbed	0.05	%	7	%
Absorbed dose (dermal route)	0.024	mg/day	2.856	mg/day
Inhalation exposure to a.s.	0.012	mg/day	0.02	mg/day
Total systemic exposure	0.036	mg/day	2.876	mg/day

PREDICTED EXPOSURE

Total systemic exposure	2.912	mg/day
Operator body weight	70	kg
Operator exposure	0.0416	mg/kg bw/day
AOEL	0.009	mg/kg bw/day
Percentage of AOEL	**462.3**	

Appendix 1.9 UK POEM – Estimated operator exposure to azoxystrobin during mixing/loading and application using hand-held (knapsack) sprayer to tomato – no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target		
Product	**A14111B**	Active substance	**azoxystrobin**
Formulation type	water-based	a.s. concentration	**80** mg/ml
Dermal absorption from product	**25** %	Dermal absorption from spray	**75** %
Container	5 litres 45 or 63 mm closure		
PPE during mix/loading	None	PPE during application	None
Dose	**2.5** l/ha	Work rate/day	**0.8** ha
Application volume	**500** l/ha	Duration of spraying	**6** h
AOEL	**0.2** mg/kg bw/day	%AOEL	**300**

EXPOSURE DURING MIXING AND LOADING

Container size	5	litres
Hand contamination/operation	0.01	ml
Application dose	2.5	litres product/ha
Work rate	0.8	ha/day
Number of operations	27	/day
Hand contamination	0.27	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0.27	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target			
Application volume	500	spray/ha		
Volume of surface contamination	50	ml/h		
Distribution	Hands	Trunk	Legs	
	25%	25%	50%	
Clothing	None	Permeable	Permeable	
Penetration	100%	20%	18%	
Dermal exposure	10	2.5	4.5	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	102	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.27	ml/day	102	ml/day
Concen. of a.s. product or spray	80	mg/ml	0.4	mg/ml
Dermal exposure to a.s.	21.6	mg/day	40.8	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	5.4	mg/day	30.6	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.02	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	0.4	mg/ml
Inhalation exposure to a.s.	0.048	mg/day
Percent absorbed	100	%
Absorbed dose	0.048	mg/day

PREDICTED EXPOSURE

Total absorbed dose	36.048	mg/day
Operator body weight	60	kg
Operator exposure	0.6008	mg/kg bw/day

%AOEL 300.4

Appendix 1.10 UK POEM – Estimated operator exposure to chlorothalonil during mixing/loading and application using hand-held (knapsack) sprayer to tomato – no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target		
Product	**A14111B**	Active substance	**chlorothalonil**
Formulation type	water-based	a.s. concentration	**400** mg/ml
Dermal absorption from product	**0.05** %	Dermal absorption from spray	**3** %
Container	5 litres 45 or 63 mm closure		
PPE during mix/loading	None	PPE during application	None
Dose	**2.5** l/ha	Work rate/day	**0.8** ha
Application volume	**500** l/ha	Duration of spraying	**6** h
AOEL	**0.009** mg/kg bw/day	%AOEL	**1188**

EXPOSURE DURING MIXING AND LOADING

Container size	5	litres
Hand contamination/operation	0.01	ml
Application dose	2.5	litres product/ha
Work rate	0.8	ha/day
Number of operations	27	/day
Hand contamination	0.27	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0.27	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target			
Application volume	500	spray/ha		
Volume of surface contamination	50	ml/h		
Distribution	Hands	Trunk	Legs	
	25%	25%	50%	
Clothing	None	Permeable	Permeable	
Penetration	100%	20%	18%	
Dermal exposure	10	2.5	4.5	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	102	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.27	ml/day	102	ml/day
Concen. of a.s. product or spray	400	mg/ml	2	mg/ml
Dermal exposure to a.s.	108	mg/day	204	mg/day
Percent absorbed	0.05	%	3	%
Absorbed dose	0.054	mg/day	6.12	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.02	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	2	mg/ml
Inhalation exposure to a.s.	0.24	mg/day
Percent absorbed	100	%
Absorbed dose	0.24	mg/day

PREDICTED EXPOSURE

Total absorbed dose	6.414	mg/day
Operator body weight	60	kg
Operator exposure	0.1069	mg/kg bw/day

%AOEL 1187.777778

Appendix 1.11 UK POEM – Estimated operator exposure to azoxystrobin during mixing/loading and application using tractor-mounted/trailed boom sprayer to cereals – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**A14111B**	Active substance	**azoxystrobin**
Formulation type	water-based	a.s. concentration	**80** mg/ml
Dermal absorption from product	**25** %	Dermal absorption from spray	**75** %
Container	10 litres 63 mm closure		
PPE during mix/loading	Gloves	PPE during application	Gloves
Dose	**1.875** l/ha	Work rate/day	**50** ha
Application volume	**100** l/ha	Duration of spraying	**6** h

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	1.875	litres product/ha
Work rate	50	ha/day
Number of operations	10	/day
Hand contamination	0.5	ml/day
Protective clothing	Gloves	
Transmission to skin	5	%
Dermal exposure to formulation	0.025	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	100	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	Gloves	Permeable	Permeable	
Penetration	10%	5%	15%	
Dermal exposure	0.65	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	6.45	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.025	ml/day	6.45	ml/day
Concen. of a.s. product or spray	80	mg/ml	1.5	mg/ml
Dermal exposure to a.s.	2	mg/day	9.675	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	0.5	mg/day	7.25625	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	1.5	mg/ml
Inhalation exposure to a.s.	0.09	mg/day
Percent absorbed	100	%
Absorbed dose	0.09	mg/day

PREDICTED EXPOSURE

Total absorbed dose	7.84625	mg/day
Operator body weight	60	kg
Operator exposure	0.131	mg/kg bw/day
AOEL	0.2	mg/kg bw/day
Percentage of AOEL	**65.5**	

Appendix 1.12 UK POEM – Estimated operator exposure to azoxystrobin during mixing/loading and application using tractor-mounted/trailed boom sprayer to tomato – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Product	**A14111B**		Active substance	**azoxystrobin**
Formulation type	water-based		a.s. concentration	**80** mg/ml
Dermal absorption from product	**25** %		Dermal absorption from spray	**75** %
Container	10 litres 63 mm closure			
PPE during mix/loading	Gloves		PPE during application	Gloves
Dose	**2.5** l/ha		Work rate/day	**50** ha
Application volume	**500** l/ha		Duration of spraying	**6** h
AOEL	**0.2** mg/kg bw/day		%AOEL	**21.7**

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	2.5	litres product/ha
Work rate	50	ha/day
Number of operations	13	/day
Hand contamination	0.65	ml/day
Protective clothing	Gloves	
Transmission to skin	5	%
Dermal exposure to formulation	0.0325	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	500	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	Gloves	Permeable	Permeable	
Penetration	10%	5%	15%	
Dermal exposure	0.65	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	6.45	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.0325	ml/day	6.45	ml/day
Concen. of a.s. product or spray	80	mg/ml	0.4	mg/ml
Dermal exposure to a.s.	2.6	mg/day	2.58	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	0.65	mg/day	1.935	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	0.4	mg/ml
Inhalation exposure to a.s.	0.024	mg/day
Percent absorbed	100	%
Absorbed dose	0.024	mg/day

PREDICTED EXPOSURE

Total absorbed dose	2.609	mg/day
Operator body weight	60	kg
Operator exposure	0.043483333	mg/kg bw/day

%AOEL	21.74166667

Appendix 1.13 UK POEM – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to cereals – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**A14111B**	Active substance	**chlorothalonil**
Formulation type	water-based	a.s. concentration	**400** mg/ml
Dermal absorption from product	**0.05** %	Dermal absorption from spray	**0.7** %
Container	10 litres 63 mm closure		
PPE during mix/loading	Gloves	PPE during application	Gloves
Dose	**1.875** l/ha	Work rate/day	**50** ha
Application volume	**100** l/ha	Duration of spraying	**6** h

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	1.875	litres product/ha
Work rate	50	ha/day
Number of operations	10	/day
Hand contamination	0.5	ml/day
Protective clothing	Gloves	
Transmission to skin	5	%
Dermal exposure to formulation	0.025	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	100	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	Gloves	Permeable	Permeable	
Penetration	10%	5%	15%	
Dermal exposure	0.65	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	6.45	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.025	ml/day	6.45	ml/day
Concen. of a.s. product or spray	400	mg/ml	7.5	mg/ml
Dermal exposure to a.s.	10	mg/day	48.375	mg/day
Percent absorbed	0.05	%	0.7	%
Absorbed dose	0.005	mg/day	0.338625	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	7.5	mg/ml
Inhalation exposure to a.s.	0.45	mg/day
Percent absorbed	100	%
Absorbed dose	0.45	mg/day

PREDICTED EXPOSURE

Total absorbed dose	0.793625	mg/day
Operator body weight	60	kg
Operator exposure	0.0132	mg/kg bw/day
AOEL	0.009	mg/kg bw/day
Percentage of AOEL	**146.7**	

Appendix 1.14 German model – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to cereals – with PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method		Tractor-mounted/trailed boom sprayer: hydraulic nozzles					
Product		**A14111B**			Active substance		**chlorothalonil**
Formulation type		Liquid			a.s. concentration		**400** g/l
Dermal absorption from product			**0.05** %		Dermal absorption from spray		**3** %
RPE during mix/loading		None			RPE during application		None
PPE during mix/loading		Gloves					
PPE during application:	Head	None	Hands	Gloves		Body	Coverall and sturdy footwear
Dose			**1.875** l product/ha		Work rate/day		**20** ha
AOEL			**0.009** mg/kg bw/day		Percent AOEL		**14.1** % AOEL

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2.4	mg/kg a.s.
Hand contamination/day	36	mg/day
Protective clothing	gloves	
Transmission to skin	1	%
Dermal exposure to a.s.	0.36	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0.0006	mg/kg a.s.
Inhalation exposure/day	0.009	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.009	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body	
Dermal contamination/kg a.s.	0.06	0.38	1.6	
Dermal contamination/day	0.9	5.7	24	
Protective clothing	none	gloves	coverall and sturdy footwear	
Transmission to skin	100	1	5	%
Total dermal exposure to a.s.	2.157	mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0.001	mg/kg a.s.
Inhalation exposure/day	0.015	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.015	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	0.36	mg/day	2.157	mg/day
Percent absorbed	0.05	%	3	%
Absorbed dose (dermal route)	0.00018	mg/day	0.06471	mg/day
Inhalation exposure to a.s.	0.009	mg/day	0.015	mg/day
Total systemic exposure	0.00918	mg/day	0.07971	mg/day

PREDICTED EXPOSURE

Total systemic exposure	0.08889	mg/day
Operator body weight	70	kg
Operator exposure	0.001269857	mg/kg bw/day
AOEL	0.009	mg/kg bw/day
Percent AOEL	14.10952381	% AOEL

Appendix 1.15 UK POEM – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to tomato – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles		
Product	**A14111B**	Active substance	**chlorothalonil**
Formulation type	water-based	a.s. concentration	**400** mg/ml
Dermal absorption from product	**0.05** %	Dermal absorption from spray	**3** %
Container	10 litres 63 mm closure		
PPE during mix/loading	Gloves	PPE during application	Gloves
Dose	**2.5** l/ha	Work rate/day	**50** ha
Application volume	**500** l/ha	Duration of spraying	**6** h
AOEL	**0.009** mg/kg bw/day	%AOEL	**95.1**

EXPOSURE DURING MIXING AND LOADING

Container size	10	litres
Hand contamination/operation	0.05	ml
Application dose	2.5	litres product/ha
Work rate	50	ha/day
Number of operations	13	/day
Hand contamination	0.65	ml/day
Protective clothing	Gloves	
Transmission to skin	5	%
Dermal exposure to formulation	0.0325	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	500	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	Gloves	Permeable	Permeable	
Penetration	10%	5%	15%	
Dermal exposure	0.65	0.05	0.375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	6.45	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.0325	ml/day	6.45	ml/day
Concen. of a.s. product or spray	400	mg/ml	2	mg/ml
Dermal exposure to a.s.	13	mg/day	12.9	mg/day
Percent absorbed	0.05	%	3	%
Absorbed dose	0.0065	mg/day	0.387	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	2	mg/ml
Inhalation exposure to a.s.	0.12	mg/day
Percent absorbed	100	%
Absorbed dose	0.12	mg/day

