Proposals for new transfer coefficient (TC) values for worker re-entry activities in vineyards

Bystander Resident Orchard Vineyard (BROV) Re-entry Project Report

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1 Abstract

To address a data gap, new transfer coefficient (TC) values have been proposed for vineyard workers handling treated grapevines when carrying out harvesting and maintenance activities. In this project, TCs for various activities are derived from pairs of concurrent worker exposure and dislodgeable foliar residue (DFR) studies. The Bystander Resident Orchard Vineyard (BROV) re-entry database considers five matched pairs of exposure and DFR studies carried out between 2004 and 2017. The studies were on wine grapes and cover hand harvesting, pruning, training and shoot lifting in vineyards in the Czech Republic, Germany, France and Italy. The test materials were all fungicides and the crop foliage was full at the times of application and re-entry.

In the exposure studies, a total of 73 workers at 16 sites were monitored for a full working day. Dermal exposure of the hands and body was measured using a combination of inner and outer dosimetry clothing, hand washes and face wipes. Partial nitrile work gloves (nitrile protective coating on the fingers and palm of the hand but permeable material on the back of the hand) were also used in two studies involving 24 workers. In the DFR studies, leaf punch samples were taken at each site to correspond, as far as possible, with the time of worker re-entry.

Potential exposure values (for both the body and the hands) showed a good correlation with the DFR values. Total (body and hands) TC values based on the BROV studies are lower than the current default values in the EFSA Guidance Document for both potential worker exposure and assuming the use of workwear with bare hands.

2 Summary

The EFSA guidance document on non-dietary exposure [1] identified a key need for additional data on transfer coefficients (TCs) and dislodgeable foliar residue (DFR) values to produce more realistic exposure assessments for situations in which workers re-enter treated crops. For grapes in particular, there is currently a lack of TC information and, in the absence of European data, the EFSA guidance recommends the use of US TC values (which are incomplete and lacking in transparency). The European Crop Protection Association (ECPA) has identified that this data gap may result in the failure of EU registrations for crop protection products for grapes. The BROV re-entry project aims to establish (and to propose to EFSA) a set of European TC values for regulatory use in worker re-entry exposure assessments for relevant activities in vineyards.

In this project, TCs for various activities are derived from pairs of concurrent worker exposure and DFR studies. The TC for the activity (cm^2/h) = exposure (µg) ÷ DFR ($µg/cm^2$) ÷ exposure time (h). The BROV re-entry database considers five matched pairs of exposure and DFR studies (presented as a total of eight study reports) carried out between 2004 and 2017. The studies were on wine grapes and covered hand harvesting, pruning, training and

shoot lifting in vineyards in the Czech Republic, Germany, France and Italy. The test materials (containing 5 different active substances) were all fungicides and the crop foliage was full at the times of application and re-entry.

In the exposure studies, 4 to 6 experienced workers were monitored for a full working day at each of 16 sites (a total of 73 workers). Dermal exposure of the hands and body was measured using a combination of inner and outer dosimetry clothing, hand washes and face wipes. In addition, partial nitrile work gloves were worn in two studies (24 workers) but only monitored in one study (20 workers). In the DFR studies, leaf punch samples were taken at each site to correspond (as closely as possible) with the time of worker re-entry. For the harvesting task, re-entry monitoring and DFR measurements took place 31 to 41 days after application and, for the crop maintenance tasks, measurements were made 0 to 2 days after application. All studies were conducted according to Good Laboratory Practice (GLP), followed appropriate guidelines and met standard quality assurance (QA) criteria.

DFR values showed a good correlation with the application rate of the active substances. Additionally, for those studies where it was possible to derive an initial DFR value from a single application (3 out of the 8 studies), a normalised value (µg/cm^2/kg a.s./ha) was calculated for comparison with the EFSA default DFR of 3 µg/cm^2/kg a.s./ha (this default value was based on a low Leaf Area Index of 2 and did not consider crop interception). At most of the sites in these 3 studies, the calculated initial DFR was well below the default value.

Across all studies, potential exposure values (for both the body and the hands) showed a good correlation with the DFR values (higher DFR values were linked to higher levels of worker exposure). This supported the proposed approach for calculating TC values. TC values (75th and 95th percentile) have been calculated for the body and hands for the various tasks monitored in the studies. Total (body and hands) TC values based on the BROV studies are lower than the current default values in the EFSA Guidance Document for both potential worker exposure and assuming the use of workwear with bare hands. Additional TC values reflecting the use of work gloves can be derived from the results.

3. Introduction

The aims of the EFSA guidance document on non-dietary exposure [1] were to review the existing data and current models for operator, bystander, resident and worker exposure and, based on this review, to propose new harmonised approaches. The EFSA Working Group (EFSA WoG) identified the following specific data gap for workers *"The [EFSA] WoG strongly recommends further collection/production of data on specific TC and DFR values to produce more realistic exposure assessments"*.

For grapes in particular, the review conducted for the EFSA guidance document identified a comparative lack of useful data in the open literature on transfer coefficients. In the absence of any European data, the current EFSA recommendation (as it appears in the guidance document) is to use the following TC values based on published literature and US EPA data, as described in Table 1.

Table 1: Current EFSA TC recommendations for grapes

Crop	Nature of task [a]	Main body parts in contact with foliage	TC (cm^2/h), total potential exposure	TC (cm^2/h) assuming arms, body and legs covered (workwear; bare hands)	TC (cm^2/h), covered body (workwear) and gloves (PPE)	Applicable for the following crops
Grapes [b]	Harvesting and other activities (e.g. leaf pulling and tying)	Hand and body	30 000	10 100	No justified proposal possible (data missing)	n.a.

(b): US EPA data were used even if the underline data are not available as it is clear that grape harvesting might be a scenario of concern for which EU data are missing. As for inspection activities, the US EPA values are considered to be appropriate, in absence of supporting data, when compared with the exposure values for other tasks.

As noted in this extract from the guidance document, the data underlying these TC values are unavailable, resulting in a lack of transparency, and the data set is incomplete as there is no separate TC value for the hands. The European Crop Protection Association (ECPA) has identified that this data gap may result in the failure of EU registrations for crop protection products for grapes.

The current EFSA-recommended TC for total potential exposure (30000 cm^2/h) is based on a US published paper (Krieger et al. 1992 [2]) and represents the maximum value for hand and body exposure for re-entry activities in tree fruit (range 4000 to 30000 cm^2/h). Using this value is likely to be very precautionary and is questionable considering the differences between grapes and tree fruit both in terms of the crop structure and the types of re-entry activities involved. Also, this value exceeds the EFSA-recommended potential dermal exposure (PDE) TC value for tree fruit of 22500 cm^2/h.

The current EFSA-recommended TC for total actual exposure (10100 cm^2/h for a worker with bare hands and normal workwear) is based on the values summarised in the US EPA Science Advisory Council for Exposure (ExpoSAC) Policy 3 [3]. These values are, in turn, based on unpublished US Agricultural Re-entry Exposure Task Force data (at present the detailed information is not available for scrutiny by European regulators or EFSA). In the ExpoSAC document, the actual dermal exposure (ADE) (workwear and bare hands) TC of 10100 cm^2/h is described as being applicable to tying/training, hand harvesting and leaf pulling tasks in grapes. The document recommends a higher TC of 19300 cm^2/h for two specific tasks: stem girdling and cane turning (both activities are performed in table grapes only). Appendix G of the EFSA guidance document also refers to this TC value of

19300 cm^2/h but states that it is applicable to "harvesting mechanically assisted": the justification for this is unclear. In addition to the TCs of 10100 and 19300 cm^2/h for the tasks as described above, the ExpoSAC document lists several TC values < 10100 cm^2/h for all other tasks in table, raisin, wine and juice varieties.

Considering the limitations of the currently available data, the ECPA BROV re-entry project aims to use European field studies to establish a set of EU TCs for relevant activities in grapes. To ensure transparency and aid open discussion, ECPA has agreed to provide the studies to regulatory authorities and to cooperate with regulators in the review and interpretation of the study results. In line with the approach taken for the Agricultural Operator Exposure Model (AOEM), the BROV project has established a joint working group which will submit its recommendations to EFSA.

4. Study design

In this project, TCs for various activities are derived from pairs of concurrent worker exposure and DFR studies based on the calculation:

TC (cm^2/h) = exposure (µg) ÷ DFR (µg/cm^2) ÷ exposure time (h)

Sites and tasks

The BROV re-entry database includes five matched pairs of exposure and DFR studies (presented as a total of eight study reports) carried out between 2004 and 2017 (mismatches in two of the study pairs are discussed later). The studies were on wine grapes and covered hand harvesting, pruning, training and shoot lifting in vineyards in the Czech Republic, Germany, France and Italy. In the exposure studies, 4 to 6 experienced workers were monitored for a full working day at each of 16 sites (a total of 73 workers). This extended database is considered to reduce substantially the current uncertainty in TC prediction for European re-entry activities in grape vines.

The details of the exposure and DFR studies are summarised in Table 2.

Table 2: BROV re-entry project, summary of studies

BROV Study ID	No of sites	Activity	Year (field work)	Location	Total number of subjects
1	6 (3 used)	Harvest DFR	2015-16	CZ, DE, FR	17
2	3	Pruning	2016	DE, IT	12
3		DFR			-
4	3	Pruning	2016	DE, FR	12
5		DFR			-
6	3	Pruning Training	2004	FR	12
7		DFR			-
8	4	Pruning Shoot lifting DFR	2017	FR, IT	20

As noted in the Introduction, the US EPA ExpoSAC) Policy 3 [3] recommends the highest ADE TC of 19300 cm^2/h for two specific tasks: stem girdling and cane turning (both activities in table grapes only). As this value exceeds the ExpoSAC ADE TC of 10100 cm^2/h for tying/training, hand harvesting and leaf pulling tasks in grapes, further evidence was sought to confirm that the tasks monitored in the BROV re-entry studies cover the likely worst case for re-entry activities in European vineyards. Based on the photographs of the activities carried out in the studies and publicly available photographs and video clips (on-line search) it appears that the cane turning process is very similar to the shoot lifting task considered in study 8 and the stem girdling activity appears to involve less contact with the treated foliage than many of the tasks investigated in the BROV studies. Information from ECPA members (through the BROV WoG), confirms that in the EU cane turning is associated with mechanically harvested grapes only, and that stem girdling is carried out (typically once a year) to improve berry size and increase sugar content in specific varieties of table or raisin grapes. Further information (with photographs) on the relative levels of worker exposure associated with a range of tasks in grapevines is provided in a UIPP

publication on good practice in grape production [4]. Overall, this information adequately demonstrates that the BROV studies covered an appropriate and representative range of tasks.

Test materials

The test materials were all fungicides approved for use on grapevines and were formulated as water-dispersible granules (3 study pairs), a suspension concentrate (1 study pair) or an oil-in-water emulsion (1 study pair). The products contained in total 6 different active substances, 5 of which were analysed in the studies.

Details of the plant protection products used are summarised in Table 3.

Table 3: Test materials

BROV Study ID	Product	Active	Foliar DT50	Formulation	Use
1	Melody Combi (Sirbel UD)	Iprovalicarb (+ Folpet, not analysed)	≥30 days (Renewal*)	WG 90 g/kg	Fungicide
2	BAS 553 01 F	Dimethomorph Dithianon	Dimethomorph: 7 days (Renewal*) Dithianon: 20 days (PPDB**)	WG 150 + 350 g/kg	Fungicide
3					
4	BAS 605 04 F	Pyrimethanil	<2 days (Renewal*)	SC 411.7 g/l	Fungicide
5					
6	Indar EW	Fenbuconazole	4.4 days (BROV)	EW 50 g/l	Fungicide
7					
8	Melody Combi (Sirbel UD)	Iprovalicarb	≥30 days (Renewal*)	WG 90 g/kg	Fungicide

* Value proposed in EFSA peer review process for the renewal of the active substance.
** Indicative value proposed by the on-line Pesticide Properties Database: a comprehensive relational database of pesticide physicochemical and ecotoxicological data developed with EU funding by the University of Hertfordshire UK.

The foliar DT50 values quoted above for the active substances are only intended to be indicative values for contextual information, and alternative values may be available from other sources. Importantly, the study involving harvesting activities (study 1) used an active substance with a sufficiently long half-life to serve as an appropriate analyte considering the extended interval between the time of application and re-entry monitoring at harvest time (i.e. to avoid errors and uncertainty caused by low or non-quantifiable DFR levels at the sampling time).

Exposure study methodology

The methodology used in the exposure monitoring studies was based on the recommendations of the OECD Guidance Document (97)148 [5]. The study subjects at each site (4 to 6 per site) were experienced workers or less experienced seasonal/casual workers under supervision. The duration of the exposure monitoring (between 4 hours and 7 hours 45 minutes) reflected the actual duration of the task being performed or a full working day. The exposure studies considered the dermal route only (additional air monitoring in some of the studies has been disregarded for the purposes of this project) using the range of dosimeters summarised in Table 4.

Table 4: Exposure monitoring matrices

Dermal exposure component	Monitoring matrix	Description	Comments
Potential body exposure (upper body)	Work jacket	Polyester cotton (65%:35%) blend long-sleeved jacket	Worn only in study 1 at sites 1 and 2 and study 8. In study 1 this was worn in conjunction with a shirt worn between the outer and inner dosimeters: in this case the residues on the shirt have been considered as ADE. In study 8 the work jacket was worn over the inner dosimeter (no mid-layer was worn). This dosimeter was sectioned to determine the distribution of contamination on the torso and arms.
Potential body exposure [1]	Outer whole-body dosimeter	Polyester cotton (65%:35%) blend long-sleeved shirt and long trousers or coverall	Sectioned to allow the distribution of contamination to be determined.

Dermal exposure component	Monitoring matrix	Description	Comments
Actual body exposure	Inner whole-body dosimeter	Polyester cotton (65%:35%) blend long-sleeved tee-shirt and long johns	Sectioned to allow the distribution of contamination to be determined. Not worn in study 6 (PDE only measured in this study).
Potential hand exposure when gloves worn (in addition to hand residues)	Partial nitrile work gloves [2]	Protective nitrile coating on palms of hands and fingers, with uncoated fabric on back of gloves to allow breathability	Worn in study 2, site 1 and study 8 only (but only sampled in the latter). Residues determined by solvent extraction at end of the study.
Actual hand exposure	Hand washes [3]	Hands washed over bowl	Sequential use of two washes each using detergent solution
Face/neck exposure	Face/neck wipes	Multi-layer cotton gauze pads moistened with detergent solution	Sequential use of two wipes
	Dust mask [4]	Disposable filtering facepiece respirator	Used by a single subject in study 2, site 1. Not used in the calculations as the results indicated that this was an unreliable dermal dosimeter.

[1] The shirt dosimeter was treated as an inner dosimeter (reflecting ADE) in the exposure calculations when a work jacket was also worn (only applies to study 1, sites 1 and 2). This differs from the approach taken in the study report itself which considered both the outer jacket and shirt as outer dosimeters (to quantify potential rather than actual exposure).

[2] The BROV WoG was confident that the type of gloves used in these studies is representative of those typically worn when carrying out these tasks. An EN Standard is under development for this type of glove which, if agreed, will allow the appropriate type of glove to be specified and will offer re-assurance that the predicted (or appropriate default) levels of protection can be achieved.

[3] Although one worker in study 1 used a single nitrile glove, the study report clarified that this was only to protect a hand wound and the calculations for this individual (as for the other workers in this study) were based on potential hand exposure (sum of glove residue and hand wash).

[4] Although one worker in study 2 used a dust mask, the data confirm that this sampling medium was not a reliable dosimeter for predicting dermal exposure to the face (see later comments).

DFR study methodology

The methodology used in the DFR studies followed the recommendations of the US EPA Guidance Series 875 [6]. DFR samples were, ideally, taken at the same time and in the same crop as the associated re-entry activity: deviations from this ideal situation are identified later in this report. For calculating a TC value, only a single DFR sample timing (concurrent with

the re-entry event) was necessary and, although study 7 reported the DFR decline resulting from each of 3 sequential applications (2 of which were after the re-entry event), data on the decline of DFR are outside the scope of the BROV project and have not been considered further in this report. The sampling method involved taking leaf punch samples from foliage within the worker contact zone. The punched area of each disc (expressed as the 2-sided leaf surface area) was 5 cm^2 (study 1) or 10 cm^2 (all other studies). Each sample represented a 2-sided area of 400 cm^2 in total, equivalent to 80 leaf discs (study 1) or 40 leaf discs (all other studies) and 3 replicate sets of samples (5 replicates for study 1) were taken at each sampling event. Foliar residues were dislodged from leaf discs using an aqueous solution (0.01%) of Aerosol OT-100 with an extraction volume of 200 ml per sample.

Quality assurance and method validation

The field and laboratory phases of all studies were GLP compliant (apart from some of the weather monitoring data). All studies also complied with the relevant guidance (OECD (97)148 for exposure measurements [5], EPA Series 875 [6] for DFR measurements and SANCO 3029/99 [7] for residues methods of analysis). Additionally, the UK HSE has undertaken a 2-stage validation process. Stage 1 of this process was to confirm that the re-entry database (available as an Excel workbook), which provides a structured summary of the information reported in the individual study reports and an analysis of these data, was an accurate reflection of the data presented in the study reports and was performing calculations correctly. Stage 2 of this process was to confirm that the methods of extraction and analysis were appropriate for each analyte and fit for purpose.

In accordance with OECD (97)148, mean procedural (laboratory) recoveries for method validation were considered to be acceptable when in the range of 70 to 110% with a RSD $\leq$ 20%.

Field recovery samples for exposure studies

In line with current practice, and following the approach taken for the bystander / resident part of the BROV project, residues measured in exposure monitoring samples were corrected for incomplete recovery only when the field recovery for that matrix was <95% for the relevant fortification level at that site. The exposure field recovery samples used either 2 or 3 fortification levels and an untreated control (UTC) for each matrix at each site, with 3 replicates at all sites apart from study 8 (the latter having 1 replicate analysed out of the 3 replicates prepared for each spiking level and the UTC for each matrix at each site). Therefore, for study 8, mean recoveries for each matrix and spiking level were calculated across all sites. The BROV WoG was content that the lack of replication for the field recovery samples in study 8 was not a concern for the reliability of the monitoring results. Field recovery samples (other than hand-wash solutions) were exposed to environmental conditions, in an area free from contamination, for the duration of the exposure monitoring period. Inner dosimeter samples were covered by a layer of unfortified outer dosimeter

material to reflect the way in which the exposure monitoring samples would have been exposed to environmental conditions over the working day.

Field recovery samples for DFR studies

In line with current practice, and following the approach taken for the bystander / resident part of the BROV project, residues measured in DFR samples were corrected for incomplete recovery only when the field recovery was <95% for the relevant fortification level at that site. The DFR field recovery samples were produced using either 2 or 3 fortification levels and an untreated control (UTC) at each site, with 3 replicates at all sites apart from study 8. The latter had a single high-level spike at each site, a single control at 3 out of 4 sites (and 2 control replicates at the other site), and 1 or 2 low level replicates per site. The BROV WoG considered this to be level of replication to be acceptable.

Travel recovery samples for exposure studies

Travel recovery samples, which according to the guidance are optional, were generated in some of the exposure studies but not always for all sites, matrices or spiking levels. These additional samples are intended to quantify degradation or loss of the analyte during transport and can be of value in the event of very low recoveries in the field fortifications. When undertaken, these travel recovery samples were produced in the same way and at the same time as the field recovery samples but, unlike the field recovery samples, the travel recovery samples were not exposed to environmental conditions but were packed and frozen immediately after fortification. These samples were shipped and stored with the field recovery and field monitoring samples.

Application and sampling details

The application details in the studies are summarised in Table 5.

Table 5: Application equipment and site details

BROV Study ID	Type	Application equipment (from description in study reports)	Plot size (ha)	Same sites for exposure and DFR [1]
1	Exposure + DFR	Commercial tractor-mounted and trailed broadcast air-assisted sprayers	0.8 – 1.5	Yes
2	Exposure	Trailed axial, crossflow, ducted broadcast air-assisted and vertical boom recirculating (tunnel) sprayers	4.0 – 4.5	No
3	DFR	Knapsack mist-blower	0.02 – 0.03	
4	Exposure	Commercial broadcast air-assisted crossflow and ducted sprayers	2.0 – 5.0	No
5	DFR	Knapsack mist-blower	0.01 – 0.03	
6	Exposure	Commercial broadcast air-assisted directed sprayer	1.5 – 2.0	Yes
7	DFR		0.006 – 0.007	
8	Exposure + DFR	Axial, crossflow, ducted, vertical boom broadcast air-assisted and vertical boom recirculating (tunnel) sprayers	1.3 – 4.1	Yes

[1] Where the same site was used for the exposure and DFR studies, the DFR sampling was carried out on a sub plot of the treated area. Where different sites were used for the exposure and DFR studies, detailed consideration has been given (below) to ensure that application rates, application timings, re-entry timings, DFR sample timings, crop details and environmental parameters were an appropriate match between the two sites.

Typical commercial equipment was used in all studies apart from in the DFR studies 3 and 5 in which knapsack mist-blowers were used. As the DFR phase of these studies was carried out on small plots, the use of hand-held equipment (as widely accepted for efficacy and residues studies) appears justified. Although commercial-scale application equipment was used in the associated exposure studies (studies 2 and 4), the BROV WoG did not consider this mismatch in the type of application equipment to be of concern. However, to confirm whether these mismatches had an influence on the study results, the TC calculations have been performed both with and without the mismatched studies (Appendix D).

Details of the application schedule and dates of DFR sampling and re-entry events are summarised in Table 6. The crop foliage was full at the times of application and re-entry. For the harvesting task, re-entry monitoring and DFR measurements took place 31 to 41 days after application and, for the crop maintenance tasks, measurements were made 0 to 2 days after application. When reported, growth stages (BBCH) at application, re-entry and DFR sampling are included in Table 6. To reflect the worst case, the target was to conduct all studies using the maximum authorised application rate and number of treatments. However, reduced rates were used at some sites based on crop and disease development, following normal commercial practice.

Table 6: Application and sampling schedule

Study	**Site**	**Application date (Growth stage BBCH)**				**Re-entry date (Growth stage)**	**DFR date (Growth stage)**
1	1	01/06/15	11/06/15	22/06/15	05/08/15	41 DAA4 (GS 89)	41 DAA4 (GS 89)
	2	27/07/15	04/08/15	17/08/15	27/08/15	31 DAA4 (GS 89)	31 DAA4 (GS 89)
	5	08/07/16	19/07/16	28/07/16	29/08/16	31 DAA4 (GS 89)	31 DAA4 (GS 89)
2	1	09/05/16 (GS 55)	20/05/16 (GS 57)	10/06/16 (GS 71)	-	0 DAA3 (GS 71)	
	2 [1]	06/06/16	15/06/16	27/06/16 (GS 71)	-	1 DAA3 (GS 73)	
	3	09/06/16	19/06/16	29/06/16 (GS 75)	-	1 DAA3 (GS 75)	
3	1	09/05/16 (GS 55)	20/05/16 (GS 57)	10/06/16 (GS 71)	-		0 DAA3 (GS 71)
	2 [1]	07/06/16 (GS 55)	18/06/16 (GS 63)	28/06/16 (GS 71)	-		0 DAA3 (GS 71)
	3	09/06/16 (GS 55-58)	19/06/16 (GS 61-65)	29/06/16 (GS 69-71)	-		1 DAA3 (GS 69-71)

Study	Site	Application date (Growth stage BBCH)				Re-entry date (Growth stage)	DFR date (Growth stage)
4 [2]	1	25/07/16 (GS 79)	-	-	-	1 DAA1 (GS 79)	
	2	19/07/16 (GS 79)	-	-	-	1 DAA1 (GS 79)	
	3	18/07/16 (GS 79)	-	-	-	1 DAA1 (GS 79)	
5 [2]	1	26/07/16 (GS 79)	-	-	-		1 DAA1 (GS 79)
	2	21/07/16 (GS 79)	-	-	-		1 DAA1 (GS 79)
	3	20/07/16 (GS 75-77)	-	-	-		1 DAA1 (GS 75-77)
6 [3]	1	23/06/04 (GS 72-73)	-	-	-	2 DAA1 (GS 72-73)	
	2	29/06/04 (GS 75)	-	-	-	1 DAA1 (GS 75)	
	3	01/07/04 (GS 73)	-	-	-	1 DAA1 (GS 73)	
7 [3]	1	23/06/04 (GS 72-73)	07/07/04	21/07/04	-		2 DAA1 (GS 72-73)
	2	29/06/04 (GS 75)	16/07/04	30/07/04	-		1 DAA1 (GS 75)
	3	01/07/04 (GS 73)	15/07/04	29/07/04	-		1 DAA1 (GS 73)

Study	Site	Application date (Growth stage BBCH)				Re-entry date (Growth stage)	DFR date (Growth stage)
8	1	23/05/17 (GS 61)	-	-	-	2 DAA1 (GS 61)	2 DAA1 (GS 61)
	2	12/06/17 (GS 65)	-	-	-	2 DAA1 (GS 65)	2 DAA1 (GS 65)
	3	20/06/17 (GS 63-75)	-	-	-	2 DAA1 (GS 63-71)	2 DAA1 (GS 63-71)
	4	18/06/17 (GS 75)	-	-	-	2 DAA1 (GS 75)	2 DAA1 (GS 75)

[1] Study 2 (exposure) and study 3 (DFR) were performed at different sites. The application dates at site 2 in these studies were not identical and, although the re-entry event was on the same day as DFR sampling, the re-entry date was 1 day after application 3 whereas the DFR sampling date was 0 days after application 3. Considering the indicative DT50s of the active substances in these studies (7 days and 20 days) this mismatch is not considered to be a major problem.

[2] Study 4 (exposure) and study 5 (DFR) were performed at different sites. The application dates at all sites in these studies were not identical. However, for all sites the re-entry event and the DFR sampling date were the same time after treatment (1 day after the single application in all cases).

[3] Study 6 (exposure) and study 7 (DFR) were performed at the same sites. Although the DFR study reported 3 applications (with a range of appropriate sample timings), the worker re-entry event was either 1 or 2 days after application 1. So, for the purposes of calculating a TC, only the first application has been considered.

In addition to the mismatches in terms of site location, application date and application method identified above for the paired studies 2 and 3 and the paired studies 4 and 5, there were also some mismatches in terms of grape variety, application rates and spray volumes. These mismatches are summarised in Table 7.

Table 7: Mismatches in paired exposure and DFR studies

Study parameter	Site	Paired studies 2 and 3		Paired studies 4 and 5	
		Study 2 Exposure	**Study 3 DFR**	**Study 4 Exposure**	**Study 5 DFR**
Location	1	Sandra, Veneto, IT		St. Martial, Aquitaine, FR[1]	St Pardon de Conques, Aquitaine, FR [1]
	2	Merdingen, Baden Württemberg, DE		Merdingen, Baden Württemberg, DE [2]	Breisach am Rhein, Baden Württemberg, DE [2]
	3	Heuchelheim, Rheinland-Pfalz, DE [3]	Partenheim, Rheinland-Pfalz, DE [3]	Heuchelheim, Rheinland-Pfalz, DE [4]	Partenheim, Rheinland-Pfalz, DE [4]
Grape variety	1	Corvina		Merlot, Cabernet Franc	Merlot
	2	Blauer Spätburgunder	Müller Thurgau	Blauer Spätburgunder	
	3	Spätburgunder Merlot	Weisser Burgunder	Dornfelder, Riesling, Merlot, Pinot Noir	Weisser Burgunder
Dose product T1 (l or kg/ha)	1	1.50	1.39	2.50	2.49
	2	1.50	1.599	2.00	2.08
	3	0.96	1.395	2.00	1.95
Dose product T2 (l or kg/ha)	1	1.50	1.483	Not applicable	
	2	1.50	1.691		
	3	1.20	1.519		
Dose product T3 (l or kg/ha)	1	1.50	1.367		
	2	1.50	1.425		
	3	1.44	1.481		
Total dose product (l or kg/ha)	1	4.50	4.24	2.50	2.49
	2	4.50	4.715	2.00	2.08
	3	3.60	4.395	2.00	1.96
Spray volume T1 (l/ha)	1	300	371	200	249
	2	350	320	250	208
	3	300	372	300	293
Spray volume T2 (l/ha)	1	300	396	Not applicable	
	2	450	338		
	3	400	405		
Spray volume T3 (l/ha)	1	300	364		
	2	550	285		
	3	400	395		

[1] Distance between the sites of the exposure and DFR parts of the study is estimated to be approximately 10 km using on-line map search information

[2] Distance between the sites of the exposure and DFR parts of the study is estimated to be approximately 8 km using on-line map search information

[3, 4] Distance between the sites of the exposure and DFR parts of the study is estimated to be approximately 45 km using on-line map search information

Where different sites were used in the exposure and DFR parts of each study, the locations were estimated to be between 8 and 45 km apart (as summarised above). Appropriate weather data (as reported in the detailed study summaries) were generated at each site. Although all these mismatches raise some uncertainties when deriving a TC from the exposure and DFR measurements, the most significant inconsistencies were considered by the BROV WoG to relate to the differences in application rate (affecting paired studies 2 and 3 only) and sampling dates (affecting paired studies 4 and 5 only). Although the application dates in study 4 (exposure) and study 5 (DFR) were not identical, for all sites in these studies the re-entry event and the DFR sampling date were the same time after treatment (1 day after the single application in all cases). So, even though the analyte in these studies had an indicative DT50 <2 days, the mismatch in the application dates (by between 1 and 2 days) is not considered to be of importance. In addition, it was specifically noted whether any rainfall occurred between the exposure and DFR sampling dates when these dates were not the same.

As the aim of the project is to calculate a TC, the mismatch in application rates is of most concern when the higher rate is used in the DFR study (a higher rate in the corresponding exposure study would result in a more precautionary TC). This situation arose for the paired studies 2 and 3 at sites 2 and 3 only, although the differences in application rate were slight. To address this, it would be possible to scale up the exposure values to account for the higher application rate in the corresponding DFR study. However, the BROV WoG concluded that this was unnecessary as the foliar residues at the time of re-entry/DFR sampling in this study resulted largely from the final application, and this final application rate matched in the exposure and DFR parts of the study. The BROV WoG also concluded that no action was necessary to address the other mismatches identified above. However, to confirm whether these mismatches had an influence on the study results, the TC calculations have been performed both with and without the mismatched studies (Appendix D).

Sample handling

Full details of the removal and sectioning of exposure dosimeters, the packaging of exposure and DFR samples and subsequent placement in frozen storage were reported in each study. Further information is provided in the detailed study summaries (Appendix A).

Environmental (weather) monitoring (non-GLP)

Environmental parameters (air temperature, relative humidity and rainfall) were recorded at each site during the trial period (i.e. from the first application to the final exposure and/or DFR sampling event). In addition, weather records covering the study period were provided from the nearest official meteorological station. Further information is provided in the detailed study summaries (Appendix A).

5 Methods of analysis

The analytical methods for each active substance were reported in the individual study reports (with additional confirmatory information being requested from the study owner when clarification was required during the review by the UK HSE). These methods have been assessed to ensure they were conducted in accordance with SANCO/3029/99 rev.4 [7] and the method validation is reported in the detailed study summaries (Appendix A).

6 Results

The key data from each study report has been entered into a MS Excel workbook (the BROV re-entry database) to allow calculations to be carried out in the same way for each study and to derive overall TC values. The BROV re-entry database was compiled by the BROV WoG from the original study reports and has been validated by the UK HSE by carrying out the following checks:

- All non-calculated values and information accurately reflect the contents of the study reports
- Values reported below the limit of quantification (LOQ) or limit of detection (LOD) have been correctly assigned the relevant LOQ and LOD values for each active substance and sampling matrix
- The relevant recovery adjustments have been made to the exposure and DFR measurements when required
- All formulae and calculated values are correct

The BROV Re-entry Database Version 15 is available as a separate document to accompany this report.

Procedural recoveries and method validation

All procedural recoveries were within the acceptable range for method validation of 70-110% (except for a value of 115% for one fortification level of the hand wash solution in study 6) with RSDs within the acceptable limit of 20%. All methods of extraction and analysis were checked and confirmed to be acceptable. Full information is provided in the detailed study summaries (Appendix A).

LOQ and LOD

The LOQ (and, where reported, the LOD) for each analyte and sampling matrix is summarised in Table 8. Further information is provided in the detailed study summaries (Appendix A).

Table 8: LOQ and LOD details

LOQ and LOD µg/sample						
Study		1	2 and 3	4 and 5	6 and 7	8
Analyte		Iprovalicarb	Dimethomorph Dithianon	Pyrimethanil	Fenbuconazole	Iprovalicarb
Outer layer	LOQ	10	0.01	0.01	7.5	0.5
	LOD	Not stated	0.003	0.002	Not stated	
	Sample	300 cm^2	100 cm^2	100 cm^2	Whole section	100 cm^2
Mid layer	LOQ	1.0	Not applicable			
	LOD	Not stated				
	Sample	300 cm^2				
Inner layer	LOQ	0.5	0.01	0.01	Not applicable	0.5
	LOD	Not stated	0.003	0.002		Not stated
	Sample	300 cm^2	100 cm^2	100 cm^2		100 cm^2
Gloves	LOQ	50	0.1	Not applicable		50
	LOD	Not stated				Not stated
	Sample	1 glove	1 glove			1 glove
Hand wash	LOQ	0.1	1	1	15	0.2
	LOD	Not stated	0.3	0.06	Not stated	
	Sample	100 ml	1 litre	1 litre	1 litre	1 litre
Face wipes	LOQ	0.1	0.01	0.01	0.75	0.02
	LOD	Not stated		0.003	Not stated	Not stated
	Sample	1 pad (100 cm^2)	2 pads (each 100 cm^2)	2 pads (each 100 cm^2)	2 pads (each 100 cm^2)	2 pads (each 100 cm^2)
Leaf disc wash	LOQ	0.01	10	10	50	2
	LOD	Not stated	1.3	1.5	Not stated	
	Sample	1 litre	1 litre	1 litre	1 litre	1 litre

For the AOEM project, the approach was to use ½ LOQ for values between LOQ and LOD and 0.01 µg/sample as a default value for the LOD. For this project (as for the BROV bystander and resident project) a default LOD of 0.01 µg/sample is not appropriate as this is no lower than the LOQ for several of the analytes in some matrices. Also, the AOEM approach of substituting a ½ LOQ value is not in line with current practice for residues studies. Therefore, in line with the approach taken for the bystander and resident part of the BROV project, measured values between LOQ and LOD have been assigned a value equivalent to the LOQ and values reported as not detected (ND) were assigned a value equivalent to the LOD. In practice, very few of the exposure measurements (7 face wipe samples in study 6) and none of the DFR measurements, other than untreated control (UTC) samples, were reported to be below the LOQ for the relevant analyte and matrix, and the above approach for assigning values has not had an influence on the calculated 75^{th} and 95^{th} percentile values.

Field recovery results exposure samples

Exposure monitoring samples were corrected for incomplete recovery only when the field recovery for that matrix was <95% for the relevant fortification level at that site.

All UTC samples in the exposure studies were reported to have residues <LOQ except for study 2 (one sample replicate at the LOQ) and study 4 (one sample replicate >LOQ). Therefore, no correction was required for residues in the UTC. However, in study 4, residue levels were not reported for face-wipe controls or hand-wash controls and, in study 8, the actual residue levels were not reported for any of the control or fortified samples (only the percentage recovery was reported). The BROV WoG was content with all these aspects of the field recovery data.

Field recovery results DFR samples

DFR measurement samples were corrected for incomplete recovery only when the field recovery was <95% for the relevant fortification level at that site. Although some recovery values for fortified samples were adjusted for low levels of residues detected in the UTC samples, there was often considerable variation in residues between the control replicates at each site. However, the BROV WoG noted that this adjustment had no impact on the DFR calculations but only served to reduce some high reported recovery levels (some >100%) to more realistic levels. Therefore, this approach of applying a correction to high recoveries in the fortified samples if residues were detected in the corresponding UTC samples was considered appropriate by the BROV WoG.

Studies 7 and 8 reported only a summary of the recovery results expressed as an overall final percentage recovery value (which may or may not have been adjusted for any residues in the UTC) and not the actual recovery values. The BROV WoG judged this to be an acceptable way of presenting the data.

Travel recovery samples for exposure studies

Travel recovery values (not conducted for all studies or, when reported, not done for all matrices/spiking levels) were, as expected, generally slightly higher than the corresponding field spike for matrices exposed to environmental conditions after field fortification. Mean recoveries for transit samples were within 70 to 110% of the fortification dose and mean RSD values were <20% in all studies.

Environmental (weather) monitoring (non-GLP)

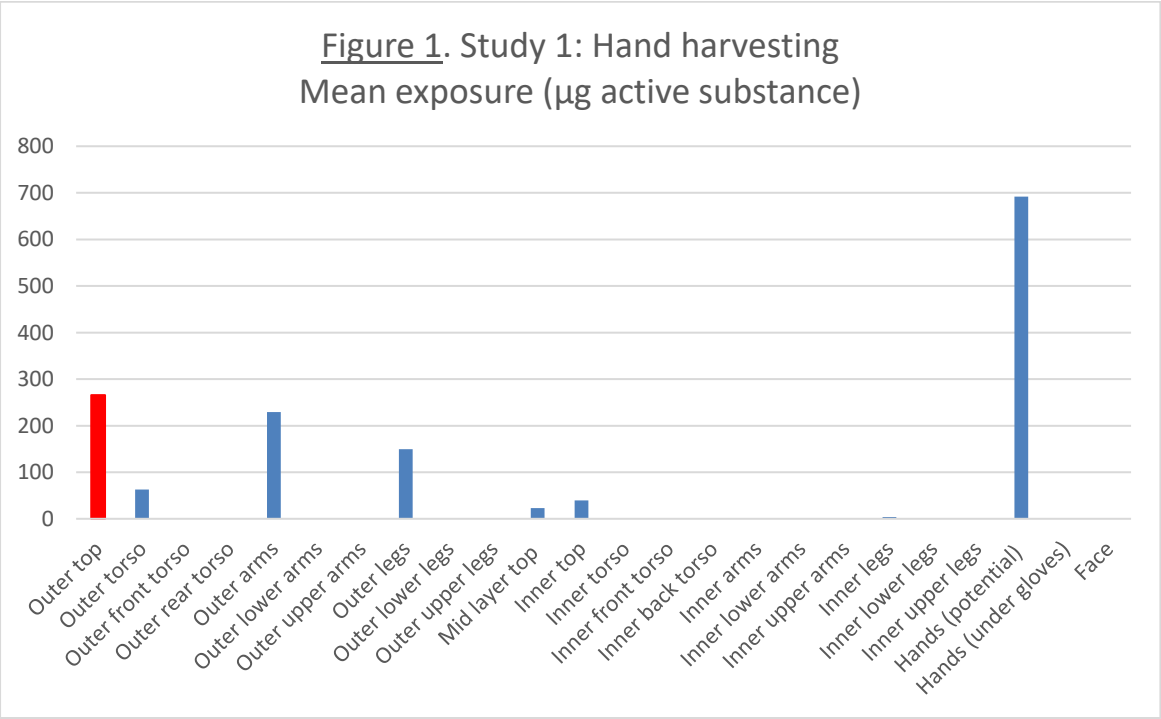
Data on air temperature, relative humidity and rainfall recorded at each site during the trial period did not indicate any adverse conditions likely to affect the study outcome. Similar evidence was provided by additional data from the nearest official meteorological station.

Where different sites were used in the exposure and DFR parts of each study, the locations were estimated to be between 8 and 45 km apart (as summarised above). Appropriate weather data (as reported in the detailed study summaries) were generated at each site and no adverse conditions affecting a specific site were noted.

It was also noted that no rainfall occurred between the exposure and corresponding DFR sampling dates when these dates were not the same in the paired studies.

Exposure results

The results of each exposure study, expressed as mean residue values (corrected for field recovery as appropriate) for all subjects at all sites, are summarised in the charts below. These exposure results have not been normalised with respect to the application rate and so give an indication of the distribution of residues associated with each task but do not provide a comparison of the absolute exposure levels between studies. Such a comparison of the different tasks is provided by the TC calculations. In the following bar charts, which show the distribution of residues in each exposure study, the individual dosimeter sections (as analysed in each study) are represented by blue bars. Totals for a region of the body are represented by red bars and, where relevant, sub-totals for smaller body areas are represented by green bars.

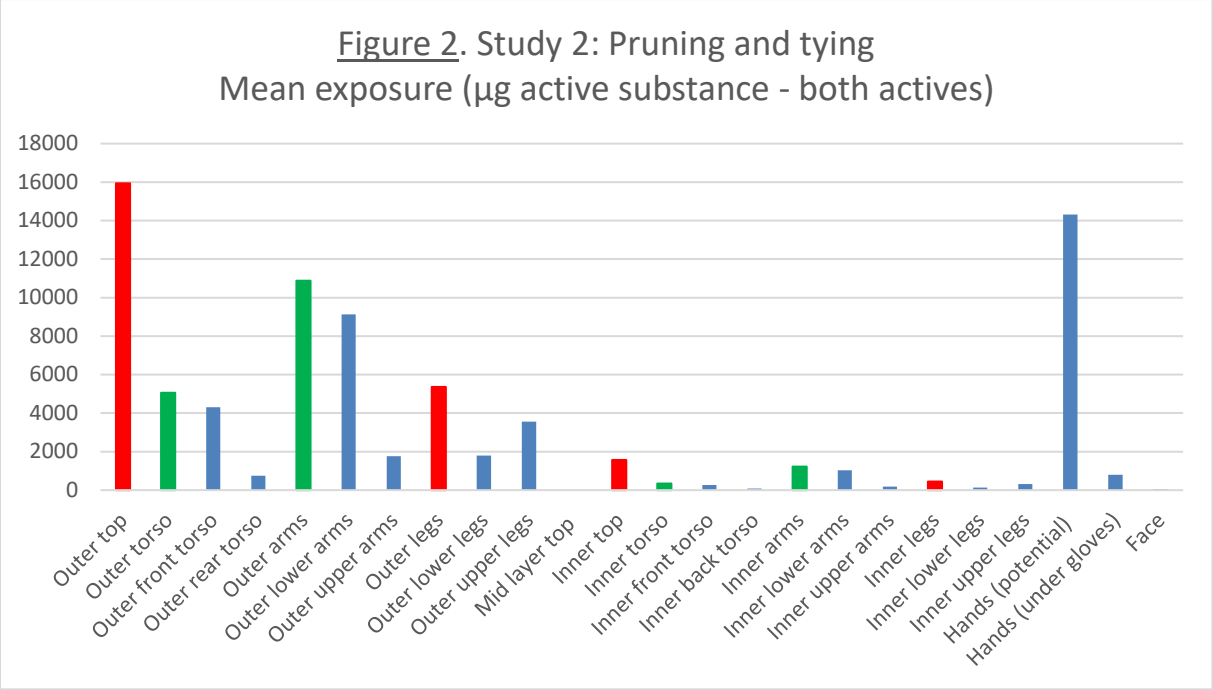


In study 1, the outer top dosimeter was sectioned (outer jacket but not shirt – see below) into torso and arms but these sections were not divided further (hence the absence of values for outer front and rear torso and outer upper and lower arms). Similarly, the outer leg dosimeter was not divided further (hence the absence of values for the outer upper and lower legs). The mid-layer dosimeter results are from the shirt at sites 1 and 2 (i.e. when a jacket was worn over this dosimeter). However, the shirt was treated as the outer top dosimeter at site 3 (i.e. when a jacket was not worn over this dosimeter). The inner top dosimeter was not divided into sections (hence the absence of values for the torso and arms). Similarly, the inner leg dosimeter (long johns) was not divided further (hence the absence of values for the inner upper and lower legs). Gloves were not worn in this study* (hence the absence of a value for hands under gloves).

*One worker in study 1 used a single nitrile glove (to protect a hand wound) and the calculations for this individual (as for the other workers in this study) were based on potential hand exposure (sum of glove residue and hand wash). For this worker, the residues on hands (under gloves) and the potential hand exposure (hands + gloves) are both within the range of potential hand exposure levels for other workers in this study. Therefore, the BROV WoG agreed that a separate consideration of actual hand exposure for this worker was not required.

Although one subject in the study 1 had a missing dosimeter (inner long johns), the overall ADE for this subject was within the range of values for other subjects and the BROV WoG agreed that it was inappropriate to correct the ADE to compensate for the missing measurement as it would have a negligible impact on the overall calculations.

The exposure distribution shows that the harvesting task carried out in this study resulted mainly in contamination to the hands. Dermal exposure to the body was mainly on the arms. Residues on the legs were higher than those measured on the torso.

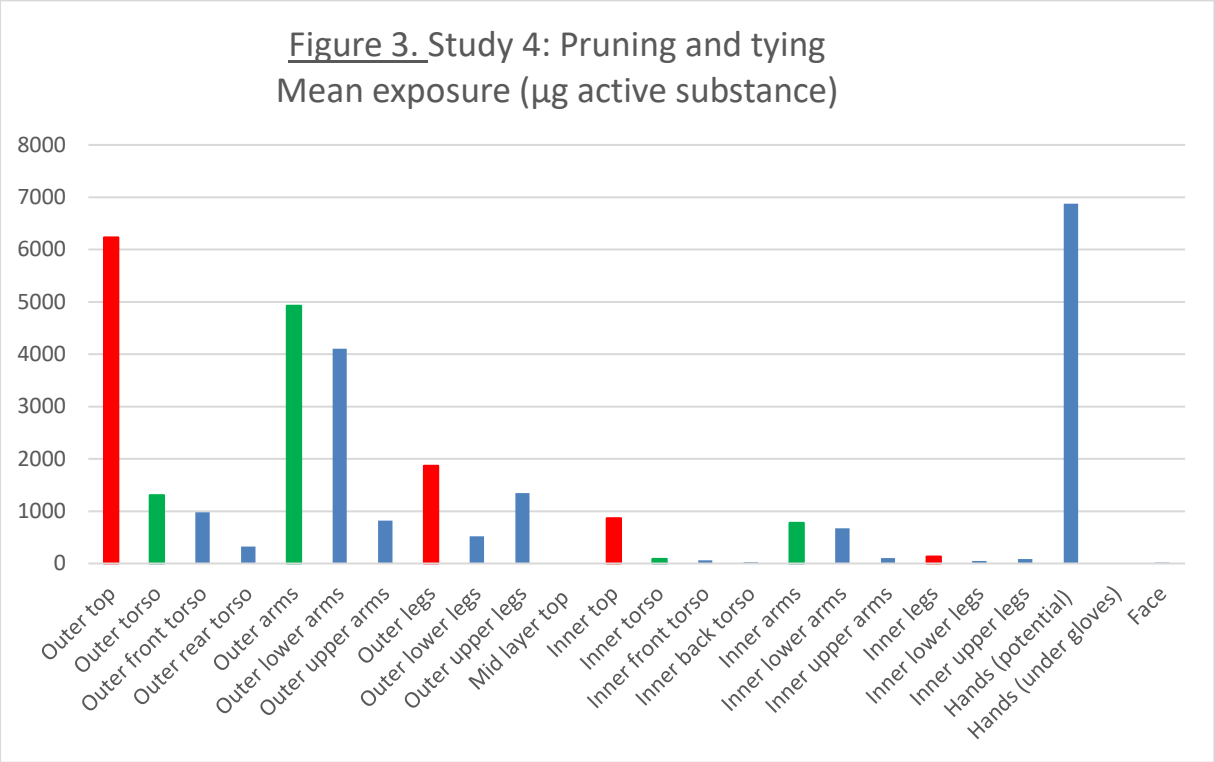


In study 2, the outer top dosimeter was sectioned into torso and arms and these sections were divided further into outer front and rear torso and outer upper and lower arms. Similarly, the outer leg dosimeter was divided further into outer upper and lower legs. A mid-layer dosimeter was not worn in this study. The inner top dosimeter was divided into sections for the torso and arms and these sections were divided further into inner front and back torso and inner upper and lower arms. Similarly, the inner leg dosimeter (long johns) was divided into inner upper and lower legs. Part-nitrile gloves were worn in this study only at site 1 but were not monitored (hence the value for hands under gloves applies only to site 1 and the value for potential hand exposure applies only to sites 2 and 3).

The exposure results for the outer dosimeter reported in study 2 were already corrected by the study authors for an assumed overall recovery level of 91.3%. Therefore, a back calculation was carried out to derive uncorrected outer dosimeter values which were then re-corrected as appropriate (i.e. for recoveries <95%).

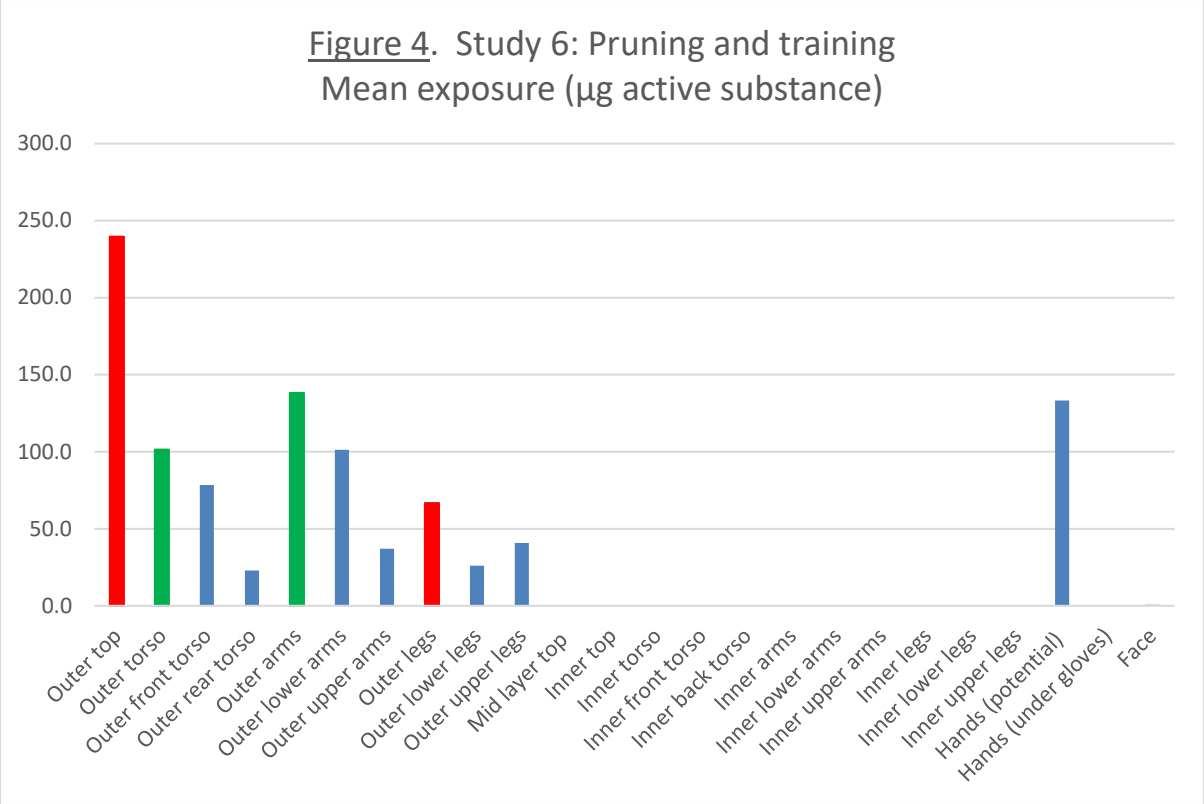
A dust mask was worn by 1 subject in study 2 at site 1. This was used (in combination with face/neck wipes) to quantify dermal exposure of the face. Residue levels on the dust mask were high in comparison to face wipes confirming that the use of a dust mask as a dermal dosimeter was unreliable as residues on this matrix were likely to have been collected mainly due to breathing. No fortification/recovery data were reported for dust masks to validate their use as a dosimeter. The BROV WoG also noted that the face wipe residues for the 2 study subjects using dust masks were within the normal range of other subjects without dust masks. Considering this, the BROV WoG agreed to exclude the dust mask measurements from the exposure calculations.

The exposure distribution shows that the pruning and tying tasks carried out in this study resulted mainly in contamination of the hands and lower arms. Contamination was also seen on the front torso and upper legs.



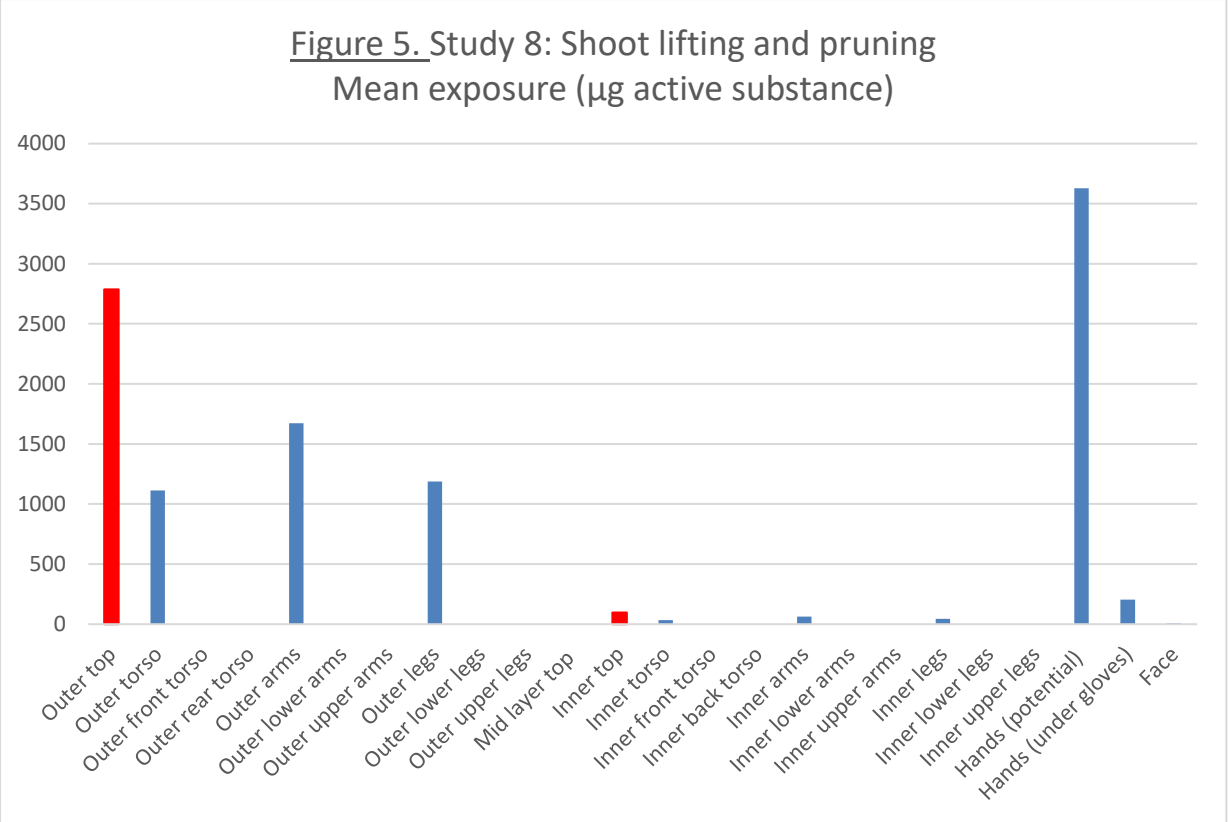
In study 4, the outer top dosimeter was sectioned into torso and arms and these sections were divided further into outer front and rear torso and outer upper and lower arms. Similarly, the outer leg dosimeter was divided further into outer upper and lower legs. A mid-layer dosimeter was not worn in this study. The inner top dosimeter was divided into sections for the torso and arms and these sections were divided further into inner front and back torso and inner upper and lower arms. Similarly, the inner leg dosimeter (long johns) was divided into inner upper and lower legs. Gloves were not worn in this study (hence the absence of a value for hands under gloves).

The exposure distribution shows that the pruning and tying tasks carried out in this study resulted mainly in contamination of the hands and, to a lesser extent, the lower arms. Contamination was also seen on the front torso and upper legs.



In study 6, the outer top dosimeter was sectioned into torso and arms and these sections were divided further into outer front and rear torso and outer upper and lower arms. Similarly, the outer leg dosimeter was divided further into outer upper and lower legs. No mid-layer or inner dosimeters were worn in this study (hence the absence of values for ADE of the body). Gloves were not worn in this study (hence the absence of a value for hands under gloves).

The exposure distribution shows that the pruning and training tasks carried out in this study resulted mainly in contamination to the hands and arms (mainly lower arms) and, to a lesser extent, the torso (mainly front torso). Contamination was also seen on the upper legs.



In study 8, the outer top dosimeter was sectioned into torso and arms, but these sections were not divided further (hence the absence of values for outer front and rear torso and outer upper and lower arms). Similarly, the outer leg dosimeter was not divided further (hence the absence of values for the outer upper and lower legs). A mid-layer was not worn in this study. The inner top dosimeter was divided into sections for the torso and arms, but these sections were not divided further (hence the absence of values for the inner front and back torso and inner upper and lower arms). Similarly, the inner leg dosimeter (long johns) was not sectioned (hence the absence of values for the upper and lower legs).

Gloves (partial nitrile work gloves) were worn in this study and levels of both potential hand exposure and hand exposure under gloves were reported. The BROV WoG was confident that the type of gloves used in this study was representative of those typically worn when carrying out similar tasks. An EN Standard is under development for this type of glove which, if agreed, will allow the appropriate type of glove to be specified and will offer re-assurance that the predicted (or appropriate default) levels of protection can be achieved.

The exposure distribution shows that the shoot lifting and pruning tasks carried out in this study resulted mainly in contamination to the hands. Dermal exposure to the body, which was also significant, was mainly on the arms, with lower levels on the legs and torso. Based on the mean exposure values presented in the graph, the partial nitrile gloves were offering a level of protection >90% (i.e. <10% penetration and transfer of glove residues to the hands).

Looking at the exposure studies as a whole, levels of exposure were lowest in study 6 (which was likely to be the result of the lower application rate of active substance in this study) and levels in study 1 were lower than those in the remaining studies (which was possibly the result of a longer interval between treatment and harvest in this study in comparison to the far shorter intervals between treatment and the crop maintenance tasks in the other studies).

DFR results

DFR values showed a good correlation with the application rate of the active substances as shown in Figure 6.

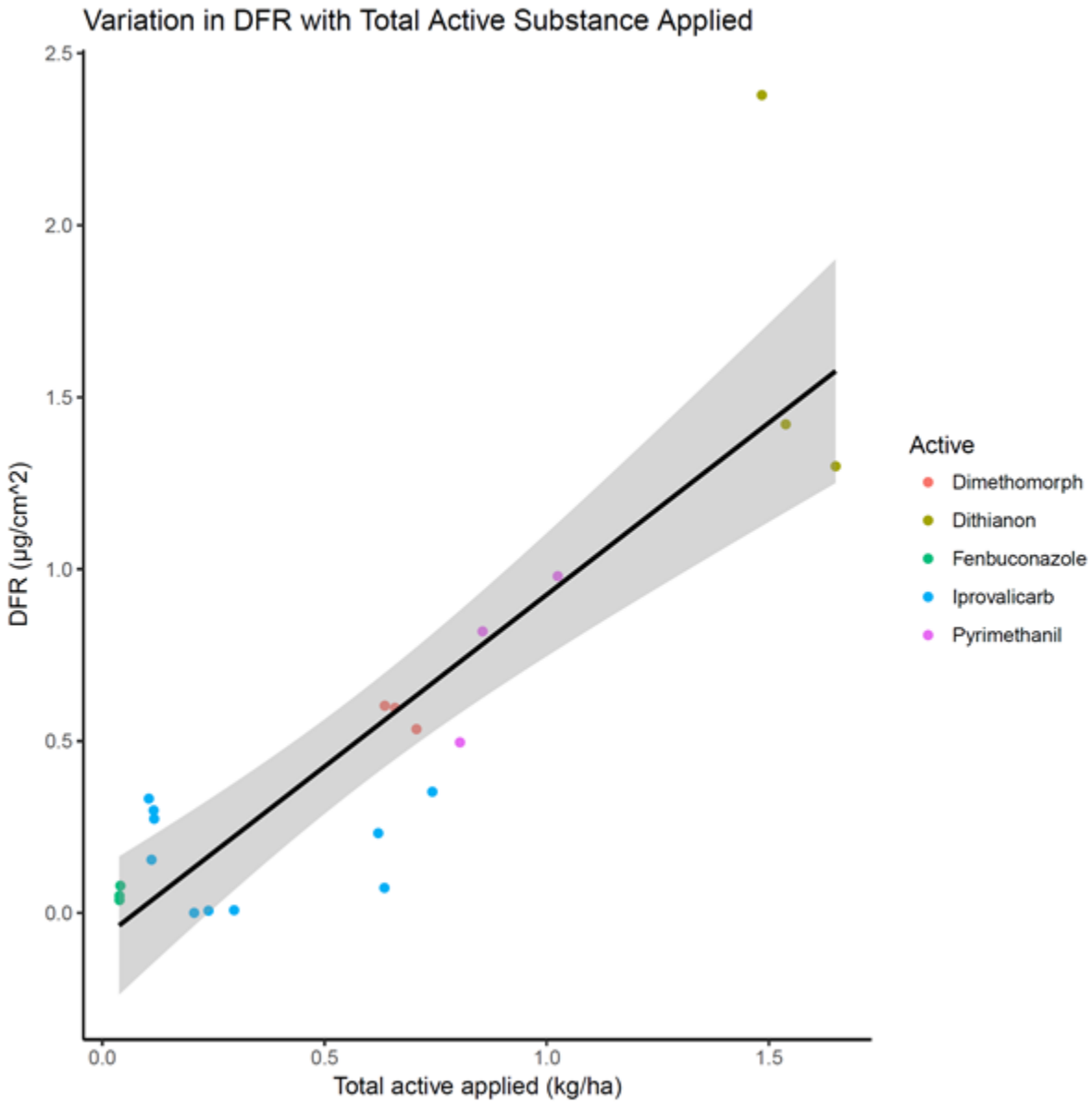


Figure 6: Relationship between DFR (µg/cm^2) and total active substance applied (kg/ha): the solid line shows linear regression and shading indicates 95 percent confidence interval of the mean.

The breakdown of the data points by active substance reflects the different total doses of the active substances in the studies. In order of increasing dose rate, the active substances are ranked: fenbuconazole (study 6/7) < iprovalicarb (study 8) < iprovalicarb (study 1) < dimethomorph (study 2 and 3) < pyrimethanil (study 4 and 5) < dithianon (study 2 and 3). The observation that the two iprovalicarb studies resulted in similar DFR values even though the application rates in these studies was different, can be explained by the fact that the higher rate was used in the harvesting study (study 1) which involved a longer interval between application and DFR sampling than the other studies. Further analysis of the relationship between applied dose and DFR is included in Appendix E.

For those studies where it was possible to derive a DFR value from a single application (3 out of the 8 studies), a normalised value (µg/cm^2/kg a.s./ha) has been calculated for comparison with the EFSA default initial DFR of 3 µg/cm^2/kg a.s./ha. At most of the sites in these 3 studies, the calculated DFR, was well below the default value. However, this is not a perfect comparison as the DFR measurements in these studies were made 1 to 2 days after application and not immediately after the spray had dried. The EFSA default value of 3 µg/cm^2/kg a.s./ha was based on a low default leaf area index (LAI) of 2 with no consideration of crop interception rates. Realistic values of LAI and interception for vines in the EU are presented in the FOCUS GW report with a maximum LAI of 4 to 6 and interception rates of 70% (flowering) and 85% (ripening). Both parameters have the impact in depleting the initial DFR. The initial DFR results are summarised in Table 9.

Table 9: Initial DFR results.

BROV Study ID	Site	DFR date	DAA	Mean DFR (µg/cm^2)	Dose kg a.s./ha	DFR (µg/cm^2/ kg a.s./ha)	% of default DFR
5	1	26/07/16	1	0.979	1.025	0.956	32%
	2	21/07/16	1	0.819	0.855	0.957	32%
	3	20/07/16	1	0.497	0.805	0.617	21%
7	1	23/06/04	2	0.055	0.038	1.472	49%
	2	29/06/04	1	0.080	0.041	1.972	66%
	3	01/07/04	1	0.050	0.038	1.302	43%
8	1	23/05/17	2	0.334	0.105	3.167*	106%
	2	12/06/17	2	0.275	0.117	2.347	78%
	3	20/06/17	2	0.155	0.111	1.401	47%
	4	18/06/17	2	0.298	0.116	2.570	86%

* This high value was the mean of 2 replicates: the third replicate was excluded from the calculations as it was < LOQ.

Comparison of exposure and DFR measurements

Across all studies, potential exposure values (for both the body and the hands) showed a good correlation with the measured DFR values. These findings support the proposed approach for calculating TC values from the exposure and DFR measurements.

A scatter plot of potential body exposure against DFR is presented in Figure 7.

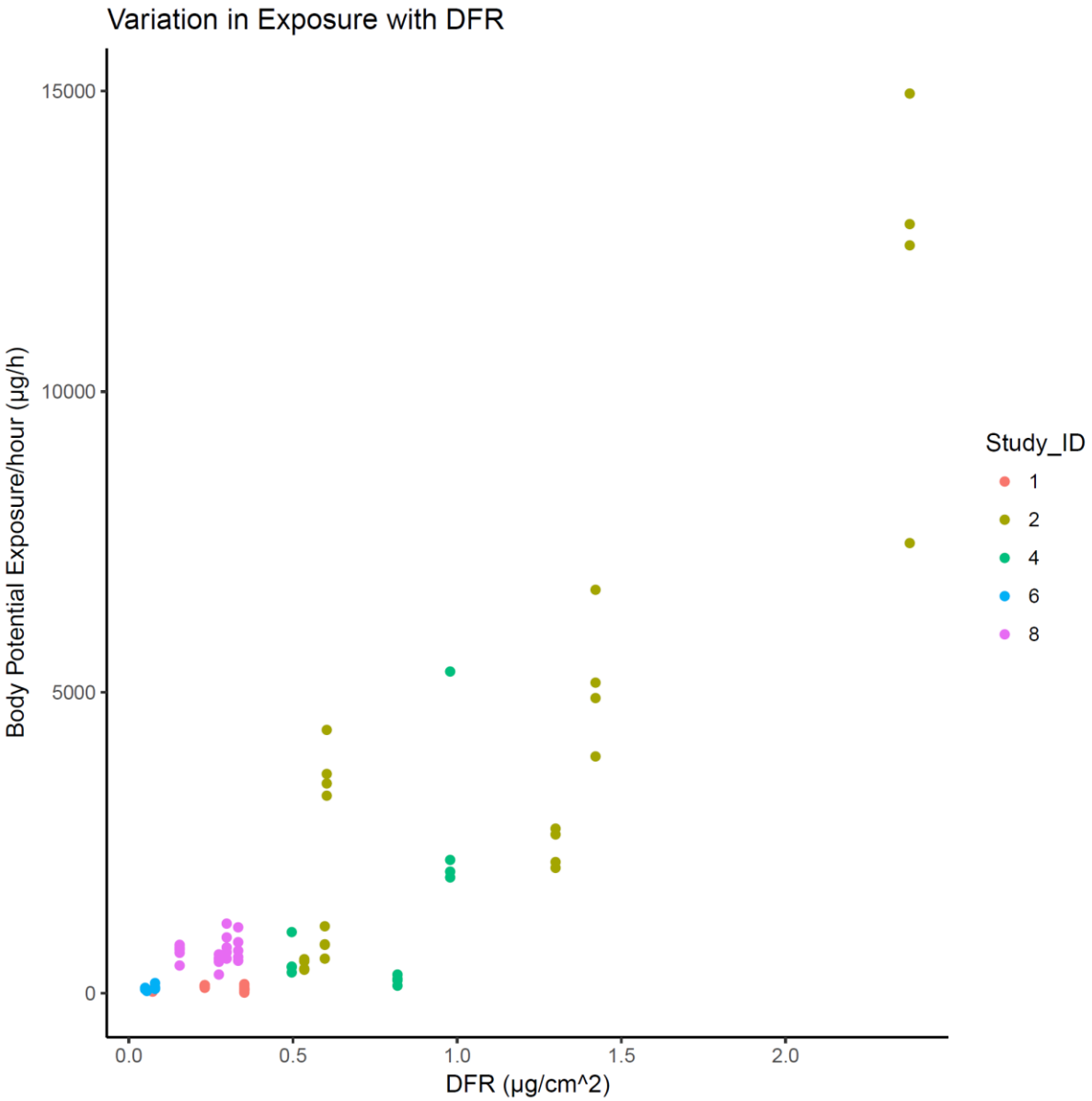


Figure 7: Body potential exposure per hour (µg/h) and DFR (µg/cm^2)

A scatter plot of potential hand exposure against DFR is presented in Figure 8.

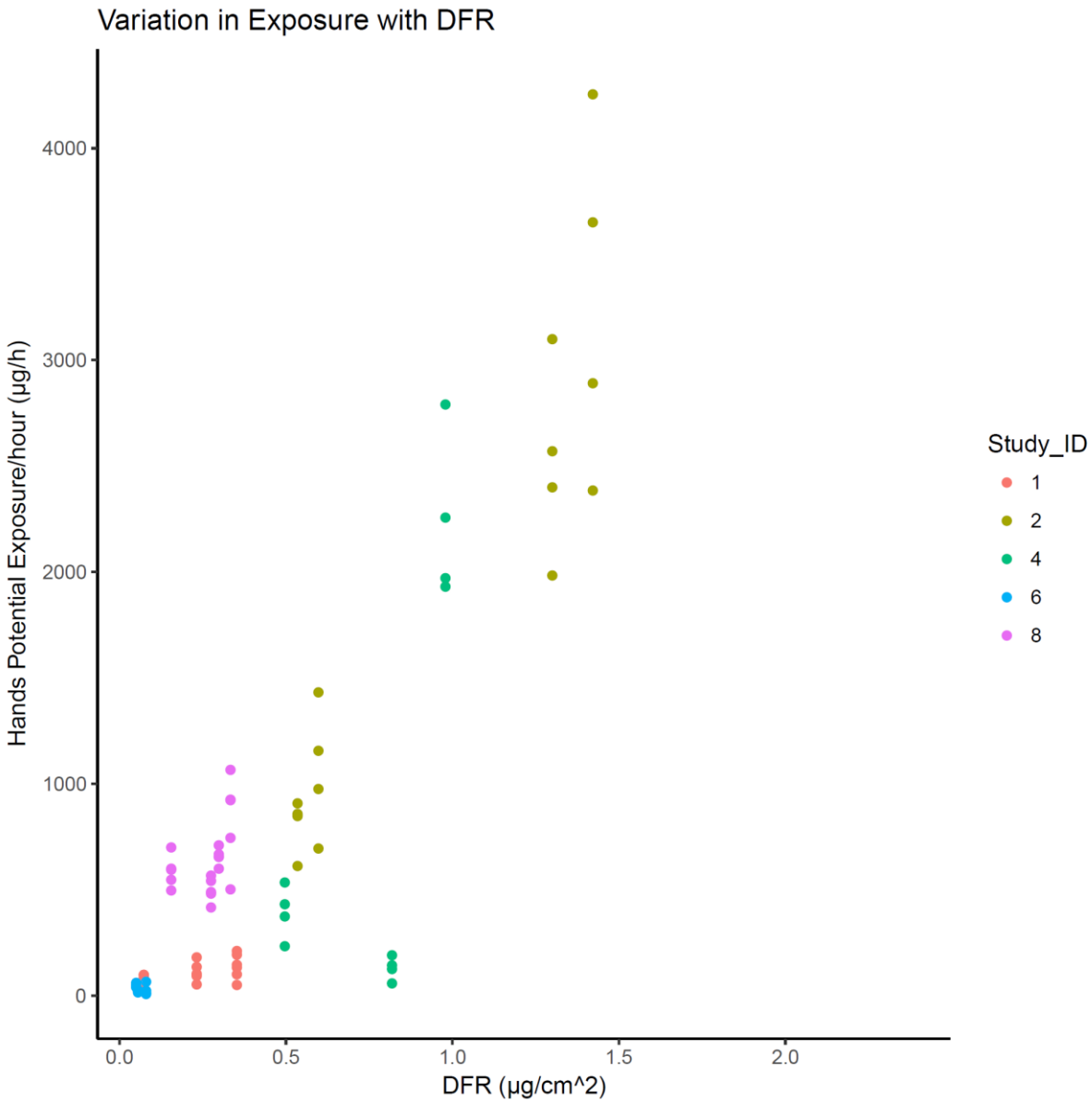


Figure 8: Hand potential exposure per hour (µg/h) and DFR (µg/cm^2)

A scatter plot of actual body exposure against DFR is presented in Figure 9.