PREDICTED EXPOSURE

Total absorbed dose	0.5135	mg/day
Operator body weight	60	kg
Operator exposure	0.008558333	mg/kg bw/day
%AOEL	95.09259259	

Appendix 1.16 German model – Estimated operator exposure to chlorothalonil during mixing/loading and application using tractor-mounted/trailed boom sprayer to tomato – with PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles				
Product	**A14111B**		Active substance		**chlorothalonil**
Formulation type	Liquid		a.s. concentration		**400** g/l
Dermal absorption from product	**0.05** %		Dermal absorption from spray		**7** %
RPE during mix/loading	None		RPE during application		None
PPE during mix/loading	Gloves				
PPE during application: Head	None	Hands	Gloves	Body	Coverall and sturdy footwear
Dose	**2.5** l product/ha		Work rate/day		**20** ha

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2.4	mg/kg a.s.
Hand contamination/day	48	mg/day
Protective clothing	gloves	
Transmission to skin	1	%
Dermal exposure to a.s.	0.48	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0.0006	mg/kg a.s.
Inhalation exposure/day	0.012	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.012	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body
Dermal contamination/kg a.s.	0.06	0.38	1.6
Dermal contamination/day	1.2	7.6	32
Protective clothing	none	gloves	coverall and sturdy footwear
Transmission to skin	100	1	5 %
Total dermal exposure to a.s.	2.876	mg/day	

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0.001	mg/kg a.s.
Inhalation exposure/day	0.02	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0.02	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	0.48	mg/day	2.876	mg/day
Percent absorbed	0.05	%	7	%
Absorbed dose (dermal route)	0.00024	mg/day	0.20132	mg/day
Inhalation exposure to a.s.	0.012	mg/day	0.02	mg/day
Total systemic exposure	0.01224	mg/day	0.22132	mg/day

PREDICTED EXPOSURE

Total systemic exposure	0.23356	mg/day
Operator body weight	70	kg
Operator exposure	0.00334	mg/kg bw/day
AOEL	0.009	mg/kg bw/day
Percentage of AOEL	**37.2**	

Appendix 1.17 UK POEM – Estimated operator exposure to azoxystrobin during mixing/loading and application using hand-held (knapsack) sprayer to tomato – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target			
Product	**A14111B**		Active substance	**azoxystrobin**
Formulation type	water-based		a.s. concentration	**80** mg/ml
Dermal absorption from product	**25** %		Dermal absorption from spray	**75** %
Container	5 litres 45 or 63 mm closure			
PPE during mix/loading	Gloves		PPE during application	Gloves and impermeable coveral
Dose	**2.5** l/ha		Work rate/day	**0.8** ha
Application volume	**500** l/ha		Duration of spraying	**6** h
AOEL	**0.2** mg/kg bw/day		%AOEL	**49.5**

EXPOSURE DURING MIXING AND LOADING

Container size	5	litres
Hand contamination/operation	0.01	ml
Application dose	2.5	litres product/ha
Work rate	0.8	ha/day
Number of operations	27	/day
Hand contamination	0.27	ml/day
Protective clothing	Gloves	
Transmission to skin	5	%
Dermal exposure to formulation	0.0135	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target			
Application volume	500	spray/ha		
Volume of surface contamination	50	ml/h		
Distribution	Hands	Trunk	Legs	
	25%	25%	50%	
Clothing	Gloves	Impermeable	Impermeable	
Penetration	10%	5%	5%	
Dermal exposure	1.25	0.625	1.25	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	18.75	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.0135	ml/day	18.75	ml/day
Concen. of a.s. product or spray	80	mg/ml	0.4	mg/ml
Dermal exposure to a.s.	1.08	mg/day	7.5	mg/day
Percent absorbed	25	%	75	%
Absorbed dose	0.27	mg/day	5.625	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.02	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	0.4	mg/ml
Inhalation exposure to a.s.	0.048	mg/day
Percent absorbed	100	%
Absorbed dose	0.048	mg/day

PREDICTED EXPOSURE

Total absorbed dose	5.943	mg/day
Operator body weight	60	kg
Operator exposure	0.09905	mg/kg bw/day

%AOEL	49.525

Appendix 1.18 UK POEM – Estimated operator exposure to chlorothalonil during mixing/loading and application using hand-held (knapsack) sprayer to tomato – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target			
Product	**A14111B**		Active substance	**chlorothalonil**
Formulation type	water-based		a.s. concentration	**400** mg/ml
Dermal absorption from product	**0.05** %		Dermal absorption from spray	**3** %
Container	5 litres 45 or 63 mm closure			
PPE during mix/loading	Gloves		PPE during application	Gloves and impermeable coveral
Dose	**2.5** l/ha		Work rate/day	**0.8** ha
Application volume	**500** l/ha		Duration of spraying	**6** h
AOEL	**0.009** mg/kg bw/day		%AOEL	**253**

EXPOSURE DURING MIXING AND LOADING

Container size	5	litres
Hand contamination/operation	0.01	ml
Application dose	2.5	litres product/ha
Work rate	0.8	ha/day
Number of operations	27	/day
Hand contamination	0.27	ml/day
Protective clothing	Gloves	
Transmission to skin	5	%
Dermal exposure to formulation	0.0135	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target			
Application volume	500	spray/ha		
Volume of surface contamination	50	ml/h		
Distribution	Hands	Trunk	Legs	
	25%	25%	50%	
Clothing	Gloves	Impermeable	Impermeable	
Penetration	10%	5%	5%	
Dermal exposure	1.25	0.625	1.25	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	18.75	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0.0135	ml/day	18.75	ml/day
Concen. of a.s. product or spray	400	mg/ml	2	mg/ml
Dermal exposure to a.s.	5.4	mg/day	37.5	mg/day
Percent absorbed	0.05	%	3	%
Absorbed dose	0.0027	mg/day	1.125	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0.02	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	2	mg/ml
Inhalation exposure to a.s.	0.24	mg/day
Percent absorbed	100	%
Absorbed dose	0.24	mg/day

PREDICTED EXPOSURE

Total absorbed dose	1.3677	mg/day
Operator body weight	60	kg
Operator exposure	0.022795	mg/kg bw/day

%AOEL 253.2777778

Appendix 1.19 Estimation of bystander exposure to azoxystrobin upon application of A14111B according to the German guidance

Estimation of bystander exposure during/after application in Field Crops, Tractor Mounted

Input parameters considered for the estimation of bystander exposure:

Intended use(s):	tomato		**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.2	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m² (adults)
				0.21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg a.s. (6 hours, adults)
	16.15	kg/person (children)		0.00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	75.00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0.2	mg/kg bw/d			

Bystander exposure towards azoxystrobin					
Adults			**Children**		
Bystander: Dermal exposure after application in tomato (via spray drift)					
$SDE_B = (AR \times D \times BSA \times DA) / BW$			$SDE_B = (AR \times D \times BSA \times DA) / BW$		
(20 x 0.29% x 1 x 75%) / 60			(20 x 0.29% x 0.21 x 75%) / 16.15		
External exposure	0.058	mg/person	External exposure	0.01218	mg/person
External exposure	0.00096667	mg/kg bw/d	External exposure	0.00075418	mg/kg bw/d
Absorbed dose:	**0.0007250**	**mg/kg bw/d**	**Absorbed dose:**	**0.0005656**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in tomato					
$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$			$SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$		
(0.001 / 360 x 0.2 x 20 x 5 x 100%) / 60			(0,00057 / 360 x 0.2 x 20 x 5 x 100%) / 16.15		
External exposure	5.5556E-05	mg/person	External exposure	3.1928E-05	mg/person
External exposure	9.2593E-07	mg/kg bw/d	External exposure	1.977E-06	mg/kg bw/d
Absorbed dose:	**0.0000009**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000020**	**mg/kg bw/d**
Total systemic exposure: $SE_B = SDE_B + SIE_B$			Total systemic exposure: $SE_B = SDE_B + SIE_B$		
Total systemic exposure (absorbed dose)	0.04355556	mg/person	Total systemic exposure (absorbed dose)	0.00916693	mg/person
Total systemic exposure (absorbed dose)	**0.0007259**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0005676**	**mg/kg bw/d**
% of AOEL:	**0.36**	**%**	**% of AOEL:**	**0.28**	**%**

Appendix 1.20 Estimation of resident exposure to azoxystrobin upon application of A14111B according to the German guidance

Estimation of resident exposure after application in Field Crops, Tractor Mounted (FCTM)

Input parameters considered for the estimation of resident exposure:

Intended use(s):	tomato		**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.2	kg a.s./ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
				2600	cm^2/h (children)
Number of applications (NA):	1		**Turf Transferable Residues (TTR):**	5	%
Body weight (BW):	60	kg/person (adults)	**Exposure Duration (H):**	2	h
	16.15	kg/person (children)	**Airborne Concentration of Vapour (ACV):**	none	
Dermal absorption (DA):	75.00	% ('worst case')	**Inhalation Rate (IR):**	16.57	m^3/d (adults),
Inhalation absorption (IA):	100	%		8.31	m^3/d (children)
Oral absorption (OA)	100	%	**Saliva Extraction Factor (SE):**	50	%
AOEL	0.2	mg/kg bw/d	**Surface Area of Hands (SA):**	20	cm^2
			Frequency of Hand to Mouth (Freq):	20	events/h
			Dislodgeable foliar residues (DFR):	20	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	25	cm^2/d

Resident exposure towards azoxystrobin					
Adults			**Children**		
Residents: Dermal exposure after application in tomato (via deposits caused by spray drift)					
$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$			$SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$		
(0.002 x 1 x 0.29% x 5% x 7300 x 2 x 75%) / 60			(0.002 x 1 x 0.29% x 5% x 2600 x 2 x 75%) / 16.15		
External exposure	0.004234	mg/person	External exposure	0.001508	mg/person
External exposure	7.0567E-05	mg/kg bw/d	External exposure	9.3375E-05	mg/kg bw/d
Absorbed dose:	**0.0000529**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000700**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
$SIE_R = (AC_V \times IR \times IA) / BW$			$SIE_R = (AC_V \times IR \times IA) / BW$		
(0 x 16.57 x 100%) / 60			(0 x 8.31 x 100%) / 16.15		
External exposure		mg/person	External exposure		mg/person
External exposure		mg/kg bw/d	External exposure		mg/kg bw/d
Absorbed dose:		**none**	**Absorbed dose:**		**none**
			Residents: Oral exposure (hand-to-mouth transfer)		
			$SOE_H = (AR \times NA \times D \times TTR \times SE \times SA \times Freq \times H \times OA) /$		
			(0.002 x 1 x 0.29% x 5% x 50% x 20 x 20 x 2 x 100%) / 16.15		
			External exposure	0.000116	mg/person
			External exposure	7.1827E-06	mg/kg bw/d
			Absorbed dose	**0.0000072**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			$SOE_O = (AR \times NA \times D \times DFR \times IgR \times OA) / BW$		
			(0.002 x 1 x 0.29% x 20% x 25 x 100%) / 16.15		
			External exposure	0.000029	mg/person
			External exposure	1.7957E-06	mg/kg bw/d
			Absorbed dose	**0.0000018**	**mg/kg bw/d**
Total systemic exposure: $SE_R = SDE_R + SIE_R$			Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$		
Total systemic exposure (absorbed dose)	0.0031755	mg/person	Total systemic exposure (absorbed dose)	0.001276	mg/person
Total systemic exposure (absorbed dose)	**0.0000529**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0000790**	**mg/kg bw/d**
% of AOEL:	**0.03**	**%**	**% of AOEL:**	**0.04**	**%**