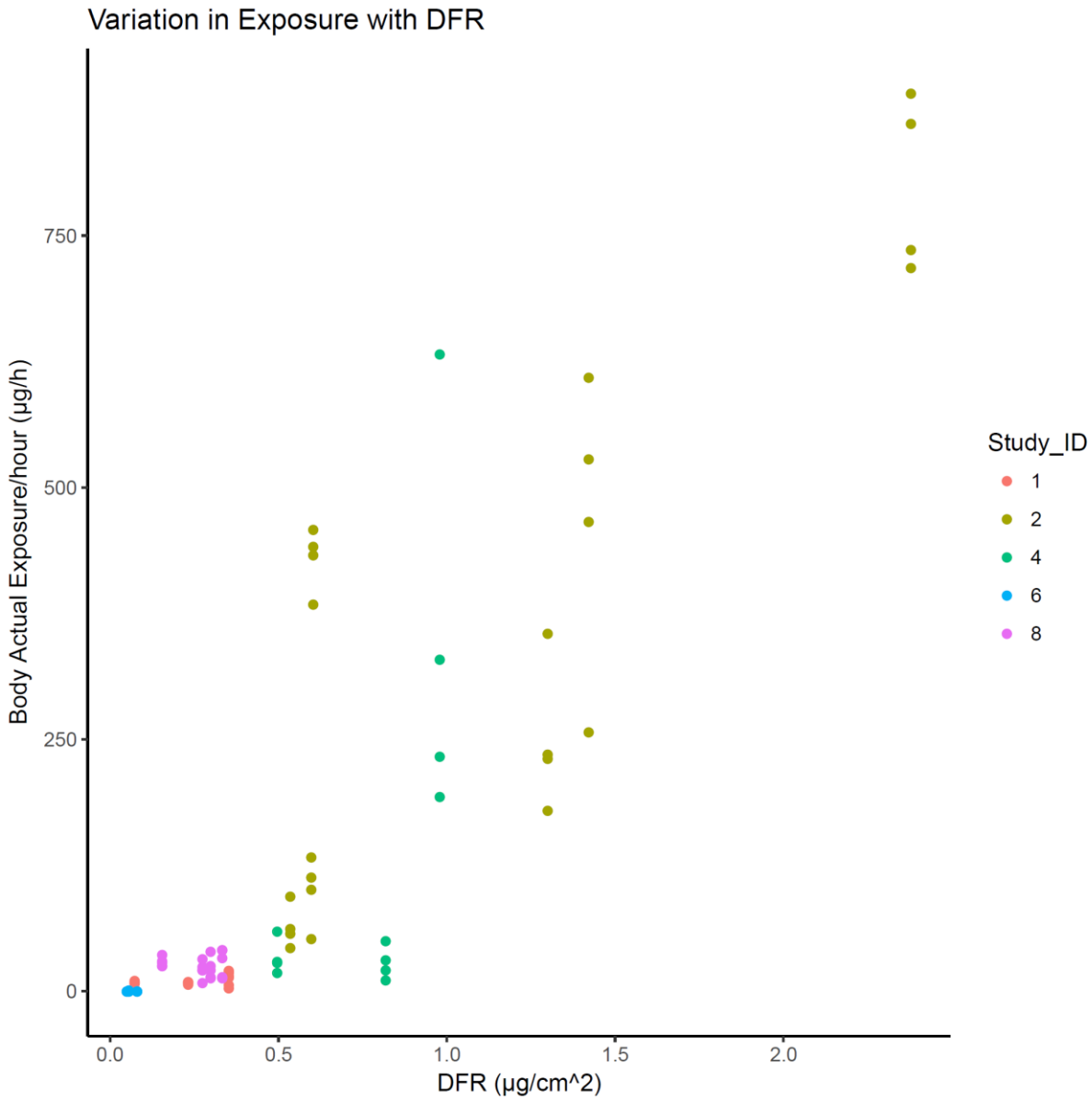


Figure 9: Actual body exposure per hour (µg/h) and DFR (µg/cm^2)

A scatter plot of actual hand exposure against DFR is presented in Figure 10.

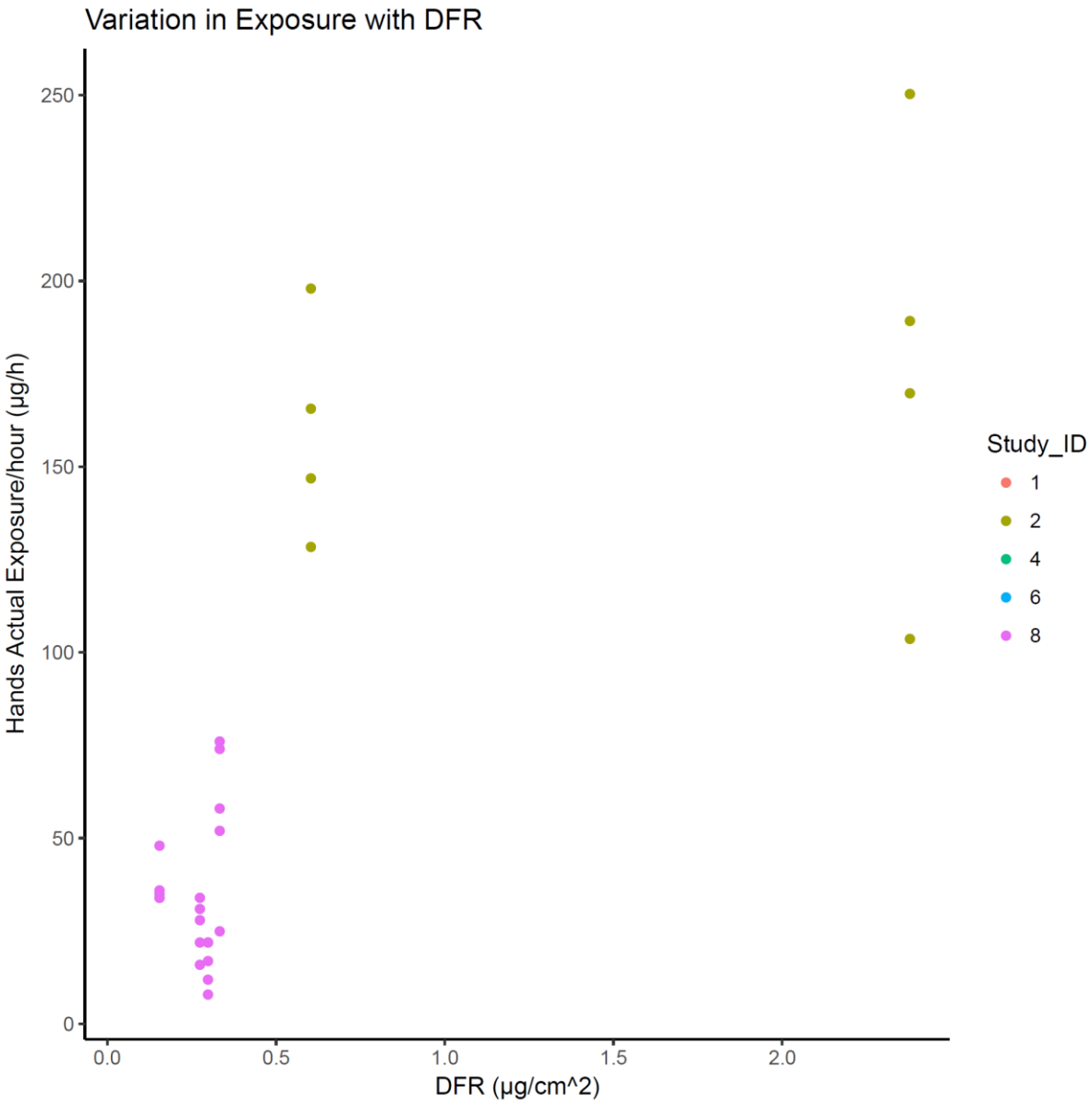


Figure 10: Actual hand exposure per hour (µg/h) and DFR (µg/cm^2)

The re-entry activities (or the combination of several tasks) undertaken by workers varied across the studies. However, the graphs above (Figures 7, 8, 9 and 10) suggest that the measured exposure levels may be more influenced by the DFR in each study (reflecting the application rate of active substance) than the nature of the task being performed.

Transfer coefficient values

TC values for each study subject were calculated by adding the exposure measurements on the relevant dosimeters*, dividing the total exposure (µg of active substance per person) by the duration of the exposure monitoring (hours) for that study subject, and then dividing the total exposure per hour for each subject by the mean DFR (µg of active substance per cm^2 of leaf surface) measured in the concurrent DFR study for the matching site. *TC values for each study subject were calculated in this way (subject to the availability of the relevant dosimeter measurements) for PDE to the body (less hands), PDE to the body (including hands), PDE to the hands, ADE to the body (less hands), ADE to the body (including hands), and ADE to the hands (under gloves).

Once these sets of TC values had been calculated for each individual study subject, overall 75^{th} and 95^{th} percentile TC values were calculated for all the study subjects. Additional 75^{th} and 95^{th} percentile TC values were calculated for the various tasks monitored in the separate studies. These TC values are summarised in Table 10. The method of calculation described above means that the percentile TC values for the body and hands may not add up to the corresponding total TC values because the latter are calculated from the sum of all relevant dosimeters for each individual study subject, whereas a given percentile value for body exposure and hand exposure will not necessarily relate to the same individual study subject.

Table 10: TC values.

Transfer Coefficient (cm^2/h)						
Task	**Potential Exposure**			**Actual Exposure**		
	Body	**Hands**	**Total [1]**	**Body [2]**	**Hands [3]**	**Total [1]**
Overall 75th centile	2500	2100	4300	190	220	410
Overall 95th centile	5400	3300	7900	640	300	990
Harvesting 75th centile	560	800	1500	60	-	-
Harvesting 95th centile	910	1300	1800	130	-	-
Pruning/training 75th centile	2900	1900	3800	340	250	980
Pruning/training 95th centile	5900	2600	6500	720	310	1000
Pruning/shoot lifting 75th centile	3400	3200	6100	140	220	350
Pruning/shoot lifting 95th centile	4900	3900	9000	200	230	420
All maintenance 75th centile	3200	2200	4500	250	220	410
All maintenance 95th centile	5700	3500	8300	660	300	990

[1] The percentile TC values for the body and hands may not add up to the corresponding total TC values because the latter are calculated from the sum of all relevant dosimeters for each individual study subject, whereas a given percentile value for body exposure and hand exposure will not necessarily relate to the same individual study subject.
[2] Body exposure beneath a single layer of long-sleeved and long-legged clothing.
[3] Actual hand exposure under work gloves (partial nitrile).

The total (body and hands) TC values for potential exposure from the BROV studies (highest 95th percentile value = 9000 cm^2/h) are lower than the current default TC value in the EFSA Guidance Document of 30000 cm^2/h).

For comparison of the BROV data with the current default TC value in the EFSA Guidance Document for actual exposure for a worker using workwear with bare hands, it is appropriate to add the BROV TC values for potential hand exposure and the values for actual body exposure. The resulting TC values are summarised in Table 11.

Table 11: TC for clothed body and bare hands.

Transfer Coefficient (cm^2/h) clothed body* and bare hands			
Task	**TC for ADE to body (less hands)**	**TC for PDE to bare hands**	**TC clothed body and bare hands**
Overall 75^{th} centile	190	2100	2300
Overall 95^{th} centile	640	3300	3600
Harvesting 75^{th} centile	60	800	920
Harvesting 95^{th} centile	130	1300	1400
Pruning/training 75^{th} centile	340	1900	2300
Pruning/training 95^{th} centile	720	2600	3200
Pruning/shoot lifting 75^{th} centile	140	3200	3300
Pruning/shoot lifting 95^{th} centile	200	3900	4100
All maintenance 75^{th} centile	250	2200	2600
All maintenance 95^{th} centile	660	3500	3900
* Single layer of long-sleeved and long-legged clothing.			

The above total (clothed body and bare hands) TC values from the BROV studies (highest 95^{th} percentile value = 4100 cm^2/h) are lower than the current default TC value in the EFSA Guidance Document of 10100 cm^2/h).

Because studies 2 and 4 provided a detailed breakdown of exposure on outer and inner dosimeter sections and study 6 provided the same detailed breakdown for the outer dosimeter only, it would be possible to use these studies in isolation to predict TC values for a lightly clothed worker wearing, for example, a tee-shirt and shorts. However, this approach would rely on a limited set of data and be based on the assumption that the distribution of contamination for the specific tasks monitored would apply to other re-entry tasks in grapevines.

Gloves (partial nitrile work gloves) were worn in study 8 (20 study subjects) and were also worn (but not monitored) at just one site in study 2 (4 study subjects). The BROV WoG was confident that the type of gloves used in this study was representative of those typically worn when carrying out similar tasks. An EN Standard is under development for this type of glove which, if agreed, will allow the appropriate type of glove to be specified and will offer re-assurance that the predicted (or appropriate default) levels of protection can be achieved. In study 8, the transfer/penetration values for these gloves, based on a comparison of the hand TCs (presented above) and supported by the exposure measurements, was 6 to 7% and this is in line with the EFSA calculator assumption of 10% transfer of foliar residues through gloves. Therefore, the BROV WoG concluded that if similar gloves were worn for other re-entry tasks in grapes, it would be appropriate to apply a default protection factor of 90% (i.e. 10% penetration and transfer) to the TC for unprotected hands for those tasks. Applying this protection value for work gloves results in the TC values presented in Table 12.

Table 12: TC values with gloves.

Transfer Coefficient (cm^2/h) body (PDE and ADE) and gloved hands					
Task	**TC for body (less hands)**		**TC for hands**	**Total TC**	
	PDE	**ADE [1]**	**Gloves [2]**	**PDE body and gloves [2]**	**ADE [1] body and gloves [2]**
Overall 75th centile	2500	190	210	2700	400
Overall 95th centile	5400	640	330	5700	970
Harvesting 75th centile	560	60	80	640	140
Harvesting 95th centile	910	130	130	1000	260
Pruning/training 75th centile	2900	340	190	3100	530
Pruning/training 95th centile	5900	720	260	6200	980
Pruning/shoot lifting 75th centile	3400	140	320	3700	460
Pruning/shoot lifting 95th centile	4900	200	390	5300	590
All maintenance 75th centile	3200	250	220	3400	470
All maintenance 95th centile	5700	660	350	6000	1000

[1] Single layer of long-sleeved and long-legged clothing.
[2] Partial nitrile work gloves (10% penetration and transfer assumed).

Transfer coefficient proposals

The TC results presented in the tables above indicate that the harvesting task (study 1) resulted in lower TC values (for PDE body, ADE body, PDE hands and total TC) than the other (crop maintenance) tasks. For tasks other than harvesting, the pruning and shoot lifting tasks (study 8) resulted in some higher TC values (for PDE body and PDE hands) than the other pruning and training activities (studies 2, 3, 4, 5, 6 and 7). However, the 95th percentile

PDE body TC and both the 75th and 95th percentile ADE body TC values for pruning and shoot lifting were lower than the corresponding values for the other pruning and training activities. Based on the graphical representations of the data and statistical analysis, it is appropriate to treat all studies as a single dataset and, in line with the current TC values for grapes recommended by the EFSA guidance document [1], propose TC values covering all re-entry tasks in grapes.

It is likely that workers harvesting and maintaining grapes may habitually wear minimal clothing, especially under hot conditions. Although it would be possible to derive modified TC values on the assumption that certain areas of the body are exposed, the exposure results show that residues on the torso were low in most studies with exposure to the body being on the arms (predominantly) and legs. Therefore, when minimal clothing is worn leaving most of the arms and legs exposed, the PDE TC values for the body provide a realistic but precautionary estimate.

Therefore, the TC values in Table 13 are proposed for all re-entry activities in grapes.

Table 13: Proposed TC values.

Proposed Transfer Coefficients (cm^2/h)					
Clothing and PPE	**TC for body (less hands)**		**TC for hands**		**Total TC**
	PDE	**ADE [1]**	**PDE**	**Gloves [2]**	
No clothing or light clothing No gloves 75th centile	3400	-	3200	-	6600
No clothing or light clothing No gloves 95th centile	5900	-	3900	-	9800
No clothing or light clothing Work gloves 75th centile	3400	-	-	320	3700
No clothing or light clothing Work gloves 95th centile	5900	-	-	390	6300
Full-length clothing No gloves 75th centile	-	340	3200	-	3500
Full-length clothing No gloves 95th centile	-	720	3900	-	4600
Full-length clothing Work gloves 75th centile	-	340	-	320	660
Full-length clothing Work gloves 95th centile	-	720	-	390	1100

[1] Single layer of long-sleeved and long-legged clothing.
[2] Partial nitrile work gloves (10% penetration and transfer assumed).

7 Conclusions

Overall the BROV re-entry data on grapes are a well-conducted set of trials which follow the appropriate guidelines for exposure and DFR studies and meet the relevant quality criteria (including those criteria applied in the production of the AOEM).

Although two of the five pairs of exposure and DFR studies used different sites in the exposure and DFR parts of the study, all mismatches that have been identified have been investigated and are not considered to affect the validity of the results and recommendations.

These studies, involving a total of 73 study subjects performing a representative range of tasks in commercial vineyards in the main wine-growing regions across the EU, provide a significant addition to the currently available re-entry exposure data. This project has addressed the data gap identified by EFSA for specific EU TC values to permit more realistic and reliable worker exposure estimates for re-entry activities in grapes. It also allows TC values to be proposed taking into account various combinations of clothing and gloves.

8 References

[1] EFSA (European Food Safety Authority), 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, 55 pp., doi:10.2903/j.efsa.2014.3874

[2] Krieger RI, Ross JH and Thongsinthusak T (1992). Assessing human exposures to pesticides. Reviews of Environmental Contamination and Toxicology. Vol 128 (1-15)

[3] The US EPA Office of Pesticide Programmes Science Advisory Council for Exposure (ExpoSAC) Policy 3

[4] UIPP Bonnes pratiques phtosanitaires en viticulture: sécurité des travailleurs viticoles

[5] OECD (Organisation for Economic Co-operation and Development), 1997. Guidance document for the conduct of studies of occupational exposure to pesticides during agricultural application. Series on testing and assessment No. 9. GD (97) 148

[6] The US EPA Office of Pesticide Programmes Series 875 Occupational and Residential Exposure Test Guidelines. Group B – Post-application Exposure Monitoring Test Guidelines. Part B, Chapter 3: Dislodgeable Foliar Residue Dissipation: Agricultural Guideline 875.2100. Part C: Quality assurance/Quality Control (QA/QC)

[7] European Commission SANCO/3029/99 rev 4**.** European Commission guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414.

[8] European and Mediterranean Plant Protection Organisation (EPPO), 2012. Dose expression for plant protection products. EPPO Bulletin (2012) 42 (3), 409 - 415.

9 Abbreviations

ABE	Actual body exposure
ADE	Actual dermal exposure
AHE	Actual hand exposure
ARETF	Agricultural Re-entry Exposure Task Force (US)
AOEM	Agricultural Operator Exposure Model
BBCH	Biologische Bundesanstalt, Bundessortenamt and Chemical industry
BROV	Bystander Resident Orchard Vineyard project
DAA [1/2/3 etc.]	Days after application [1/2/3 etc.]
DFR	Dislodgeable foliar residue
ECPA	European Crop Protection Association
EFSA	European Food Safety Authority
EU	European Union
EW	Oil-in-water emulsion
ExpoSAC	Science Advisory Council for Exposure (US EPA)
GLP	Good laboratory practice
LAI	Leaf area index
LOD	Limit of detection
LOQ	Limit of quantification
LWA	Leaf wall area
LWH	Leaf wall height
ND	Non-detect / not detected
OECD	Organisation for Economic Co-operation and Development
PBE	Potential body exposure
PDE	Potential dermal exposure
PHE	Potential hand exposure
PHI	Pre-harvest interval
QA	Quality assurance
RSD	Relative standard deviation
SC	Suspension concentrate
TC	Transfer coefficient
UIPP	L'Union des Industries de la Protection des Plantes
UTC	Untreated control
WG	Water-dispersible granule
WoG	Working Group

Appendix A: Detailed study summaries and evaluations

The following studies were submitted in support of the BROV worker re-entry project and are summarised and evaluated in this section.

BROV Study ID	Study owner code	Study title	Author	Report number	Study year (field phase)	Report year
1	ECPA	Iprovalicarb, measurement of worker re-entry exposure (combined with dislodgeable foliar residue determination) during crop harvesting of grapes following application of a WG formulation containing iprovalicarb, northern and southern Europe, 2015	J M Wiseman	CEMR-7088	2015-16	2017
2	BASF 1-1	Determination of worker re-entry exposure associated to typical worker re-entry activities (pruning/tying up) in vineyards following treatment with BAS 553 01 F in Italy and Germany, 2016	I Thouvenin	734687	2016	2017
3	BASF 1-2	Determination of dislodgeable foliar residues of dimethomorph (BAS 550 F) and dithianon (BAS 216 F) after application of BAS 553 01 F to grapevines, 2016	Ch.H. Roussel	734687_1	2016	2017
4	BASF 2-1	Determination of worker re-entry exposure associated to typical worker re-entry activities (pruning/tying up) in vineyards following treatment with BAS 605 04 F in France and Germany, 2016	I Thouvenin	799911_1	2016	2017
5	BASF 2-2	Determination of dislodgeable foliar residues of pyrimethanil (BAS 605 F) after application of BAS 605 04 F to grapevines, 2016	Ch.H. Roussel	799911_1	2016	2017
6	DOW 1-1	Determination of dermal exposure to re-entry workers during pruning and training of grapevines in France, 2004	J. Perkins, G. Jones	AF/8247/DE	2004	2006

BROV Study ID	Study owner code	Study title	Author	Report number	Study year (field phase)	Report year
7	DOW 1-2	Dissipation of dislodgeable foliar residues of fenbuconazole from vines treated with Indar EW	G. Jones	AF/8246/DE	2004	2006
8	UIPP	Determination of worker re-entry exposure (combined with dislodgeable foliar residues) associated to typical worker re-entry activities (shoot lifting) in vines in France and Italy, 2017	I. Thouvenin	ChR-17-28350	2017	2018

Study 1

Report CEMR-7088. 'Measurement of worker re-entry exposure (combined with dislodgeable foliar residue determination) during crop harvesting of grapes following application of a WG formulation containing iprovalicarb, northern and southern Europe, 2015'

Author:	J. M. Wiseman
Date (final report):	06/10/2017
Study 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. EPA Occupational and Residential Exposure Test Guidelines: OPPTS 875.1100 Dermal Exposure Outdoor. US EPA February 1996.
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substances:	Iprovalicarb (in formulation with folpet, latter not analysed)
Product:	Melody Combi (Sirbel UD)
Crop:	Grapevine
Location:	France (2 sites), Germany (3 sites) and the Czech Republic (1 site): • Site 1 Ortenberg, Baden, Germany • Site 2 Uherský Ostroh, Czech Republic • Site 3 Beauvoisin, Nimes, France* • Site 4 Mülheim, Mosel, Germany* • Site 5 Ihringen, Freiburg, Germany • Site 6 Marsillargues, France* * The exposure samples were not analysed at sites 3, 4 or 6 because the very low foliar residues found at these sites at harvest time would not have resulted in meaningful exposure data. The

low DFR measurements at these sites were attributed to a combination of heavy rainfall before sampling (site 3), reduced application rates (sites 4 and 6) and the extended interval between the final treatment and harvest (sites 3 and 4).

Aim.

The purpose of this study was to determine the potential and actual dermal exposure of workers carrying out harvesting activities in grapevines. Concurrent measurements of dislodgeable foliar residues (DFR) at the time of re-entry were made at each site to permit the calculation of transfer coefficient (TC) values for the harvesting task.

Test material.

The study was carried out using the fungicide 'Melody Combi' ('Sirbel UD'), a water-dispersible granule (WG) formulation containing a nominal 90 g/kg iprovalicarb (in formulation with 563 g/kg folpet, latter not analysed).

Study design.

Potential and actual dermal exposure to foliar residues was measured for experienced workers carrying out harvesting activities in grapevines. The field portion of the study was carried out at six commercial vineyards at 2 sites in France, 3 sites in Germany and 1 site in the Czech Republic. The vines (wine varieties Müller-Thurgau at site 1, Pinot Blanc at site 2, Carignan at site 3, Riesling at site 4, Pinot Noir at site 5 and Carignan, Grenache and Merlot at site 6) were planted in row widths of 2.0 m (site 5), 2.5 m (sites 1, 4 and 6), or 3.0 m (sites 2 and 3). Crop height was reported to be 1.8 m (sites 3 and 6) or 2.1 m (sites 1, 2, 4 and 5) and the foliage was full at the time of the study. The treated plot areas were 1.0 ha (sites 1, 2 and 5), 1.5 ha (site 3), 0.8 ha (site 4) or 1.3 ha (site 6).

Treatment details.

The product was applied up to 4 times at each site before worker re-entry as described in Table A1.1. The application equipment was typical commercial broadcast air-assisted sprayers (no further details were provided).

Table A1.1: Treatment details.

Site	Treatment no.	Date of treatment	Growth stage (BBCH)	Application rate* (g a.s./ha)	Application volume (l/ha)
1	1	01/06/15	89	110	400
	2	11/06/15	89	140	800
	3	22/06/15	89	160	1200
	4	05/08/15	89	220	1200
2	1	27/07/15	89	160	722
	2	04/08/15	89	150	715
	3	17/08/15	89	170	770
	4	27/08/15	89	160	735
3	1	07/08/15	89	120	210
	2	17/08/15	89	120	210
4	1	23/07/15	89	50	500
	2	08/08/15	89	100	800
	3	22/08/15	89	150	1200
5	1	08/07/16	89	150	300
	2	19/07/16	89	200	300
	3	28/07/16	89	200	300
	4	29/08/16	89	200	300
6	1	24/08/16	89	90	400
	2	02/09/16	89	120	400

* The doses (reduced where appropriate) reflected the crop / disease development at each site.

Re-entry activities.

Workers re-entered the treated crop for harvesting activities after the following intervals from the final application: 31 days (sites 2 and 5), 32 days (site 6), 43 days (sites 1 and 3) or 47 days (site 4). The minimum pre-harvest interval (PHI) of the product was 28 days. Five workers were monitored at site 1, 6 workers at site 2, and 6 workers at site 5: giving a total of 17 study subjects (8 male and 9 female). Workers were not monitored at sites 3, 4 or 6. Each re-entry monitoring period was a full working day at each site.

At site 1, workers harvested without protective gloves. They used secateurs to cut the bunches and placed them in crates which were filled to a weight of about 20 kg. Full crates were passed under the vines and emptied into a trailer. When required, workers also pulled leaves off the vines to expose the bunches. A total of 2100 kg of grapes was harvested by a group of 10 workers, 5 of whom were monitored in the study over a full day (the actual working duration was 309 minutes).

At site 2, workers harvested without protective gloves (although worker 6 wore a single nitrile glove on her right hand to protect a cut). They used secateurs to cut the bunches and placed them in buckets. Full buckets were emptied into crates (each containing about 30 kg of

grapes) on a trailer. A total of 1220 kg of grapes was harvested by the 6 workers being monitored over a full day (the actual working duration was 358 minutes).

At site 5, workers harvested without protective gloves. They used secateurs to cut the bunches and placed them in buckets which were occasionally passed under the vines. Full buckets were emptied into a hopper (containing about 300 kg of grapes) on a trailer. When required, workers also pulled leaves off the vines to expose the bunches. A total of 3104 kg of grapes was harvested by the 6 workers being monitored over a full day (the actual working duration was 443 minutes).

No unexpected incidents were reported for any of the workers which were likely to have influenced the study results.

Exposure assessment.
Dermal exposure was assessed using whole-body dosimetry, hand washes and face/neck wipes. Gloves were not worn (except for a single nitrile glove worn by one worker to protect a hand cut). Details of the exposure sampling matrices are described in Table A1.2.

Table A1.2: Exposure sampling matrices.

Body area	Sampling matrix	Description
Arms, torso (outer layer only worn at sites 1 and 2)	Whole body dosimeter	65% polyester/35% cotton long-sleeved jacket. Cut into sections for analysis (arms and torso) to evaluate deposition on specific body parts.
Arms, legs, torso (outer layer) (mid layer when outer jacket worn at sites 1 and 2)	Whole body dosimeter	Two-piece 65% polyester/35% cotton long-sleeved, long-legged garments. Analysed as separate parts (top and bottom sections).
Arms, legs, torso (inner layer)	Whole body dosimeter	Two-piece 100% cotton long-sleeved, long-legged underwear. Analysed as separate parts (top and bottom sections).
Hands	Hand wash	A single (site 2) or repeated (sites 1 and 5) hand wash using a total of 1000 ml of a 0.01% aqueous solution of Aerosol OT-100 over a bowl. Taken before work (discarded), before lunch (and other breaks) and at the end of the monitoring period. A 100 ml aliquot was retained from each hand wash sample in a HDPE bottle.
Hands (one worker at site 2)	Disposable nitrile glove	A single nitrile glove was worn on the right hand of one worker to protect a cut. This was not considered to be a protective glove and the glove residue was added to the hand wash residue for this worker.
Face, neck	Face / neck wipes	A single wipe (site 2) or 2 sequential wipes (sites 1 and 5), each using a multi-layer cotton gauze pad (10 cm x 10 cm) moistened with 4 ml of Aerosol OT solution. Taken before work (discarded), before

		lunch (and other breaks) and at the end of the monitoring period. All wipes for an individual subject were collected together in a HDPE bottle.

At the end of monitoring, dosimeter sections were wrapped in aluminium foil and bagged. All samples were stored on ice in a cool box at each site before being deep frozen until the time of extraction for analysis.

Dislodgeable foliar residue (DFR) sampling.
Each test site was divided into 3 sub-plots for DFR sampling and 1 sample was collected from each sub-plot using a leaf punch directly into a pre-labelled jar. Samples were taken from the areas of the crop likely to be in contact with workers during harvesting. Each sample consisted of 80 leaf discs, each disc with a 2-sided area of 5 cm^2, giving a total leaf area per sample of 400 cm^2. Samples were also taken from untreated plots to produce fortified and control leaf wash solutions. The leaf punch was cleaned with acetone and de-ionised water after each sample.

Leaf discs were washed twice by adding, each time, 100 ml of a 0.01% aqueous solution of Aerosol OT-100 to each sampling jar for 10 minutes on a reciprocating platform shaker. The dislodging solutions for each sample were combined and frozen.

Environmental monitoring.
Air temperature, relative humidity, wind speed and wind direction were monitored at each site between 2 and 5 times during the re-entry activities. Air temperatures during re-entry ranged from 13.3 to 28.7 ºC across the 3 sites used for exposure monitoring and relative humidity ranged from 32% to 72%. Winds were generally light (the peak values recorded were 7 m/s at sites 1 and 5, 3.9 m/s at site 2, and ≤ 1.8 m/s at the other sites).

No adverse weather events likely to affect the study results were reported.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.
Field recovery samples were produced for all sampling matrices to assess, and correct for, the recovery of the active substance from each matrix. The dermal exposure matrices were fortified using the analytical standard in water and the dislodging solutions (DFR measurement) were fortified using the analytical standard in acetonitrile.

Three sets of field fortifications at 2 spiking levels and an untreated control were prepared for each exposure sampling matrix on each day of monitoring at each site as described in Table A1.3. Three sets of field fortifications at 3 spiking levels and an untreated control were prepared for the leaf wash (DFR) solution on each day of re-entry at each site as described in Table A1.4.

Fortified outer and inner dosimeter samples (the latter covered by a layer of unfortified outer dosimeter material) were exposed to the same environmental conditions for the same period of time as the monitoring garments, but positioned away from sources of contamination. Hand wash and face wipe recovery samples were stored on ice in a cool box immediately after spiking before being deep frozen.

Field recovery results for the exposure matrices are summarised in Table A1.3.

Table A1.3: Field recovery results for exposure matrices.

Matrix	Fortification level (µg/specimen)	% recovery (sum of isomers) (3 replicates x 3 sites)					
		Site 1		Site 2		Site 5	
		Mean	RSD	Mean	RSD	Mean	RSD
Outer dosimeter	100 (100x LOQ)	94	4.0	96	3.9	99	3.6
	5000 (5000x LOQ)	109	7.2	86	7.8	92	2.5
Inner dosimeter	5 (10x LOQ)	104	7.9	108	9.9	59*	9.9*
	250 (500x LOQ)	96	3.6	82	6.7	100	3.8
Face wipe	1 (10x LOQ)	117	3.5	117	3.0	96	1.2
	50 (500x LOQ)	105	3.9	93	3.8	89	0.6
Hand wash (100 ml)	10 (100x LOQ)	98	9.8	92	1.7	90	10.1
	500 (5000x LOQ)	105	4.2	101	4.5	90	0.0
Nitrile glove	100 (2x LOQ)	**	**	87	16.1	**	**
	5000 (100x LOQ)	**	**	109	1.1	**	**

* Excluded due to a fortification error, therefore n = 6
** Glove field recovery only conducted where worn (site 2 only)

Field recovery results for the leaf wash (DFR) samples are summarised in Table A1.4.

Table A1.4: Field recovery results for DFR samples.

Matrix	Fortification level (µg/specimen)	% recovery (sum of isomers) (3 replicates x 6 sites)						
			Site 1	Site 2	Site 3	Site 4	Site 5	Site 6
Leaf wash (200 ml)	4 (2000x LOQ)	Mean	114	160	86	172	108	108
		RSD	70.7	38.4	15.9	49.5	7.1	1.9
	40 (20000x LOQ)	Mean	117	118	96	75	122	106
		RSD	7.0	2.2	10.8	48.7	6.1	6.2
	400 (200000x LOQ)	Mean	86	99	100	80	105	102
		RSD	21.3	2.6	5.9	19.7	7.2	4.5

Recoveries at sites 1 and 4 were corrected for residues in the control samples
At site 2, residues in control samples were variable (and occasionally high) and the recoveries have not been corrected. Although residues in the control would have a significant impact on the reported recovery values at the lowest fortification level, the middle fortification level is the appropriate (nearest) value to use when correcting the leaf punch samples.

Mean recoveries for all matrices used in the exposure and DFR calculations were considered acceptable (generally within the 70% - 120% range). Mean RSD values were generally within acceptable limits (≤ 20% except for the DFR samples described above).

This evaluation has corrected monitoring and DFR samples for which field recoveries were <95% (based on the mean recovery for nearest fortification level): this is in line with the agreed UK HSE / BROV approach.

Travel recovery samples.
Additional travel recovery samples (not exposed to environmental conditions) were generated for each exposure matrix (3 replicates at the high and low fortification levels) at sites 2 and 5. The results are summarised in Table A1.5.

Table A1.5: Travel recovery samples.

Matrix	Fortification level (µg/specimen)	% recovery (sum of isomers) (2 sites x 3 replicates)			
		Site 2		Site 5	
		Mean	RSD	Mean	RSD
Outer dosimeter	100 (100x LOQ)	100	8.2	107	10.5
	5000 (5000x LOQ)	115	3.1	97	4.7
Inner dosimeter	5 (10x LOQ)	88	1.1	100	2.0
	250 (500x LOQ)	106	13.7	109	2.9
Face wipe	1 (10x LOQ)	110	8.6	106	6.0
	50 (500x LOQ)	82	3.9	90	1.3
Hand wash (100 ml)	10 (100x LOQ)	109	1.9	92	8.5
	500 (5000x LOQ)	105	1.9	89	1.7
Nitrile glove (site 2 only)	100 (2x LOQ)*	112	2.7	-	-
	5000 (100x LOQ)*	109	4.0	-	-
* n=3					

All mean travel recoveries were within acceptable limits.

Results.
All measured residue levels were greater than the LOQ for every matrix and so it was not necessary to substitute the LOQ for measured values between LOQ and LOD or to substitute the LOD for values reported as non-detectable.

No statistical tests were conducted for outliers in the exposure data set. Several values were noticeably higher or lower than others in the data set for a given matrix, but all values were included in the calculations since there was no experimental basis for exclusion. Values were only excluded if the samples were compromised in the field, during transit, or during analysis.

The exposure results, with residues corrected for samples with <95% field recovery, are presented in Table A1.6.

Table A1.6: Exposure results.

Iprovalicarb residues on dermal monitoring matrices (µg – sum of isomers)											
Site	Worker	Inner top	Inner bottom	Outer jacket torso	Outer jacket arms	Outer bottom	Outer or mid-layer top**	Hand wash	Glove	Face wipe	Total
1	1	5.92	Missing	88.63*	450.8*	88.34*	39.10*	275.2	-	0.56	948.6
	2	11.66	4.55	94.37*	348.3*	213.8*	17.16*	534.0	-	1.18	1225.0
	3	6.46	3.04	55.35*	274.9*	110.1*	25.24*	937.9	-	0.99	1414.1
	4	11.28	5.05	108.7*	256.1*	135.5*	28.02*	697.5	-	1.05	1243.3
	5	9.76	4.39	99.27*	322.4*	122.8*	31.91*	473.8	-	0.52	1064.9
2	6	1.80	1.21	27.58	123.5	9.28	11.46	273.2	313.2*	0.51	761.7
	7	29.46	1.06	62.18	222.3	58.77	23.27	346.2	-	1.06	744.3
	8	19.34	1.49	69.61	200.1	79.72	24.33	580.3	-	1.38	976.2
	9	36.62	0.75	20.60	120.9	31.83	25.15	505.7	-	0.40	742.0
	10	23.39	2.02	48.68	105.8	58.61	22.93	408.4	-	1.62	671.5
	11	7.18	1.56	15.16	93.47	20.15	5.18	244.3	-	0.43	387.5
5	23	37.00*	4.94*	-	-	234.7	257.3	1568.7*	-	2.51	2105.1
	24	126.4*	7.54*	-	-	488.9	221.8	1069.0*	-	1.18	1914.7
	25	87.50*	8.07*	-	-	207.0	220.2	1431.4*	-	3.92	1958.1
	26	98.60*	8.42*	-	-	559.3	441.5	983.5*	-	4.95	2096.2
	27	17.70*	2.77*	-	-	29.12	51.08	738.8*	-	0.50	840.0
	28	139.83	8.08*	-	-	93.91	114.0	379.4*	-	2.71	737.9

* Values corrected for recovery (at closest fortification level for the matrix at the same site) when field recovery was <95%

** Treated as an outer dosimeter when an outer jacket was not worn (site 5) and as an inner dosimeter when an outer jacket was worn (sites 1 and 2)

The DFR results, with residues corrected for samples with <95% field recovery, are presented in Table A1.7.