Appendix 1.21 Estimation of bystander exposure to chlorothalonil upon application of A14111B according to the German guidance

Estimation of bystander exposure during/after application in Field Crops, Tractor Mounted

Input parameters considered for the estimation of bystander exposure:

Intended use(s):	tomato		**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	1	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m² (adults)
				0.21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg a.s. (6 hours, adults)
	16.15	kg/person (children)		0.00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	7.00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0.009	mg/kg bw/d			

Bystander exposure towards chlorothalonil					
Adults			**Children**		
Bystander: Dermal exposure after application in tomato (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(100 x 0.29% x 1 x 7%) / 60			(100 x 0.29% x 0.21 x 7%) / 16.15		
External exposure	0.29	mg/person	External exposure	0.0609	mg/person
External exposure	0.00483333	mg/kg bw/d	External exposure	0.0037709	mg/kg bw/d
Absorbed dose:	**0.0003383**	**mg/kg bw/d**	**Absorbed dose:**	**0.0002640**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in tomato					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0.001 / 360 x 1 x 20 x 5 x 100%) / 60			(0,00057 / 360 x 1 x 20 x 5 x 100%) / 16.15		
External exposure	0.00027778	mg/person	External exposure	0.00015964	mg/person
External exposure	4.6296E-06	mg/kg bw/d	External exposure	9.885E-06	mg/kg bw/d
Absorbed dose:	**0.0000046**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000099**	**mg/kg bw/d**
Total systemic exposure: $SE_B = SDE_B + SIE_B$			Total systemic exposure: $SE_B = SDE_B + SIE_B$		
Total systemic exposure (absorbed dose)	0.02057778	mg/person	Total systemic exposure (absorbed dose)	0.00442264	mg/person
Total systemic exposure (absorbed dose)	**0.0003430**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0002738**	**mg/kg bw/d**
% of AOEL:	**3.81**	**%**	**% of AOEL:**	**3.04**	**%**

Appendix 1.22 Estimation of resident exposure to chlorothalonil upon application of A14111B according to the German guidance

Estimation of resident exposure after application in Field Crops, Tractor Mounted (FCTM)

Input parameters considered for the estimation of resident exposure:

Intended use(s):	tomato		**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	1	kg a.s./ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
				2600	cm^2/h (children)
Number of applications (NA):	1		**Turf Transferable Residues (TTR):**	5	%
Body weight (BW):	60	kg/person (adults)	**Exposure Duration (H):**	2	h
	16.15	kg/person (children)	**Airborne Concentration of Vapour (ACV):**	0.001	mg/m3
Dermal absorption (DA):	7.00	% ('worst case')	**Inhalation Rate (IR):**	16.57	m^3/d (adults),
Inhalation absorption (IA):	100	%		8.31	m^3/d (children)
Oral absorption (OA)	30	%	**Saliva Extraction Factor (SE):**	50	%
AOEL	0.009	mg/kg bw/d	**Surface Area of Hands (SA):**	20	cm^2
			Frequency of Hand to Mouth (Freq):	20	events/h
			Dislodgeable foliar residues (DFR):	20	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	25	cm^2/d

Resident exposure towards chlorothalonil					
Adults			**Children**		
Residents: Dermal exposure after application in tomato (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0.01 x 1 x 0.29% x 5% x 7300 x 2 x 7%) / 60			(0.01 x 1 x 0.29% x 5% x 2600 x 2 x 7%) / 16.15		
External exposure	0.02117	mg/person	External exposure	0.00754	mg/person
External exposure	0.00035283	mg/kg bw/d	External exposure	0.00046687	mg/kg bw/d
Absorbed dose:	**0.0000247**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000327**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0.001 x 16.57 x 100%) / 60			(0.001 x 8.31 x 100%) / 16.15		
External exposure	0.01657	mg/person	External exposure	0.00831	mg/person
External exposure	0.00027617	mg/kg bw/d	External exposure	0.00051455	mg/kg bw/d
Absorbed dose:	**0.0002762**	**mg/kg bw/d**	**Absorbed dose:**	**0.0005146**	**mg/kg bw/d**
			Residents: Oral exposure (hand-to-mouth transfer)		
			SOE_H = (AR x NA x D x TTR x SE x SA x Freq x H x OA) /		
			(0.01 x 1 x 0.29% x 5% x 50% x 20 x 20 x 2 x 30%) / 16.15		
			External exposure	0.00058	mg/person
			External exposure	3.5913E-05	mg/kg bw/d
			Absorbed dose	**0.0000108**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			SOE_O = (AR x NA x D x DFR x IgR x OA) / BW		
			(0.01 x 1 x 0.29% x 20% x 25 x 30%) / 16.15		
			External exposure	0.000145	mg/person
			External exposure	8.9783E-06	mg/kg bw/d
			Absorbed dose	**0.0000027**	**mg/kg bw/d**
Total systemic exposure: SE_R = SDE_R + SIE_R			Total systemic exposure: SE_R = SDE_R + SIE_R + SOE_H + SOE_O		
Total systemic exposure (absorbed dose)	0.0180519	mg/person	Total systemic exposure (absorbed dose)	0.0090553	mg/person
Total systemic exposure (absorbed dose)	**0.0003009**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0005607**	**mg/kg bw/d**
% of AOEL:	**3.34**	**%**	**% of AOEL:**	**6.23**	**%**

Appendix 1.23 Estimation of worker exposure for crop inspection in cereals for azoxystrobin upon application of A14111B according to the EUROPOEM II approach

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	3	µg/cm²/kg a.s.
Application rate (AR):	0.15	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	2		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	75	% ('worst case')			
			Work rate per day (WR):	2	h/d
AOEL	0.2	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in cereals					
Worker exposure towards azoxystrobin					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 3600 x 2 x 0.15 x 2 x 75%) / 60			(3 x 300 x 2 x 0.15 x 2 x 75%) / 60		
External dermal exposure	6.48	mg/person	External dermal exposure	0.54	mg/person
External dermal exposure	0.11	mg/kg bw/d	External dermal exposure	0.01	mg/kg bw/d
Total systemic exposure	4.86	mg/person	Total systemic exposure	0.41	mg/person
Total systemic exposure	**0.081000**	**mg/kg bw/d**	**Total systemic exposure**	**0.006750**	**mg/kg bw/d**
% of AOEL	**40.5**	**%**	**% of AOEL**	**3.38**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 2200 x 2 x 0.15 x 2 x 75%) / 60			(3 x 2200 x 2 x 0.15 x 2 x 5% x 75%) / 60		
External dermal exposure	3.96	mg/person	External dermal exposure	0.20	mg/person
External dermal exposure	0.07	mg/kg bw/d	External dermal exposure	0.003	mg/kg bw/d
Total systemic exposure	4.95	mg/person	Total systemic exposure	0.02	mg/person
Total systemic exposure	**0.049500**	**mg/kg bw/d**	**Total systemic exposure**	**0.002475**	**mg/kg bw/d**
% of AOEL	**24.8**	**%**	**% of AOEL**	**1.24**	**%**

Total potential exposure	**0.130500**	**mg/kg bw/d**	**% of AOEL**	**65.3**	**%**
Total actual exposure	**0.056250**	**mg/kg bw/d**	**% of AOEL**	**28.1**	**%**
Total exposure with PPE	**0.009225**	**mg/kg bw/d**	**% of AOEL**	**4.6**	**%**

Appendix 1.24 Estimation of worker exposure for crop inspection in cereals for azoxystrobin upon application of A14111B according to the EUROPOEM II approach (refined DFR)

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	1.2534	µg/cm²/kg a.s.
Application rate (AR):	0.15	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	2		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	75	% ('worst case')			
			Work rate per day (WR):	2	h/d
AOEL	0.2	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in cereals					
Worker exposure towards azoxystrobin					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(1.2534 x 3600 x 2 x 0.15 x 2 x 75%) / 60			(1.2534 x 300 x 2 x 0.15 x 2 x 75%) / 60		
External dermal exposure	2.71	mg/person	External dermal exposure	0.23	mg/person
External dermal exposure	0.05	mg/kg bw/d	External dermal exposure	0.00	mg/kg bw/d
Total systemic exposure	2.03	mg/person	Total systemic exposure	0.17	mg/person
Total systemic exposure	**0.033842**	**mg/kg bw/d**	**Total systemic exposure**	**0.002820**	**mg/kg bw/d**
% of AOEL	**16.9**	**%**	**% of AOEL**	**1.41**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(1.2534 x 2200 x 2 x 0.15 x 2 x 75%) / 60			(1.2534 x 2200 x 2 x 0.15 x 2 x 5% x 75%) / 60		
External dermal exposure	1.65	mg/person	External dermal exposure	0.08	mg/person
External dermal exposure	0.03	mg/kg bw/d	External dermal exposure	0.001	mg/kg bw/d
Total systemic exposure	2.07	mg/person	Total systemic exposure	0.00	mg/person
Total systemic exposure	**0.020681**	**mg/kg bw/d**	**Total systemic exposure**	**0.001034**	**mg/kg bw/d**
% of AOEL	**10.3**	**%**	**% of AOEL**	**0.52**	**%**

Total potential exposure	**0.054523**	**mg/kg bw/d**	**% of AOEL**	**27.3**	**%**
Total actual exposure	**0.023501**	**mg/kg bw/d**	**% of AOEL**	**11.8**	**%**
Total exposure with PPE	**0.003854**	**mg/kg bw/d**	**% of AOEL**	**1.9**	**%**

Appendix 1.2425 Estimation of worker exposure for crop inspection in cereals for azoxystrobin upon application of A14111B according to the EUROPOEM II approach (refined TC)

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	3	µg/cm^2/kg a.s.
Application rate (AR):	0.15	kg a.s./ha	**Transfer coefficient (TC):**	1100	cm^2/person/h
Number of applications (NA):	2		**Work rate per day (WR):**	2	h/d
Body weight (BW):	60	kg/person	**PPE**	5	%
Dermal absorption (DA):	75	% ('worst case')			
AOEL	0.2	mg/kg bw/d			

Worker exposure towards chlorothalonil					
Without PPE			**With PPE**		
Worker (re-entry): Systemic dermal exposure after application in cereals					
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 1100 x 2 x 0.15 x 2 x 75%) / 60			(3 x 1100 x 2 x 0.15 x 2 x 5% x 75%) / 60		
External dermal exposure	1.98	mg/person	External dermal exposure	0.10	mg/person
External dermal exposure	0.03	mg/kg bw/d	External dermal exposure	0.00	mg/kg bw/d
Total systemic exposure	1.49	mg/person	Total systemic exposure	0.07	mg/person
Total systemic exposure	**0.024750**	**mg/kg bw/d**	**Total systemic exposure**	**0.001238**	**mg/kg bw/d**
% of AOEL	**12.4**	**%**	**% of AOEL**	**0.6**	**%**

Appendix 1.26 Estimation of worker exposure for crop inspection in cereals for azoxystrobin upon application of A14111B according to the EUROPOEM II approach (refined TC and DFR)

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	1.2534	µg/cm²/kg a.s.
Application rate (AR):	0.15	kg a.s./ha	**Transfer coefficient (TC):**	1100	cm²/person/h
Number of applications (NA):	2		**Work rate per day (WR):**	2	h/d
Body weight (BW):	60	kg/person	**PPE**	5	%
Dermal absorption (DA):	75	% ('worst case')			
AOEL	0.2	mg/kg bw/d			

Worker exposure towards azoxystrobin					
Without PPE			**With PPE**		
Worker (re-entry): Systemic dermal exposure after application in cereals					
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(1.2534 x 1100 x 2 x 0.15 x 2 x 75%) / 60			(1.2534 x 1100 x 2 x 0.15 x 2 x 5% x 75%) / 60		
External dermal exposure	0.83	mg/person	External dermal exposure	0.04	mg/person
External dermal exposure	0.01	mg/kg bw/d	External dermal exposure	0.00	mg/kg bw/d
Total systemic exposure	0.62	mg/person	Total systemic exposure	0.03	mg/person
Total systemic exposure	**0.010341**	**mg/kg bw/d**	**Total systemic exposure**	**0.000517**	**mg/kg bw/d**
% of AOEL	**5.2**	**%**	**% of AOEL**	**0.3**	**%**