Table A1.7: DFR results.

Iprovalicarb residues in leaf wash samples: DFR (µg/cm^2 - sum of isomers)						
	Replicate					Mean
	1	2	3	4	5	
Site 1	0.2846	0.1867	0.2601	0.1521	0.2754	0.2318
Site 2	0.0558	0.0454	0.0850	0.0906	0.0872	0.0728
Site 3	0.0013	0.0100	0.0010	0.0001	0.0147	0.0063*
Site 4	0.0084	0.0048	0.0131	0.0075	0.0106	0.0089
Site 5	0.4495	0.3404	0.3908	0.3141	0.2679	0.3526
Site 6	0.0003	0.0002	0.0001	0.0004	0.0003	0.0003

* Mean value corrected for recovery (at closest fortification level for the leaf wash solution at the same site) when field recovery was <95%

Annex: method of analysis for iprovalicarb and method validation.

Dermal exposure matrices: analytical method 00947 (MR-103/05)

Principle of the method

Outer and inner dosimeter samples were extracted with an appropriate volume of 2-propanol on a horizontal shaker for approximately 30 minutes. A 1 ml aliquot was evaporated to dryness and the extract was reconstituted with 1 ml acetonitrile/water solution containing the internal standard iprovalicarb-d7. The sample was filtered using a 45 µm GHP Acrodisc before HPLC-MS/MS analysis.

Face/neck wipe samples (including the detergent added in the field) were extracted with 50 ml of 2-propanol on a horizontal shaker for approximately 30 minutes. A 1 ml aliquot was evaporated to dryness and the extract was reconstituted with 2 ml acetonitrile/water solution containing the internal standard iprovalicarb-d7. The sample was filtered using a 45 µm GHP Acrodisc before HPLC-MS/MS analysis.

A 1 ml aliquot of a 50 ml sub-sample of hand wash solution was evaporated to dryness and reconstituted with 2 ml acetonitrile/water solution containing the internal standard iprovalicarb-d7. The sample was filtered using a 45 µm GHP Acrodisc before HPLC-MS/MS analysis.

Protective gloves were extracted with 500 ml/glove of 2-propanol solution. A 0.05 – 0.1 ml aliquot was evaporated to dryness and the extract was reconstituted with 1 – 5 ml acetonitrile/water solution containing the internal standard iprovalicarb-d7. The sample was filtered using a 45 µm GHP Acrodisc before HPLC-MS/MS analysis.

Analysis was performed by HPLC-MS/MS using a Merck Superspher 60 RP-select B column (12.5 cm x 0.4 cm, 4 µm), at 40 ºC in positive ion mode for detection, monitoring the following mass transition: m/z 328→ 119 (stable-labelled internal standard SZX 0722-O-isopropyl-d7). A gradient elution was used (mobile phase A: water/acetonitrile 90:10, v:v and 0.1 ml acetic acid/l, mobile phase B: acetonitrile and 0.1 ml acetic acid/l).

Stability of extracts

Storage stability of iprovalicarb in all matrices was tested by determination of recovery at a range of fortification levels for 24 – 105 days at 4 – 8 ºC.

Table A1.8: Stability of extracts.

Matrix	Storage days	Fortification level (µg/specimen)	% Mean recoveries (n)	% RSD
Hand wash solution	0	0.1	91 (5)	2.7
	26		101 (5)	1.3
	105		101 (5)	1.2
	0	100	93 (5)	4.6
	26		101 (5)	1.9
	105		104 (5)	0.7
Under garment	0	0.5	89 (5)	5.5
	30		90 (5)	10.2
	104		91 (5)	7.7
	0	50	89 (5)	14.9
	30		87 (5)	12.6
	104		88 (5)	14.3
Gauze pads	0	0.1	95 (5)	2.6
	29		85 (5)	9.3
	104		96 (5)	2.9
	0	10	89 (5)	14.9
	29		93 (5)	5.2
	104		102 (5)	18.2
Outer garments, shirt	0	1	104 (5)	9.4
	26		96 (5)	4.4
	92		99 (5)	4.2
	0	100	106 (5)	3.9
	26		106 (5)	0.8
	92		107 (5)	1.7
Outer garments, jacket	0	1	106 (5)	5.5
	24		102 (5)	3.9
	92		97 (5)	5.7
	0	100	101 (5)	12.3
	24		105 (5)	2.5
	92		106 (5)	1.5
Protective gloves	0	50	96 (5)	7.4
	30		95 (5)	4.3
	85		97 (5)	6.6
	0	5000	105 (5)	4.3
	30		103 (5)	2.7
	85		107 (5)	3.5

Iprovalicarb was stable in all matrices for at least 24 – 105 days storage between 4 – 8 ºC.

Matrix effects

The method used an internal standard (stable labelled iprovalicarb-d7) for quantification. Any influence from the matrix in the samples affects the analyte iprovalicarb in the same way as the internal standard. There was no influence of the matrix on the results of the validation and therefore validation of iprovalicarb was conducted using solvent-based standards.

Validation summary

HPLC-MS/MS is a highly specific technique and a single mass transition was monitored. Chromatograms of standard solutions, control samples and fortified samples have been presented showing no interferences >30% LOQ at the retention time of interest. Accuracy

was assessed at 2 fortification levels for the analyte in each matrix of interest corresponding to the LOQ and either 100x or 1000x LOQ depending on the matrix; in all cases mean recovery was within the acceptable range of 70 – 110%. To assess method precision, 5 determinations were made at each fortification level and the RSDs were within the acceptable limit of 20%. The overall RSDs were between 3.8 and 10.6%. The linear range is appropriate for the expected values from field samples for all matrices (adjusting volumes and dilutions during sample preparation) and was determined using internal standards which compensates for any possible matrix effects. The LOQ of the method is 1 µg/specimen for outer garments, 0.5 µg/specimen for under garments, 0.1 µg/specimen for gauze pads and hand wash solutions and 50 µg/specimen for protective gloves. Although the method of analysis is not fully validated in accordance with SANCO/3029/99 rev.4, as 5 rather than 7 determinations of precision have been made at each fortification level, it is fit for purpose.

Table A1.9: Validation data summary for iprovalicarb residues in dosimeter, hand wash solution and face/neck wipe samples

Matrix	LOQ (µg/specimen)	Recovery fortification level (µg/specimen)	% recovery range (mean, n)	Repeatability % RSD (n)	Linearity	Specificity
Outer garments, jacket	1	1 100	98 – 114 (106, 5) 85 – 120 (101, 5)	5.5 12.3 Overall 9.1 (10)	0.025 – 50 µg/l [gauze pads approx. 0.0025 – 5 µg/specimen] [hand wash solution approx. 0.0025 – 5 µg/specimen] [protective gloves approx. 0.125 – 2500 µg/specimen] 11 standards, y = 0.481*x* + 0.0046, r = 0.9981	Acceptable chromatograms presented for standard, control and fortified samples. No interferences >30% LOQ.
Outer garments, shirts	1	1 100	13* – 111 (102, 4) 101 – 112 (106, 5)	9.4 (5) 3.9 (5) Overall: 6.8 (10)		
Under garments	0.5	0.5 50	84 – 95 (89, 5) 72 – 104 (89, 5)	5.5 (5) 14.9 (5) Overall: 10.6 (10)		
Face and neck gauze pads	0.1	0.1 10	93 – 98 (95, 5) 85 – 100 (89, 5)	2.6 (5) 14.9 (5) Overall: 4.6 (10)		
Hand wash solution	0.1	0.1 100	88 – 94 (91, 5) 89 – 100 (93, 5)	2.7 (5) 4.6 (5) Overall: 3.8 (10)		
Protective gloves	50	50 5000	87 – 101 (97, 5) 96 – 104 (100, 5)	5.9 (5) 2.8 (5) Overall: 4.7 (10)		

* Statistical outlier by Dixon's Q-Test, where:
Q = (suspect value – nearest value) / (largest value – smallest value)
= (13 – 88) / (111 – 13)
= 0.765 > Q crit, n=5 at 95% confidence interval (0.710)

Leaf wash solution (DFR): analytical method 01318 (MR-11/019)

Principle of the method

Iprovalicarb residues from a 400 cm^2 sample of leaf punch discs in 200 ml of a 0.01% aqueous solution of Aerosol OT-100 were analysed. 40 ml of acetonitrile was added to the 200 ml leaf wash sample and shaken for 1 minute. A 1 ml aliquot of the solution was transferred into a centrifuge tube and 0.1 ml of the internal standard (stable labelled iprovalicarb-d7) was added. After homogenisation, the solution was filtered and transferred into a HPLC vial for analysis.

Analysis was performed by HPLC-MS/MS using a Superlco Ascentis Express C18 column (2.7 µm, 50 mm x 2 mm) at 65 ºC in positive ion mode for detection, monitoring the following mass transitions: m/z 321 → 119 (quantification) and 321 → 203 (confirmatory). A gradient elution was used (mobile phase A: Mili-Q water/methanol (9:1, v:v) + 10 mM ammonium formate + 120 µl/l formic acid, mobile phase B: Mili-Q water/methanol (1:9, v:v) + 10 mM ammonium formate + 120 µl/l formic acid).

Matrix effects

The method used an internal standard (stable labelled iprovalicarb-d7) for quantification. Any influence from the matrix in the samples affects the analyte iprovalicarb in the same way as the internal standard. There was no influence of the matrix on the results of the validation and therefore validation of iprovalicarb was conducted using solvent-based standards.

Stability of extracts

The stability of iprovalicarb in grape leaf punch washing solution was tested by determination at a fortification level of 0.2 µg/l for 41 days at 6 ± 3 ºC under dark conditions.

Table A1.10: Stability of extracts.

Mass transition m/z 321 →119					
Matrix	**Storage days**	**Fortification level**		**Recovery % range (mean, n)**	**Mean deviation % from day 0**
		0.2 mg/l	0.1 µg/cm^2		
Iprovalicarb S/R diastereomer	0			95 – 113 (103, 7)	3.8
	41			95 – 107 (102, 7)	
Iprovalicarb S/S diastereomer	0			97 – 111 (105, 7)	4.9
	41			93 – 109 (103, 7)	

Iprovalicarb S/R- and S/S-diastereomers were stable in grape leaf punch washing solutions for at least 41 days storage at 6 ± 3 ºC under dark conditions.

Validation summary

HPLC-MS/MS is a highly specific technique and two mass transitions (3 ions) were monitored. For the quantification and confirmatory mass transitions, chromatograms of standard solutions, control and fortified samples have been presented showing no

interferences >30% LOQ at the retention time of interest. Although the chromatograms of the control and fortified samples provided are from tomato leaf washing solution, the matrices can be considered sufficiently similar, so it is unlikely to interfere with the specificity of the method. Accuracy was assessed at 4 fortification levels for the analyte in the matrix of interest (an additional fortification level at the revised LOQ of 0.01 µg/l was performed) and in all cases the mean recovery was within the acceptable range of 70 – 110%. To assess method precision, at least 5 determinations were made at each fortification level and RSDs were within the acceptable limit of 20%. The overall RSDs were between 9.5 – 10%. The linear range is appropriate for the nominal test concentration and was determined using internal standards, which compensates for any possible matrix effects. The LOQ of the method is 0.01 µg/l. Although the method of analysis is not fully validated in accordance with SANCO/3029/99 rev.4, as 5 rather than 7 determinations of precision have been made at the LOQ fortification level, it is fit for purpose.

Table A1.11: Validation data summary for iprovalicarb residues in grape leaf disc washing solutions

Analyte	Mass transition m/z	LOQ† (µg/l)	Recovery fortification level*		% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
			(µg/l)	(µg/cm² leaf surface area)				
Iprovalicarb S/R diastereomer	321 → 119	0.01	0.01† 8.34 83.4 834	0.000005 0.00417 0.0417 0.417	73 – 100 (88, 5) 77 – 120 (98, 7) 97 – 113 (103, 7) 96 – 105 (100, 7)	12.2 (5) 12.9 (7) 6.2 (7) 3.1 (7) Overall: 9.9 (26)	2.085 – 1042.5 µg/l [approx. 2.502 - 1251 µg/l leaf washing solution] [equivalent to 0.001251 – 0.6255 µg/cm²] 7 standards, y = 25.8x – 0.27, r =0.9995	Acceptable chromatogram presented for standard samples. No interference >30% LOQ. Identity confirmed by additional mass transition.
Iprovalicarb S/S diastereomer		0.01	0.01† 11.66 116.6 1166	0.000005 0.00583 0.0583 0.583	76 – 112 (90, 5) 71 – 107 (96, 7) 97 – 111 (105, 7) 92 – 106 (98, 7)	15.1 (5) 12.4 (7) 4.0 (7) 4.9 (7) Overall: 9.5 (26)	2.085 – 1042.5 µg/l [approx. 2.502 - 1251 µg/l leaf washing solution] [equivalent to 0.001251 – 0.6255 µg/cm²] 7 standards, y = 7.43x – 0.0899, r =0.9998	Acceptable chromatogram presented for standard samples. No interference >30% LOQ. Identity confirmed by additional mass transition.
Iprovalicarb S/R diastereomer	321 → 203	0.01	0.01† 8.34 83.4 834	0.000005 0.00417 0.0417 0.417	81 – 107 (90, 5) 73 – 105 (94, 7) 93 – 113 (101, 7) 95 – 106 (99, 7)	12.9 (5) 10.9 (7) 6.8 (7) 3.7(7)	2.915 – 1457.5 µg/l [approx. 3.498 – 1749 µg/l leaf	Acceptable chromatogram presented for standard samples.

Analyte	Mass transition m/z	LOQ† (µg/l)	Recovery fortification level*		% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
			(µg/l)	(µg/cm^2 leaf surface area)				
						Overall: 9.5 (26)	washing solution] [equivalent to 0.001749 – 0.8745 µg/cm^2] 7 standards, y = 24.4x – 0.0865 r =0.9994	No interference >30% LOQ.
Iprovalicarb S/S diastereomer		0.01	0.01† 11.66 116.6 1166	0.000005 0.00583 0.0583 0.583	74 – 109 (89, 5) 69 – 104 (94, 7) 95 – 107 (103, 7) 91 – 106 (98, 7)	15.0 (5) 12.8 (7) 3.6 (7) 5.2 (7) Overall: 10.0 (26)	2.915 – 1457.5 µg/L [approx. 3.498 – 1749 µg/l leaf washing solution] [equivalent to 0.001749 – 0.8745 µg/cm^2] 7 standards, y = 6.89x – 0.0379 r =0.9996	Acceptable chromatogram presented for standard samples. No interference >30% LOQ.

*The fortification levels as the sum of S,R- and S,S-diastereomers are 20, 200 and 2000 µg/l corresponding to 0.01, 0.1 and 1.0 µg/cm^2.

† Additional validation was carried at the revised LOQ of 0.01 µg/l

Study 2

Report ChR-16-24264. 'Determination of worker re-entry exposure associated to typical worker re-entry activities (pruning/tying up) in vineyards following treatment with BAS 553 01 F in Italy and Germany, 2016'

Author:	I. Thouvenin
Date (final report):	24/03/2017
Study 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.
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substances:	Dimethomorph (BAS 550 F) and Dithianon (BAS 216 F)
Product:	BAS 553 01 F
Crop:	Grapevine
Location:	Italy (1 site) and Germany (2 sites): • Site 1 (IT01) Sandra, Veneto, Italy • Site 2 (DE02) Merdingen, Baden Württemberg, Germany • Site 3 (DE03) Heuchelheim bei Frankenthal, Rheinland Pfalz, Germany

Aim.
The purpose of this study was to determine the potential and actual dermal exposure and inhalation exposure of workers carrying out maintenance activities in grapevines. Concurrent measurements of dislodgeable foliar residues (DFR) at the time of re-entry (in the associated study ChR-16-24265) permit the calculation of transfer coefficient (TC) values for these re-entry tasks.

Test material.
The study was carried out using the fungicide 'BAS 553 01 F', a water-dispersible granule (WG) formulation containing a nominal 15% dimethomorph (BAS 550 F) and 35% dithianon (BAS 216 F).

Study design.
Potential dermal exposure to foliar residues was measured for experienced workers (with between 1 and 20 years' experience) carrying out hand pruning and training (tying up) activities in grapevines. The field portion of the study was carried out at three commercial vineyards at 1 site in Italy and 2 sites in Germany. The vines (wine varieties 'Corvina' at site 1, Blauer Spätburgunder at site 2 and Spätburgunder Merlot at site 3) were planted 1.0 to 1.2 m apart in row widths of 2.5 m (site 1), 1.8 m (site 2) or 2.0 m (site 3). Plant height was reported to be approximately 2.0 m and the foliage was full at the time of the study.

Treatment details.
The product was applied 3 times at each site before worker re-entry as described in Table A2.1. The application equipment included a representative range of axial fan, crossflow and ducted air-assisted sprayers and tunnel sprayers.

Table A2.1: Treatment details.

Site	Treatment no.	Date of treatment	Growth stage (BBCH)	Maximum application rate* (g a.s./ha)		Actual application rate (g a.s./ha)		Application volume (l/ha)
				Dime	Dith	Dime	Dith	
1	1	09/05/2016	GS 71	225	525	225	525	300
	2	20/05/2016	GS 71	225	525	225	525	300
	3**	10/06/2016	GS 71	225	525	225	525	300
2	1	06/06/2016	GS 73	225	525	225	525	350
	2	15/06/2016	GS 73	225	525	225	525	450
	3	27/06/2016	GS 73	225	525	225	525	550
3	1	09/06/2016	GS 73-75	225	525	144	336	300
	2	19/06/2016	GS 73-75	225	525	180	420	400
	3	29/06/2016	GS 73-75	225	525	216	504	400

Dime = dimethomorph
Dith = dithianon
* equivalent to maximum individual dose on the product label of 1.5 kg of product/ha with reduced doses (equivalent to 0.96 to 1.44 kg of product/ha) being used at Site 3 based on crop development.
** application delayed (21-day interval from previous application) due to adverse weather conditions

The study report confirms that no other dimethomorph or dithianon products (or morpholine fungicides) were used were used at any of the sites during the 2016 growing season.

Re-entry activities.
Workers re-entered the treated crop on the day of the final treatment at site 1 or 1 day after the final treatment at site 2 and site 3. Four workers were monitored for each site, giving a total of 12 study subjects (10 male and 2 female). Each daily re-entry period was a full working day at sites 2 and 3 or half a day at site 1 (to allow the pesticide application made that morning to dry on the foliage before re-entry).

Workers at site 1 lifted and tied up the vine shoots. The upper wire was moved upwards on the supporting posts and the shoots were repositioned on the wires. Between the team of 4 workers, a total row length of 5900 m was lifted and tied in half a day (the actual working duration ranged from 279 to 288 minutes).

At site 2, workers pruned the crop to remove leaves around the bunches of grapes. A few shoots were also repositioned on the wires. Between the team of 4 workers, a total row length of 2650 m was pruned in a full day (the actual working duration ranged from 445 to 449 minutes).

At site 3, workers pruned the crop to remove leaves around the bunches of grapes. A few shoots were also repositioned on the wires. Between the team of 4 workers, a total row length of 5100 m was pruned in a full day (the actual working duration ranged from 446 to 448 minutes).

No unexpected incidents were reported for any of the workers which were likely to influence the study results.

Dislodgeable foliar residue (DFR) samples were collected on the day of re-entry (or within 1 day) as part of the concurrent study 734687-1. The dermal exposure data were used in conjunction with the DFR measurements to generate a transfer coefficient (TC) for the re-entry activities.

Exposure assessment.
Dermal exposure was assessed using whole-body dosimetry, hand washes and face/neck wipes. Protective gloves (partial nitrile) were worn at one site (site 1) but were not analysed for residues: the workers spontaneously requested these because the crop had been sprayed only a few hours earlier. A single operator (operator 4, site 1) wore a dust mask (which he provided) at his own request. Although inhalation exposure was also measured in this study, this route of exposure has not been considered further as it is not relevant for the calculation of TC values. Details of the sampling matrices are presented in Table A2.2.

Table A2.2: Exposure sampling matrices.

Body area	Sampling matrix	Description
Arms, legs, torso (outer layer)	Whole body dosimeter	One-piece 65% polyester/35% cotton coverall. Cut into sections for analysis (upper and lower arms, upper and lower legs, and front and back torso) to evaluate deposition on specific body parts.
Arms, legs, torso (inner layer)	Whole body dosimeter	Two-piece 100% cotton long-armed, long-legged underwear. Cut into sections for analysis (upper and lower arms, upper and lower legs, and front and back torso) to evaluate deposition on specific body parts.
Hands	Hand wash	Single hand wash using 1000 ml of a 0.01% aqueous solution of Aerosol OT-100 over a metal bowl. Taken before work (discarded), before lunch (and other breaks) and at the end of the monitoring period. A 50 ml aliquot was retained from each hand wash sample in a 125 ml HDPE bottle.
Face, neck	Face / neck wipes	Two sequential wipes, each using a multi-layer cotton gauze pad (10 cm x 10 cm) moistened with 4 ml of Aerosol OT-100 solution. Taken before work (discarded), before lunch (and other breaks) and at the end of the monitoring period. All wipes for an individual subject were collected together in a 250 ml HDPE bottle.
Face (additional sample for Operator 4, Site 1)	Dust mask	Disposable respirator used as dermal dosimeter

At the end of monitoring, dosimeter sections were wrapped in aluminium foil and bagged. All samples were stored on ice in a cool box at each site before being deep frozen until the time of extraction for analysis.

Environmental monitoring (non-GLP).
Air temperature, relative humidity, rainfall, wind speed and wind direction were recorded at local weather stations over the period from application to re-entry. These weather stations were located 3.5 to 15 km from site 1, 25 km from site 2 and 20 km from site 3. During application, wind speed was reported to be < 3m/s at all locations and daily air temperatures ranged from 14.2 - 26.5 ºC at site 1, 9.8 - 23.7 ºC at site 2 and 15.2 - 24.0 ºC at site 3. No rainfall was recorded at any of the 3 sites between the dates of application and re-entry.

Additionally, environmental conditions were monitored at each site itself 4 times (at sites 1 and 3) to 6 times (at site 2) during the re-entry activities. Air temperatures during re-entry ranged from 21.8 to 34.2 ºC across all 3 sites and relative humidity ranged from 21% to 64%. Winds were generally absent or light (the peak value recorded was 3.2 m/s).

No adverse weather events likely to affect the study results were reported.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.
Field recovery samples were produced for all sampling matrices to assess, and correct for, the recovery of the active substance from each matrix. These samples were fortified using the analytical standard in acetonitrile.

Three sets of field fortifications at 2 spiking levels were prepared for each matrix on each day of monitoring at each site as described in Table A2.3. Additionally, 1 set of untreated control recovery samples was produced for each matrix on each day at each site.

Fortified outer and inner dosimeter samples (the latter covered by a layer of unfortified outer dosimeter material) were exposed to the same environmental conditions for the same period of time as the monitoring garments, but positioned away from sources of contamination. Hand wash and face wipe recovery samples were stored on ice in a cool box immediately after spiking before being deep frozen.

Although a single worker (site 1, worker 4) used a dust mask, which was sampled as a dermal dosimeter, no field recovery data were generated for this matrix.

Field recovery results for dimethomorph are summarised in Table A2.3 (air sampling media not included).

Table A2.3: Dimethomorph field recovery results.

Matrix	Dimethomorph fortification level (µg/specimen)	Dimethomorph mean % recovery (3 replicates x 3 sites)				Dimethomorph recovery %RSD			
		Site 1	Site 2	Site 3	Mean	Site 1	Site 2	Site 3	Overall
Outer dosimeter	1.0 (100x LOQ)	98	101	98	99	1.2	0.6	1.4	1.7
	100 (10000x LOQ)	98	102	102	100	3.5	1.5	2.6	3.1
Inner dosimeter	0.1 (10x LOQ)	89	79	78	82	4.1	0.3	4.2	7.3
	10 (1000x LOQ)	87	77	96	80	1.0	1.0	1.7	7.0
Face wipe	0.1 (10x LOQ)	102	105	107	105	0.0	0.0	1.4	2.3
	10 (1000x LOQ)	106	104	104	104 [1]	4.5	0.6	0.7	2.6
Hand wash Site 1*	0.01 (0.2x LOQ)	116				1.0			
	10 (200x LOQ)	100				3.4			
Hand wash Sites 2 & 3	0.1 (2x LOQ)		108	106	110 [2]		1.9	1.1	4.2 [2]
	100 (2000x LOQ)		101	98	100 [2]		2.0	2.7	2.7 [2]
Partial nitrile gloves	0.1 (LOQ)	Because of unacceptable results, the partial nitrile gloves (worn only at Site 1) were not used as a sampling matrix							
	100 (1000x LOQ)								

* Part nitrile gloves (not sampled) were worn at this site.
[1] n = 8.
[2] includes all 3 sites.

For dimethomorph, mean recoveries ranged from 80% to 110% for all matrices used in the exposure calculations and were considered acceptable (within the 70% - 120% range). Mean RSD values were within acceptable limits (≤ 20%).

Field recovery results for dithianon are summarised in Table A2.4 (air sampling media not included).

Table A2.4: Dithianon field recovery results.

Matrix	Dithianon fortification level (µg/specimen)	Dithianon mean % recovery (3 replicates x 3 sites)				Dithianon recovery %RSD			
		Site 1	Site 2	Site 3	Mean	Site 1	Site 2	Site 3	Overall
Outer dosimeter	1.0 (100x LOQ)	41	59	46	48.8	2.8	1.9	2.6	17
	100 (10000x LOQ)	52	77	62	63.7	2.3	2.8	4.7	18
Inner dosimeter	0.1 (10x LOQ)	34	42	43	39.6	7.2	7.4	2.3	11
	10 (1000x LOQ)	64	66	67	65.7	12.6	0.4	8.6	7.9
Face wipe	0.1 (10x LOQ)	67	73	77	72.5	4.9	17.5	3.3	11
	10 (1000x LOQ)	112	108	111	110 [1]	1.0	3.2	3.2	2.8
Hand wash Site 1*	0.01 (0.2x LOQ)	100				3.8			
	10 (200x LOQ)	97				1.7			
Hand wash Sites 2 & 3	0.1 (2x LOQ)		112	110	107 [2]		1.0	1.1	5.5 [2]
	100 (2000x LOQ)		96	101	98 [2]		3.6	2.1	2.9 [2]
Partial nitrile gloves	0.1 (LOQ)	Because of unacceptable results, the partial nitrile gloves (worn only at Site 1) were not used as a sampling matrix							
	100 (1000x LOQ)								

* Part nitrile gloves (not sampled) were worn at this site.
[1] n = 8.
[2] includes all 3 sites.

For dithianon, mean recoveries ranged from 39.6% to 110% for all matrices used in the exposure calculations (i.e. not all within the 70% - 120% acceptable range). Mean RSD values were within acceptable limits (≤ 20%).

The study authors corrected monitoring samples for which field recoveries were <95% (based on the mean recovery for nearest fortification level): this is in line with the agreed UK HSE / BROV approach.

Travel recovery samples.
Additional travel recovery samples (not exposed to environmental conditions) were generated for each matrix (3 replicates at the high fortification level and 1 control sample) and at all sites. The results for dimethomorph and dithianon are summarised in Table A2.5 and A2.6, respectively.

Table A2.5: Dimethomorph travel recovery results.

Matrix	Dimethomorph fortification level (µg/specimen)	Dimethomorph mean % recovery (3 sites x 3 replicates)	Dimethomorph recovery % RSD
Outer dosimeter	100 (10000x LOQ)	104	2.2
Inner dosimeter	10 (1000x LOQ)	95.9	1.9
Face wipe	10 (1000x LOQ)	106	3.2
Hand wash site 1*	10 (200x LOQ)	101	5.3
Hand wash sites 2 & 3	100 (2000x LOQ)		

* Part nitrile gloves (not sampled) were worn at this site.

Table A2.6: Dithianon travel recovery results.

Matrix	Dithianon fortification level (µg/specimen)	Dithianon mean % recovery (3 sites x 3 replicates)	Dithianon recovery % RSD
Outer dosimeter	100 (10000x LOQ)	109	3.5
Inner dosimeter	10 (1000x LOQ)	93.5	8.1
Face wipe	10 (1000x LOQ)	111	2.2
Hand wash site 1*	10 (200x LOQ)	99.6	7.7
Hand wash sites 2 & 3	100 (2000x LOQ)		

* Part nitrile gloves (not sampled) were worn at this site.

All mean travel recoveries for both analytes were within acceptable limits.

Results.
All measured residue levels for both analytes were greater than the LOQ for every matrix and so it was not necessary to substitute the LOQ for measured values between LOQ and LOD or to substitute the LOD for values reported as non-detectable.

No statistical tests were conducted for outliers in the exposure data set. Several values were noticeably higher or lower than others in the data set for a given matrix, but all values were included in the calculations since there was no experimental basis for exclusion. Values were only excluded if the samples were compromised in the field, during transit, or during analysis.

The results, with residues corrected for samples with <95% field recovery, are presented in Table A2.7 and Table A2.8.

Table A2.7: Dimethomorph exposure results.

Dimethomorph residues on dermal monitoring matrices µg											
Site	Worker	Dosimeter	Lower arm	Upper arm	Front torso	Back torso	Lower leg	Upper leg	Face neck	Hands	Total
1	1	Outer	5264	1392	3636	799	612	1449	58.0	-	15600
		Inner	1040*	228*	280*	74.0*	41.3*	130*		597 [b]	
	2	Outer	7000	1187	29.5	810	813	1905	37.4	-	14378
		Inner	1070*	196*	210*	110*	89.0*	126*		795 [b]	
	3	Outer	9436	1848	3708	796	714	2229	28.0	-	21458
		Inner	943*	218*	250*	105*	77.3*	166*		940 [b]	
	4	Outer	8680	1624	2444	446	573	1554	152 [a] 21.9	-	18065
		Inner	1070*	161*	126*	540*	44.3*	90.3*		690 [b]	
2	5	Outer	1624	164	414	90.0	531	807	8.97	6725	10604
		Inner	42.0*	16.3*	33.8*	10.3*	51.6*	85.8*		-	
	6	Outer	1133	111	382	132	384	414	7.73	6345	9258
		Inner	203*	23.9*	36.0*	9.53*	24.1*	52.4*		-	
	7	Outer	920	211	378	177	369	1500	13.6	4575	8677
		Inner	107*	23.3*	27.3*	20.5*	66.8*	288*		-	
	8	Outer	931	137	298	161	336	600	7.03	6375	9166
		Inner	114*	17.4*	23.6*	15.6*	57.1*	92.8*		-	
3	9	Outer	1834	500	1022	250	393	1338	10.7	8640	14734
		Inner	360	87.0	72.3	28.3	40.0	159		-	
	10	Outer	1362	168	662	111	1038	543	12.9	5195	9467
		Inner	174	33.5	58.8	15.1	34.3	59.1		-	
	11	Outer	3500	409	1246	319	576	1227	31.6	7255	15523
		Inner	398	87.1	193	44.0	51.3	186		-	
	12	Outer	1267	354	1289	209	468	1581	11.1	10665	16672
		Inner	368	63.8	125	32.0	23.8	215		-	

* values corrected for recovery (at closest fortification level for the matrix at the same site) when field recovery was <95%

[a] dust mask for worker 4 (unreliable dermal dosimeter) not used in calculations

[b] actual hand exposure under part nitrile gloves

Table A2.8: Dithianon exposure results.

Dithianon residues on dermal monitoring matrices µg											
Site	Worker	Dosimeter	Lower arm	Upper arm	Front torso	Back torso	Lower leg	Upper leg	Face neck	Hands	Total
1	1	Outer	896*	2171*	7743*	1130*	1229*	2835*	222	-	19630
		Inner	1753*	347*	460*	122*	79.8*	161*		482 [b]	
	2	Outer	14220*	2220*	6330*	950*	1799*	3485*	119	-	33049
		Inner	1863*	288*	347*	174*	177*	169*		908 [b]	
	3	Outer	18110*	3429*	6895*	1080*	1808*	3942*	86.8	-	39082
		Inner	1412*	297*	387*	151*	115*	181*		1189 [b]	
	4	Outer	17429*	3011*	4754*	391*	1215*	2821*	131 [a]	-	32986
		Inner	1790*	202*	221*	78.2*	97.4*	111*	67.6	798 [b]	
2	5	Outer	6440*	730*	1713*	287*	2232*	2722*	64.1	17800	32822
		Inner	158*	60.0*	143*	31.1*	174*	268*		-	
	6	Outer	5231*	466*	1650*	444*	1870*	1630*	39.9	23200	35649
		Inner	691*	82.5*	112*	30.7*	71.4*	131*		-	
	7	Outer	3714*	912*	1689*	841*	1545*	5086*	45.1	14850	30412
		Inner	409*	94.8*	79.1*	63.0*	250*	834*		-	
	8	Outer	4110*	644*	1430*	316*	1484*	2651*	22.4	19100	30896
		Inner	435*	58.8*	62.4*	38.4*	240*	304*		-	
3	9	Outer	7758*	2141*	4024*	989*	1436*	5275*	26.3	27250	51221
		Inner	1148*	295*	201*	77.3*	132*	469*		-	
	10	Outer	6242*	801*	3030*	286*	4088*	2477*	32.2	17800	36027
		Inner	676*	108*	163*	42.0*	109*	173*		-	
	11	Outer	13934*	1670*	4776*	876*	2119*	4554*	97.9	21500	52507
		Inner	1449*	265*	502*	131*	135*	499*		-	
	12	Outer	5165*	1400*	5041*	582*	1936*	5981*	39.0	31700	54464
		Inner	1303*	187*	359*	83.7*	65.0*	623*		-	

* values corrected for recovery (at closest fortification level for the matrix at the same site) when field recovery was <95%

[a] dust mask for worker 4 (unreliable dermal dosimeter) not used in calculations

[b] actual hand exposure under part nitrile gloves

The study authors reported minimum, maximum, geometric mean, 75th percentile and 95th percentile exposure values based on the PDE, ADE and inhalation measurements. These calculated exposure values are not presented in this study summary as, for the purposes of the BROV project, it is appropriate to base such calculations on the combined database for all studies.

Annex: method of analysis for dimethomorph and dithianon and method validation.

Principle of the method

Outer dosimeter and dust mask samples were extracted with an appropriate volume (700 ml for arms, 1500 ml for legs, 1800 ml for torso and 30 ml for dust mask) of acetonitrile with 0.1% acetic acid on a horizontal shaker for 1 hour. A 0.5 ml aliquot was taken and mixed with 0.5 ml of water with 0.1% of acetic acid to give a final sample volume of 1 ml. The final 1 ml sample was further diluted by a factor of 5, 500 or 2000 to be within the calibration range.

Inner dosimeter samples were extracted with an appropriate volume (400 ml for arms, 600 ml for legs and 1000 ml for torso) of acetonitrile with 0.1% acetic acid on a horizontal shaker for 0.5 hour. A 0.5 ml aliquot was taken and mixed with 0.5 ml of water with 0.1% of acetic acid to give a final sample volume of 1 ml. The final 1 ml sample was further diluted by a factor of 5, 50 or 1000 to be within the calibration range.

Face/neck wipe samples (including the detergent added in the field) were extracted with 100 ml of acetonitrile with 0.1% acetic acid on a horizontal shaker for 0.5 hours. A 0.5 ml aliquot was taken and mixed with 0.5 ml of water with 0.1% acetic acid to give a final sample volume of 1 ml. The final 1 mL sample was further diluted by a factor of 50 or 500 to be within the calibration range.

A 0.5 ml aliquot of the 1000 ml hand wash solution was taken and mixed with 0.5 ml acetonitrile with 0.2% acetic acid. The 1 ml sample was further diluted with water/acetonitrile (1/1 v/v) with 0.1% acetic acid by a factor of 250 or 5000 to be within the calibration range.

Analysis was performed by LC-MS/MS using a Waters Acquity UPLC BEH C18 column (50 mm x 2.1 mm, 1.7 µm) at 60 °C in positive ion mode for detection, monitoring the following mass transitions for dimethomorph: m/z 388 → 301 (quantification) and m/z 388 → 165 (confirmatory) and in negative ion mode for detection, monitoring the following mass transition for dithianon: m/z 296 → 264 (quantification) and m/z 296 → 238 (confirmatory). A gradient elution was used (mobile phase A: water + 0.1 % formic acid, mobile phase B: acetonitrile + 0.1 % formic acid).

Matrix effects

Matrix matched standards were quantified against standards in acetonitrile/water (1:1, v:v) with 0.1% acetic acid at 5.0 ng/ml, 1.0 ng/ml, 0.25 ng/ml and 0.05 ng/ml. The matrix effect was calculated as a ratio of the mean peak area in matrix matched standards to the mean peak area in solvent standards expressed as a percentage.

Table A2.9: Matrix effects.

Matrix	Fortification level (ng/ml)	Dimethomorph mass transition (m/z)	Matrix effect (%)	Dithianon mass transition (m/z)	Matrix effect (%)
Face/neck wipe	5.0	388 → 301	4	296 → 264	6
	0.25		11		12
	0.05		8		6
	5.0	388 → 165	3	296 → 238	9
	0.25		2		6
	0.05		-3		0
Hand wash solution	5.0	388 → 301	-9	296 → 264	-4
	0.25		-3		4
	0.05		1		7
	5.0	388 → 165	-12	296 → 238	-2
	0.25		-3		7
	0.05		3		5
Inner dosimeter	5.0	388 → 301	3	296 → 264	0
	0.25		-3		-8
	0.05		2		5
	5.0	388 → 165	0	296 → 238	3
	0.25		-7		-5
	0.05		-2		8
Outer dosimeter	5.0	388 → 301	-5	296 → 264	4
	0.25		-9		3
	0.05		-12		-3
	5.0	388 → 165	-3	296 → 238	7
	0.25		-6		2
	0.05		-5		3

No significant matrix effects (>20%) were observed therefore calibration could be performed with standards in acetonitrile/water (1:1 v:v) with 0.1% acetic acid.

Validation summary

LC-MS/MS is a highly specific technique and two mass transitions (3 ions) were monitored for dimethomorph and dithianon. Chromatograms of standard solutions, control samples and fortified samples have been presented showing no interferences >30% LOQ at the retention time of interest. Accuracy was assessed at 4 fortification levels for the analyte in each matrix of interest corresponding to the LOQ and 10 – 50,000x LOQ depending on the matrix; in most cases mean recovery was within the acceptable range of 70 – 110%. For dimethomorph in face/neck wipes and dithianon in air filters, hand wash solution and outer dosimeter/dust mask, mean recovery at one fortification level was just outside the acceptable range 111 – 114%. To assess method precision, at least 7 determinations were made at each fortification level and the RSDs were within the acceptable limits of 20%. The overall RSDs were between 2.3 – 15%. The linear range is appropriate for the expected values from field samples for all matrices and was determined using solvent-based standards as no significant matrix effects were observed. The LOQ of the method is 0.01 µg/sample for dosimeters, 0.01 µg/sample for face/neck wipes and 0.05 µg/sample for hand wash solution. Although the method of analysis is not fully validated in accordance with SANCO/3029/99 rev.4, for dimethomorph in face/neck wipes and for dithianon in hand wash solution and outer

dosimeter/dust mask as mean recovery at one fortification level was just outside the acceptable range, it is fit for purpose.

Table A2.10: Validation data summary of dimethomorph and dithianon residues on dosimeter, hand wash solution and face/neck wipes

Matrix	Active substance	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Outer dosimeter and dust mask	Dimethomorph	388 → 301	0.01	0.01 1.0 100 500	95 – 113 (99, 9) 102 – 108 (104, 6) 95 – 114 (106, 9) 102 – 107 (105, 7)	7.1 (9) 2.0 (6) 4.7 (9) 2.0 (7) Overall: 5.2 (31)	0.015 – 25 ng/ml 10 standards, y = $5.68x10^5x + 2.13x10^3$, r = 0.9997	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ. Identity confirmed by additional mass transition.
Inner dosimeter			0.01	0.01 0.1 10 200	85 – 109 (91, 9) 95 – 97 (96, 7) 95 – 101 (97, 9) 100 – 113 (105, 7)	9.0 (9) 1.1 (7) 2.1 (9) 3.9 (7) Overall: 7.0 (32)		
Face/neck wipes			0.01	0.01 0.1 10 200	110 – 118 (114, 8) 102 – 116 (109, 7) 108 – 113 (110, 8) 102 – 115 (107, 7)	3.4 (8) 4.7 (7) 1.3 (8) 5.1 (7) Overall: 4.2 (30)		
Hand wash solution			0.05	0.05 0.1 100 1500	106 – 112 (109, 8) 109 – 112 (110, 8) 104 – 115 (108, 8) 103 – 112 (108, 7)	1.7 (8) 0.9 (8) 3.2 (8) 2.5 (7) Overall: 2.3 (31)		
Outer dosimeter and dust mask		388 → 165	0.01	0.01 1.0 100 500	90 – 114 (97, 9) 101 – 104 (103, 6) 96 – 114 (105, 9) 102 – 109 (106, 7)	8.5 (9) 1.6 (6) 4.6 (9) 1.9 (7) Overall: 6.2 (31)	0.015 – 25 ng/ml 10 standards, y = $2.01x10^5x + 73.9$, r = 0.9998	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ.

Matrix	Active substance	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Inner dosimeter			0.01	0.01 0.1 10 200	88 – 109 (94, 9) 96 – 98 (96, 7) 96 – 100 (99, 9) 102 – 113 (105, 7)	8.3 (9) 1.4 (7) 1.2 (9) 3.9 (7) Overall: 6.2 (32)		
Face/neck wipes			0.01	0.01 0.1 10 200	107 – 115 (110, 8) 102 – 116 (109, 7) 107 – 111 (110, 8) 104 – 117 (108, 7)	2.9 (8) 5.4 (7) 2.0 (8) 4.9 (7) Overall: 3.7 (30)		
Hand wash solution			0.05	0.05 0.1 100 1500	103 – 113 (109, 8) 109 – 113 (110, 8) 101 – 115 (107, 8) 102 – 111 (108, 7)	2.9 (8) 1.3 (8) 3.8 (8) 2.7 (7) Overall: 2.9 (31)		
Outer dosimeter and dust mask	Dithianon	296 → 264	0.01	0.01 1.0 100 500	82 – 92 (86, 9) 108 – 112 (110, 6) 95 – 113 (105, 9) 105 – 112 (108, 7)	4.0 (9) 1.6 (6) 5.1 (9) 2.4 (7) Overall: 10.0 (31)	0.015 – 10 ng/ml 9 standards, y = $3.28x10^5x$ + 663, r = 0.9998	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ. Identity confirmed by additional mass transition.
Inner dosimeter			0.01	0.01 0.1 10 200	76 – 86 (82, 9) 93 – 102 (99, 7) 101 – 110 (107, 9) 101 – 116 (106, 7)	4.3 (9) 3.0 (7) 2.7 (9) 4.5 (7) Overall: 12.0 (32)		

Matrix	Active substance	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Face/neck wipes			0.01	0.01 0.1 10 200	90 – 113 (103, 8) 89 – 108 (98, 7) 102 – 111 (108, 8) 105 – 118 (110, 7)	6.6 (8) 7.5 (7) 4.8 (8) 4.4 (7) Overall: 7.1 (30)		
Hand wash solution			0.05	0.05 0.1 100 1500	75 – 84 (80, 8) 79 – 102 (85, 8) 107 – 117 (110, 8) 103 – 112 (108, 7)	4.7 (8) 9.5 (8) 2.8 (8) 3.2 (7) Overall: 15.0 (31)		
Outer dosimeter and dust mask		296 → 238	0.01	0.01 1.0 100 500	85 – 94 (92, 9) 109 – 113 (111, 6) 98 – 115 (107, 9) 105 – 111 (108, 7)	7.8 (9) 1.2 (6) 4.8 (9) 2.0 (7) Overall: 2.0 (31)	0.015 – 10 ng/ml 9 standards, y = $6.15x10^4x + 86.3$, r = 0.9998	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ.
Inner dosimeter			0.01	0.01 0.1 10 200	80 – 88 (84, 9) 90 – 105 (98, 7) 104 – 111 (107, 9) 106 – 111 (108, 7)	4.1 (9) 4.8 (7) 2.1 (9) 1.7 (7) Overall: 11.0 (32)		
Face/neck wipes			0.01	0.01 0.1 10 200	95 – 100 (97, 8) 94 – 110 (101, 7) 103 – 114 (108, 8) 103 – 116 (110, 7)	2.8 (8) 6.0 (7) 3.6 (8) 4.2 (7) Overall: 6.6 (30)		

Matrix	Active substance	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Hand wash solution			0.05	0.05 0.1 100 1500	76 – 88 (81, 8) 79 – 103 (86, 8) 106 – 119 (111, 8) 105 – 112 (108, 7)	6.1 (8) 9.5 (8) 3.6 (8) 2.2 (7) Overall: 15.0 (31)		

Study 3

Report ChR-16-24265. 'Determination of dislodgeable foliar residues of dimethomorph (BAS 550 F) and dithianon (BAS 216 F) after application of BAS 553 01 F to grapevines, 2016'

Author:	Ch. H. Roussel
Date (final report):	05/05/2017
Study guidelines:	EPA Assessment Guidelines Series 875 Occupational and Residential Exposure Test Guidelines, Group B Post-application Exposure Monitoring Test Guideline, Part B, Chapter 3 – Dislodgeable Foliar Residue Dissipation: Agricultural (Guideline 875.2100).
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substances:	Dimethomorph (BAS 550 F) and Dithianon (BAS 216 F)
Product:	BAS 553 01 F
Crop:	Grapevine
Location:	Italy (1 site) and Germany (2 sites): • Site IT01 Sandra, Veneto, Italy • Site DE02 Merdingen, Baden Württemberg, Germany • Site DE03 Partenheim, Rheinland-Pfalz, Germany

Aim.
The purpose of this study was to determine the dislodgeable foliar residues (DFR) of dimethomorph and dithianon on vine leaves after applications of BAS 553 01 F in sites in Italy and Germany. Concurrent measurements of worker exposure during re-entry activities (in the associated study ChR-16-24264) permit the calculation of transfer coefficient (TC) values for these tasks.

Test material.
The study was carried out using the fungicide 'BAS 553 01 F', a water-dispersible granule (WG) formulation containing a nominal 15% dimethomorph (BAS 550 F) and 35% dithianon (BAS 216 F).

Study design.
Dislodgeable foliar residues (DFR) of dimethomorph and dithianon on vine leaves after multiple applications of BAS 553 01 F were determined. The field portion of the study was carried out at 3 commercial vineyards at 1 site in Italy and 2 sites in Germany. The vines (wine varieties Corvina at site IT01, Müller-Thurgau at site DE02 and Weisser Burgunder at site DE03) were planted 1.0 m (sites IT01 and DE03) or 1.2 m (site DE02) apart in row widths of 2.0 m (sites DE02 and DE03) or 2.5 m (site IT01). Crop height was reported to be 1.90 m (site IT01), 2.00 m (site DE02) or 2.05 m (site DE03) with a leaf wall height of

1.10 m (site IT01), 1.00 m (site DE02) or 1.20 m (site DE03). The foliage at all sites was full at the time of the study. The treated plot areas were 225 m^2 (site IT01), 327 m^2 (DE02) or 200 m^2 (DE03) and were divided into 3 sub-plots to provide 3 replicate samples at each site for each sampling interval.

Treatment details.
The product was applied 3 times at each site before worker re-entry as summarised in Table A3.1. Knapsack mist blowers (Maruyama at site IT01 and Solo at sites DE02 and DE03), of the type used in efficacy and residues trials to mimic typical commercial broadcast air-assisted sprayers, were used.

Table A3.1: Treatment details.

Site	Treatment no.	Date of treatment	Growth stage (BBCH)	Application rate (g a.s./ha)			Application volume (l/ha)
				Dime	Dith	% of target*	
IT01	1	09/05/16	55	215	487	92.7	371
	2	20/05/16	57	230	519	98.9	396
	3	10/06/16	71	212	478	91.1	364
DE02	1	07/06/16	55	248	560	106.6	320
	2	18/06/16	63	262	592	112.7	338
	3	28/06/16	71	221	499	95.0	285
DE03	1	09/06/16	55-58	216	488	93.0	372
	2	19/06/16	61-65	235	532	101.3	405
	3	29/06/16	69-71	230	518	98.7	395

Dime = dimethomorph
Dith = dithianon
* Target application rate equivalent to 1.5 kg of product/ha.

Applications were planned at 10-day intervals but, because of adverse weather conditions, this was extended for applications 2 and 3 at site IT01 (11 and 21 days after previous application, respectively) and for application 2 at site DE02 (11 days after the previous application).

A record was provided of all pesticides applied at each site during the 2016 season: no other products containing dimethomorph or dithianon were used before or during the studies.

Dislodgeable foliar residue (DFR) sampling.
Leaf samples were taken from each of the 3 sub-plots at each site using a leaf punch with discs collected directly into a pre-labelled jar. Samples were taken from all areas of the crop likely to be in contact with workers during crop maintenance activities. Each sample consisted of 40 leaf discs, each disc with a 2-sided area of 10 cm^2, giving a total leaf area per sample of 400 cm^2. Samples were also taken from untreated plots to produce fortified and control leaf wash solutions. The leaf punch was cleaned with acetone and de-ionised water after each sample.

Leaf disc samples from treated plots were taken at each site before each application and immediately after each application (once the spray had dried on the foliage). Additional samples from treated plots were taken at intervals of 1, 3, 5, 7, 10, 14 (± 1) and 21 (± 1) days after the final application. Leaf disc samples from untreated control plots were taken at the time of each application (to the treated plots) and at intervals (varying between sites) of either 7, 13 - 14 or 21 days after the final application.

Dislodging of the residues from the leaf samples was carried out within a few hours of sampling by mechanically shaking the discs twice for 10 minutes in a 0.01% aqueous solution of Aerosol OT-100 acidified with 0.1% acetic acid (2x 100 ml washes for 40-disc samples). 20 ml aliquots of the extraction solutions were deep frozen within 8 hours of sampling until analysis.

Environmental monitoring.
Air temperature and rainfall data were provided by the nearest meteorological station to each site (10 km from IT01, 25 km from DE02 and 18 km from DE03) from the first application date to the final sampling date, together with comparative historical data for the same period in other years.

Additionally, air and soil temperature, relative humidity, cloud cover, wind direction, wind speed and rainfall were monitored at each trial site during each application. Rainfall was also monitored throughout the rest of the field phase.

No adverse weather events likely to affect the study results were reported.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.
Field recovery samples were produced on 4 or 5 occasions at each site to assess, and correct for, the recovery of the active substances from the leaf disk wash solution. Each set of recovery samples consisted of one unfortified blank solution, 3 replicates fortified at 10x LOQ and 3 replicates fortified at 1000x LOQ. The dislodging solutions were fortified using the analytical standard in acetonitrile and 0.1% acetic acid. All samples were prepared using matrix-loaded dislodging solutions (i.e. the solution having been used to wash untreated control discs before fortification).

Field recovery results for the leaf wash (DFR) samples taken after application 3 are summarised in Table A3.2. Although field recovery samples were also taken 0 DAA1, 0 DAA2, 7 DAA3, 13-14 DAA3 and 21 DAA3, these results are not relevant for the calculation of the DFR at the time of worker re-entry (0 - 1 DAA3) and have not been considered further in this summary.

Table A3.2: Field recovery results.

Sample timing	Fortification level (µg/200 ml specimen)	% recovery (3 replicates x 3 sites)						
		Analyte	Dimethomorph (BAS 550 F)			Dithianon (BAS 216 F)		
		Site	IT 01	DE 02	DE 03	IT 01	DE 02	DE 03
0 - 1 DAA3	20 (10x LOQ)	Mean	119	108	110	45	97	97
		%RSD	9	3	6	13	11	2
	2000 (1000x LOQ)	Mean	106	108	93	110	109	103
		%RSD	7	1	3	6	2	23
Dimethomorph and dithianon recoveries at site DE 02 were corrected for residues in the control samples.								

Mean recoveries for leaf wash solutions were considered acceptable (generally within the 70% - 120% range). Mean RSD values were generally within acceptable limits (≤ 20%). For dithianon, low level field fortifications at site IT01 gave varying and unexpectedly low recoveries, indicating that possibly the pH was not sufficiently adjusted with acidic acid for dithianon stabilization.

This evaluation has corrected DFR samples for which field recoveries were <95% (based on the mean recovery for the nearest fortification level): this is in line with the agreed UK HSE / BROV approach.

Results.
All measured residue levels were greater than the LOQ and so it was not necessary to substitute the LOQ for measured values between LOQ and LOD or to substitute the LOD for values reported as non-detectable.

No statistical tests were conducted for outliers in the data set. Several values were noticeably higher or lower than others, but all values were included in the calculations since there was no experimental basis for exclusion. Values were only excluded if the samples were compromised in the field, during transit or during analysis.

The DFR results, for the sample timing 0 - 1 DAA3 with residues corrected for samples with <95% field recovery, are presented in Table A3.3. Although DFR samples were also taken 0 DAA1, 0 DBA2, 0 DAA2, 0 DBA3, 3 DAA3, 5 DAA3, 7 ± 1 DAA3, 10 ± 1 DAA3, 14 ± 1 DAA3 and 21 ± 1 DAA3, these results are not relevant for the calculation of the DFR at the time of worker re-entry (0 - 1 DAA3) and have not been considered further in this summary.

Table A3.3: DFR results.

Residues in leaf wash samples: DFR (µg/cm^2)							
Analyte		Dimethomorph (BAS 550 F)			Dithianon (BAS 216 F)		
Sample timing	Site	IT01	DE02	DE03	IT01	DE02	DE03
0-1 DAA3	Mean	0.603	0.535	0.598	2.379*	1.300	1.422
	%RSD	9.9	6.1	25.5	5.1	6.0	14.8
* Mean value corrected for recovery (at closest fortification level for the leaf wash solution at the same site) when field recovery was <95%							

Annex: method of analysis for dimethomorph and dithianon and method validation.

Principle of the method

Dimethomorph and dithianon residues extracted from 400 cm^2 of leaf punch discs in 200 ml of a 0.01% aqueous solution of Aerosol OT-100 dislodging solution were analysed. A 0.2 ml aliquot of the solution was pipetted into 0.8 ml of acetonitrile/water (1:1, v:v) with 0.1% acetic acid to reach a final volume of 1 ml. The extracts were further diluted with acetonitrile/water (1:1, v:v) with 0.1% acetic acid) to be within the calibration range of the analytical equipment.

Analysis was performed by LC-MS/MS using a Waters Acquity UPLC BEH C18 column (50 mm x 2.1 mm, 1.7 µm), at 60 ºC in positive ion mode for detection, monitoring the following mass transitions for dimethomorph: m/z 388 → 301 (quantification) and m/z 388 → 165 (confirmatory) and in negative ion mode for detection, monitoring the following mass transitions for dithianon: m/z 296 → 264 (quantification) and m/z 296 → 238 (confirmatory). A gradient elution was used (mobile phase A: water + 0.1 % formic acid, mobile phase B: acetonitrile + 0.1 % formic acid).

Matrix effects

Matrix matched standards were quantified against standards in acetonitrile/water (1:1, v:v) with 0.1% acetic acid at 5.0 ng/ml, 1.0 ng/ml, 0.25 ng/ml and 0.05 ng/ml. The matrix effect was calculated as a ratio of the mean peak area in matrix matched standards to the mean peak area in solvent standards expressed as a percentage.

Table A3.4: Matrix effects.

Matrix	Fortification level (ng/ml)	Dimethomorph mass transition (m/z)	Matrix effect (%)	Dithianon mass transition (m/z)	Matrix effect (%)
Leaf washing solution (0.01% OT-100 solution)	5.0	388 → 301	-5.9	296 → 264	10
	1.0		7.4		12
	0.25		6.1		0.2
	5.0	388 → 165	-4.5	296 → 238	3.8
	1.0		8.8		11
	0.25		-2.1		1.6
Leaf washing solution (site IT01)	5.0	388 → 301	-9.6	296 → 264	-8.8
	1.0		-2.5		-13
	0.25		4.9		-3.2
	5.0	388 → 165	-8.1	296 → 238	-11
	1.0		-0.5		-11
	0.25		-4.4		-6.3
Leaf washing solution (site DE02)	5.0	N/A		296 → 264	-1.2
	1.0				2.4
	0.25				11
	5.0	N/A		296 → 238	-3.2
	1.0				2.7
	0.25				12
Leaf washing solution (site DE03)	5.0	388 → 301	-12	296 → 264	-7.6
	1.0		4.9		-12
	0.25		6.1		2.2
	5.0	388 → 165	-9.0	296 → 238	-10
	1.0		-2.3		-12
	0.25		-1.0		-1.1

No significant matrix effects (>20%) were observed, therefore, calibration could be performed with standards in acetonitrile/water (1:1, v:v) with 0.1% acetic acid.

Validation summary

LC-MS/MS is a highly specific technique and two mass transitions (3 ions) were monitored for dimethomorph and dithianon. Chromatograms of standard solutions, control samples and fortified samples have been presented showing no interferences >30% LOQ at the retention time of interest. Accuracy was assessed at 3 fortification levels for the analyte in leaf wash solution corresponding to the LOQ, 10x LOQ and 1000x LOQ; in all cases mean recovery was within (or very slightly over) the acceptable range of 70 – 110%. To assess method precision, at least 7 determinations were made at each fortification level and the RSDs were within the acceptable limit of 20%. The overall RSDs were between 4.3 and 8.1%. The linear range is appropriate for the expected values from field samples and was determined using solvent-based standards as no significant matrix effects were observed. The LOQ of the method is 0.01 µg/ml for leaf wash solution. Although the method of analysis is not fully validated in accordance with SANCO/3029/99 rev.4, as mean recovery at one fortification level was just outside the acceptable range, it is fit for purpose.

Table A3.5: Validation data summary for dimethomorph and dithianon residues in leaf washing solution samples

Matrix	Active substance	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Grape leaf washing solution	Dimethomorph	388 → 301	0.010 µg/ml	0.010 µg/ml 0.1 µg/ml 10 µg/ml	106 – 112 (109, 9) 102 – 117 (108, 7) 103 – 123 (111, 9)	1.8 (9) 4.5 (7) 6.6 (9) Overall: 4.7 (25)	0.025 - 10 ng/ml [equivalent to 0.00125 – 25 µg/ml] 8 standards, y = $1.04x10^{6}x + 1.71x10^{3}$, r = 0.9999	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ. Identity confirmed by additional mass transition.
		388 → 165	0.010 µg/ml	0.010 µg/ml 0.1 µg/ml 10 µg/ml	102 – 113 (108, 9) 98 – 109 (104, 7) 101 – 119 (108, 9)	3.0 (9) 4.1 (7) 5.1 (9) Overall: 4.3 (25)	0.025 - 10 ng/ml [equivalent to 0.00125 – 25 µg/ml] 8 standards, y = $3.69x10^{5}x + 718$, r = 0.9998	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ.
	Dithianon	296 → 264	0.010 µg/ml	0.010 µg/ml 0.1 µg/ml 10 µg/ml	93 – 111 (101, 9) 89 – 102 (99, 7) 97 – 120 (111, 9)	5.8 (9) 4.8 (7) 7.5 (9) Overall: 8.1 (25)	0.025 - 10 ng/ml [equivalent to 0.00125 – 25 µg/ml] 8 standards, y = $4.2x10^{5}x - 2.01x10^{3}$, r = 0.9995	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ. Identity confirmed by additional mass transition.

Matrix	Active substance	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
		296 → 238	0.010 µg/ml	0.010 µg/ml 0.1 µg/ml 10 µg/ml	93 – 104 (99, 9) 90 – 100 (97, 7) 96 – 115 (108, 9)	3.7 (9) 3.8 (7) 6.2 (9) Overall: 6.6 (25)	0.025 - 10 ng/ml [equivalent to 0.00125 – 25 µg/ml] 8 standards, y = $7.76x10^4x$ - 455, r = 0.9998	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ.

Study 4

Report ChR-16-26172. 'Determination of worker re-entry exposure associated to typical worker re-entry activities (pruning) in vineyards following treatment with BAS 605 04 F in France and Germany, 2016'

Author:	I. Thouvenin
Date (final report):	31/01/2017
Study 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.
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substances:	Pyrimethanil (BAS 605 F)
Product:	BAS 605 04 F
Crop:	Grapevine
Location:	France (1 site) and Germany (2 sites): • Site 1 (FR01) Saint-Martial, Aquitaine, France • Site 2 (DE02) Merdingen, Baden Württemberg, Germany • Site 3 (DE03) Heuchelheim bei Frankenthal, Rheinland Pfalz, Germany

Aim.
The purpose of this study was to determine the potential and actual dermal exposure and inhalation exposure of workers carrying out maintenance activities in grapevines. Concurrent measurements of dislodgeable foliar residues (DFR) at the time of re-entry (in the associated study ChR-16-26173) permit the calculation of transfer coefficient (TC) values for these re-entry tasks.

Test material.
The study was carried out using the fungicide 'BAS 605 04 F', a suspension concentrate (SC) formulation containing a nominal 400 g/l pyrimethanil (BAS 605 F).

Study design.
Potential dermal exposure to foliar residues was measured for experienced workers (with between 1 and 10 years' experience) carrying out hand pruning activities in grapevines. The field portion of the study was carried out at three commercial vineyards at 1 site in France and 2 sites in Germany. The vines (wine varieties Merlot, Cabernet Franc at site 1, Blauer Spätburgunder at site 2 and Dornfelder, Riesling, Merlot and Pinot Noir at site 3) were planted 1.0 to 1.2 m apart in row widths of 3.0 m (site 1), 1.8 m (site 2) or 2.0 m (site 3). Plant height was reported to be approximately 2.0 m and the foliage was full at the time of the study.

Treatment details.
The product was applied once at each site before worker re-entry as in Table A4.1. The application equipment included a representative range of crossflow and ducted air-assisted sprayers.

Table A4.1: Treatment details.

Site	Treatment no.	Date of treatment	Growth stage (BBCH)	Maximum application rate* (g a.s./ha)	Actual application rate (g a.s./ha)	Application volume (l/ha)
1	1	25/07/2016	GS 79	1000	1000	200
2	1	19/07/2016	GS 79	800	800	250
3	1	18/07/2016	GS 79	800	800	300
* equivalent to maximum individual dose on the product label of 2.5 litres of product/ha at site 1 with a reduced dose equivalent to 2.0 litres of product/ha used at sites 2 and 3 based on crop development.						

The study report confirms that no other pyrimethanil products (or anilinopyrimidine fungicides) were used were used at any of the sites during the 2016 growing season.

Re-entry activities.
Workers re-entered the treated crop 1 day after treatment at all sites. Four workers were monitored at each site, giving a total of 12 study subjects (11 male and 1 female). Each re-entry monitoring period was a full working day at each site.

At site 1, workers pruned the vines to remove leaves from the bunches of grapes. Only one side of the row was pruned: leaves on the other side were left in place to protect the bunches of grapes from the afternoon sun. The vines at this site had previously been mechanically pruned. Some long shoots were repositioned and some wires were moved. Between the team of 4 workers, a total row length of 6800 m was lifted and tied in a full day (the actual working duration ranged from 447 to 450 minutes).

At site 2, workers pruned the crop to remove leaves around the bunches of grapes. Only one side of the row was pruned: leaves on the other side were left in place to protect the bunches of grapes from the afternoon sun. Some shoots were repositioned on the wires and some wires were moved. Between the team of 4 workers, a total row length of 3600 m was pruned in a full day (the actual working duration ranged from 463 to 470 minutes).

At site 3, workers pruned the crop to remove leaves around the bunches of grapes. Only one side of the row was pruned: leaves on the other side were left in place to protect the bunches of grapes from the afternoon sun. The vines at this site had previously been mechanically pruned and there were only a few long shoots to be moved. Between the team of 4 workers, a total row length of 4800 m was pruned in a full day (the actual working duration ranged from 444 to 449 minutes).

No unexpected incidents were reported for any of the workers which were likely to influence the study results.

Dislodgeable foliar residue (DFR) samples were collected within 1 to 2 days of re-entry as part of the concurrent study ChR-16-26173. The dermal exposure data were used in conjunction with the DFR measurements to generate a transfer coefficient (TC) for the re-entry activities.

Exposure assessment.
Dermal exposure was assessed using whole-body dosimetry, hand washes and face/neck wipes. Gloves were not worn. Although inhalation exposure was also measured in this study, this route of exposure has not been considered further as it is not relevant for the calculation of TC values. Details of the sampling matrices are summarised in Table A4.2.

Table A4.2: Sampling matrices.

Body area	Sampling matrix	Description
Arms, legs, torso (outer layer)	Whole body dosimeter	One-piece 65% polyester/35% cotton coverall. Cut into sections for analysis (upper and lower arms, upper and lower legs, and front and back torso) to evaluate deposition on specific body parts.
Arms, legs, torso (inner layer)	Whole body dosimeter	Two-piece 100% cotton long-armed, long-legged underwear. Cut into sections for analysis (upper and lower arms, upper and lower legs, and front and back torso) to evaluate deposition on specific body parts.
Hands	Hand wash	Single hand wash using 1000 ml of 0.01% aqueous solution of Aerosol OT-100 over a metal bowl. Taken before work (discarded), before lunch (and other breaks) and at the end of the monitoring period. A 50 ml aliquot was retained from each hand wash sample in a 125 ml HDPE bottle.
Face, neck	Face / neck wipes	Two sequential wipes, each using a multi-layer cotton gauze pad (10 cm x 10 cm) moistened with 4 ml of Aerosol OT solution. Taken before work (discarded), before lunch (and other breaks) and at the end of the monitoring period. All wipes for an individual subject were collected together in a 250 ml HDPE bottle.

At the end of monitoring, dosimeter sections were wrapped in aluminium foil and bagged. All samples were stored on ice in a cool box at each site before being deep frozen until the time of extraction for analysis.

Environmental monitoring (non-GLP).
Air temperature, relative humidity, rainfall, wind speed and wind direction were recorded at local weather stations over the period from application to re-entry. These weather stations were located between 7 km (site 1) and 20 km (site 3) from the study sites. During

application, wind speed was reported to be < 3 m/s at all locations and daily air temperatures ranged from 14.5 – 28.4 ºC at site 1, 14.9 – 31.0 ºC at site 2 and 16.0 – 30.4 ºC at site 3. No rainfall was recorded at any of the 3 sites between the dates of application and re-entry.

Additionally, environmental conditions were monitored at each site itself 4 times during the re-entry activities. Air temperatures during re-entry ranged from 15.5 to 37.7 ºC across all 3 sites and relative humidity ranged from 30% to 83%. Winds were generally absent or light (the peak value recorded was 2.9 m/s).

No adverse weather events likely to affect the study results were reported.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.
Field recovery samples were produced for all sampling matrices to assess, and correct for, the recovery of the active substance from each matrix. These samples were fortified using the analytical standard in methanol.

Three sets of field fortifications at 2 spiking levels were prepared for each matrix on each day of monitoring at each site as described in Table A4.3. Additionally, 1 set of untreated control recovery samples was produced for each matrix on each day at each site.

Fortified outer and inner dosimeter samples (the latter covered by a layer of unfortified outer dosimeter material) were exposed to the same environmental conditions for the same period of time as the monitoring garments, but positioned away from sources of contamination. Hand wash and face wipe recovery samples were stored on ice in a cool box immediately after spiking before being deep frozen.

Field recovery results are summarised in Table A4.3 (air sampling media not included).

Table A4.3: Field recovery results.

Matrix	Fortification level (µg/specimen)	Mean % recovery (3 replicates x 3 sites)			
		Site 1	Site 2	Site 3	Mean
Outer dosimeter	1.0* (100x LOQ)	92	88	87	89
	100 (10000x LOQ)	92	88	95	91
Inner dosimeter	0.1 (10x LOQ)	93	86	93	90
	10 (1000x LOQ)	106	105	109	107
Face wipe	0.1 (10x LOQ)	96	97	89	94[1]
	10 (1000x LOQ)	99	98	98	98
Hand wash	0.1 (2x LOQ)	90	88	90	89
	100 (2000x LOQ)	106	95	98	99

* 0.1 µg at site 3 – this deviation had no impact as the measured residue levels on the outer dosimeter were closer to the high fortification level.
[1] n = 8.

Mean recoveries ranged from 89% to 107% for all matrices used in the exposure calculations and were considered acceptable (within the 70% - 120% range). Mean RSD values were within acceptable limits (≤ 20%).

For outer dosimeters, the study authors presented the results already corrected for 91.3% recovery: these results have been back-calculated to derive uncorrected values. This evaluation has corrected monitoring samples for which field recoveries were <95% (based on the mean recovery for nearest fortification level): this is in line with the agreed UK HSE / BROV approach.

Travel recovery samples.
Additional travel recovery samples (not exposed to environmental conditions) were generated for each matrix (3 replicates at the high fortification level and 1 control sample) and at all sites. The results are summarised in Table A4.4.

Table A4.4: Travel recovery results.

Matrix	Fortification level (µg/specimen)	Mean % recovery (3 sites x 3 replicates)	Recovery % RSD
Outer dosimeter	100 (10000x LOQ)	97	1.5
Inner dosimeter	10 (1000x LOQ)	102	2.2
Face wipe	10 (1000x LOQ)	99	3.0
Hand wash	100 (2000x LOQ)	102	4.5

All mean travel recoveries were within acceptable limits.

Results.
All measured residue levels were greater than the LOQ for every matrix and so it was not necessary to substitute the LOQ for measured values between LOQ and LOD or to substitute the LOD for values reported as non-detectable.

No statistical tests were conducted for outliers in the exposure data set. Several values were noticeably higher or lower than others in the data set for a given matrix, but all values were included in the calculations since there was no experimental basis for exclusion. Values were only excluded if the samples were compromised in the field, during transit, or during analysis.

The results, with residues corrected for samples with <95% field recovery, are presented in Table A4.5.

Table A4.5: Exposure results.

Pyrimethanil residues on dermal monitoring matrices µg											
Site	Worker	Dosimeter	Lower arm	Upper arm	Front torso	Back torso	Lower leg	Upper leg	Face neck	Hands	Total
1	1	Outer	5887*	1301*	1130*	596*	673*	4052*	46	14680	29755
		Inner	888	118	68	38	20	258			
	2	Outer	18758*	4331*	4353*	1267*	1304*	5098*	67	20800	60617
		Inner	3272	483	245	110	204	324			
	3	Outer	7244*	747*	1341*	654*	925*	1764*	15	16930	31350
		Inner	1296	196	56	44	23	114			
	4	Outer	6421*	2287*	2063*	659*	938*	1710*	39	14410	30947
		Inner	1632	360	183	66	60	119			
2	5	Outer	649*	123*	160*	62*	337*	267*	3	1485	3321
		Inner	159	8.2	9.2	5.4	35	18			
	6	Outer	267*	59*	122*	39*	278*	123*	2	454	1430
		Inner	27	3.3	8.4	3.1	34	10			
	7	Outer	804*	236*	272*	121*	317	310*	6	979	3430
		Inner	251	25	21	10	53	24			
	8	Outer	747*	95*	215*	59*	211*	171*	18	1108	2771
		Inner	77	7.8	15	3.7	25	18			
3	9	Outer	1165	186	493	98	254	852	15	2783	6040
		Inner	97	16	28	7.8	18	27			
	10	Outer	4634	431	738	131	456	696	14	3191	10712
		Inner	206	20	51	19	80	46			
	11	Outer	1680	22	497	134	275	459	9	1746	5029
		Inner	111	12	27	6.8	25	25			
	12	Outer	1018	21	396	72	272	675	6	3993	6584
		Inner	53	9.6	26	6.2	11	25			
* values corrected for recovery (at closest fortification level for the matrix at the same site) when field recovery was <95%											

The study authors reported minimum, maximum, geometric mean, 75th percentile and 95th percentile exposure values based on the PDE, ADE and inhalation measurements. These calculated exposure values are not presented in this study summary as, for the purposes of the BROV project, it is appropriate to base such calculations on the combined database for all studies.

Annex: method of analysis for pyrimethanil and method validation.

Principle of the method

Outer dosimeter samples were extracted with an appropriate volume (700 ml for arms, 1500 ml for legs and 1800 ml for torso) of methanol on a horizontal shaker for 1 hour. A 0.5 ml aliquot was taken and mixed with 0.5 ml of water to give a final sample volume of 1 ml. The final 1 ml sample was further diluted by a factor of 5, 500 or 5000 with water/methanol (1/1 v/v) to be within the calibration range.