Appendix 1.257 Estimation of worker exposure for hand-harvesting tomato for azoxystrobin upon application of A14111B according to the EUROPOEM II approach

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	tomato		**Dislodgeable foliar residues (DFR):**	3	µg/cm²/kg a.s.
Application rate (AR):	0.2	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	1		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	75	% ('worst case')			
			Work rate per day (WR):	8	h/d
AOEL	0.2	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in tomato					
Worker exposure towards azoxystrobin					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 3600 x 8 x 0.2 x 1 x 75%) / 60			(3 x 300 x 8 x 0.2 x 1 x 75%) / 60		
External dermal exposure	17.28	mg/person	External dermal exposure	1.44	mg/person
External dermal exposure	0.29	mg/kg bw/d	External dermal exposure	0.02	mg/kg bw/d
Total systemic exposure	12.96	mg/person	Total systemic exposure	1.08	mg/person
Total systemic exposure	**0.216000**	**mg/kg bw/d**	**Total systemic exposure**	**0.018000**	**mg/kg bw/d**
% of AOEL	**108.0**	**%**	**% of AOEL**	**9.00**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 2200 x 8 x 0.2 x 1 x 75%) / 60			(3 x 2200 x 8 x 0.2 x 1 x 5% x 75%) / 60		
External dermal exposure	10.56	mg/person	External dermal exposure	0.53	mg/person
External dermal exposure	0.18	mg/kg bw/d	External dermal exposure	0.009	mg/kg bw/d
Total systemic exposure	13.20	mg/person	Total systemic exposure	0.11	mg/person
Total systemic exposure	**0.132000**	**mg/kg bw/d**	**Total systemic exposure**	**0.006600**	**mg/kg bw/d**
% of AOEL	**66.0**	**%**	**% of AOEL**	**3.30**	**%**

Total potential exposure	**0.348000**	**mg/kg bw/d**	**% of AOEL**	**174.0**	**%**
Total actual exposure	**0.150000**	**mg/kg bw/d**	**% of AOEL**	**75.0**	**%**
Total exposure with PPE	**0.024600**	**mg/kg bw/d**	**% of AOEL**	**12.3**	**%**

Appendix

1.268 Estimation of worker exposure for crop inspection in cereals for chlorothalonil upon application of A14111B according to the EUROPOEM II approach

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	3	µg/cm²/kg a.s.
Application rate (AR):	0.75	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	2		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	3	% ('worst case')			
			Work rate per day (WR):	2	h/d
AOEL	0.009	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in cereals					
Worker exposure towards chlorothalonil					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 3600 x 2 x 0.75 x 2 x 3%) / 60			(3 x 300 x 2 x 0.75 x 2 x 3%) / 60		
External dermal exposure	32.40	mg/person	External dermal exposure	2.70	mg/person
External dermal exposure	0.54	mg/kg bw/d	External dermal exposure	0.05	mg/kg bw/d
Total systemic exposure	0.97	mg/person	Total systemic exposure	0.08	mg/person
Total systemic exposure	**0.016200**	**mg/kg bw/d**	**Total systemic exposure**	**0.001350**	**mg/kg bw/d**
% of AOEL	**180.0**	**%**	**% of AOEL**	**15.00**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 2200 x 2 x 0.75 x 2 x 3%) / 60			(3 x 2200 x 2 x 0.75 x 2 x 5% x 3%) / 60		
External dermal exposure	19.80	mg/person	External dermal exposure	0.99	mg/person
External dermal exposure	0.33	mg/kg bw/d	External dermal exposure	0.017	mg/kg bw/d
Total systemic exposure	0.99	mg/person	Total systemic exposure	0.02	mg/person
Total systemic exposure	**0.009900**	**mg/kg bw/d**	**Total systemic exposure**	**0.000495**	**mg/kg bw/d**
% of AOEL	**110.0**	**%**	**% of AOEL**	**5.50**	**%**

Total potential exposure	**0.026100**	**mg/kg bw/d**	**% of AOEL**	**290.0**	**%**
Total actual exposure	**0.011250**	**mg/kg bw/d**	**% of AOEL**	**125.0**	**%**
Total exposure with PPE	**0.001845**	**mg/kg bw/d**	**% of AOEL**	**20.5**	**%**

Appendix 1.29 Estimation of worker exposure for crop inspection in cereals for chlorothalonil upon application of A14111B according to the EUROPOEM II approach (refined DFR)

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	0.8405	µg/cm²/kg a.s.
Application rate (AR):	0.75	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	2		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	3	% ('worst case')			
			Work rate per day (WR):	2	h/d
AOEL	0.009	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in cereals					
Worker exposure towards chlorothalonil					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(0.8405 x 3600 x 2 x 0.75 x 2 x 3%) / 60			(0.8405 x 300 x 2 x 0.75 x 2 x 3%) / 60		
External dermal exposure	9.08	mg/person	External dermal exposure	0.76	mg/person
External dermal exposure	0.15	mg/kg bw/d	External dermal exposure	0.01	mg/kg bw/d
Total systemic exposure	0.27	mg/person	Total systemic exposure	0.02	mg/person
Total systemic exposure	**0.004539**	**mg/kg bw/d**	**Total systemic exposure**	**0.000378**	**mg/kg bw/d**
% of AOEL	**50.4**	**%**	**% of AOEL**	**4.20**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(0.8405 x 2200 x 2 x 0.75 x 2 x 3%) / 60			(0.8405 x 2200 x 2 x 0.75 x 2 x 5% x 3%) / 60		
External dermal exposure	5.55	mg/person	External dermal exposure	0.28	mg/person
External dermal exposure	0.09	mg/kg bw/d	External dermal exposure	0.005	mg/kg bw/d
Total systemic exposure	0.28	mg/person	Total systemic exposure	0.0013	mg/person
Total systemic exposure	**0.002774**	**mg/kg bw/d**	**Total systemic exposure**	**0.000139**	**mg/kg bw/d**
% of AOEL	**30.8**	**%**	**% of AOEL**	**1.54**	**%**

Total potential exposure	**0.007312**	**mg/kg bw/d**	**% of AOEL**	**81.2**	**%**
Total actual exposure	**0.003152**	**mg/kg bw/d**	**% of AOEL**	**35.0**	**%**
Total exposure with PPE	**0.000517**	**mg/kg bw/d**	**% of AOEL**	**5.7**	**%**

Appendix 1.2730 Estimation of worker exposure for crop inspection in cereals for chlorothalonil upon application of A14111B according to the EUROPOEM II approach (refinement with TC)

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	3	µg/cm²/kg a.s.
Application rate (AR):	0.75	kg a.s./ha	**Transfer coefficient (TC):**	1100	cm²/person/h
Number of applications (NA):	2		**Work rate per day (WR):**	2	h/d
Body weight (BW):	60	kg/person	**PPE**	5	%
Dermal absorption (DA):	3	% ('worst case')			
AOEL	0.009	mg/kg bw/d			

Worker exposure towards chlorothalonil					
Without PPE			**With PPE**		
Worker (re-entry): Systemic dermal exposure after application in cereals					
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 1100 x 2 x 0.75 x 2 x 3%) / 60			(3 x 1100 x 2 x 0.75 x 2 x 5% x 3%) / 60		
External dermal exposure	9.90	mg/person	External dermal exposure	0.50	mg/person
External dermal exposure	0.17	mg/kg bw/d	External dermal exposure	0.01	mg/kg bw/d
Total systemic exposure	0.30	mg/person	Total systemic exposure	0.01	mg/person
Total systemic exposure	**0.004950**	**mg/kg bw/d**	**Total systemic exposure**	**0.000248**	**mg/kg bw/d**
% of AOEL	**55.0**	**%**	**% of AOEL**	**2.8**	**%**

Appendix 1.31 Estimation of worker exposure for crop inspection in cereals for chlorothalonil upon application of A14111B according to the EUROPOEM II approach (refined TC and DFR)

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	cereals		**Dislodgeable foliar residues (DFR):**	0.8405	µg/cm^2/kg a.s.
Application rate (AR):	0.75	kg a.s./ha	**Transfer coefficient (TC):**	1100	cm^2/person/h
Number of applications (NA):	2		**Work rate per day (WR):**	2	h/d
Body weight (BW):	60	kg/person	**PPE**	5	%
Dermal absorption (DA):	3	% ('worst case')			
AOEL	0.009	mg/kg bw/d			

Worker exposure towards chlorothalonil					
Without PPE			**With PPE**		
Worker (re-entry): Systemic dermal exposure after application in cereals					
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(0.8405 x 1100 x 2 x 0.75 x 2 x 3%) / 60			(0.8405 x 1100 x 2 x 0.75 x 2 x 5% x 3%) / 60		
External dermal exposure	2.77	mg/person	External dermal exposure	0.14	mg/person
External dermal exposure	0.05	mg/kg bw/d	External dermal exposure	0.00	mg/kg bw/d
Total systemic exposure	0.08	mg/person	Total systemic exposure	0.00	mg/person
Total systemic exposure	**0.001387**	**mg/kg bw/d**	**Total systemic exposure**	**0.000069**	**mg/kg bw/d**
% of AOEL	**15.4**	**%**	**% of AOEL**	**0.8**	**%**

Appendix 1.~~28~~32 Estimation of worker exposure for hand-harvesting tomato for chlorothalonil upon application of A14111B according to the EUROPOEM II approach

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	tomato		**Dislodgeable foliar residues (DFR):**	3	µg/cm²/kg a.s.
Application rate (AR):	1	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	1		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	7	% ('worst case')			
			Work rate per day (WR):	8	h/d
AOEL	0.009	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in tomato					
Worker exposure towards chlorothalonil					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 3600 x 8 x 1 x 1 x 7%) / 60			(3 x 300 x 8 x 1 x 1 x 7%) / 60		
External dermal exposure	86.40	mg/person	External dermal exposure	7.20	mg/person
External dermal exposure	1.44	mg/kg bw/d	External dermal exposure	0.12	mg/kg bw/d
Total systemic exposure	6.05	mg/person	Total systemic exposure	0.50	mg/person
Total systemic exposure	**0.100800**	**mg/kg bw/d**	**Total systemic exposure**	**0.008400**	**mg/kg bw/d**
% of AOEL	**1120.0**	**%**	**% of AOEL**	**93.33**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(3 x 2200 x 8 x 1 x 1 x 7%) / 60			(3 x 2200 x 8 x 1 x 1 x 5% x 7%) / 60		
External dermal exposure	52.80	mg/person	External dermal exposure	2.64	mg/person
External dermal exposure	0.88	mg/kg bw/d	External dermal exposure	0.044	mg/kg bw/d
Total systemic exposure	6.16	mg/person	Total systemic exposure	0.27	mg/person
Total systemic exposure	**0.061600**	**mg/kg bw/d**	**Total systemic exposure**	**0.003080**	**mg/kg bw/d**
% of AOEL	**684.4**	**%**	**% of AOEL**	**34.22**	**%**

Total potential exposure	**0.162400**	**mg/kg bw/d**	**% of AOEL**	**1804.4**	**%**
Total actual exposure	**0.070000**	**mg/kg bw/d**	**% of AOEL**	**777.8**	**%**
Total exposure with PPE	**0.011480**	**mg/kg bw/d**	**% of AOEL**	**127.6**	**%**

Appendix 1.2933 Estimation of worker exposure for hand-harvesting tomato crops for chlorothalonil upon application of A14111B. According to the EUROPOEM II approach and incorporating data on dislodgeable foliar residues

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

Intended use(s):	tomato		**Dislodgeable foliar residues (DFR):**	0.4118	µg/cm²/kg a.s.
Application rate (AR):	1	kg a.s./ha	**Body potential (TC):**	3600	cm²/hr
Number of applications (NA):	1		**Body Actual (TC):**	300	cm²/hr
Body weight (BW):	60	kg/person	**Hand Potential (TC):**	2200	cm²/hr
Dermal absorption (DA):	7	% ('worst case')			
			Work rate per day (WR):	8	h/d
AOEL	0.009	mg/kg bw/d	**PPE**	5	%

Worker (re-entry): Systemic dermal exposure after application in tomato					
Worker exposure towards chlorothalonil					
Without PPE - Body - potential			**Body - Actual**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(0.4118 x 3600 x 8 x 1 x 1 x 7%) / 60			(0.4118 x 300 x 8 x 1 x 1 x 7%) / 60		
External dermal exposure	11.86	mg/person	External dermal exposure	0.99	mg/person
External dermal exposure	0.20	mg/kg bw/d	External dermal exposure	0.02	mg/kg bw/d
Total systemic exposure	0.83	mg/person	Total systemic exposure	0.07	mg/person
Total systemic exposure	**0.013836**	**mg/kg bw/d**	**Total systemic exposure**	**0.001153**	**mg/kg bw/d**
% of AOEL	**153.7**	**%**	**% of AOEL**	**12.81**	**%**

Without PPE -Hands - potential			**Hands - with PPE**		
SDE_W = (DFR x TC x WR x AR x NA x DA) / BW			SDE_W = (DFR x TC x WR x AR x NA x PPE x DA) / BW		
(0.4118 x 2200 x 8 x 1 x 1 x 7%) / 60			(0.4118 x 2200 x 8 x 1 x 1 x 5% x 7%) / 60		
External dermal exposure	7.25	mg/person	External dermal exposure	0.36	mg/person
External dermal exposure	0.12	mg/kg bw/d	External dermal exposure	0.006	mg/kg bw/d
Total systemic exposure	0.85	mg/person	Total systemic exposure	0.01	mg/person
Total systemic exposure	**0.008456**	**mg/kg bw/d**	**Total systemic exposure**	**0.000423**	**mg/kg bw/d**
% of AOEL	**94.0**	**%**	**% of AOEL**	**4.70**	**%**

Total potential exposure	**0.022292**	**mg/kg bw/d**	**% of AOEL**	**247.7**	**%**
Total actual exposure	**0.009609**	**mg/kg bw/d**	**% of AOEL**	**106.8**	**%**
Total exposure with PPE	**0.001576**	**mg/kg bw/d**	**% of AOEL**	**17.5**	**%**

Appendix 2: Detailed evaluation of DFR study relied on (CP 7.2.3, CP 7.2.3.1)

Report:	K-CP 7.2.3.1/01Roussel, C. (2015). Chlorothalonil and Azoxystrobin - Determination of Dislodgeable Foliar Residues of Chlorothalonil and Azoxystrobin on wheat leaves after one application of A14111B in Northern Europe (UK and Northern France), 2014. Staphyt, 23 rue de Moeuvres, F-62860 Inchy en Artois, France Study Dates: 22 May 2014 – 03 September 2015. Report Number ChR-14-19410 (Syngenta file No. A14111B_11228)

Guidelines

OECD Series on Testing and Assessment No. 9 ”Guidance document on the conduct of studies of occupational exposure to pesticides during agricultural application ”, Paris 1997. OCDE/GD(97)148.
European Commission Guidance for Generating and Reporting Methods of Analysis in Support of Pre-registration Requirements for Annex II (Part A, Section 4) of Directive 91/414, SANCO/3029/99 revision 4 (11 Jul 2000).
Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009 (for residue studies), specifically OECD Test Guideline 509, (Crop field trials) and OECD (2011) Guidance Document on Crop Field Trials (Series on Testing and Assessment No. 164 and Series on Pesticides No. 66).
This study was conducted in broad compliance with the U.S. EPA Series 875.2100 Occupational and Residential Exposure Test Guidelines. Foliar Dislodgeable Residue Dissipation (February 1996)

GLP

Fully GLP compliant study.

Executive Summary

Four dislodgeable foliar residue field trials on wheat were conducted in the United Kingdom and Northern France during 2014.

Azoxystrobin and chlorothalonil were applied to wheat as A14111B, a suspension concentrate (SC) formulation containing 80 g of azoxystrobin and 400 g of chlorothalonil per litre. One application was made at 200 and 1000 g per hectare respectively for azoxystrobin and chlorothalonil at BBCH 69.

Wheat leaves were weighed and their weight was compared to an average surface weight ratio determined at two occasions during each trial in order to estimate the leaf surface of each specimen. Leaf surface ratios were determined at 0 days after application 1 (DAA1) or the day before and 21 DAA1. 12 samples of wheat leaves were weighed, scanned and the leaves’ image was then processed to allow calculation of the leaf area to weight ratio.

Following the application, wheat leaves samples were collected in triplicate at 0 DAA1 as soon as spray deposit had dried and 8 hours (+/-1) after application; then 1, 2, 3, 5, 7, 14-15, 21-22 and 28-29 days after application. In trial UK01, sampling at 28 DAA1 was not performed because the leaves were already too dry. Each specimen was made of 20 wheat leaves and represented 2 upper leaves taken on 10 shoots randomly chosen.

Once returned to the field laboratory at the field test site, the leaves samples underwent two dislodging procedures using a washing solution of 0.01% w/v Aerosol OT100. After both washing solutions have been pooled and thoroughly mixed, each final solution was divided in two different vessels (400 ml each). Washing solution for azoxystrobin analysis was frozen without any addition while solution for chlorothalonil analysis was acidified with HCl 1M.

For each trial, two series of field fortifications have been prepared with 2 fortification levels and three replicates for each series.

Samples were analysed for azoxystrobin and chlorothalonil.

Some untreated samples appear to have small contaminations. Most of them were outliers: In trial UK01, one value above LOQ for azoxystrobin and another one above LOQ for chlorothalonil. In trial FR04: 2 values out of 6 just above LOQ (0.06 and 0.07 respectively for chlorothalonil One trial was clearly contaminated at a very low level. The contamination observed at 0 DAA1 was representing 0.03% of the residue level. It was assumed that this contamination was originated by an insufficient cleaning process after the previous trial (FR04) had been processed with the same equipment. These contaminations have been considered without impact on the study results.

This section discusses uncorrected results. The mean residues of azoxystrobin and chlorothalonil in total leaf washing specimens are summarised from each trial in the following table.

Sampling interval (days)	**Azoxystrobin residue (µg/cm^2) Mean Uncorrected**			
	Trial 1	**Trial 2**	**Trial 3**	**Trial 4**
0 DAA (<1 HAA)	0.197274	0.1090112	0.256480	0.234057
0 DAA (8 HAA)	0.139074	0.130319	0.191454	0.167726
1 DAA	0.087667	0.128377	0.150748	0.063579
2 DAA	0.164798	0.135038	0.185798	0.078148
3 DAA	0.048267	0.163796	0.171044	0.049432
5 DAA	0.010200	0.114250	0.142064	0.048904
7 DAA	0.036558	0.097354	0.114390	0.051728
14 DAA	0.006727	0.079629	0.108389	0.047942
21 DAA	0.005076	0.014475	0.004549	0.009173

Sampling interval (days)	Chlorothalonil residue (µg/cm^2) Mean Uncorrected			
	Trial 1	Trial 2	Trial 3	Trial 4
0 DAA (<1 HAA)	0.566384	0.467546	0.527439	0.653522
0 DAA (8 HAA)	0.446222	0.286406	0.447930	0.711402
1 DAA	0.706845	0.295515	0.397389	0.382758
2 DAA	0.644190	0.270775	0.466705	0.354731
3 DAA	0.492122	0.595452	0.348478	0.357628
5 DAA	0.383307	0.474213	0.333197	0.413468
7 DAA	0.498692	0.374266	0.277854	0.384168
14 DAA	0.192450	0.213949	0.368633	0.294651
21-22 DAA	0.134716	0.405253	0.192508	0.141877

I. MATERIALS AND METHODS

A MATERIALS

A1 Test System, Test Item and Reference Item

Test system	The following test system is representative of the crop group required for product registration: Wheat (Triticum aestivum) EPPO - Code: TRZAW	
Test Item(s)	Formulation – Company Code	A14111B
	Formulation Content and Type	080/400 SC
	Batch No.	GRA1A063B/1
	Valid until:	End of Dec 2014 (re-analysis date)
	Active ingredients	Azoxystrobin Chlorothalonil
	Nominal Content in Formulation (nominal)	80 g/L azoxystrobin 400 g/L chlorothalonil
	Actual Content in Formulation (actual)	74.7 g/L azoxystrobin 384 g/L chlorothalonil
	Stability	The test item is assumed to be stable for the period of use in the study, pending concurrent batch re-analysis since it was stored below 30°C

A2 Test Facilities

The Field Phase was conducted at four sites in Northern France and the United Kingdom between 10 June 2014 and 16 July 2014.

The Analytical Phase was conducted at The Analytical Phase was conducted at Eurofins Agroscience Services Chem SAS, Vergèze, France between 25 November 2014 – 29 July 2015.

B FIELD PHASE

Four dislodgeable foliar residue field trials on wheat were conducted in the United Kingdom and Northern France during 2014.

Details of the application of chlorothalonil and azoxystrobin to wheat in trials ChR-14-19410 UK01, ChR-14-19410 FR02, ChR-14-19410 FR03 and ChR-14-19410 FR04 are summarised in Table AP2-1.

Table AP2-1: Treatment details for Trials ChR-14-19410 UK01, ChR-14-19410 FR02, ChR-14-19410 FR03 and ChR-14-19410 FR0

Trial. ChR-19410-	Applications	Application date(s)	Formulation Code	Product rate (L/ha)	Actual spray volume (L/ha)	Growth stage at application (BBCH)	AI application rate (g ai/ha)		
							AI Name	Actual	Target
UK01	1	24 Jun 2014	A14111B	2.615	208	69	Azoxystrobin	209	200
							Chlorothalonil	1046	1000
FR02	1	12 Jun 2014	A14111B	2.445	194	69	Azoxystrobin	196	200
							Chlorothalonil	978	1000
FR03	1	11 Jun 2014	A14111B	2.487	297	69	Azoxystrobin	199	200
							Chlorothalonil	995	1000
FR04	1	10 Jun 2014	A14111B	2.487	198	69	Azoxystrobin	199	200
							Chlorothalonil	995	1000

B5 Sampling

Following the application, wheat leaves samples were collected in triplicate at 0 DAA1 as soon as spray deposit had dried and 8 hours (+/-1) after application; then 1, 2, 3, 5, 7, 14-15, 21-22 and 28-29 days after application. In trial UK01, sampling at 28 DAA1 was not performed because the leaves were already too dry. Each specimen was made of 20 wheat leaves and represented 2 upper leaves taken on 10 shoots randomly chosen.

On each sampling date, the leaves were taken in places kept untouched since application. Three replicates were sampled on each sampling date. 20 leaves were sampled from sub sampling area: each sample was made of 2 upper leaves on 10 shoots randomly selected in order to represent the upper part of foliage susceptible to be in contact with a worker entering the wheat field.

The leaves specimens were transferred to the test site under ‘cool’ conditions using blue ice.

B6 Leaf washing

All specimens of 20 leaves underwent a dislodging process at the test site within 4 hours of sampling. This procedure consists of mechanically shaking the foliage for 10 minutes with two sequential 400ml washes with an aqueous solution of 0.01% w/v Aerosol OT100 (dislodging solution).

Half the final solution was transferred into a bottle identified for chlorothalonil analysis. This bottle was acidified with 3 vials of HCl 1M (1.2 ml each) and wrapped in aluminium foil. The remaining 400 ml bottle was identified for azoxystrobin analysis. Both bottles were stored in freezers until shipment.