Inner dosimeter samples were extracted with an appropriate volume (400 ml for arms, 500 ml for legs and 1000 ml for torso) of methanol on a horizontal shaker for 0.5 hour. A 0.5 ml aliquot was taken and mixed with 0.5 ml of water to give a final sample volume of 1 ml. The

final 1 ml sample was further diluted by a factor of 5, 50 or 1000 with water/methanol (1/1 v/v) to be within the calibration range.

Face/neck wipe samples (including the detergent added in the field) were extracted with 50 ml of methanol on a horizontal shaker for 0.5 hour. A 0.5 ml aliquot was taken and mixed with 0.5 ml of water to give a final sample volume of 1 ml. The final 1 mL sample was further diluted by a factor of 50 or 100 with water/methanol (1/1 v/v) to be within the calibration range.

A 0.5 ml aliquot of the 1000 ml hand wash solution was taken and mixed with 0.5 ml methanol. The 1 ml sample was further diluted by a factor of 500 or 2000 with water/methanol (1/1 v/v) to be within the calibration range.

Analysis was performed by LC-MS/MS using a Waters Acquity UPLC BEH C18 column (50 mm x 2.1 mm, 1.7 µm) at 40 °C in positive ion mode for detection, monitoring the following mass transitions: m/z 200 → 107 (quantification) and m/z 200 → 82 (confirmatory). A gradient elution was used (mobile phase A: water + 0.1 % formic acid, mobile phase B: methanol + 0.1 % formic acid).

Matrix effects

Matrix matched standards were quantified against standards in methanol/water (1/1, v/v) at 5.0 ng/ml, 0.5 ng/ml and 0.1 ng/ml. The matrix effect was calculated as a ratio of the mean peak area in matrix matched standards to the mean peak area in solvent standards expressed as a percentage.

Table A4.6: Matrix effects.

Matrix	Fortification level (ng/ml)	Mass transition (m/z)	Matrix effect (%)
Hand wash solution	5.0	200 → 107	4.0
	0.5		-2.1
	0.1		-6.7
	5.0	200 → 82	1.6
	0.5		-1.6
	0.1		-9.8
Face/neck wipes	5.0	200 → 107	1.7
	0.5		6.8
	0.1		14.0
	5.0	200 → 82	-9.8
	0.5		0.3
	0.1		5.0
Inner dosimeter	5.0	200 → 107	-9.8
	0.5		-7.9
	0.1		-13.0
	5.0	200 → 82	-12.0
	0.5		-6.8
	0.1		-5.7
Outer dosimeter	5.0	200 → 107	-6.3
	0.5		-9.4
	0.1		-14.0
	5.0	200 → 82	-7.9
	0.5		-9.2
	0.1		-14.0

No significant matrix effects (>20%) were observed therefore calibration could be performed with standards in methanol/water (1:1 v:v).

Validation summary

LC-MS/MS is a highly specific technique and two mass transitions (3 ions) were monitored. Chromatograms of standard solutions, control samples and fortified samples have been presented showing no interferences >30% LOQ at the retention time of interest. Accuracy was assessed at 4 fortification levels for the analyte in each matrix of interest corresponding to the LOQ and 10 – 100,000x LOQ depending on the matrix; in all cases mean recovery was within the acceptable range of 70 – 110%. To assess method precision, at least 7 determinations were made at each fortification level and the RSDs were within the acceptable limits of 20%. The overall RSDs were between 3.3 and 10%. The linear range is appropriate for the expected values from field samples for all matrices and was determined using solvent-based standards as no significant matrix effects were observed. The LOQ of the method is 0.01 µg/patch for dosimeters, 0.01 µg/sample for face/neck wipes and 0.05 µg/sample for hand wash solution. The method is satisfactorily validated in accordance with SANCO/3029/99 rev.4.

Table A4.7: Validation data summary of pyrimethanil residues on dosimeter, hand wash solution and face/neck wipes

Matrix	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Outer dosimeter	200 → 107	0.01	0.01 1 100 1000	77 – 102 (86, 11) 101 – 105 (103, 7) 92 – 109 (104, 11) 102 – 107 (104, 7)	9.4 (11) 1.6 (7) 5.2 (11) 1.6 (7) Overall: 10 (36)	0.03 – 10 ng/ml 12 standards, y = $7.45x10^5x + 1.51x10^4$, r = 0.9998	Acceptable chromatograms presented for standard, control and fortified samples. No interferences >30% LOQ. Identity confirmed by additional mass transition.
Inner dosimeter		0.01	0.01 0.1 10 200	76 – 95 (82, 10) 92 – 98 (94, 7) 96 – 104 (100, 10) 104 – 110 (106, 7)	9.4 (10) 1.4 (7) 2.0 (10) 2.1 (7) Overall: 11 (34)		
Face/neck wipes		0.01	0.01 0.1 10 50	99 – 106 (96, 8) 97 – 104 (101, 7) 102 – 112 (107, 7) 89 – 93 (91, 8)	5.8 (8) 2.3 (7) 2.8 (7) 1.7 (8) Overall: 6.8 (30)		
Hand wash		0.05	0.05 0.1 100 1000	100 – 103 (102, 7) 97 – 101 (99, 7) 104 – 109 (107, 7) 95 – 107 (101, 7)	1.1 (7) 1.6 (7) 1.7 (7) 3.6 (7) Overall: 3.6 (28)		

Matrix	**Mass transition m/z**	**LOQ (µg/sample)**	**Recovery fortification level (µg/sample)**	**% Recoveries range (mean, n)**	**Repeatability %RSD (n)**	**Linearity**	**Specificity**
Outer dosimeter	200 → 82	0.01	0.01 1 100 1000	80 – 105 (87, 11) 100 – 105 (103, 7) 91 – 109 (103, 11) 100 – 107 (102, 7)	9.7 (11) 1.9 (7) 5.8 (11) 2.3 (7) Overall: 9.3 (36)	0.03 – 10 ng/ml 12 standards, y = $4.23x10^5x + 7.22x10^3$, r = 0.9999	Acceptable chromatograms presented for standard, control and fortified samples. No interferences >30% LOQ.
Inner dosimeter		0.01	0.01 0.1 10 200	76 – 98 (85, 10) 93 – 96 (94, 7) 95 – 102 (99, 10) 102 – 107 (105, 7)	8.3 (10) 1.3 (7) 2.2 (10) 2.2 (7) Overall: 9.1 (34)		
Face/neck wipes		0.01	0.01 0.1 10 50	96 – 114 (103, 8) 95 – 101 (99, 7) 102 – 107 (106, 7) 87 – 94 (98, 8)	7.2 (8) 2.0 (7) 2.1 (7) 2.4 (8) Overall: 7.1 (30)		
Hand wash		0.05	0.05 0.1 100 1000	97 – 102 (99, 7) 95 – 101 (98, 7) 101 – 109 (106, 7) 95 – 108 (101, 7)	1.9 (7) 2.0 (7) 2.7 (7) 3.8 (7) Overall: 4.0 (28)		

Study 5

Report ChR-16-26173. 'Determination of dislodgeable foliar residues of pyrimethanil (BAS 605 F) after application of BAS 605 04 F to grapevine, Southern France and Germany, 2016'

Author:	Ch. H. Roussel
Date (final report):	03/02/2017
Study guidelines:	EPA Assessment Guidelines Series 875 Occupational and Residential Exposure Test Guidelines, Group B Post-application Exposure Monitoring Test Guideline, Part B, Chapter 3 – Dislodgeable Foliar Residue Dissipation: Agricultural (Guideline 875.2100).
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substances:	Pyrimethanil (BAS 605 F)
Product:	BAS 605 04 F
Crop:	Grapevine
Location:	France (1 site) and Germany (2 sites): • Site FR01 St Pardon de Conques, Aquitaine, France • Site DE02 Breisach am Rhein, Baden Württemberg, Germany • Site DE03 Partenheim, Rheinland-Pfalz, Germany

Aim.
The purpose of this study was to determine the dislodgeable foliar residues (DFR) of pyrimethanil on vine leaves after applications of BAS 605 04 F in sites in Southern France and Germany. Concurrent measurements of worker exposure during re-entry activities (in the associated study ChR-16-26172) permit the calculation of transfer coefficient (TC) values for these tasks.

Test material.
The study was carried out using the fungicide 'BAS 605 04 F', a suspension concentrate (SC) formulation containing a nominal 400 g/l (actual 411.7 g/l) pyrimethanil (BAS 605 F).

Study design.
Dislodgeable foliar residues (DFR) of pyrimethanil on vine leaves after either multiple or single applications of BAS 605 04 F were determined. The field portion of the study was carried out at 3 commercial vineyards at 1 site in France and 2 sites in Germany. The vines (wine varieties Merlot at site FR01, Blauer Spätburgunder at site DE02 and Weisser Burgunder at site DE03) were planted 1.0 m (sites FR01 and DE03) or 1.2 m (site DE02) apart in row widths of 2.0 m (sites FR01 and DE03) or 1.8 m (site DE02). Crop height was reported to be 1.60 m (site FR01), 2.00 m (site DE02) or 1.955 m (site DE03) with a leaf wall height of 1.10 m (site FR01), 1.30 m (site DE02) or 1.00 m (site DE03). The foliage at all

sites was full at the time of the study. At each site, 4 plots were established as described in Table A5.1.

Table A5.1: Plot details.

Plot	Target individual dose		Number of treatments
	Product l/ha	Pyrimethanil g/ha	
1	Untreated		
2	2.5	1000	3
3	2.5	1000	1
4	2.0	800	1

As this study has been used in conjunction with the concurrent exposure study to derive TC values, only the plots which match the application regime in the exposure study have been considered in this evaluation: plot 3 (1x 1000 g a.s./ha) at site 1 and plot 4 (1x 800 g a.s./ha) at sites 2 and 3. The treated plot areas were 180 m^2 (site FR01), 310 m^2 (DE02) or 150 m^2 (DE03) and were divided into 3 sub-plots to provide 3 replicate samples at each site for each sampling interval.

Treatment details.

As explained above, this evaluation considers only the plot 3 treatment at site 1 (a single treatment of 1000 g a.s./ha) and the plot 4 treatment at sites 2 and 3 (a single application of 800 g a.s./ha). Knapsack mist blowers (Solo at all sites), of the type used in efficacy and residues trials to mimic typical commercial broadcast air-assisted sprayers, were used. Treatment details for the plots of interest are summarised in Table A5.2.

Table A5.2: Treatment details.

Site	Plot	Treatment no.	Date of treatment	Growth stage (BBCH)	Application rate (based on 411.7 g a.s./l)		Application volume (l/ha)
					g a.s/ha	% of target*	
FR01	3	1	26/07/16	79	1025	102.5	249
DE02	4	1	21/07/16	79	856	107.0	208
DE03	4	1	20/07/16	75-77	805	100.6	293
* Target application rate of 1000 g a.s./ha (equivalent to 2.5 litres of product/ha) at site FR01 and 800 g a.s./ha (2.0 litres of product/ha) at sites DE02 and DE03.							

A record was provided of all pesticides applied at each site during the 2016 season: no other products containing pyrimethanil were used before or during the studies.

Dislodgeable foliar residue (DFR) sampling.

Leaf samples were taken from each of the 3 sub-plots at each site using a leaf punch with discs collected directly into a pre-labelled jar. Samples were taken from all areas of the crop likely to be in contact with workers during crop maintenance activities. Each sample consisted of 40 leaf discs, each disc with a 2-sided area of 10 cm^2, giving a total leaf area per sample of 400 cm^2. Samples were also taken from untreated plots to produce fortified and

control leaf wash solutions. The leaf punch was cleaned with acetone and de-ionised water after each sample.

Leaf disc samples were taken at each site before each application and immediately after each application (once the spray had dried on the foliage). Additional samples were taken at intervals of 1, 3, 5, 7, 10, 14 (or 15) and 21 (or 22) days after the final application.

Dislodging of the residues from the leaf samples was carried out within a few hours of sampling by mechanically shaking the discs twice for 10 minutes in a 0.01% aqueous solution of Aerosol OT-100 (2x 100 ml washes for 40-disc samples). 20 ml aliquots of the extraction solutions were deep frozen within 8 hours of sampling until analysis.

Environmental monitoring.
Air temperature and rainfall data were provided by the nearest meteorological station to each site (0 km from FR01, 16 km from DE02 and 18 km from DE03) from the first application date to the final sampling date, together with comparative historical data for the same period in other years.

Additionally, air and soil temperature, relative humidity, cloud cover, wind direction, wind speed and rainfall were monitored at each trial site during each application. Rainfall was also monitored throughout the rest of the field phase.

No adverse weather events likely to affect the study results were reported.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.
Field recovery samples were produced at each site at the time of each application and at intervals of 7 and 14 days after the final application to assess, and correct for, the recovery of the active substances from the leaf disk wash solution. Each set of recovery samples consisted of one unfortified blank solution, 3 replicates fortified at 10x LOQ and 3 replicates fortified at 1000x LOQ. The dislodging solutions were fortified using the analytical standard in methanol. All samples were prepared using matrix-loaded dislodging solutions (i.e. the solution having been used to wash untreated control discs before fortification).

As this study has been used in conjunction with the concurrent exposure study to derive TC values, only the plots which match the application regime in the exposure study have been considered in this evaluation. Hence, field recovery results for the leaf wash (DFR) samples taken after the single application to plot 3 at site FR01 and plot 4 at sites DE02 and DE03 are summarised in Table A5.3. Although field recovery samples were also taken 7 and 14 days after application to these plots, these results are not relevant for the calculation of the DFR at the time of worker re-entry (1 DAA1) and have not been considered further in this summary.

Table A5.3: Field recovery results.

Sample timing	Fortification level (µg/200 ml specimen)	% recovery (3 replicates x 3 sites)			
		Site	FR01	DE 02	DE 03
1 DAA1	20 (10x LOQ)	Mean	82	83	111
		%RSD	2	2	7
	2000 (1000x LOQ)	Mean	94	91	85
		%RSD	2	1	4
No residues were detected in untreated control samples.					

Mean recoveries for leaf wash solutions were acceptable (within the 70% - 120% range). Mean RSD values were within acceptable limits (≤ 20%).

This evaluation has corrected DFR samples for which field recoveries were <95% (based on the mean recovery for the nearest fortification level): this is in line with the agreed UK HSE / BROV approach.

Results.

All measured residue levels were greater than the LOQ and so it was not necessary to substitute the LOQ for measured values between LOQ and LOD or to substitute the LOD for values reported as non-detectable.

No statistical tests were conducted for outliers in the data set. Several values were noticeably higher or lower than others, but all values were included in the calculations since there was no experimental basis for exclusion. Values were only excluded if the samples were compromised in the field, during transit or during analysis.

As this study has been used in conjunction with the concurrent exposure study to derive TC values, only the plots which match the regime in the exposure study have been considered in this evaluation. Hence, results for the leaf wash (DFR) samples taken 1 day after the single application to plot 3 at site FR01 and plot 4 at sites DE02 and DE03 are summarised in Table A5.4. Although samples were also taken at each site immediately after each application and at intervals of 3, 5, 7, 10, 14 (or 15) and 21 (or 22) days after the final application, these results are not relevant for the calculation of the DFR at the time of worker re-entry (1 DAA1) and have not been considered further in this summary.

Table A5.4: DFR results.

Residues in leaf wash samples: DFR (µg/cm^2)				
Sample timing	Site	FR01	DE02	DE03
1 DAA1	Mean	0.802*	0.681*	0.497
	%RSD	0.30	0.08	0.36
* Mean value corrected for recovery (at closest fortification level for the leaf wash solution at the same site) when field recovery was <95%				

Annex: method of analysis for pyrimethanil and method validation.

Principle of the method

Pyrimethanil residues extracted from 400 cm^2 of leaf punch discs in 200 ml of a 0.01% aqueous solution of Aerosol OT-100 dislodging solution were analysed. A 20 ml aliquot of the solution was diluted with 80 ml of methanol/water (1:1, v:v) to reach a final volume of 100 ml. The extracts were further diluted with methanol/water (1:1, v:v) to be within the calibration range of the analytical equipment.

Analysis was performed by LC-MS/MS using a Waters Acquity UPLC BEH C18 column (50 mm x 2.1 mm, 1.7 µm), at 40 ºC in positive ion mode for detection, monitoring the following mass transitions: m/z 200 → 107 (quantification) and m/z 200 → 82 (confirmatory). A gradient elution was used (mobile phase A: water + 0.1 % formic acid, mobile phase B: methanol + 0.1 % formic acid).

Matrix effects

Matrix matched standards were quantified against standards in methanol/water (1:1, v:v) at 5.0 ng/ml, 0.5 ng/ml and 0.1 ng/ml. The matrix effect was calculated as a ratio of the mean peak area in matrix-matched standards to the mean peak area in solvent standards expressed as a percentage.

Table A5.5: Matrix effects.

Matrix	Fortification level (ng/ml)	Mass transition (m/z)	Matrix effect (%)
Leaf washing solution	5.0	200 → 107	-3.5
	0.5		1.1
	0.1		-10.9
	5.0	200 → 82	-0.6
	0.5		1.4
	0.1		0.9

No significant matrix effects (>20%) were observed, therefore, calibration could be performed with standards in methanol/water (1:1, v:v).

Validation summary

LC-MS/MS is a highly specific technique and two mass transitions (3 ions) were monitored. Chromatograms of standard solutions, control samples and fortified samples have been presented showing no interferences >30% LOQ at the retention time of interest. Accuracy was assessed at 3 fortification levels for the analyte in leaf wash solution corresponding to the LOQ, 10x LOQ and 1000x LOQ; in all cases mean recovery was within the acceptable range of 70 – 110%. To assess method precision, at least 7 determinations were made at each fortification level and the RSDs were within the acceptable limit of 20%. The overall RSDs were between 3.3 and 3.5%. The linear range is appropriate for the expected values from field

samples and was determined using solvent-based standards as no significant matrix effects were observed. The LOQ of the method is 0.01 µg/ml for leaf wash solution. The method of analysis is fully validated in accordance with SANCO/3029/99 rev.4.

Table A5.6: Validation data summary for pyrimethanil and dithianon residues in leaf washing solution samples

Matrix	Mass transition m/z	LOQ (µg/sample)	Recovery fortification level (µg/sample)	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Grape leaf washing solution	200 → 107	0.010 µg/ml	0.010 µg/ml 0.1 µg/ml 10 µg/ml	96 – 104 (98, 9) 99 – 104 (101, 7) 98 – 107 (103, 9)	2.8 (9) 1.9 (7) 2.9 (9) Overall: 3.3 (25)	0.03 – 10 ng/ml [approx. 0.0015 – 25 µg/ml leaf dislodging solution] 11 standards, $y = 3.69x10^5x + 5.46x10^3$, r = 0.9999	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ. Identity confirmed by additional mass transition.
	200 → 82	0.010 µg/ml	0.010 µg/ml 0.1 µg/ml 10 µg/ml	95 – 105 (98, 9) 98 – 104 (101, 7) 98 – 108 (104, 9)	2.8 (9) 2.2 (7) 3.2 (9) Overall: 3.5 (25)	0.03 – 10 ng/ml [approx. 0.0015 – 25 µg /ml leaf dislodging solution] 11 standards, $y = 2.04x10^5x + 2.86x10^3$, r = 0.9998	Acceptable chromatograms presented for standard, fortified and control samples. No interferences >30% LOQ.

Study 6

Report AF/8247/DE. Determination of dermal exposure to re-entry workers during pruning and training of grapevines in France, 2004

Author:	J. Perkins and G. Jones
Date (final report):	04/08/2006
Study guidelines:	EPA Assessment Guidelines Series 875 Occupational and Residential Exposure Test Guidelines, Group B Post-application Exposure Monitoring Test Guideline
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substance:	Fenbuconazole
Product:	Indar EW
Crop:	Grapevine
Location:	France (3 sites): • Site 1 (AF/8247/DE/1) Tarn-et-Garonne (near Albi) • Site 2 (AF/8247/DE/2) Maine-et-Loire (near Montauban) • Site 3 (AF/8247/DE/3) Tarn (near Gennes) Note: Site numbers 2 and 3 in this worker exposure study are referred to in the concurrent DFR study as sites numbers 3 and 2, respectively.

Aim.
The purpose of this study was to determine the potential dermal exposure of workers carrying out maintenance activities in grapevines. Concurrent measurements of dislodgeable foliar residues (DFR) at the time of re-entry (in the associated study AF/8246/DE) permit the calculation of transfer coefficient (TC) values for these re-entry tasks.

Test material.
The study was carried out using the fungicide 'Indar EW', an oil-in-water emulsion formulation containing a nominal 50 g/l fenbuconazole.

Study design.
Potential dermal exposure to foliar residues was measured for experienced workers (and some less experienced seasonal staff working under supervision) carrying out hand pruning and training activities in grapevines. The field portion of the study was carried out at three commercial vineyards near Albi and Montauban in Southern France and near Gennes in Northern France. The vines (wine varieties 'Syrah' at Sites 1 and 3 and 'Cabernet Franc' at Site 2) were planted 1.0 to 1.1 m apart in row widths of 2.0 m (sites 2 and 3) or 2.5 m (site 1). Plant height ranged from 150 to 180 cm and the foliage was full at the time of the study.

The treated plots consisted of 2.0, 1.49 and 1.8 ha of grapevines at Sites 1, 2 and 3, respectively. A subplot of these treated areas (1 row by 29 vines, approximately 30 m by

2.5 m) was used for DFR sampling as part of the concurrent study AF/8246/DE. Untreated (control) plots (1 row by 12 vines, approximately 12.5 m by 2.5 m) located a suitable distance upwind of the treated area were also used in the concurrent DFR sampling study.

Treatment details.
The product 'Indar EW' was applied at each site using a broadcast air-assisted sprayer (no further details given) in accordance with normal commercial practice. A single treatment was applied at each site before worker re-entry as described in Table A6.1 (a total of 3 applications at each site was reported for the concurrent DFR sampling study but, as the re-entry event occurred after the first application, this worker exposure study considers only a single application).

Table A6.1: Treatment details.

Site	Date of treatment	Growth stage (BBCH)	Target application rate (g a.s./ha)	Actual application rate (g a.s./ha)	Application volume (l/ha)
1	23/06/2004	GS 72 to 73	37.5*	38.0	190
2	29/06/2004	GS 73	37.5*	37.4	121
3	01/07/2004	GS 75	37.5*	38.5	206

* equivalent to maximum individual dose on the product label of 0.75 litres of product/ha.

A full list of the pesticide products applied at each site in the current growing season (2004) and the previous seasons (2001 - 2003 for Site 1 and Site 3, and 2002 - 2003 for Site 2) was reported and confirms that no other fenbuconazole products were used at any site during these periods.

Re-entry activities.
Workers re-entered the treated crop 1 day after treatment at Site 2 and Site 3 and 2 days after treatment at Site 1. Four workers were monitored for each site, giving a total of 12 study subjects (5 male and 7 female). Each daily re-entry period was approximately 4 hours.

Workers at Site 1 trained the vine shoots through the espalier wires and also pruned some shoots from the vines by pulling them off by hand. It took 247 minutes to carry out this work on 2.0 ha of crop.

At Site 2, workers trained vine shoots through the espalier wires and secured the vines by pinching wires together using plastic clips. It took 251 minutes to carry out this work on 1.49 ha of crop.

At Site 3, workers moved espalier wires up the metal supporting poles (notched at approximately 10 cm intervals) to 'sandwich' the vines. Any shoots still hanging in the row were then threaded through the wires and shoots growing lower down on the vine were pruned by pulling them off by hand. It took 240 minutes to carry out this work on 1.8 ha of crop.

No unexpected incidents were reported for any of the workers which were likely to influence the study results.

Dislodgeable foliar residue (DFR) samples were collected on the day of re-entry at each site as part of the concurrent study AF/8246/DE. The dermal exposure data were used in conjunction with the DFR measurements to generate a transfer coefficient (TC) for the re-entry activities.

Exposure assessment.
Dermal exposure was assessed using whole-body dosimetry (outer dosimeter only), hand washes and face/neck wipes. Protective gloves were not used. Only potential dermal exposure (PDE) was measured. Details of the sampling matrices are summarised in Table A6.2.

Table A6.2: Sampling matrices.

Body area	Sampling matrix	Description
Arms, legs, torso	Whole body dosimeter	One-piece 65% polyester/35% cotton coverall. Cut into 6 sections for analysis (upper and lower arms, upper and lower legs, and front and back torso) to evaluate deposition on specific body parts.
Hands	Hand wash	Two sequential hand washes, each using 250 ml of a 0.01% aqueous solution of Aerosol OT-100.
Face, neck	Face / neck wipes	Two sequential wipes, each using an 8-layer cotton gauze pad (10 cm x 10 cm) moistened with 4 ml of Aerosol OT-100 solution.

Environmental monitoring (non-GLP).
Air temperature and relative humidity were recorded at each site on the day of worker re-entry activities. Air temperatures during the study ranged from 24 ºC (Site 1) to 30 °C (Site 3) and relative humidity ranged from 34% (Site 2) to 86% (Site 3). The foliage was dry at all sites. In addition, monthly weather data were presented from the nearest meteorological stations (data for June 2004 from 10 km away from Site 1, data for July 2004 from 8 km away from Site 2, and data for June 2004 from 12 km away from Site 3).

No adverse weather events likely to affect the study results were reported.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.
Field recovery samples were produced for all sampling matrices to assess, and correct for, the recovery of the active substance from each matrix. These samples were fortified using the analytical standard in methanol.

Three sets of field fortifications at 3 spiking levels were prepared for each matrix on each day of monitoring at each site as described in Table A6.3. Additionally, 2 sets of untreated control recovery samples were produced for each matrix on each day at each site.

Fortified outer dosimeter specimens were exposed to the same environmental conditions for the same period of time as the monitoring garments but positioned away from sources of contamination. Hand wash and face wipe specimens were frozen immediately after spiking.

Field recovery results are summarised in Table A6.3.

Table A6.3: Field recovery results.

Matrix	Fortification level (µg/specimen)	Mean % recovery (3 replicates x 3 sites)				Recovery %RSD			
		Site 1	Site 2	Site 3	Mean	Site 1	Site 2	Site 3	Overall
Outer dosimeter	7.5 (LOQ)	97	101[1]	99	99[1]	4.1	-	1.5	3.0
	75.0 (10x LOQ)	97	98	95	97	4.1	2.6	2.8	3.2
	18000 (2400x LOQ)	96	106	95	99	1.6	3.8	0.6	5.9
Face wipe	0.75 (LOQ)	89	102	103	98	5.6	4.8	17.5	12.0
	15.0 (20x LOQ)	97	92	148	112	7.2	6.7	26.5	29.8
	1800 (2400x LOQ)	97	103	90	97	4.1	6.0	13.4	9.3
Hand wash	7.5 (LOQ)	78	108[2]	72	83[2]	11.2	-	3.8	20.5
	75.0 (10x LOQ)	74	74	65	71	11.5	8.9	3.5	10.1
	18000 (2400x LOQ)	74	91[2]	96	87[2]	2.8	-	6.1	13.1

[1] n = 8 An outlier (28% recovery) was rejected (based on Dixon's test) and not included in the mean. Procedural recovery at this spike level was 103% with a RSD of 3.6%.
[2] n = 8 One specimen was lost (damaged sample container)

Mean recoveries ranged from 71% to 112% for all matrices and were considered acceptable (within the 70% - 120% range) and mean RSD values were generally within acceptable limits (≤ 20%).

Although the study authors corrected all monitoring samples for which field recoveries were <100% (based on the mean recovery for nearest fortification level) this is not in line with the agreed UK HSE / BROV approach of applying a correction to monitoring samples only when the corresponding field recoveries were <95%. Exposure values have, therefore, been recalculated.

Travel recovery samples.
Additional travel recovery samples (not exposed to environmental conditions) were generated for each matrix (two replicates) at just one fortification level (high) and at just one site. The results are summarised in Table A6.4.

Table A6.4: Travel recovery results.

Matrix	Fortification level (µg/specimen)	Mean % recovery (1 site x 2 replicates)	Range %
Outer dosimeter	18000 (2400x LOQ)	87	85 - 88
Face wipe	1800(2400x LOQ)	95	95 - 95
Hand wash	18000 (2400x LOQ)	115	100 - 130

Results.

For exposure samples with residues < LOQ, the study authors' reported approach was to assign a value of ½ LOQ as the final value (i.e. without correction for recovery) for each matrix. For the AOEM project the approach was to use ½ LOQ for values between LOQ and LOD and 0.01 µg/sample as a default value for the LOD. The agreed BROV approach is to substitute the LOQ for measured values between LOQ and LOD and to substitute the LOD for values reported as ND. However, for this study there were no monitoring samples with residues < LOQ.

No statistical tests were conducted for outliers in the exposure data set. Several values were noticeably higher or lower than others in the data set for a given matrix, but all values were included in the calculations since there was no experimental basis for exclusion. Values were only excluded if the samples were compromised in the field, during transit, or during analysis.

All the dosimeter results were reported already corrected for recovery (i.e. results from all matrices with field recoveries <100% were corrected for incomplete recovery). Therefore, to follow the agreed BROV approach of only correcting samples with <95% recovery, the reported values were back-calculated to derive an uncorrected value, which was then re-corrected using the 95% cut-off. The results are presented in Table A6.5.

Table A6.5: Results.

Residues on monitoring matrices µg										
Site	Operator	Lower arm	Upper arm	Front torso	Rear torso	Lower leg	Upper leg	Face neck	Hands	Total
1	1	91.69	17.89	54.61	21.43	15.64	15.04	2.206*	103.4*	321.9
	2	80.64	11.79	41.89	12.11	17.42	15.47	0.407*	66.48*	246.2
	3	61.51	11.83	56.93	16.51	27.15	24.07	0.903*	103.4*	302.3
	4	46.00	6.025	30.42	5.93	27.34	22.10	0.668*	96.02*	234.5
2	5	136.8	50.12	81.15	28.46	39.75	58.49	0.4028	96.39	491.6
	6	78.80	34.03	94.57	18.46	26.44	41.93	0.3672	36.14	330.7
	7	100.5	47.85	81.82	23.77	33.35	47.22	0.2599	60.24	395.0
	8	187.8	87.85	142.2	51.73	56.07	188.2	0.8878	277.1	991.8
3	9	118.7	46.56	92.39	26.74	15.72	21.23	0.4714	241.9*	563.7
	10	83.05	37.65	60.11	18.05	11.83	25.73	0.2004	158.5*	395.2
	11	111.0	44.01	91.22	21.55	23.45	17.42	1.041	200.2*	509.9
	12	117.8	48.43	113.6	30.87	16.96	11.96	1.051	158.5*	499.3
* values corrected for recovery (at closest fortification level for the matrix at the same site) when field recovery was <95%										

The study authors reported geometric mean, 75th percentile and 95th percentile exposure values based on the PDE measurements. Additionally, the authors calculated:

- 'Total dermal exposure' (to reflect the wearing of long-sleeved and long-legged clothing) = 10% of the residue on the outer dosimeter + hand wash + face wipe
- 'Modified total dermal exposure' (to reflect the wearing of short-sleeved and short-legged clothing as likely in hot conditions) = 10% of dosimeter trunk + 10% of dosimeter upper legs + 10% of dosimeter upper arms + dosimeter lower arms + dosimeter lower legs + hand wash + face wipe.

These calculated exposure values are not presented in this study summary as, for the purposes of the BROV project, it is appropriate to base such calculations on the combined database for all studies.

The study authors also calculated the mean distribution of total residues to be 26% on the hands, 25% on the lower arms, 7% on the lower legs, 19% on the front torso and <10% on all other body parts.

These distribution calculations are not presented in this study summary as, for the purposes of the BROV project, it is appropriate to base such calculations on the combined database for all studies.

Although the study authors proposed a range of Transfer Coefficient values (hands only, PDE, 'total dermal exposure' and 'modified total dermal exposure') based on the results from this study in conjunction with the concurrent Dislodgeable Foliar Residue (DFR) study, these values are not presented in this study summary as, for the purposes of the BROV project, it is appropriate to base such calculations on the combined database for all studies.

Annex: method of analysis for fenbuconazole and method validation.

Principle of the method

200 ml of methanol was added to 3 face wipes and ultrasonicated for 2 minutes, and a 1 ml aliquot was taken and diluted with the mobile phase (0.1% acetic acid in 1:1 methanol/water). 1 to 2 litres of methanol were added to a piece of dosimeter material and ultrasonicated for 2 minutes, and a 1 ml aliquot was taken and diluted with the mobile phase. A 500 ml sample of hand wash solution was extracted by ultrasonication, if necessary in methanol.

All extracts were further diluted before analysis by a factor of at least 10, as required, to be within the calibration range of the analytical method.

Analysis was performed by LC-MS/MS using a Hypersil BDS C18 5 µm column, 150 mm x 2.1 mm, monitoring the following mass transition: m/z 337 → 125 (quantification). A gradient elution was used (mobile phase A: 0.1% acetic acid in water, mobile phase B: 0.1% acetic acid in methanol).

Validation summary

LC-MS/MS is a highly specific technique and a single mass transition was monitored. Chromatograms of standard solutions, control, fortified and reagent samples have been presented showing no interferences >30% of the LOQ at the retention time of interest. Accuracy was assessed at least at 2 fortification levels for the analyte in each matrix of interest corresponding to the LOQ and between 240 – 2400x the LOQ and in most cases, except for hand washing solution matrix at the LOQ fortification level, the mean recovery was within the acceptable range of 70 – 110%. To assess method precision, at least 5 determinations were made at each fortification level in all matrices and RSDs were within the acceptable limit of 20%. The overall RSDs were between 8.3 – 13.2%. The linear range is appropriate for the expected values in the field samples (samples were further diluted with the mobile phase). The LOQ of the method is 7.5 µg/sample in outer dosimeter and hand wash solution, and 0.75 µg/sample in face/neck wipes. Although the method of analysis is not fully validated in accordance with SANCO/3029/99 rev. 4, as 5 rather than 7 determinations of precision have been made in at each fortification level for outer dosimeter, hand wash solution and face/neck wipes, the method of analysis is fit for purpose.

Table A6.6: Validation data of fenbuconazole residues on outer dosimeters, hand wash solutions and face/neck wipes

Matrix	LOQ (µg/sample)	Recovery fortification level	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Outer dosimeter	7.5	7.5 µg/ml 18000 µg/ml	90 – 107 (100, 5) 97 – 128 (107, 5)	7.2 (5) 12.6 (5) Overall: 10.4 (10)	0.005 – 0.025 µg/ml 6 standards, $y = 2.8461x10^{7}x + 41686$, $r^2 = 0.9889$	Acceptable chromatograms presented for standard, control and fortified samples. No interferences > 30% LOQ.
Hand wash solution	7.5	0.015 µg/ml 3.6 µg/ml	109 – 120 (115, 5) 80 – 95 (91, 5)	3.8 (5) 7.5 (5) Overall: 13.2 (10)		
Face/neck wipes	0.75	0.75 µg/ml 1800 µg/ml	99 – 106 (103, 5) 94 – 129 (105, 5)	2.6 (5) 13.5 (5) Overall: 9.4 (10)		

Study 7

Report AF/8246/DE. Dissipation of dislodgeable foliar residues of fenbuconazole from vines treated with Indar EW

Author:	G. Jones
Date (final report):	24/08/2005 (study completion date)
Study guidelines:	EPA Assessment Guidelines Series 875 Occupational and Residential Exposure Test Guidelines, Group B Post-application Exposure Monitoring Test Guideline, Part B, Chapter 3 – Dislodgeable Foliar Residue Dissipation: Agricultural (Guideline 875.2100).
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substance:	Fenbuconazole
Product:	Indar EW
Crop:	Grapevine
Location:	France (3 sites): • Site 1 (AF/8246/DE/1) Tarn-et-Garonne (near Albi) • Site 2 (AF/8246/DE/2) Tarn (near Gennes) • Site 3 (AF/8246/DE/3) Maine-et-Loire (near Montauban) Note: Site numbers 2 and 3 in the concurrent worker exposure study are referred to in this DFR study as sites numbers 3 and 2, respectively.

Aim.
The purpose of this study was to determine dislodgeable foliar residue (DFR) levels on grape foliage at the time of worker re-entry. Concurrent measurements of dermal exposure for workers (in the associated study AF/8247/DE) permit the calculation of transfer coefficient (TC) values for the re-entry tasks.

Test material.
The study was carried out using the fungicide 'Indar EW', an oil-in-water emulsion formulation containing a nominal 50 g/l fenbuconazole.

Study design.
Dislodgeable foliar residue (DFR) studies were carried out at three commercial vineyards near Albi and Montauban in Southern France and near Gennes in Northern France. The vines (wine varieties 'Syrah' at sites 1 and 2 and 'Cabernet Franc' at site 3) were planted 1.0 to 1.1 m apart in row widths of 2.0 m (sites 2 and 3) or 2.5 m (site 1). Plant height ranged from 150 to 180 cm and the foliage was full at the time of the study.