On two sampling events (1DBA and 22DAA) one extra field specimen of 20 leaves was taken in C1 plot to produce blank leaf wash solution. After the leaf washing procedure, 50 mL of control leaf wash specimens were added to 6 labelled bottles (125 ml). For azoxystrobin: 3 leaf wash specimens were each spiked with 100 µL of a solution containing 0.125 µg/mL (low rate fortification). In addition, 3 leaf wash specimens were each spiked with 100 µL of a solution containing 150 µg/mL. For chlorothalonil: 3 vial filled with 0.9 ml of acetonitrile were each spiked with 100 µL of a solution containing 0.125 µg/mL (low rate fortification). In addition, 3 other vials were each spiked with 100 µL of a solution containing 750 µg/mL. The fortified vial spiking were done with a micro pipet or Hamilton syringe. The leaf wash solution spiking were done by emptying the fortified vials in the leaf wash specimens and adding them (without the lid) into the solution. Then, the final solution was acidified with 500 µL of HCl 1M. Leaf wash specimens were kept deep frozen at or below -18°C during transport and storage prior to analysis.

C ANALYTICAL PHASE

Samples of wash solutions were analysed by Method GRM057/05A. The analytical method has been validated for analysis of chlorothalonil and azoxystrobin in leaf wash solutions. Determination of azoxystrobin was by LC-MS/MS. Determination of chlorothalonil was by GC-MS/MS. Field fortifications were analysed alongside the field specimens to demonstrate the stability of azoxystrobin and chlorothalonil in the leaf wash solutions.

II RESULTS AND DISCUSSION

A RESULTS OF ANALYSIS OF FIELD TRIAL SAMPLES

A1 Results of Trial Number ChR-14-19410 UK01

Residues of azoxystrobin and chlorothalonil in total leaf wash specimens from wheat leaves taken from Trial ChR-14-19410 UK01 are shown in Table AP2-2 and Table AP2-3.

Table AP2-2: Azoxystrobin residues in/on leaf washes from wheat treated at 200 g AI/ha

Sample No. ChR-14-19410 UK01-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin		
						Total Residue† (µg/L) Uncorrected	Residue (µg/cm^2) Uncorrected	Residue (µg/cm^2) Uncorrected Mean*
7-AZX	1 x 0.2	0DAA	-	966	Total washings 1	245.42	0.203249	0.197274
8-AZX	1 x 0.2	0DAA	-	841	Total washings 2	178.88	0.170160	
9-AZX	1 x 0.2	0DAA	-	950	Total washings 3	259.37	0.218414	
10-AZX	1 x 0.2	0DAA	8HAA	963	Total washings 1	234.77	0.195031	0.139074
11-AZX	1 x 0.2	0DAA	8HAA	988	Total washings 2	125.20	0.101380	
12-AZX	1 x 0.2	0DAA	8HAA	1116	Total washings 3	168.53	0.120810	
13-AZX	1 x 0.2	1DAA	-	818	Total washings 1	53.85	0.052669	0.087667
14-AZX	1 x 0.2	1DAA	-	1032	Total washings 2	194.39	0.150687	
15-AZX	1 x 0.2	1DAA	-	977	Total washings 3	72.84	0.059646	
16-AZX	1 x 0.2	2DAA	-	870	Total washings 1	208.78	0.191980	0.164798
17-AZX	1 x 0.2	2DAA	-	870	Total washings 2	175.69	0.161552	
18-AZX	1 x 0.2	2DAA	-	1006	Total washings 3	177.13	0.140861	
19-AZX	1 x 0.2	3DAA	-	951	Total washings 1	128.19	0.107837	0.048267
20-AZX	1 x 0.2	3DAA	-	973	Total washings 2	30.36	0.024962	
21-AZX	1 x 0.2	3DAA	-	933	Total washings 3	14.00	0.012001	
22-AZX	1 x 0.2	5DAA	-	1478	Total washings 1	26.50	0.014345	0.010200
23-AZX	1 x 0.2	5DAA	-	1351	Total washings 2	10.76	0.006374	

Sample No. ChR-14-19410 UK01-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin Total Residue† (µg/L) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected Mean*
24-AZX	1 x 0.2	5DAA	-	1385	Total washings 3	17.11	0.009880	
25-AZX	1 x 0.2	7DAA	-	1068	Total washings 1	51.79	0.038796	
26-AZX	1 x 0.2	7DAA	-	1104	Total washings 2	39.54	0.028651	0.036558
27-AZX	1 x 0.2	7DAA	-	1186	Total washings 3	62.60	0.042228	
28-AZX	1 x 0.2	15DAA	-	844	Total washings 1	7.18	0.006808	
29-AZX	1 x 0.2	15DAA	-	863	Total washings 2	7.62	0.007061	0.006727
30-AZX	1 x 0.2	15DAA	-	1069	Total washings 3	8.43	0.006311	
31-AZX	1 x 0.2	21DAA	-	729	Total washings 1	4.97	0.005455	
32-AZX	1 x 0.2	21DAA	-	778	Total washings 2	3.17	0.003262	0.005076
33-AZX	1 x 0.2	21DAA	-	715	Total washings 3	5.82	0.006512	
1-AZX	Control	1DBA	-	1034	Total washings 1	<0.05	<0.00005	-
2-AZX	Control	1DBA	-	1038	Total washings 2	<0.05	<0.00005	-
3-AZX	Control	1DBA	-	1074	Total washings 3	<0.05	<0.00005	-
4-AZX	Control	0DAA	-	976	Total washings 1	<0.05	<0.00005	-
5-AZX	Control	0DAA	-	995	Total washings 2	<0.05	<0.00005	-
6-AZX	Control	0DAA	-	977	Total washings 3	<0.05	<0.00005	-
34-AZX	Control	22DAA	-	914	Total washings 1	<0.05	<0.00005	-
35-AZX	Control	22DAA	-	704	Total washings 2	<0.05	<0.00005	-
36-AZX	Control	22DAA	-	782	Total washings 3	0.14	0.000144	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to azoxystrobin

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

Note: The contamination of the controls being at maximum 2% of the residues found in the treated samples, there is no impact on the study.

Table AP2-4: Chlorothalonil residues in/on leaf washes from wheat treated at 1000 g AI/ha

Sample No. ChR-14-19410 UK01-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
7-CTN	1 x 1	0DAA	-	966	Total washings 1	708.23	0.586526	
8-CTN	1 x 1	0DAA	-	841	Total washings 2	694.41	0.660553	0.566384
9-CTN	1 x 1	0DAA	-	950	Total washings 3	536.84	0.452074	
10-CTN	1 x 1	0DAA	8HAA	963	Total washings 1	518.70	0.430907	
11-CTN	1 x 1	0DAA	8HAA	988	Total washings 2	592.85	0.480042	0.446222
12-CTN	1 x 1	0DAA	8HAA	1116	Total washings 3	596.67	0.427718	
13-CTN	1 x 1	1DAA	-	818	Total washings 1	700.39	0.684982	
14-CTN	1 x 1	1DAA	-	1032	Total washings 2	887.95	0.688332	0.706845
15-CTN	1 x 1	1DAA	-	977	Total washings 3	912.54	0.747221	
16-CTN	1 x 1	2DAA	-	870	Total washings 1	882.79	0.811763	
17-CTN	1 x 1	2DAA	-	870	Total washings 2	664.91	0.611409	0.644190
18-CTN	1 x 1	2DAA	-	1006	Total washings 3	640.57	0.509399	
19-CTN	1 x 1	3DAA	-	951	Total washings 1	598.52	0.503487	
20-CTN	1 x 1	3DAA	-	973	Total washings 2	586.21	0.481984	0.492122
21-CTN	1 x 1	3DAA	-	933	Total washings 3	572.51	0.490895	
22-CTN	1 x 1	5DAA	-	1478	Total washings 1	895.31	0.484607	0.383307
23-CTN	1 x 1	5DAA	-	1351	Total washings 2	471.04	0.278927	

Sample No. ChR-14-19410 UK01-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
24-CTN	1 x 1	5DAA	-	1385	Total washings 3	668.93	0.386385	
25-CTN	1 x 1	7DAA	-	1068	Total washings 1	714.43	0.535152	
26-CTN	1 x 1	7DAA	-	1104	Total washings 2	454.84	0.329592	0.498692
27-CTN	1 x 1	7DAA	-	1186	Total washings 3	935.95	0.631333	
28-CTN	1 x 1	15DAA	-	844	Total washings 1	270.06	0.255982	
29-CTN	1 x 1	15DAA	-	863	Total washings 2	199.87	0.185279	0.192450
30-CTN	1 x 1	15DAA	-	1069	Total washings 3	181.85	0.136090	
31-CTN	1 x 1	21DAA	-	729	Total washings 1	132.57	0.145483	
32-CTN	1 x 1	21DAA	-	778	Total washings 2	111.81	0.114971	0.134716
33-CTN	1 x 1	21DAA	-	715	Total washings 3	128.43	0.143695	
1-CTN	Control	1DBA	-	1034	Total washings 1	<0.05	<0.00005	-
2-CTN	Control	1DBA	-	1038	Total washings 2	<0.05	<0.00005	-
3-CTN	Control	1DBA	-	1074	Total washings 3	<0.05	<0.00005	-
4-CTN	Control	0DAA	-	976	Total washings 1	<0.05	<0.00005	-
5-CTN	Control	0DAA	-	995	Total washings 2	0.77	0.000619	-
6-CTN	Control	0DAA	-	977	Total washings 3	<0.05	<0.00005	-
34-CTN	Control	22DAA	-	914	Total washings 1	<0.05	<0.00005	-
35-CTN	Control	22DAA	-	704	Total washings 2	<0.05	<0.00005	-
36-CTN	Control	22DAA	-	782	Total washings 3	<0.05	<0.00005	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to chlorothalonil

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

† Total extraction residue = Sample extraction residue + flask extraction residue

Note: The contamination of the controls being at maximum 0.8% of the residues found in the treated samples, there is no impact on the study.

Residues of azoxystrobin and chlorothalonil in total leaf wash specimens from wheat leaves taken from Trial ChR-14-19410 FR02 are shown in Table AP2-4 and Table AP2-5.

Table AP2-4: Azoxystrobin residues in/on leaf washes from wheat treated at 200 g AI/ha

Sample No. ChR-14-19410 FR02-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin Total Residue† (µg/L) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected Mean*
46-AZX	1 x 0.2	0DAA	-	795	Total washings 1	236.56	0.238051	
47-AZX	1 x 0.2	0DAA	-	941	Total washings 2	252.02	0.214255	0.221822
48-AZX	1 x 0.2	0DAA	-	704	Total washings 3	187.58	0.213160	
49-AZX	1 x 0.2	0DAA	8HAA	820	Total washings 1	156.44	0.152623	
50-AZX	1 x 0.2	0DAA	8HAA	910	Total washings 2	178.32	0.156764	0.152034
51-AZX	1 x 0.2	0DAA	8HAA	724	Total washings 3	132.78	0.146715	
52-AZX	1 x 0.2	1DAA	-	893	Total washings 1	213.10	0.190908	
53-AZX	1 x 0.2	1DAA	-	769	Total washings 2	116.68	0.121385	0.149795
54-AZX	1 x 0.2	1DAA	-	688	Total washings 3	117.90	0.137092	
55-AZX	1 x 0.2	2DAA	-	1074	Total washings 1	272.50	0.202982	
56-AZX	1 x 0.2	2DAA	-	896	Total washings 2	104.54	0.093343	0.157535
57-AZX	1 x 0.2	2DAA	-	726	Total washings 3	159.97	0.176280	

Sample No. ChR-14-19410 FR02-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin Total Residue† (µg/L) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected Mean*
58-AZX	1 x 0.2	3DAA	-	1069	Total washings 1	204.69	0.153184	0.191152
59-AZX	1 x 0.2	3DAA	-	868	Total washings 2	311.22	0.286835	
60-AZX	1 x 0.2	3DAA	-	751	Total washings 3	125.26	0.133436	
61-AZX	1 x 0.2	5DAA	-	836	Total washings 1	135.06	0.129243	0.133281
62-AZX	1 x 0.2	5DAA	-	836	Total washings 2	166.91	0.159721	
63-AZX	1 x 0.2	5DAA	-	729	Total washings 3	101.04	0.110879	
64-AZX	1 x 0.2	7DAA	-	956	Total washings 1	144.15	0.120628	0.113607
65-AZX	1 x 0.2	7DAA	-	964	Total washings 2	157.82	0.130971	
66-AZX	1 x 0.2	7DAA	-	872	Total washings 3	97.25	0.089221	
67-AZX	1 x 0.2	15DAA	-	1008	Total washings 1	106.61	0.084609	0.079629
68-AZX	1 x 0.2	15DAA	-	874	Total washings 2	92.38	0.084557	
69-AZX	1 x 0.2	15DAA	-	998	Total washings 3	86.98	0.069720	
70-AZX	1 x 0.2	21DAA	-	674	Total washings 1	9.09	0.010788	0.014475
71-AZX	1 x 0.2	21DAA	-	524	Total washings 2	10.79	0.016480	
72-AZX	1 x 0.2	21DAA	-	661	Total washings 3	13.35	0.016156	
40-AZX	Control	1DBA	-	863	Total washings 1	0.28	0.000263	-
41-AZX	Control	1DBA	-	745	Total washings 2	0.12	0.000128	-
42-AZX	Control	1DBA	-	919	Total washings 3	0.17	0.000150	-
43-AZX	Control	0DAA	-	919	Total washings 1	<0.05	<0.00005	-
44-AZX	Control	0DAA	-	848	Total washings 2	<0.05	<0.00005	-
45-AZX	Control	0DAA	-	963	Total washings 3	<0.05	<0.00005	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to azoxystrobin

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

Note: The samples at 28 DAA were not presented in this table because the area could not be determined. The leaf weight was too low to calculate leaf surface with average ratio.
The contamination of the controls being at maximum 3% of the residues found in the treated samples, there is no impact on the study.

Table AP2-5: Chlorothalonil residues in/on leaf washes from wheat treated at 1000 g AI/ha

Sample No. ChR-14-19410 FR02-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
46-CTN	1 x 1	0DAA	-	795	Total washings 1	778.49	0.783387	0.545575
47-CTN	1 x 1	0DAA	-	941	Total washings 2	498.95	0.424190	
48-CTN	1 x 1	0DAA	-	704	Total washings 3	377.65	0.429148	
49-CTN	1 x 1	0DAA	8HAA	820	Total washings 1	314.44	0.306773	0.334114
50-CTN	1 x 1	0DAA	8HAA	910	Total washings 2	373.74	0.328562	
51-CTN	1 x 1	0DAA	8HAA	724	Total washings 3	332.14	0.367006	
52-CTN	1 x 1	1DAA	-	893	Total washings 1	372.96	0.334116	0.344812
53-CTN	1 x 1	1DAA	-	769	Total washings 2	335.35	0.348872	
54-CTN	1 x 1	1DAA	-	688	Total washings 3	302.25	0.351449	
55-CTN	1 x 1	2DAA	-	1074	Total washings 1	552.93	0.411863	0.315881
56-CTN	1 x 1	2DAA	-	896	Total washings 2	236.39	0.211067	
57-CTN	1 x 1	2DAA	-	726	Total washings 3	294.68	0.324714	
58-CTN	1 x 1	3DAA	-	1069	Total washings 1	806.16	0.603302	0.694877

Sample No. ChR-14-19410 FR02-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
59-CTN	1 x 1	3DAA	-	868	Total washings 2	890.99	0.821193	
60-CTN	1 x 1	3DAA	-	751	Total washings 3	619.70	0.660135	
61-CTN	1 x 1	5DAA	-	836	Total washings 1	591.65	0.566169	
62-CTN	1 x 1	5DAA	-	836	Total washings 2	469.49	0.449272	0.553259
63-CTN	1 x 1	5DAA	-	729	Total washings 3	587.15	0.644335	
64-CTN	1 x 1	7DAA	-	956	Total washings 1	495.72	0.414825	
65-CTN	1 x 1	7DAA	-	964	Total washings 2	723.94	0.600776	0.436754
66-CTN	1 x 1	7DAA	-	872	Total washings 3	321.18	0.294660	
67-CTN	1 x 1	15DAA	-	1008	Total washings 1	312.89	0.248323	
68-CTN	1 x 1	15DAA	-	874	Total washings 2	307.87	0.281807	0.213949
69-CTN	1 x 1	15DAA	-	998	Total washings 3	139.37	0.111716	
70-CTN	1 x 1	21DAA	-	674	Total washings 1	351.39	0.417085	
71-CTN	1 x 1	21DAA	-	524	Total washings 2	261.15	0.398704	0.405253
72-CTN	1 x 1	21DAA	-	661	Total washings 3	330.47	0.399969	
40-CTN	Control	1DBA	-	863	Total washings 1	0.19	0.000181	-
41-CTN	Control	1DBA	-	745	Total washings 2	0.12	0.000134	-
42-CTN	Control	1DBA	-	919	Total washings 3	0.18	0.000156	-
43-CTN	Control	0DAA	-	919	Total washings 1	0.08	0.000067	-
44-CTN	Control	0DAA	-	848	Total washings 2	0.07	0.000071	-
45-CTN	Control	0DAA	-	963	Total washings 3	0.07	0.000054	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to chlorothalonil

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

† Total extraction residue = Sample extraction residue + flask extraction residue

Note: The samples at 28 DAA were not presented in this table because the area could not be determined. The leaf weight was too low to calculate leaf surface with average ratio.

Note: The contamination of the controls being at maximum 0.1% of the residues found in the treated samples, there is no impact on the study.

Residues of azoxystrobin and chlorothalonil in total leaf wash specimens from wheat leaves taken from Trial ChR-14-19410 FR03 are shown in Table AP2-6 and Table AP2-7.

Table AP2-6: Azoxystrobin residues in/on leaf washes from wheat treated at 200 g AI/ha

Sample No. ChR-14-19410 FR03-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin Total Residue† (µg/L) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected Mean*
85-AZX	1 x 0.2	0DAA	-	694	Total washings 1	224.59	0.258896	
86-AZX	1 x 0.2	0DAA	-	593	Total washings 2	196.76	0.265444	0.256480
87-AZX	1 x 0.2	0DAA	-	668	Total washings 3	204.66	0.245098	
88-AZX	1 x 0.2	0DAA	8HAA	749	Total washings 1	190.14	0.203092	
89-AZX	1 x 0.2	0DAA	8HAA	777	Total washings 2	180.43	0.185770	0.191454
90-AZX	1 x 0.2	0DAA	8HAA	807	Total washings 3	187.12	0.185500	
91-AZX	1 x 0.2	1DAA	-	783	Total washings 1	151.57	0.154863	
92-AZX	1 x 0.2	1DAA	-	765	Total washings 2	138.40	0.144728	0.150748
93-AZX	1 x 0.2	1DAA	-	757	Total washings 3	144.45	0.152652	
94-AZX	1 x 0.2	2DAA	-	725	Total washings 1	158.17	0.174529	
95-AZX	1 x 0.2	2DAA	-	746	Total washings 2	168.22	0.180397	0.185798

Sample No. ChR-14-19410 FR03-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin Total Residue† (µg/L) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected Mean*
96-AZX	1 x 0.2	2DAA	-	665	Total washings 3	168.30	0.202469	
97-AZX	1 x 0.2	3DAA	-	861	Total washings 1	168.82	0.156859	
98-AZX	1 x 0.2	3DAA	-	907	Total washings 2	194.75	0.171777	0.171044
99-AZX	1 x 0.2	3DAA	-	1007	Total washings 3	232.24	0.184497	
100-AZX	1 x 0.2	5DAA	-	846	Total washings 1	150.92	0.142712	
101-AZX	1 x 0.2	5DAA	-	877	Total washings 2	145.94	0.133123	0.142064
102-AZX	1 x 0.2	5DAA	-	883	Total washings 3	165.96	0.150358	
103-AZX	1 x 0.2	7DAA	-	997	Total washings 1	132.83	0.106586	
104-AZX	1 x 0.2	7DAA	-	924	Total washings 2	135.16	0.117024	0.114390
105-AZX	1 x 0.2	7DAA	-	849	Total washings 3	126.88	0.119559	
106-AZX	1 x 0.2	14DAA	-	865	Total washings 1	91.42	0.084548	
107-AZX	1 x 0.2	14DAA	-	726	Total washings 2	114.88	0.126585	0.108389
108-AZX	1 x 0.2	14DAA	-	786	Total washings 3	112.04	0.114034	
109-AZX	1 x 0.2	21DAA	-	559	Total washings 1	3.65	0.005220	
110-AZX	1 x 0.2	21DAA	-	573	Total washings 2	3.03	0.004234	0.004549
111-AZX	1 x 0.2	21DAA	-	546	Total washings 3	2.86	0.004193	
79-AZX	Control	0DBA	-	934	Total washings 1	<0.05	<0.00005	-
80-AZX	Control	0DBA	-	917	Total washings 2	<0.05	<0.00005	-
81-AZX	Control	0DBA	-	919	Total washings 3	<0.05	<0.00005	-
82-AZX	Control	0DAA	-	665	Total washings 1	<0.05	<0.00005	-
83-AZX	Control	0DAA	-	852	Total washings 2	<0.05	<0.00005	-
84-AZX	Control	0DAA	-	801	Total washings 3	<0.05	<0.00005	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to azoxystrobin

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

Note: The samples at 28 DAA were not presented in this table because the area could not be determined. The leaf weight was too low to calculate leaf surface with average ratio.

Table AP2-7: Chlorothalonil residues in/on leaf washes from wheat treated at 1000 g AI/ha

Sample No. ChR-14-19410 FR03-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
85-CTN	1 x 1	0DAA	-	694	Total washings 1	442.14	0.509667	
86-CTN	1 x 1	0DAA	-	593	Total washings 2	419.22	0.565559	0.527439
87-CTN	1 x 1	0DAA	-	668	Total washings 3	423.42	0.507092	
88-CTN	1 x 1	0DAA	8HAA	749	Total washings 1	404.40	0.431939	
89-CTN	1 x 1	0DAA	8HAA	777	Total washings 2	457.99	0.471543	0.447930
90-CTN	1 x 1	0DAA	8HAA	807	Total washings 3	444.16	0.440307	
91-CTN	1 x 1	1DAA	-	783	Total washings 1	437.94	0.447452	
92-CTN	1 x 1	1DAA	-	765	Total washings 2	363.77	0.380409	0.397389
93-CTN	1 x 1	1DAA	-	757	Total washings 3	344.72	0.364305	
94-CTN	1 x 1	2DAA	-	725	Total washings 1	368.85	0.407007	
95-CTN	1 x 1	2DAA	-	746	Total washings 2	384.53	0.412368	0.466705

Sample No. ChR-14-19410 FR03-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
96-CTN	1 x 1	2DAA	-	665	Total washings 3	482.74	0.580742	
97-CTN	1 x 1	3DAA	-	861	Total washings 1	284.12	0.263990	
98-CTN	1 x 1	3DAA	-	907	Total washings 2	245.80	0.216804	0.348478
99-CTN	1 x 1	3DAA	-	1007	Total washings 3	710.74	0.564639	
100-CTN	1 x 1	5DAA	-	846	Total washings 1	378.05	0.357497	
101-CTN	1 x 1	5DAA	-	877	Total washings 2	385.10	0.351285	0.333197
102-CTN	1 x 1	5DAA	-	883	Total washings 3	320.98	0.290808	
103-CTN	1 x 1	7DAA	-	997	Total washings 1	270.67	0.217190	
104-CTN	1 x 1	7DAA	-	924	Total washings 2	343.45	0.297359	0.277854
105-CTN	1 x 1	7DAA	-	849	Total washings 3	338.55	0.319012	
106-CTN	1 x 1	14DAA	-	865	Total washings 1	316.49	0.292707	
107-CTN	1 x 1	14DAA	-	726	Total washings 2	403.08	0.444164	0.368633
108-CTN	1 x 1	14DAA	-	786	Total washings 3	362.57	0.369027	
109-CTN	1 x 1	21DAA	-	559	Total washings 1	127.38	0.182300	
110-CTN	1 x 1	21DAA	-	573	Total washings 2	149.97	0.209378	0.192508
111-CTN	1 x 1	21DAA	-	546	Total washings 3	126.84	0.185848	
79-CTN	Control	0DBA	-	934	Total washings 1	<0.05	<0.00005	-
80-CTN	Control	0DBA	-	917	Total washings 2	<0.05	<0.00005	-
81-CTN	Control	0DBA	-	919	Total washings 3	<0.05	<0.00005	-
82-CTN	Control	0DAA	-	665	Total washings 1	<0.05	<0.00005	-
83-CTN	Control	0DAA	-	852	Total washings 2	<0.05	<0.00005	-
84-CTN	Control	0DAA	-	801	Total washings 3	-	-	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to chlorothalonil

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

† Total extraction residue = Sample extraction residue + flask extraction residue

Note: The samples of 28 DAA were not presented in this table because the area could not be determined. The leaf weight was too low to calculate leaf surface with average ratio.