The treated plots consisted of 2.0, 1.8 and 1.49 ha of grapevines at sites 1, 2 and 3, respectively. A subplot of these treated areas (1 row by 29 vines, approximately 30 m by 2.5 m) was used for DFR sampling at each site. These subplots were split into 3 areas for

sampling (9 vines per area with 1 vine at either end). Additional untreated (control) plots (1 row by 12 vines, approximately 12.5 m by 2.5 m) were located a suitable distance upwind of the treated area (at least 10 m) at each site.

Treatment details.
The product 'Indar EW' was applied at each site using a broadcast air-assisted sprayer (no further details given) in accordance with normal commercial practice. Three treatments were applied at each site as described in Table A7.1. However, in the concurrent worker exposure study, the crop was re-entered after the first application and, for calculating TC values, only the DFR after the first application is of relevance.

Table A7.1: Treatment details.

	Site 1	Site 2	Site 3
First application (T1)			
Date of treatment	23/06/2004	01/07/2004	29/06/2004
Growth stage BBCH	72-73	75	73
Application rate*	37.7 g a.s./ha	38.4	40.6
Application volume	188	205	131
Second application (T2)			
Date of treatment	07/07/2004	15/07/2004	16/07/2004
Interval from previous application	14 days	14 days	17 days
Growth stage BBCH	77	77	77
Application rate*	37.9 g a.s./ha	38.8	40.2
Application volume	208	207	139
Third application (T3)			
Date of treatment	21/07/2004	29/07/2004	30/07/2004
Interval from previous application	14 days	14 days	14 days
Growth stage BBCH	79	79	77
Application rate*	37.7 g a.s./ha	37.5	40.0
Application volume	201	200	128
* The target application rate (representing the maximum individual dose on the product label) was 0.75 litres of product/ha (37.5 g a.s./ha).			

A full list of the pesticide products applied at each site in the current growing season (2004) was reported and confirmed that no other fenbuconazole products were used at any site during this period.

Dislodgeable foliar residue sampling.
Leaf disc samples were taken at each site before each application and immediately after each application (once the spray had dried on the foliage). Additional samples were taken at site 1 at intervals of 2,3,7,10 and 14 days after the final application, and at sites 2 and 3 at an

interval of 14 days after the final application. The sampling schedule is summarised in Table A7.2.

Table A7.2: Sampling schedule.

Sample	Description	Site 1	Site 2	Site 3
S1 Treated and control	Before first application (T1)	23/06/2004	01/07/2004	29/06/2004
S2 Treated only	Immediately after first application (T1)	23/06/2004	01/07/2004	29/06/2004
S3 Treated only	1-2 DAT1	25/06/2004	02/07/2004	30/06/2004
S4 Treated and control	Before second application (T2)	07/07/2004	15/07/2004	16/07/2004
S5 Treated only	Immediately after second application (T2)	07/07/2004	15/07/2004	16/07/2004
S6 Treated and control	Before third application (T3)	21/07/2004	29/07/2004	30/07/2004
S7 Treated only	Immediately after third application (T3)	21/07/2004	29/07/2004	30/07/2004
S8 Treated and control	1 DAT3	22/07/2017		
S9 Treated and control	3 DAT3	24/07/2004		
S10 Treated and control	7 DAT3	28/07/2004		
S11 Treated and control	10 DAT3	31/07/2004		
S12 (S8 at sites 2 and 3) Treated and control	14 DAT3	04/08/2004	12/08/2004	13/08/2004
The total study duration was 42 days at all sites				

Samples were taken using a leaf punch (5 cm^2 punched area = 10 cm^2 double sided sample). At each sample timing, except for the S1 sampling of the untreated control (UTC) plot, 40 leaf disc specimens were taken (total double-sided leaf surface area 400 cm^2). For S1 sampling of the untreated plot, 80 leaf disc specimens taken (total double-sided surface leaf area 800 cm^2) to generate additional specimens for field fortification procedures.

When taking samples, the sampling area was split into 4 quadrants (2 either side of the row) of equal foliar density, and 10 (or 20 for the UTC plot at S1) leaf punches were taken from

the top, middle and bottom of each quadrant, in areas likely to be contacted by workers when carrying out their activities. Each sample was placed in a capped container and assigned a unique number which was used for identification and tracking throughout the study. The samples were transported in cool boxes to test facility for dislodging.

Dislodging of the residues from the leaf samples was carried out within 4 to 5 hours of sampling by mechanically shaking the discs twice for 10 mins in a 0.01% aqueous solution of Aerosol OT-100 (2x 100 ml washes for 40-disc samples and 2x 200 ml for 80-disc samples). 25 ml aliquots of the extraction solutions were deep frozen within 8 hours of sampling until analysis.

Environmental monitoring (non-GLP).
Air temperature and relative humidity were recorded at each site on the day of sampling. Air temperatures during the study period ranged from 21 ºC (site 1) to 32 °C (site 3) and relative humidity ranged from 38% (site 2) to 79% (site 2). The foliage was dry at all sites. In addition, monthly weather data were presented from the nearest meteorological stations (data for June, July and August 2004 from 10 km away from site 1; data for July and August 2004 from 8 km away from site 2; and data for June, July and August 2004 from 12 km away from site 3). Rainfall throughout the trial period was below the historical average at site 1 and slightly above the historical average at site 2 and site 3.

No adverse weather events likely to affect the study results were reported.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.
Field fortification specimens (at least 3 replicates) were produced at the first sample timing (S1) at each site. Each replicate consisted of leaf disc washings from the control plot (24 ml) fortified with the appropriate standard solution (1 ml) to produce the concentrations described in Table A7.3. An unfortified (control) solution (25 ml) using just the washing solution was also produced. The LOQ was 1µg/sample = 0.004 µg/ml (equivalent to 0.0025 µg/cm^2 for a sample surface area of 400 cm^2).

Table A7.3: Field recovery results.

Matrix	Fortification level [1]	Mean % recovery			Recovery %RSD [4]
		Site 1	Site 2	Site 3	
Leaf disc wash	0.03 µg/ml (0.015 µg/cm^2) [2]	68 (n = 3)	97 (n = 3)	719 [3] (n = 7)	24.8 [5]
	0.3 µg/ml (0.15 µg/cm^2) [2]	80 (n = 3)	97 (n = 3)	97 (n = 3)	10.7
	3.0µg/ml (1.5 µg/cm^2) [2]	42 (n = 9)	85 (n = 3)	83 (n = 4)	34.7
[1] All unfortified control recovery samples were at or below the LOQ with the exception of site 3 where a mean residue level of 0.0356 µg/ml was recorded.					

[2] Based on 200 ml recovered wash solution and 400 cm^2 total (double-sided) surface area of each disc sample
[3] Report concludes 'probable error during fortification process'
[4] RSD for means across the 3 sites as recovery results for individual replicates was not reported
[5] Excluding anomalous result for site 3

Residue levels above the LOQ were not found in any of the leaf washings from the untreated plots.

Mean recoveries (average across all sites for each fortification level excluding the anomalous low level fortification result at site 3) ranged from 70% to 91% and were considered acceptable (within the 70% - 120% range). In the absence of recovery values for individual replicates, it is not possible to confirm that the %RSDs for the mean values were within acceptable limits (≤ 20%).

Results

Although the study authors corrected all monitoring samples for which field recoveries were <100% (based on the mean recovery for nearest fortification level) this is not in line with the agreed UK HSE / BROV approach of applying a correction to monitoring samples only when the corresponding field recoveries were <95%. Exposure values have, therefore, been recalculated.

The DFR results following the first application (i.e. at the time of worker re-entry) are summarised in Table A7.4.

Table A7.4: DFR results.

Site	Sample timing	Replicate (sub-plot)	DFR value (µg/cm^2)	Uncorrected mean DFR (µg/cm^2)	RSD	Recovery (%)	Corrected mean DFR (µg/cm^2)
1	2 DAA1	1	0.0453	0.0444	0.003	80	0.0555
	2 DAA1	2	0.0408				
	2 DAA1	3	0.0471				
2	1 DAA1	1	0.0848	0.0801	0.007	97	0.0801
	1 DAA1	2	0.0835				
	1 DAA1	3	0.0718				
3	1 DAA1	1	0.0469	0.0500	0.003	97	0.0500
	1 DAA1	2	0.0532				
	1 DAA1	3	0.0499				

Although the study authors calculated DFR decline, with the more extensive data from Site 1 resulting in a DT50 ranging from 3.44 to 5.39 days (mean 4.39 days), these decline calculations are not relevant to the calculation of TC values based on DFR at the time of worker re-entry (i.e. after the first application).

Annex: method of analysis for fenbuconazole and method validation.

Principle of the method

Residues of fenbuconazole were analysed in a 0.01% aqueous solution of Aerosol OT-100 containing either a total of 800 cm^2 of leaf punch discs (in 400 ml of solution) or 400 cm^2 leaf punch discs (in 200 ml of solution). A 1 ml aliquot was transferred to a 10 ml volumetric flask and diluted with 0.1% acetic acid in 50:50 methanol/water. The extract was filtered and transferred for analysis. Extracts were further diluted, if necessary, prior to analysis to be within the calibration range of the method.

Analysis was performed by LC-MS/MS using a Hypersil BDS C18 5 µm column, 150 mm x 2.1 mm, monitoring the following mass transition: m/z 337 → 125 (quantification). A gradient elution was used (mobile phase A: 0.1% acetic acid in water, mobile phase B: 0.1% acetic acid in methanol).

Validation summary

LC-MS/MS is a highly specific technique and a single mass transition was monitored. Chromatograms of standard solutions, control, fortified and reagent samples have been presented showing no interferences >30% LOQ at the retention time of interest. Accuracy was assessed at 2 fortification levels for the analyte in the dislodging solution corresponding to the LOQ and 600x the LOQ and the mean recovery was within the acceptable range of 70 – 110%. To assess method precision, at least 7 determinations were made at each fortification level and RSDs were within the acceptable limit of 20%. The linear range is appropriate for the expected values in the field samples (samples were further diluted with the mobile phase). The LOQ of the method for the leaf washing solution is equivalent to a foliar residue of 0.0025 µg/cm^2. The method of analysis is validated in accordance with SANCO/3029/99 rev. 4 and is fit for purpose.

Table A7.5: Validation data of fenbuconazole residues in grape leaf washing solution

Matrix	LOQ (µg/sample)	Recovery fortification level	% Recoveries range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Grape leaf washing solution	0.0025 (µg/cm^2)	0.0025 (µg/cm^2) 1.5 (µg/cm^2)	69 – 95 (81, 9) 78 – 92 (85, 7)	9.5 (9) 6.2 (7) Overall: 8.3 (16)	0.00025 – 0.025 µg/ml [equivalent to 0.00125 – 0.125 µg/cm^2] 7 standards, y = 9x10^{7}x + 105258, r = 0.9930	Acceptable chromatograms presented for standard, control and fortified samples. No interferences > 30% LOQ.

Study 8

Report ChR-17-28350. 'Determination of worker re-entry exposure (combined with dislodgeable foliar residues) associated to typical worker re-entry activities (shoot lifting) in vines in France and Italy, 2017'

Author:	I. Thouvenin
Date (final report):	19/01/2018
Study 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. EPA Occupational and Residential Exposure Test Guidelines: OPPTS 875.2100 Foliar Dislodgeable Residue Dissipation. US EPA February 1996.
GLP:	GLP compliance certificate, compliance statement and QA statement provided for both field phase and analytical phase of the study
Active substances:	Iprovalicarb (in formulation with folpet, latter not analysed)
Product:	Sirbel UD
Crop:	Grapevine
Location:	Italy (1 site) and France (3 sites): • Workers 1-5: site IT01 Veneto, Italy • Workers 6-10: site FR02 Charente, France • Workers 11-15: site FR04 Alsace, France • Workers 16-20: site FR03 Champagne, France

Aim.
The purpose of this study was to determine the potential and actual dermal exposure of workers carrying out maintenance (shoot lifting) activities in grapevines. Concurrent measurements of dislodgeable foliar residues (DFR) at the time of re-entry were made at each site to permit the calculation of transfer coefficient (TC) values for the re-entry task.

Test material.
The study was carried out using the fungicide 'Sirbel UD', a water-dispersible granule (WG) formulation containing a nominal 90 g/kg iprovalicarb (in formulation with 563 g/kg folpet, latter not analysed). The test material was applied in tank mix with other products at sites IT01 and FR04.

Study design.
Potential and actual dermal exposure to foliar residues was measured for experienced workers (with between 1 and 40 years' experience) carrying out shoot lifting in grapevines. The field portion of the study was carried out at four commercial vineyards at 1 site in Italy and 3 sites in France. The vines (wine varieties Moscato and Merlot at site IT01, Ugni Blanc at site FR02, Pinot Auxerrois, Muscat, Pinot Gris, Pinot Noir and Gewurztraminer at site FR04, and Chardonnay, Pinot Noir and Pineau Meunier at site FR03) were planted 0.9 m to 1.2 m apart

in row widths of 2.5 m (site IT01), 3.0 m (site FR02), 1.6 m (site FR04) or 1.1 m (site FR03). Crop height was reported to be 1.8 m at site IT01, 2.0 m at site FR02, 1.9 m at site FR04 and 1.5 m at site FR03 and the foliage was full at the time of the study. The treated plot areas were 4.0 ha at site IT01, 4.1 ha at site FR02, 1.9 ha at site FR04 and 1.3 ha at site FR03.

Treatment details.
The product was applied once at each site before worker re-entry as described in Table A8.1. The application equipment included a representative range of commercial broadcast vineyard sprayers: an air-assisted (axial fan) sprayer at site IT01, a recirculating vertical boom straddle sprayer (2-row) at site FR02, and an air-assisted (cross-flow) sprayer at site FR04, and an air-assisted vertical boom straddle sprayer (6-row) at site FR03.

Table A8.1: Treatment details.

Site	Date of treatment	Growth stage (BBCH)	Application rate* (g a.s./ha)			Spray volume (l/ha)
			Target	Actual	Actual as % of target	
IT01	23/05/17	61	117	105	90	450
FR02	12/06/17	65	117	117	100	180
FR04	18/06/17	63 – 75*	117	116	99	160
FR03	20/06/17	75	117	111	95	148
* Range of crop growth stages due to frost.						

Re-entry activities.
Workers re-entered the treated crop for maintenance activities (mainly shoot lifting) 2 days (a minimum of 44 hours) after a single application of the product at each site. Five workers were monitored at each site, giving a total of 20 study subjects (16 male and 4 female). Each re-entry monitoring period was a full working day at each site.

At site IT01, the shoots had not been previously lifted in the season. Workers lifted shoots and tucked them between the wires and also carried out pruning to remove suckers at the base of the plant. Workers carried out the tasks individually: dealing with one side of each row before returning down the other side to repeat the tasks. The working time at this site was from 6 hours 2 minutes to 6 hours 11 minutes. The estimated length of row lifted per worker was 3300 m.

At site FR02, the shoots had not been previously lifted in the season. Workers adjusted the height of the wires on the posts, lifted shoots and tucked them between the wires, and positioned clips between the pairs of wires to retain the shoots. Workers carried out the tasks as a pair, working together on opposite sides of the same row. The working time at this site was from 5 hours 58 minutes to 6 hours 9 minutes. The estimated length of row lifted per worker was 3850 m.

At site FR04, the shoots had been mechanically lifted earlier in the season. Workers lifted shoots and tucked them between the wires, positioned clips between the pairs of wires to retain the shoots, and carried out pruning to remove suckers at the base of the plant and shoots at the top of the plant extending above the row height. Workers carried out the tasks individually: dealing with one side of each row before returning down the other side to repeat the tasks. The working time at this site was from 5 hours 46 minutes to 5 hours 52 minutes. The estimated length of row lifted per worker was 1600 m.

At site FR03, the shoots had been lifted earlier in the season. Workers adjusted the height of the wires on the posts, lifted shoots and tucked them between the wires, and positioned clips between the pairs of wires to retain the shoots. Workers carried out the tasks individually: dealing with one side of each row before returning down the other side to repeat the tasks. The working time at this site was from 5 hours 8 minutes to 6 hours 0 minutes. The estimated length of row lifted per worker was 2000 m.

No unexpected incidents were reported for any of the workers which were likely to influence the study results.

Exposure assessment.
Dermal exposure was assessed using whole-body dosimetry, glove sampling, hand washes and face/neck wipes. Partial nitrile work gloves were used by all workers. Details of the exposure sampling matrices are presented in Table A8.2.

Table A8.2: Exposure sampling matrices.

Body area	Sampling matrix	Description
Arms, legs, torso (outer layer)	Whole body dosimeter	Two-piece 65% polyester/35% cotton long-sleeved, long-legged garments. Sectioned and analysed as separate parts (top torso, arms and bottom sections).
Arms, legs, torso (inner layer)	Whole body dosimeter	Two-piece 100% cotton long-sleeved, long-legged underwear. Sectioned and analysed as separate parts (top torso, arms and bottom sections).
Hands (potential exposure)	Gloves	Partial nitrile gloves: polyamide knitted gloves with palm and fingers coated with nitrile. The gloves were taken off during breaks.
Hands (actual exposure)	Hand wash	A single hand wash using 1000 ml of 0.4% Esemtan solution over a metal bowl. Taken before work (discarded), before lunch (and other breaks) and at the end of the monitoring period. A 50 ml aliquot was retained from each hand wash sample in a HDPE bottle.

Body area	Sampling matrix	Description
Face, neck	Face / neck wipes	Two sequential wipes, each using a multi-layer cotton gauze pad (10 cm x 10 cm) moistened with 4 ml of 0.4 Esemtan solution. Taken before work (discarded), before lunch (and other breaks) and at the end of the monitoring period. All wipes for an individual subject were collected together.

At the end of monitoring, dosimeter sections, gloves and wipes were wrapped in aluminium foil and bagged. All samples were stored on ice in a cool box at each site before being deep frozen until the time of extraction for analysis.

Dislodgeable foliar residue (DFR) sampling.
Three replicate leaf disc samples were taken in the treated field(s) at each site both before application (0 – 1 day before treatment) and on the day of worker re-entry (2 days after application). An additional 4 replicate samples were taken before treatment at each site to produce fortified and control leaf wash solutions.

Each sample, which was taken with a leaf punch directly into a pre-labelled jar, consisted of 40 leaf discs, each disc with a 2-sided area of 10 cm^2, giving a total leaf area per sample of 400 cm^2. The leaf punch was cleaned with ethanol after each sample.

Samples were taken from the areas of the crop likely to be in contact with workers during shoot lifting.

Within a few hours of sampling (within 2 hours for the samples taken at the time of re-entry), leaf disc samples were washed twice by adding, each time, 100 ml of 0.01% Aerosol OT solution to each sampling jar for 10 minutes on a reciprocating platform shaker. The dislodging solutions for each sample were combined and frozen.

Environmental monitoring (non-GLP).
Air temperature, relative humidity, wind speed and wind direction were monitored at each site 4 times during the re-entry activities. Air temperatures during re-entry ranged from 18.8 to 38.2 ºC and relative humidity ranged from 31% to 86%. Winds were generally light (the peak values recorded were 3.5 m/s at site IT01, 2.3 m/s at site FR02, 2.3 m/s at site FR04 and 2.8 m/s at site FR03).

The only rainfall in the 2-day period between application and re-entry occurred at site FR02 (2.6 mm during the afternoon of the day before re-entry). During the re-entry activities a small amount of rain occurred at sites IT01 and FR02 but was not considered enough to stop the work or to affect the study results.

Method of analysis and method validation.
See Annex to this study summary.

Field recovery samples.

Field recovery samples were produced for all sampling matrices to assess, and correct for, the recovery of the active substance from each matrix. The dermal exposure matrices and dislodging solutions (DFR measurement) were fortified using the analytical standard in acetonitrile.

Three sets of field fortifications at 2 spiking levels and an untreated control were prepared for each exposure sampling matrix and the leaf wash solution on each day of monitoring at each site as described in Table A8.3.

Fortified outer and inner dosimeter samples (the latter covered by a layer of unfortified outer dosimeter material) were exposed to the same environmental conditions for the same period of time as the monitoring garments, but positioned away from sources of contamination. Hand wash, face wipe and DFR recovery samples were stored on ice in a cool box immediately after spiking before being deep frozen.

Field recovery results for the exposure matrices and leaf disc wash (DFR) samples are summarised in Table A8.3.

When recovery levels measured from the first set of field spiked specimens were higher than 70% at the low and high fortification rates, the second and third sets of fortified samples were not analysed.

For DFR dislodging solutions, blank controls were contaminated at site FR04 and, as a result, residue levels in samples fortified at low level at this site could not be interpreted.

Table A8.3: Field recovery results.

Matrix	Fortification level (µg/specimen)	% recovery (1 replicate x 4 sites) n = 4					
		Site IT01	Site FR02	Site FR04	Site FR03	Mean	RSD
Outer dosimeter	0.5 (1x LOQ)	104	92.7	95.7	93.7	97	5.3
	50 (100x LOQ)	111	110	107	104	108	2.9
Inner dosimeter	0.5 (1x LOQ)	106	96.3	92.9	94.1	97	6.1
	50 (100x LOQ)	127	103	102	101	108	11.6
Face wipe	0.01 (1x LOQ)	119	97.3	93.1	103	103	11.0
	1.0 (100x LOQ)	103	106	109	106	106	2.3
Hand wash (50 ml)	0.01 (1x LOQ)	97.9	96.1	97.6	96.9	97	0.8
	1 (100x LOQ)	109	106	106	103	106	2.3
Part-nitrile glove	50 (1x LOQ)	92.8	85.0	64.5	89.3	83	15.3
	5000 (100x LOQ)	110	123	110	104	112	7.2
Leaf disc wash (200 ml)	0.4 (1x LOQ)	73.5* 90.3*	105	**	109	94	17.1
	40 (100x LOQ)	106	106	103	102	104	2.0

* Two replicates reported at this site
** No value due to high levels of contamination in control

Mean recoveries for all matrices used in the exposure and DFR calculations were considered acceptable (generally within the 70% - 120% range). Mean RSD values were within acceptable limits (≤ 20%).

The agreed UK HSE / BROV approach is to correct exposure monitoring and DFR samples for which field recoveries were <95% (based on the mean recovery for the nearest fortification level). However, based on this approach, it was unnecessary to correct any of the results in this study.

Travel recovery samples.
Additional travel recovery samples (not exposed to environmental conditions) were generated for each exposure matrix (3 replicates at the high fortification level and a single control) at sites IT01, FR02 and FR04. These samples were frozen immediately after fortification. Since field fortification samples gave acceptable recoveries, travel recovery specimens were not analysed.

Results.
All measured residue levels were greater than the LOQ for every matrix and so it was not necessary to substitute the LOQ for measured values between LOQ and LOD or to substitute the LOD for values reported as non-detectable.

No statistical tests were conducted for outliers in the exposure data set. Several values were noticeably higher or lower than others in the data set for a given matrix, but all values were included in the calculations since there was no experimental basis for exclusion. Values were only excluded if the samples were compromised in the field, during transit, or during analysis.

The exposure results are presented in Table A8.4. None of the values required correction for field recovery.

Table A8.4: Exposure results.

Iprovalicarb residues on dermal monitoring matrices (µg)											
Site	Worker	Inner torso	Inner arms	Inner legs	Outer torso	Outer arms	Outer legs	Hand wash	Gloves	Face wipe	Total
IT01	1	63.7	125	51.3	1436	2084	1328	348	4139	8.30	9583
	2	41.0	95.7	103	1812	3004	1685	458	5265	14.4	12478
	3	14.7	29.7	28.1	749	1863	975	151	2904	5.79	6720
	4	45.7	117	29.0	1195	2212	732	466	6076	13.0	10886
	5	21.0	39.7	19.1	635	1642	945	319	5335	6.35	8962
FR02	6	7.30	28.3	12.3	530	962	300	99.0	2406	2.83	4348
	7	59.6	106	17.1	1221	1909	554	206	3204	6.86	7284
	8	44.5	65.7	11.7	1352	1624	400	131	2740	6.08	6375
	9	47.7	60.8	24.7	1211	1504	615	175	3154	11.7	6804
	10	34.9	69.6	10.8	1032	1719	294	191	2772	9.40	6133
FR04	11	57.3	73.1	93.8	2359	1869	2247	129	3681	4.15	10513
	12	13.3	27.9	41.0	678	1113	1473	48.0	3470	2.75	6867
	13	31.0	59.9	39.9	1516	1922	1755	126	3970	12.2	9432

Iprovalicarb residues on dermal monitoring matrices (µg)											
	14	18.3	25.7	24.3	1081	1403	1379	70.2	3727	5.63	7734
	15	10.2	19.0	87.6	533	1310	2426	95.6	3767	1.77	8250
FR03	16	30.5	58.8	33.4	879	1458	968	173	2639	5.97	6246
	17	25.5	87.6	46.9	1169	2100	1310	210	3287	3.26	8239
	18	29.1	74.8	70.0	1187	1611	1528	202	3366	4.21	8072
	19	21.5	38.6	88.3	602	819	1191	210	2768	3.98	5742
	20	40.3	82.7	85.0	1093	1334	1663	285	3872	3.47	8458

The DFR results are presented in Table A8.5. None of the values required correction because the corresponding field recovery levels at the nearest fortification level were all ≥ 95%.

Table A8.5: DFR results.

Iprovalicarb residues in leaf wash samples: DFR (µg/cm^2)				
	Replicate			Mean
	1	2	3	
Site IT01	0.360	0.308	*	0.334*
Site FR02	0.338	0.238	0.248	0.275
Site FR04	0.288	0.271	0.336	0.298
Site FR03	0.166	0.150	0.150	0.155
* n = 2: anomalous residue level in this replicate (below LOQ) was excluded for calculation of mean.				

The study authors reported arithmetic mean, 75th percentile and 95th percentile exposure values based on the PDE and ADE measurements. These calculated exposure values are not presented in this study summary as, for the purposes of the BROV project, it is appropriate to base such calculations on the combined database for all studies.

Annex: method of analysis for iprovalicarb and method validation.

Dermal exposure matrices

Principle of the method

Outer and inner dosimeter samples were extracted with an appropriate volume (see Table A8.6) of methanol on a horizontal shaker for approximately 60 minutes. A 1 ml aliquot was evaporated to dryness and the extract was reconstituted with 1 ml acetonitrile/water (50/50 v/v). 0.05 ml of the internal standard iprovalicarb-D7 was added to a 0.5 ml aliquot of the extract and diluted in 4.45 ml acetonitrile/water (50/50 v/v). A 0.5 ml aliquot of the final sample was taken for analysis.

Table A8.6: Extraction details.

Matrix	Volume of extraction solvent (ml)	Evaporated aliquot (ml)	Final analytical solution concentration (specimen/ml)
Outer arms	2000	4	0.002
Outer legs	4000	8	0.002
Outer torso	4000	8	0.002

Matrix	Volume of extraction solvent (ml)	Evaporated aliquot (ml)	Final analytical solution concentration (specimen/ml)
Inner arms	1500	3	0.002
Inner legs	2000	4	0.002
Inner torso	1500	3	0.002

For inner and outer dosimeters, analysis was performed by LC-MS/MS using a Merck Superspher 60 RP-select B column (12.5 cm x 0.4 cm, 4 µm), at 40 ºC in positive ion mode for detection, monitoring the following mass transitions: m/z 321 → 119 (quantification) and 321 → 203 (confirmatory). A gradient elution was used (mobile phase A: water/acetonitrile 90/10, v/v and 0.1 ml acetic acid/l, mobile phase B: acetonitrile and 0.1 ml acetic acid/l).

For the extraction and analysis of face/neck wipe samples, hand wash solution and protective gloves, see method of analysis for Study 1 (ECPA).

Stability of extracts

Storage stability of iprovalicarb in outer and inner dosimeter matrices was tested by determination of recovery at the LOQ of 0.5 µg/specimen for 10 days at 4 ºC.

Table A8.7: Stability of extracts.

Mass transition m/z 321 → 119				
Matrix	Storage days	Fortification level (µg/specimen)	% recovery range (mean, n)	% RSD
Inner dosimeter	10	0.5	92 – 104 (97, 5)	4.9
Outer dosimeter	10	0.5	92 – 97 (95, 5)	2.4

Iprovalicarb was stable in outer and inner dosimeter matrices for at least 10 days storage at 4 ºC. For storage stability of face/neck wipe samples, hand wash solution and protective gloves, see method of analysis for Study 1 (ECPA).

Validation summary: outer and inner dosimeter matrices

LC-MS/MS is a highly specific technique and two mass transitions (3 ions) were monitored. For the quantification and confirmatory mass transitions, chromatograms of standard solutions have been presented showing no interferences >30% of LOQ at the retention time of interest. Accuracy was assessed at 2 fortification levels for the analyte in the matrix of interest corresponding to the LOQ and 100x LOQ and in all cases the mean recovery was within the acceptable range of 70 – 110%. To assess method precision, 5 determinations were made at each fortification level and the RSDs were within the acceptable limit of 20%. The overall RSDs were between 2.3 and 13.1%. The linear range is appropriate for the expected values from field samples for all matrices (out of range specimens were diluted in acetonitrile/water solution by the appropriate factor) and was determined using internal standards which compensates for any possible matrix effects. The LOQ of the method is 0.5 µg/specimen for inner and outer dosimeters. Although the method of analysis is not fully

validated in accordance with SANCO/3029/99 rev.4, as 5 rather than 7 determinations of precision have been made at each fortification level, it is fit for purpose.

Validation summary: face/neck wipe samples, hand wash solution and protective gloves. See method of analysis for Study 1 (ECPA).

Table A8.8: Validation data summary for iprovalicarb residues in outer and inner dosimeter samples

Active	Matrix	Analyte (transition m/z)	LOQ (µg/specimen)	Recovery fortification level (µg/specimen)	% recovery range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Iprovalicarb	Outer dosimeter	321 →119	0.5	0.5 50	79 – 92 (83, 5) 100 – 109 (106, 5)	6.0 4.1 Overall: 13.1	0.025 – 50 ng/ml [approx. 0.125 – 250 µg/specimen] 11 standards, y = 0.48x + 0.00337 r = 0.9999	Acceptable chromatograms presented for standard, control, and fortified samples. No interference > 30% LOQ. Identity confirmed by additional mass transition.
	Inner dosimeter		0.5	0.5 50	103 – 110 (108, 5) 104 – 108 (105, 5)	2.6 1.6 Overall: 2.3	0.025 – 50 ng/ml [approx. 0.125 – 250 µg/specimen] 11 standards, y = 0.48x + 0.00337 r = 0.9999	
	Outer dosimeter	321 → 203	0.5	0.5 50	83 – 106 (92, 5) 94 – 108 (104, 5)	10.3 5.2 Overall: 9.8	0.025 – 50 ng/ml [approx. 0.125 – 250 µg/specimen] 11 standards, y = 0.195x + 0.00145 r = 0.9999	Acceptable chromatograms presented for standard, control, and fortified samples. No interference > 30% LOQ.

Active	Matrix	Analyte (transition m/z)	LOQ (µg/specimen)	Recovery fortification level (µg/specimen)	% recovery range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
	Inner dosimeter		0.5	0.5 50	93 – 105 (97, 5) 102 – 108 (104, 5)	4.9 2.4 Overall: 5.1	0.025 – 50 ng/ml [approx. 0.125 – 250 µg/specimen] 11 standards, y = 0.195x + 0.00145 r = 0.9999	

Leaf wash solution (DFR)

Principle of the method

Iprovalicarb residues from a 400 cm^2 sample of leaf punch discs in 200 ml of a 0.01% aqueous solution of Aerosol OT-100 were analysed. 40 ml of acetonitrile was added to the 200 ml leaf wash sample and shaken for 1 minute. A 0.06 ml aliquot of the solution was transferred into a vial and 0.1 ml of the internal standard (stable labelled iprovalicarb-D7) was added together with 0.84 ml of acetonitrile/water (50/50 v/v). After homogenisation, the solution was analysed.

Analysis was performed by HPLC-MS/MS using a Superlco Ascentis Express C18 column (2.7 µm, 50 mm x 2 mm) at 65 ºC in positive ion mode for detection, monitoring the following mass transitions: m/z 321 → 119 (quantification) and 321 → 203 (confirmatory). A gradient elution was used (mobile phase A: Mili-Q water/methanol (9:1, v:v) + 10 mM ammonium formate + 120 µl/l formic acid, mobile phase B: Mili-Q water/methanol (1:9, v:v) + 10 mM ammonium formate + 120 µl/l formic acid).

Stability of extracts

Storage stability of iprovalicarb in the leaf wash matrices was tested by determination of recovery at the LOQ of 0.4 µg/specimen for 8 days at 4 ºC.

Table A8.9: Stability of extracts.

Mass transition m/z 321 → 119				
Matrix	Storage days	Fortification level (µg/specimen)	% recovery range (mean, n)	% RSD
Leaf wash solution	8	0.4	94 – 114 (103, 5)	8.2

Iprovalicarb was stable in leaf wash solution for at least 8 days storage at 4 ºC.

Validation summary

LC-MS/MS is a highly specific technique and two mass transitions (3 ions) were monitored. For the quantification and confirmatory mass transitions, chromatograms of standard solutions have been presented showing no interferences >30% of LOQ at the retention time of interest. Accuracy was assessed at 2 fortification levels for the analyte in the matrix of interest corresponding to the LOQ and 100x LOQ and in all cases the mean recovery was within the acceptable range of 70 – 110%. To assess method precision, 5 determinations were made at each fortification level and the RSDs were within the acceptable limit of 20%. The overall RSDs were between 4.9 and 5.6%. The linear range is appropriate for the expected values from field samples for all matrices (out of range specimens were diluted in acetonitrile/water solution by the appropriate factor) and was determined using internal standards which compensates for any possible matrix effects. The LOQ of the method is 0.4 µg/specimen of 200 ml leaf washing solution. Although the method of analysis is not fully validated in accordance with SANCO/3029/99 rev.4, as 5 rather than 7 determinations of precision have been made at each fortification level, it is fit for purpose.

Table A8.10: Validation data summary for iprovalicarb residues in grape leaf disc washing solutions

Active	Matrix	Analyte (transition m/z)	LOQ (µg/specimen)	Recovery fortification level (µg/specimen)	% recovery range (mean, n)	Repeatability %RSD (n)	Linearity	Specificity
Iprovalicarb	Leaf punches washing solution*	321 →119	0.4	0.4 40	97 – 107 (102, 5) 109 – 112 (110, 5)	3.9 1.3 Overall: 4.9	0.025 – 50 ng/ml [approx. 0.0005 – 1 µg/mL, equivalent to 0.1 – 200 µg/specimen] 11 standards, y = 0.48x + 0.00337 r = 0.9999	Acceptable chromatograms presented for standard, control, and fortified samples. No interference > 30% LOQ. Identity confirmed by additional mass transition.
	Leaf punches washing solution*	321 → 203	0.4	0.4 40	97 – 106 (101, 5) 106 – 112 (110, 5)	4.2 2.1 Overall: 5.6	0.025 – 50 ng/ml [approx. 0.0005 – 1 µg/mL, equivalent to 0.1 – 200 µg/specimen] 11 standards, y = 0.195x + 0.00145 r = 0.9999	Acceptable chromatograms presented for standard, control, and fortified samples. No interference > 30% LOQ.

*Specimen = 200 ml of leaf washing solution

Appendix B: Database description and analysis

The database consists of five exposure studies (two of which also include DFR measurements) and three supplementary DFR studies. In total the database provides 73 records of exposure for individuals with associated concurrent DFR measurements (for 37 records) or estimates where DFR samples were not taken from same site used for exposure monitoring. The contributions to the database, i.e. number of records associated with each individual exposure study, active substance, formulation type, activity and country location, are shown in Table B1.

Table B1: Numbers of exposure records associated with individual studies, active substances, formulation types, activities, and country locations

Study	Active	Formulation	Activity	Country
BASF1: 24	Dimethomorph: 12	EW: 12	Harvesting: 17	Czech Rep.: 6
BASF2: 12	Dithianon: 12	SC: 12	Pruning: 36	France: 31
DOW1: 12	Fenbuconazole: 12	WG: 61	Pruning and training: 12	Germany: 35
ECPA: 17	Iprovalicarb: 37		Shoot-lifting/pruning: 20	Italy: 13
UIPP: 20	Pyrimethanil: 12			

Tables B2 to B4 show summary statistics of the raw and calculated variables from the database. Histograms of the data are also shown in Figure B1.

Table B2: Observed activity durations (hours), DFR (µg/cm^2) and potential and actual dermal exposures on the body and hands (µg a.s.)

	Duration	DFR	Body actual exposure	Body potential exposure	Hand actual exposure	Hand potential exposure
Minimum	4.00	0.050	0.8	101	48	36
1st quartile	5.15	0.155	47	536	146	506
Median	6.00	0.333	152	3349	210	2963
Mean	6.13	0.544	773	8992	375	5215
3rd quartile	7.43	0.603	839	7521	511	5723
Maximum	7.83	2.379	4705	71049	1189	31700

Table B3: Observed total exposures: body and hand potential; body actual and hand potential; body potential and hand actual; and body and hand actual (µg a.s.)