Residues of azoxystrobin and chlorothalonil in total leaf wash specimens from wheat leaves taken from Trial ChR-14-19410 FR04 are shown in Table AP2-8 and Table AP2-9.

Table AP2-8: Azoxystrobin residues in/on leaf washes from wheat treated at 200 g AI/ha

Sample No. ChR-14-19410 FR04-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin Total Residue† (µg/L) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected Mean*
124-AZX	1 x 0.2	0DAA	-	797	Total washings 1	227.04	0.227890	
125-AZX	1 x 0.2	0DAA	-	815	Total washings 2	272.83	0.267810	0.234057
126-AZX	1 x 0.2	0DAA	-	769	Total washings 3	198.47	0.206471	
127-AZX	1 x 0.2	0DAA	8HAA	831	Total washings 1	176.28	0.169699	
128-AZX	1 x 0.2	0DAA	8HAA	753	Total washings 2	138.94	0.147615	0.167726
129-AZX	1 x 0.2	0DAA	8HAA	657	Total washings 3	152.64	0.185863	
130-AZX	1 x 0.2	1DAA	-	775	Total washings 1	69.78	0.072031	0.063579

Sample No. ChR-14-19410 FR04-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Azoxystrobin Total Residue† (µg/L) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected	Azoxystrobin Residue (µg/cm^2) Uncorrected Mean*
131-AZX	1 x 0.2	1DAA	-	809	Total washings 2	52.47	0.051881	
132-AZX	1 x 0.2	1DAA	-	732	Total washings 3	61.14	0.066823	
133-AZX	1 x 0.2	2DAA	-	740	Total washings 1	54.86	0.059305	
134-AZX	1 x 0.2	2DAA	-	764	Total washings 2	103.41	0.108285	0.078148
135-AZX	1 x 0.2	2DAA	-	824	Total washings 3	68.86	0.066854	
136-AZX	1 x 0.2	3DAA	-	819	Total washings 1	49.32	0.048181	
137-AZX	1 x 0.2	3DAA	-	773	Total washings 2	42.92	0.044420	0.049432
138-AZX	1 x 0.2	3DAA	-	907	Total washings 3	63.14	0.055694	
139-AZX	1 x 0.2	5DAA	-	800	Total washings 1	37.42	0.037422	
140-AZX	1 x 0.2	5DAA	-	732	Total washings 2	48.98	0.053531	0.048904
141-AZX	1 x 0.2	5DAA	-	857	Total washings 3	59.73	0.055758	
142-AZX	1 x 0.2	7DAA	-	748	Total washings 1	45.79	0.048972	
143-AZX	1 x 0.2	7DAA	-	700	Total washings 2	49.71	0.056806	0.051728
144-AZX	1 x 0.2	7DAA	-	785	Total washings 3	48.48	0.049404	
145-AZX	1 x 0.2	14DAA	-	734	Total washings 1	39.02	0.042531	
146-AZX	1 x 0.2	14DAA	-	663	Total washings 2	40.82	0.049256	0.047942
147-AZX	1 x 0.2	14DAA	-	821	Total washings 3	53.40	0.052039	
148-AZX	1 x 0.2	21DAA	-	655	Total washings 1	7.12	0.008702	
149-AZX	1 x 0.2	21DAA	-	570	Total washings 2	7.17	0.010065	0.009173
150-AZX	1 x 0.2	21DAA	-	692	Total washings 3	7.57	0.008753	
118-AZX	Control	1DBA	-	831	Total washings 1	<0.05	<0.00005	-
119-AZX	Control	1DBA	-	824	Total washings 2	<0.05	<0.00005	-
120-AZX	Control	1DBA	-	819	Total washings 3	-**	-	-
121-AZX	Control	0DAA	-	855	Total washings 1	<0.05	<0.00005	-
122-AZX	Control	0DAA	-	813	Total washings 2	<0.05	<0.00005	-
123-AZX	Control	0DAA	-	793	Total washings 3	<0.05	<0.00005	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to azoxystrobin

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

**Not enough samples was remained for analysis after use for tests

Note: The samples at 28 DAA were not presented in this table because the area could not be determined. The leaf weight was too low to calculate leaf surface with average ratio.

Table AP2-9: Chlorothalonil residues in/on leaf washes from wheat treated at 1000 g AI/ha

Sample No. ChR-14-19410 FR04-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
124-CTN	1 x 1	0DAA	-	797	Total washings 1	624.37	0.626717	
125-CTN	1 x 1	0DAA	-	815	Total washings 2	659.69	0.647545	0.653522
126-CTN	1 x 1	0DAA	-	769	Total washings 3	659.71	0.686303	
127-CTN	1 x 1	0DAA	8HAA	831	Total washings 1	621.14	0.597966	
128-CTN	1 x 1	0DAA	8HAA	753	Total washings 2	703.90	0.747839	0.711402
129-CTN	1 x 1	0DAA	8HAA	657	Total washings 3	647.47	0.788400	

Sample No. ChR-14-19410 FR04-	Number and Nominal Rate of Application (kg ai/ha)	Sampling Interval (days)	Sampling Interval (hours)	Area (cm^2)	Matrix	Chlorothalonil Total Residue† (µg/L) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected	Chlorothalonil Residue (µg/cm^2) Uncorrected Mean*
130-CTN	1 x 1	1DAA	-	775	Total washings 1	459.13	0.473943	0.382758
131-CTN	1 x 1	1DAA	-	809	Total washings 2	371.39	0.367259	
132-CTN	1 x 1	1DAA	-	732	Total washings 3	280.97	0.307072	
133-CTN	1 x 1	2DAA	-	740	Total washings 1	269.28	0.291109	0.354731
134-CTN	1 x 1	2DAA	-	764	Total washings 2	389.90	0.408274	
135-CTN	1 x 1	2DAA	-	824	Total washings 3	375.76	0.364811	
136-CTN	1 x 1	3DAA	-	819	Total washings 1	380.16	0.371343	0.357628
137-CTN	1 x 1	3DAA	-	773	Total washings 2	342.20	0.354155	
138-CTN	1 x 1	3DAA	-	907	Total washings 3	393.85	0.347386	
139-CTN	1 x 1	5DAA	-	800	Total washings 1	364.66	0.364662	0.413468
140-CTN	1 x 1	5DAA	-	732	Total washings 2	401.93	0.439264	
141-CTN	1 x 1	5DAA	-	857	Total washings 3	467.58	0.436479	
142-CTN	1 x 1	7DAA	-	748	Total washings 1	333.56	0.356744	0.384168
143-CTN	1 x 1	7DAA	-	700	Total washings 2	342.66	0.391608	
144-CTN	1 x 1	7DAA	-	785	Total washings 3	396.57	0.404151	
145-CTN	1 x 1	14DAA	-	734	Total washings 1	253.06	0.275813	0.294651
146-CTN	1 x 1	14DAA	-	663	Total washings 2	217.99	0.263037	
147-CTN	1 x 1	14DAA	-	821	Total washings 3	354.16	0.345104	
148-CTN	1 x 1	21DAA	-	655	Total washings 1	122.10	0.149126	0.141877
149-CTN	1 x 1	21DAA	-	570	Total washings 2	93.48	0.131197	
150-CTN	1 x 1	21DAA	-	692	Total washings 3	125.69	0.145310	
118-CTN	Control	1DBA	-	831	Total washings 1	<0.05	<0.00005	-
119-CTN	Control	1DBA	-	824	Total washings 2	0.06	0.000057	-
120-CTN	Control	1DBA	-	819	Total washings 3	<0.05	<0.00005	-
121-CTN	Control	0DAA	-	855	Total washings 1	0.07	0.000068	-
122-CTN	Control	0DAA	-	813	Total washings 2	<0.05	<0.00005	-
123-CTN	Control	0DAA	-	793	Total washings 3	<0.05	<0.00005	-

DBA: Days before application; DAA: Days after application; HAA: Hours after application

The application rate refers to chlorothalonil

No correction of results for control residues has been performed.

For residues <LOQ, the LOQ was used for the calculation of the mean except where all values were <LOQ in which case the mean is reported as <LOQ.

*Mean values calculated on unrounded values.

† Total extraction residue = Sample extraction residue + flask extraction residue

Note: The samples of 28 DAA were not presented in this table because the area could not be determined. The leaf weight was too low to calculate leaf surface with average ratio.

III CONCLUSIONS

Uncorrected residues of azoxystrobin and chlorothalonil in total leaf washing specimens from wheat leaves treated at 200 and 1000 g per hectare respectively for azoxystrobin and chlorothalonil at BBCH 69 are summarised in Tables AP2-10 and AP2-11.

Some untreated samples appear to have small contaminations. Most of them were outliers: In trial UK01, one value above LOQ for azoxystrobin and another one above LOQ for chlorothalonil. In trial FR04: 2 values out of 6 just above LOQ (0.06 and 0.07 respectively for chlorothalonil One trial was clearly contaminated at a very low level. The contamination observed at 0 DAA1 was representing 0.03% of the residue level. It was assumed that this contamination was originated by an insufficient cleaning process after the previous trial (FR04) had been processed with the same equipment. These contaminations have been considered without impact on the study results.

Table AP2-10: Summary of azoxystrobin residues from wheat leaves following application at 200 g AI/ha

Sampling interval (days)	Azoxystrobin residue (µg/cm^2) Mean Uncorrected			
	Trial 1	Trial 2	Trial 3	Trial 4
0 DAA (<1 HAA)	0.197274	0.1090112	0.256480	0.234057
0 DAA (8 HAA)	0.139074	0.130319	0.191454	0.167726
1 DAA	0.087667	0.128377	0.150748	0.063579
2 DAA	0.164798	0.135038	0.185798	0.078148
3 DAA	0.048267	0.163796	0.171044	0.049432
5 DAA	0.010200	0.114250	0.142064	0.048904
7 DAA	0.036558	0.097354	0.114390	0.051728
14 DAA	0.006727	0.079629	0.108389	0.047942
21 DAA	0.005076	0.014475	0.004549	0.009173

Table AP2-11: Summary of chlorothalonil residues from wheat leaves following application at 1000 g AI/ha

Sampling interval (days)	Chlorothalonil residue (µg/cm^2) Mean Uncorrected			
	Trial 1	Trial 2	Trial 3	Trial 4
0 DAA (<1 HAA)	0.566384	0.467546	0.527439	0.653522
0 DAA (8 HAA)	0.446222	0.286406	0.447930	0.711402
1 DAA	0.706845	0.295515	0.397389	0.382758
2 DAA	0.644190	0.270775	0.466705	0.354731
3 DAA	0.492122	0.595452	0.348478	0.357628
5 DAA	0.383307	0.474213	0.333197	0.413468
7 DAA	0.498692	0.374266	0.277854	0.384168
14 DAA	0.192450	0.213949	0.368633	0.294651
21-22 DAA	0.134716	0.405253	0.192508	0.141877

(C Roussel, 2015)