	Total potential exposure	Total body actual + hand potential exposure	Total body potential + hand actual	Total actual exposure
Minimum	235	37	1942	133
1st quartile	976	569	3646	294
Median	6246	3088	4785	388
Mean	11302	5766	13878	1312
3rd quartile	10514	5977	16291	2553
Maximum	71367	35633	72238	5040

Table B4: Observed hourly potential and actual exposures on the body and hands (µg a.s./h)

	Body actual exposure/hour	**Body potential exposure/hour**	**Hand actual exposure/hour**	**Hand potential exposure/hour**
Minimum	0.2	13.7	8.2	8.6
1st quartile	8.8	94.6	24.2	92.0
Median	25.1	540.8	35.3	488.4
Mean	126.3	1515.2	72.7	738.8
3rd quartile	112.6	1112.3	109.8	857.6
Maximum	890.7	14957.7	250.3	4255.0

Calculated transfer coefficients for body and hand exposures and total exposures are shown in Tables B5 and B6.

Table B5: Calculated transfer coefficients for body and hand exposures (cm^2/h)

	Actual TC body	**Potential TC body**	**Actual TC hand**	**Potential TC hand**
Minimum	8	39	27	72
1st quartile	43	726	74	550
Median	115	1610	120	1350
Mean	169	2019	149	1460
3rd quartile	193	2542	223	2069
Maximum	759	7254	238	4505

Table B6: Calculated transfer coefficients for total body and hand exposures (cm^2/h)

	Total TC body potential + hand potential	**Total TC body actual + hand potential**	**Total TC body potential + hand actual**	**Total TC body actual + hand actual**
Minimum	226	86	1175	76
1st quartile	1184	807	2291	182
Median	2631	1800	3193	337
Mean	3310	1749	3764	374
3rd quartile	4268	2353	5338	415
Maximum	9167	4734	7582	1046

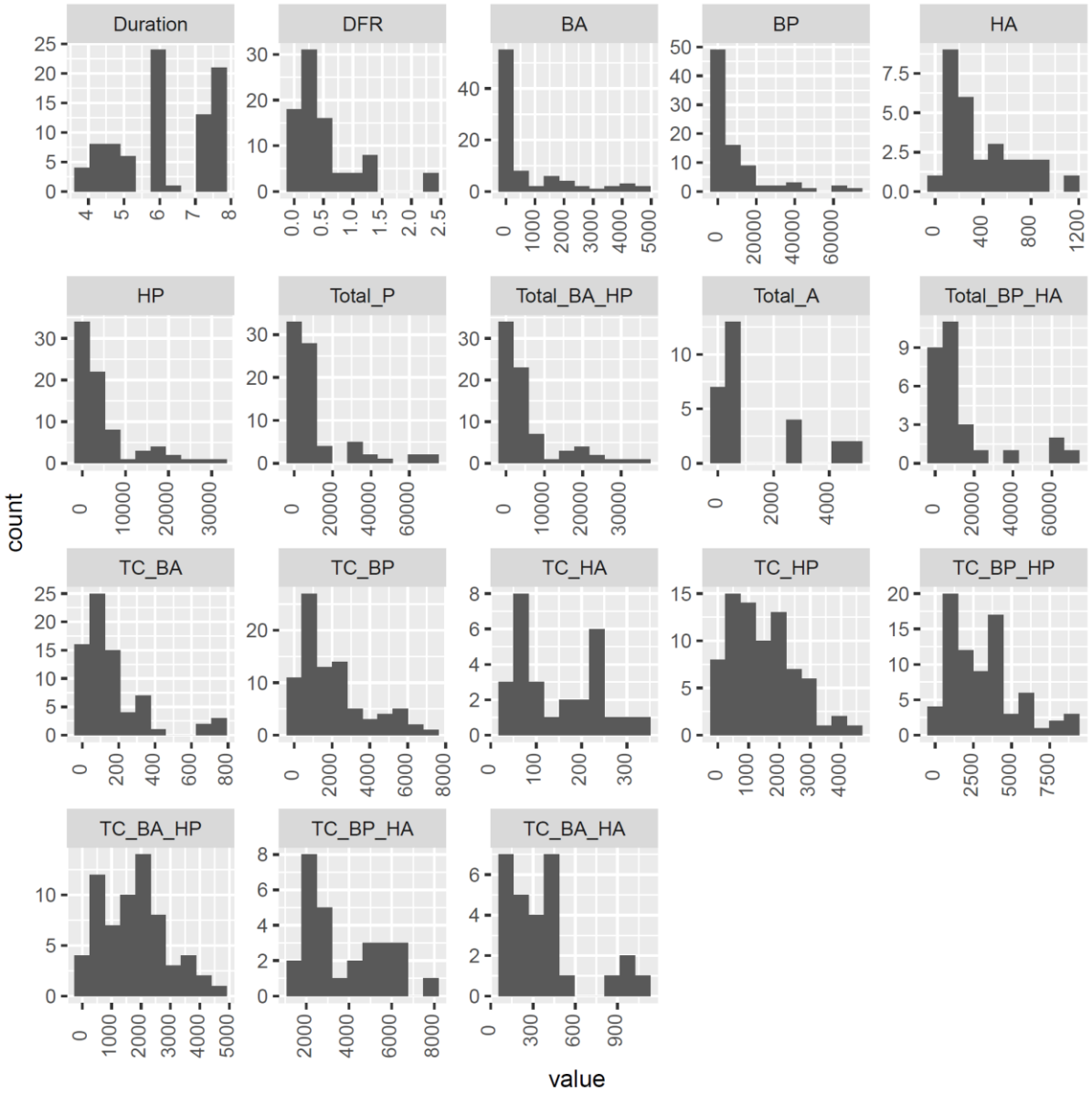


Figure B1: Histograms of BROV worker database values

Duration = re-entry task duration (hours),
DFR = dislodgeable foliar residue (µg/cm^2),
BA = body actual exposure (µg),
BP = body potential exposure (µg),
HA = hand actual exposure (µg),
HP = hand potential exposure (µg),
Total_P = total body and hand potential exposure (µg),
Total_BA_HP = total body actual and hand potential exposure (µg),
Total_A = total body and hand actual exposure (µg),
BA_hour = body actual exposure/hour (µg/h),
BP_hour = body potential exposure/hour (µg/h),
HA_hour = hand actual exposure/hour (µg/h),
HP_hour = hand potential exposure/hour (µg/h),
TC_BA = transfer coefficient for body actual exposure (cm^2/h),
TC_BP = transfer coefficient for body potential exposure (cm^2/h),
TC_HA = transfer coefficient for hand actual exposure (cm^2/h),

TC_HP = transfer coefficient for hand potential exposure (cm^2/h),
TC_BP_HP = transfer coefficient for sum of body and hand potential exposure (cm^2/h),
TC_BA_HP = transfer coefficient for sum of body actual and hand potential exposure (cm^2/h),
TC_BP_HA = transfer coefficient for sum of body potential and hand actual exposure (cm^2/h) and
TC_BA_HA = transfer coefficient for sum of body and hand actual exposure (cm^2/h)

The distributions of DFR and exposures in Figure B1 illustrate that much of the data are not normally distributed.

Pairwise plots exploring the relationships between the DFR levels and body and hand exposure are shown in Figure B2. An additional pairwise plot (not included here), to explore the relationships between the five active substances, three formulation types and DFR levels, showed no differences related to active substance or formulation type. Correlations are apparent between potential and actual exposure, and between potential body and hand exposure. Actual hand exposure values are relatively limited in both number and range.

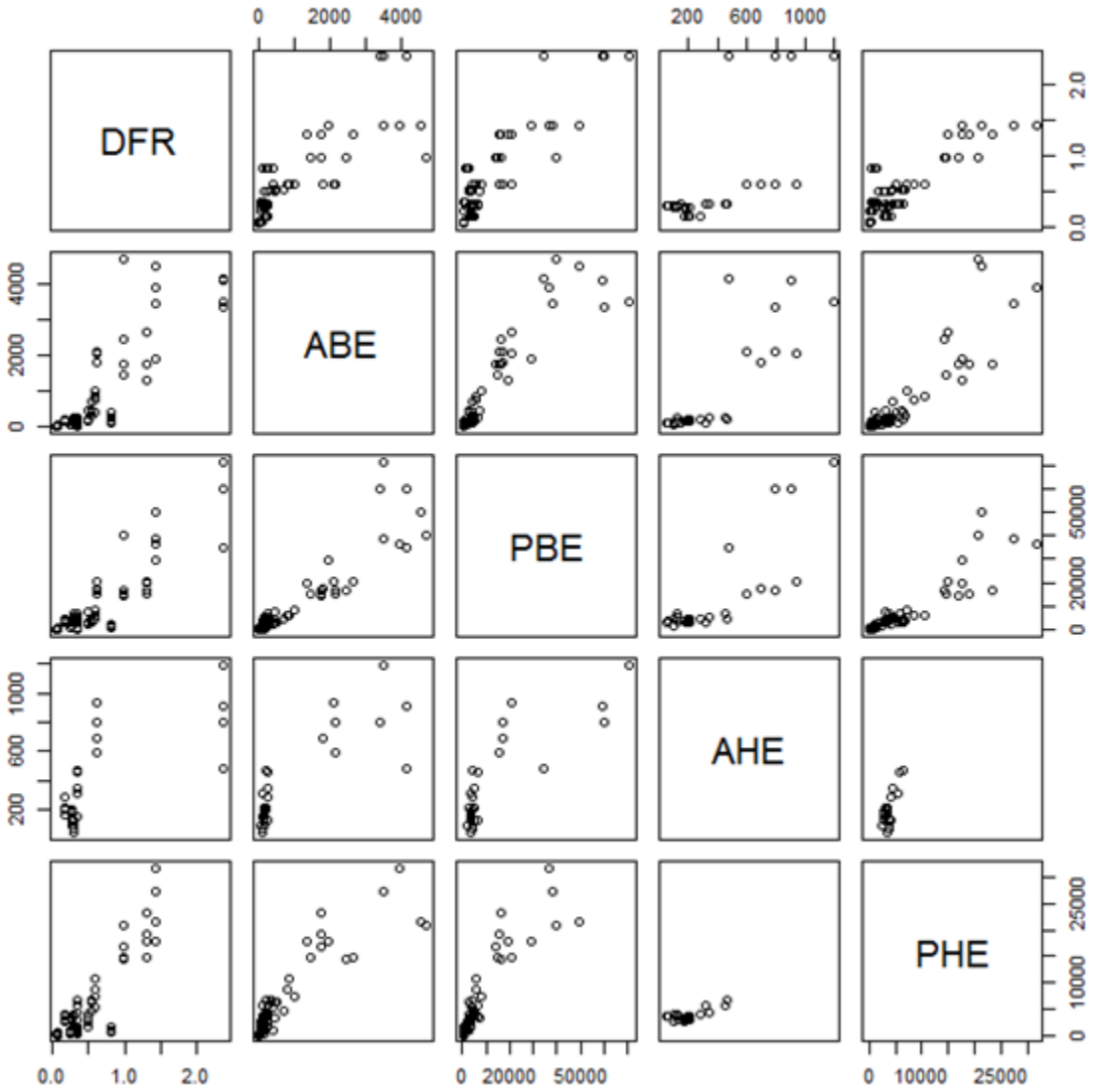


Figure B2: Pairwise plots of DFR level and body and hand exposure, where ABE = actual body exposure, PBE = potential body exposure, AHE = actual hand exposure, and PHE = potential hand exposure.

To illustrate the possible relationships between DFR data and exposure, Figures B3 to B6 show plots of hourly exposure data against DFR including these data sources.

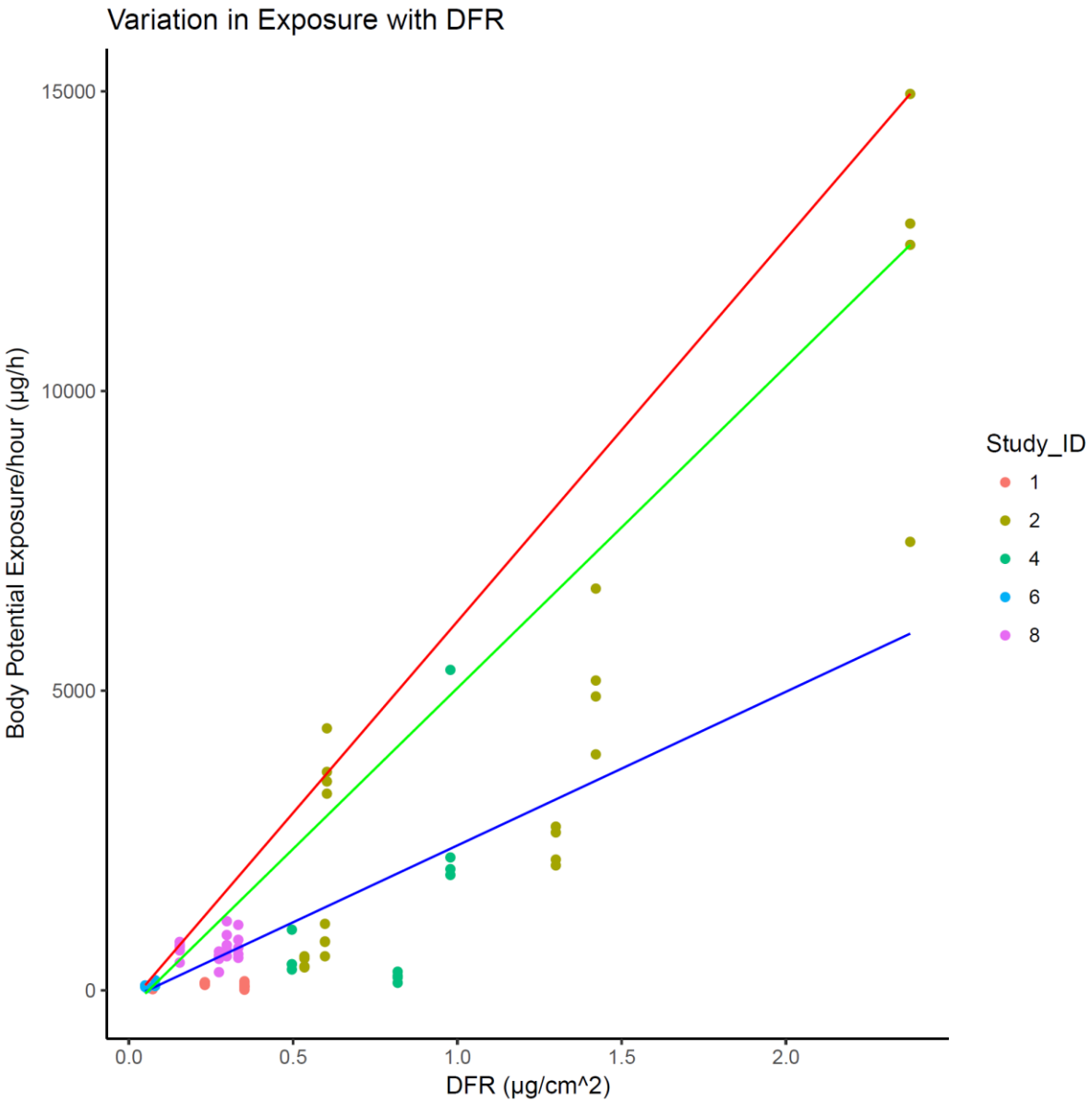


Figure B3: Plot of body potential exposure per hour (µg/h) and DFR level (µg/cm^2) showing source of data. Fitted lines show quantile regressions, showing red 95th, green 75th, and blue 50th percentiles.

The data cover a good range of DFR levels, showing an apparently clear relationship between the residue and exposure levels, but fewer data are available for the highest DFR:exposure combinations and it is noted that these are from a single study.

Quantile regression has been used to illustrate the relationship trends within the data, as it is less sensitive to outliers, and makes no assumptions of normality in the data.

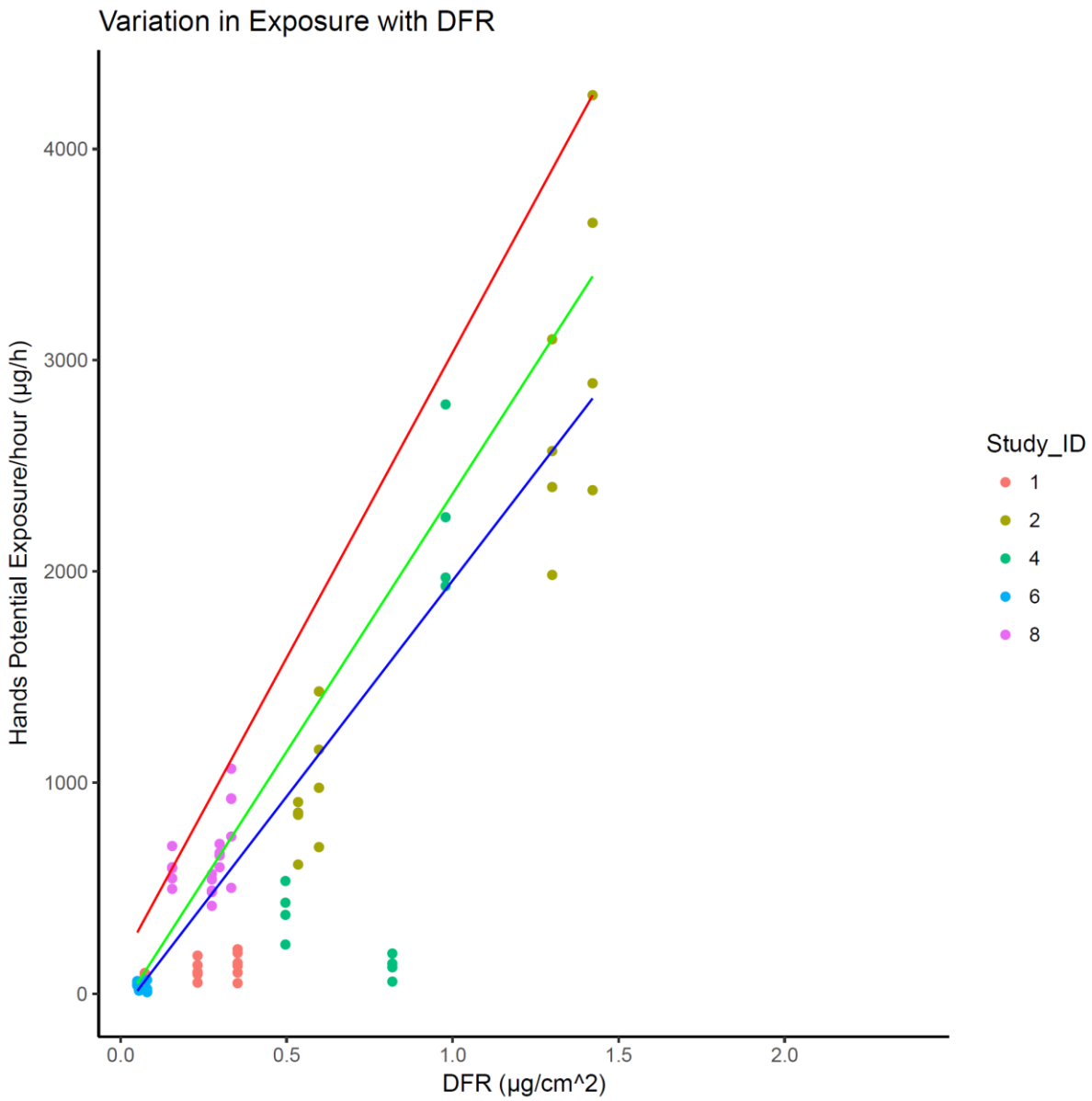


Figure B4: Plot of hand potential exposure per hour (µg/h) and DFR level (µg/cm^2) showing source of data. Fitted lines show quantile regressions, showing red 95th, green 75th, and blue 50th percentiles.

The observed data cover the lower ¾ of the range of DFR levels observed in the studies, showing an apparently clear relationship between potential hand exposure and DFR, but with no data for the highest DFR any extrapolation to potential exposures from DFRs above 1.5 µg/cm^2 is uncertain.

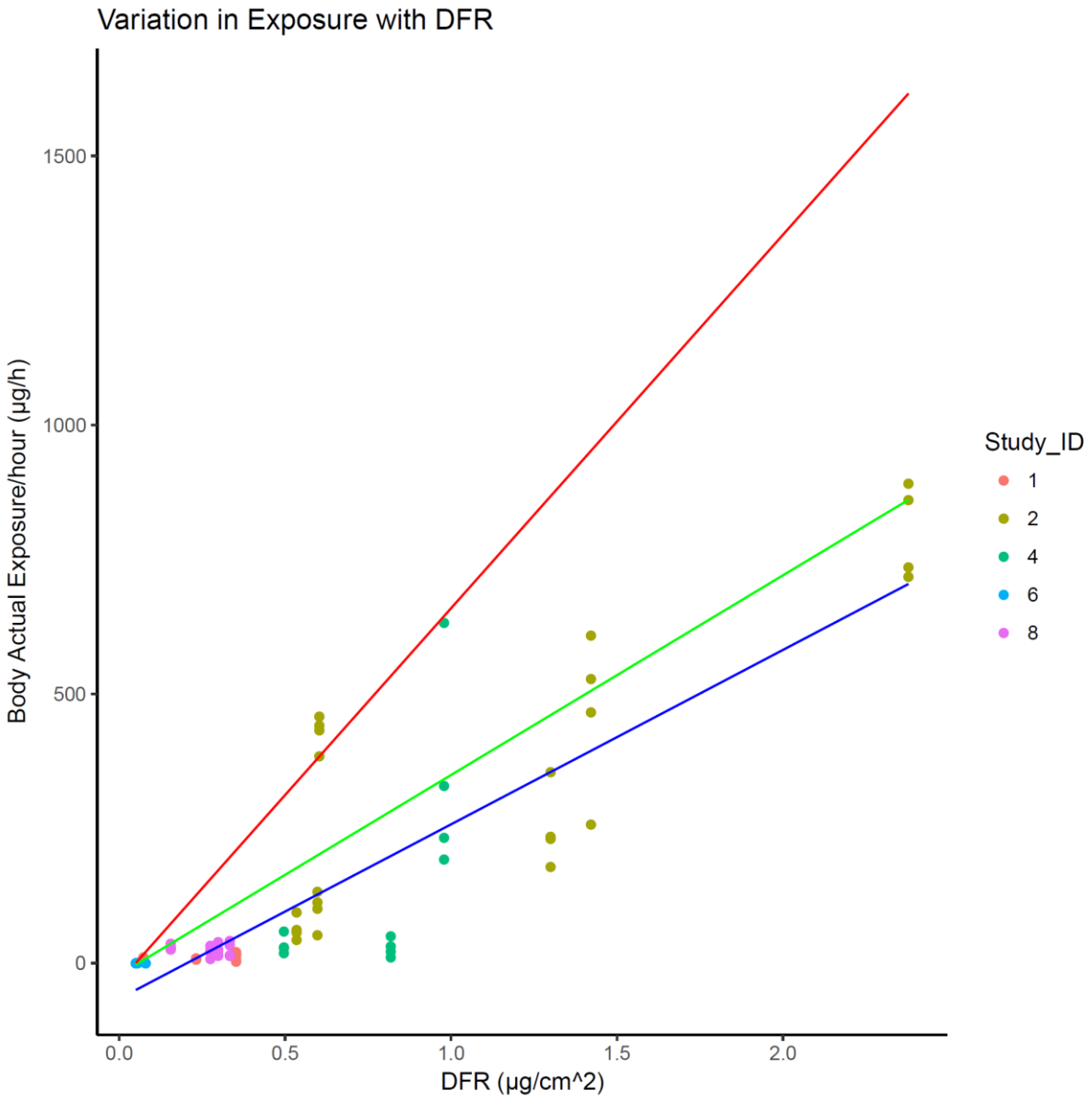


Figure B5: Plot of body actual exposure per hour (µg/h) and DFR level (µg/cm^2) showing data source. The two BASF studies have some uncertainties regarding DFR data. Bold blue line shows linear regression, thin blue lines show 95th and 75th percentile quantile regression.

The data cover a range of DFR levels, and show an apparently clear relationship between DFR and exposure, but fewer data are available for the highest DFR:exposure combinations and at and above the median DFR level the exposure data appear to be limited to observations well below expected 95th percentiles.

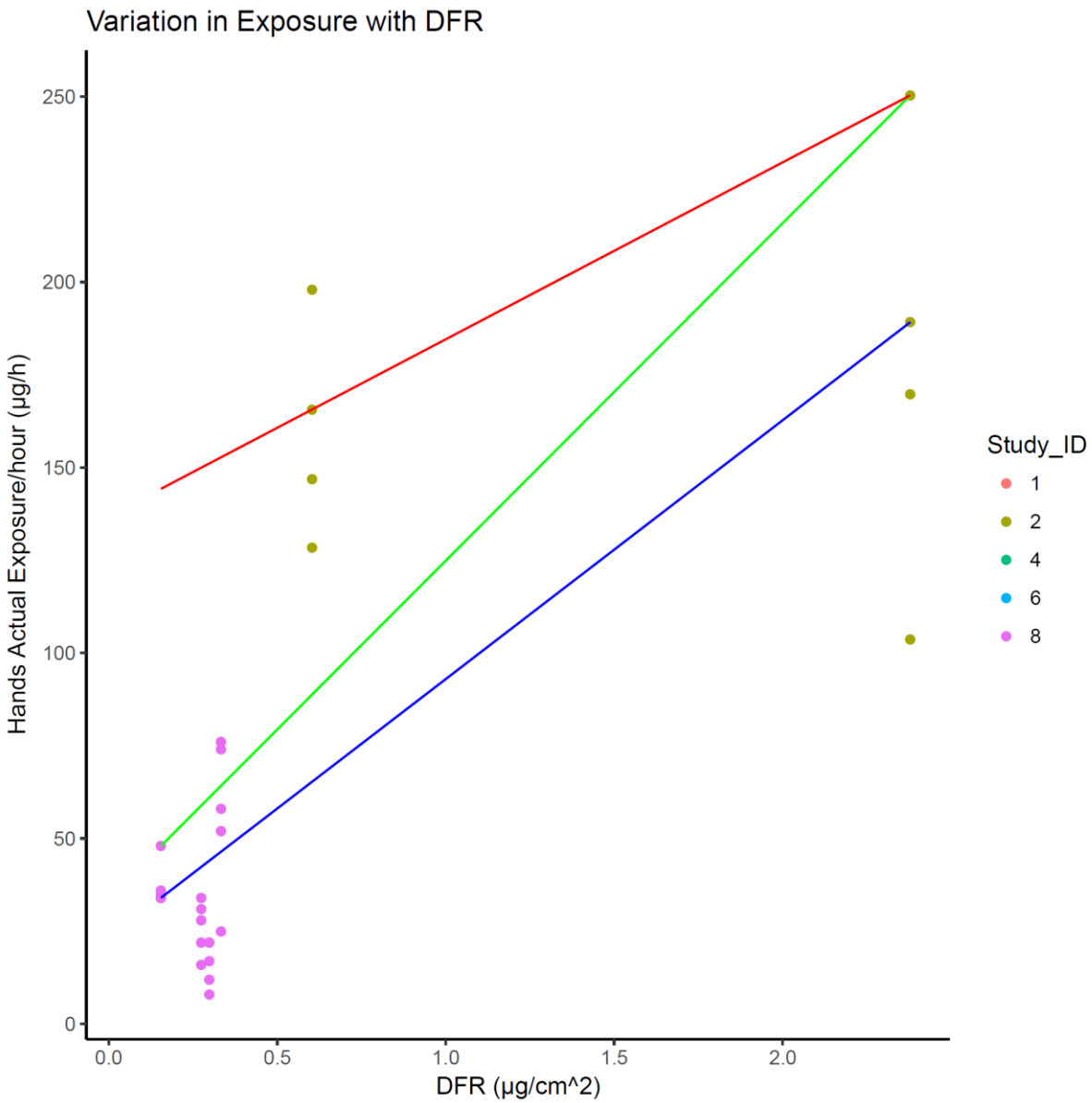


Figure B1: Plot of hand actual exposure per hour (µg/h) and DFR level (µg/cm^2) showing data source (only the BASF 1 and UIPP studies measured actual hand exposure under gloves). Fitted lines show quantile regressions, showing red 95th, green 75th, and blue 50th percentiles.

The data were only measured at the extremes of the range of DFR levels and in two studies, therefore there is high uncertainty about any observed trend and, with the limited data available, the quantile regression results are tentative.

Appendix C: Leaf wall height information, leaf wall area calculations and photographic record of studies

In a 3-dimensional crop such as grapevines, an application rate expressed simply as a dose per hectare of ground area, may not accurately reflect the dose reaching the target foliage. Measurements or estimates of leaf wall height (LWH) at the time of application, re-entry or DFR sampling are useful to predict the dose on the foliage and to allow this to be compared to the measured DFR. Leaf wall height information is also useful as evidence of the similarity of the crop structure in the exposure and DFR parts of the studies when these were conducted at different sites (paired studies 2 and 3 and paired studies 4 and 5).

In some cases, described below, measurements of leaf wall height were reported either in the final study report or in the form of raw data in the field notes of the study supervisors. Where these measurements were not available, it has been possible to estimate leaf wall height from photographs.

Where photographs have been relied on, scanned images were viewed at the maximum possible size without loss of clarity. Measurements, to the nearest millimetre, were made at 3 points in each photograph. At each measurement point, the overall height of the aerial part of the grape vine and the corresponding leaf wall height were measured. The leaf wall height was expressed as a percentage of the total crop height and the leaf wall height in metres was then calculated by multiplying the percentage value by the total crop height value reported in the studies (although the latter value was sometimes an approximate measurement covering multiple sites within a study). To validate this approach, measurements from photographs were also taken for those studies where leaf wall heights were reported (studies 3, 5 and 8): in these studies the reported leaf wall height was similar to the value calculated from the photographs.

Study 1: ECPA

In this study, the DFR measurements and the corresponding re-entry exposure measurements were performed on the same crop at the same location. Therefore, leaf wall height information is not required to justify any mismatch between sites.

The overall crop height was reported at each site but there were no measurements of leaf wall height.

Although representative photographs from all 6 sites are presented in Table C1, exposure data (and the resulting TC values) were only generated from sites 1, 2 and 5 due to low DFR levels at the other sites.

Table C1: Study 1

Site	Details	Representative photograph
1	Location: Ortenberg, Germany Variety: Müller-Thurgau Row width: 2.5 m	
2	Location: Uherský Ostroh, Czech Republic Variety: Pinot blanc Row width: 3.0 m	
3	Location: Beauvoisin, France Variety:Carignan Row width: 3.0 m	
4	Location: Mülheim, Germany Variety: Riesling Row width: 2.5 m	
5	Location: Ihringen, Germany Variety: Pinot noir Row width: 2.0 m	
6	Location: Marsillargues, France Variety: Carignan, Grenache, Merlot Row width: 2.5 m	

The analysis of the photographs is summarized in Table C2.

Table C2: Leaf wall height calculations.

Site	Reported crop height (m)	Leaf wall height as a percentage of total crop height from photographic measurements (%)				Calculated leaf wall height (m)
		Position 1	Position 2	Position 3	Mean	
1	2.1	63	66	76	68	1.4
2	2.1	73	63	70	69	1.4
3	1.8	80	85	84	83	1.5
4	2.1	86	90	88	88	1.8
5	2.1	71	73	69	71	1.5
6	1.8	76	71	77	75	1.3

Studies 2 and 3: BASF 1-1 (Re-entry) and 1-2 (DFR)

In these studies, the DFR measurements and the corresponding re-entry exposure measurements were performed on different grape varieties for sites 2 and 3 and at different locations for site 3. Therefore, leaf wall height information is useful to justify these mismatches between sites.

The overall crop heights were reported at each site as were the leaf wall heights in the DFR plots. However, there were no measurements of leaf wall height in the exposure studies. Representative photographs from all sites are presented in Table C3.

Table C3: Studies 2 and 3.

Site	Exposure study		DFR study	
	Details	Representative photograph	Details	Representative photograph
1	Location: Sandra, Veneto, IT Variety: Corvina Row width: 2.5 m		Location: Same Variety: Same Row width: 2.5 m	
2	Location: Merdingen, Baden Württemberg, DE Variety: Blauer Spätburgunder Row width: 1.8 m		Location: Same Variety: Müller Thurgau Row width: 2.0 m	
3	Location: Heuchelheim, Rheinland-Pfalz, DE Variety: Spätburgunder Merlot Row width: 2.0 m		Location: Partenheim, Rheinland-Pfalz, DE Variety: Weisser Burgunder Row width: 2.0 m	

An initial comparison of these photographs suggests that the crop structure and size is similar at the mismatched sites (the exposure and DFR studies at sites 2 and 3). The analysis of the photographs is summarized in Table C4 with reported measurements for comparison.

Table C4: Leaf wall height calculations.

Site	Reported crop height (m)	Leaf wall height as a percentage of total crop height from photographic measurements (%)				Calculated or reported leaf wall height (m)
		Position 1	Position 2	Position 3	Mean	
1 Exposure	2.0	63	58	59	60	1.2
1 DFR	1.9	Measured values reported in study				1.1
2 Exposure	2.0	53	52	60	55	1.1
2 DFR	2.0	Measured values reported in study				1.0
3 Exposure	2.0	58	62	58	59	1.2
3 DFR	2.05	Measured values reported in study				1.2

The predicted leaf wall height values for the exposure study sites are almost identical to the reported values for the corresponding DFR study sites. The similarity of the size and structure of the crops at the corresponding sites is also evident from an initial comparison of the photographs. This provides some justification for the use of the results from non-identical sites (the exposure and DFR studies at sites 2 and 3) to calculate TC values.

Studies 4 and 5: BASF 2-1 (Re-entry) and 2-2 (DFR)

In these studies, the DFR measurements and the corresponding re-entry exposure measurements were performed on different grape varieties for sites 1 and 3 and at different locations for sites 1, 2 and 3. Therefore, leaf wall height information is useful to justify these mismatches between sites.

The overall crop heights were reported at each site as were the leaf wall heights in the DFR plots. However, there were no measurements of leaf wall height in the exposure studies.

Representative photographs from all sites are presented in Table C5.

Table C5: Studies 4 and 5.

Site	Exposure study		DFR study	
	Details	Representative photograph	Details	Representative photograph
1	Location: St. Martial, Aquitaine, FR Variety: Merlot, Cabernet Franc Row width: 3.0 m		Location: St Pardon de Conques, Aquitaine, FR Variety: Merlot Row width: 2.0 m	
2	Location: Merdingen, Baden Württemberg, DE Variety: Blauer Spätburgunder Row width: 1.8 m		Location: Breisach am Rhein, Baden Württemberg, DE Variety: Same Row width: 1.8 m	
3	Location: Heuchelheim, Rheinland-Pfalz, DE Variety: Dornfelder, Riesling, Merlot, Pinot Noir Row width: 2.0 m		Location: Partenheim, Rheinland-Pfalz, DE Variety: Weisser Burgunder Row width: 2.0 m	

An initial comparison of these photographs suggests that the crop structure and size is similar for the exposure and DFR studies at site 1 but the crop structure appears different in the exposure and DFR studies at sites 2 and 3. The analysis of the photographs is summarized in Table C6 with reported measurements for comparison.

Table C6: Leaf wall height calculations.

Site	Reported crop height (m)	Leaf wall height as a percentage of total crop height from photographic measurements (%)				Calculated or reported leaf wall height (m)
		Position 1	Position 2	Position 3	Mean	
1 Exposure	2.0	72	76	72	73	1.5
1 DFR	1.6	Measured values reported in study				1.1
2 Exposure	2.0	72	68	65	68	1.4
2 DFR	2.0	Measured values reported in study				1.3
3 Exposure	2.0	77	72	75	75	1.5
3 DFR	1.95	Measured values reported in study				1.0

The predicted leaf wall height values for the exposure study sites differ by between 0.1 and 0.5 m from the reported values for the corresponding DFR study sites. Differences in the size and structure of the corresponding crops at sites 2 and 3 is also evident from an initial comparison of the photographs. This provides some justification for investigating whether the TC values derived from these studies differ from those based on the other studies which use identical sites for the exposure and DFR measurements.

Studies 6 and 7: Dow 1-1 (exposure) and 1-2 (DFR)

In these studies, the DFR measurements and the corresponding re-entry exposure measurements were performed on the same crop at the same location. Therefore, leaf wall height information is not required to justify any mismatch between sites.

The overall crop height was reported only as a range across all sites (1.5 to 1.8 m). No measurements of leaf wall height were reported and no further information on crop height or leaf wall height are available in the raw data or field notes.

It is not possible to predict leaf wall height from photographs as none is available.

Study 8: UIPP

In this study, the DFR measurements and the corresponding re-entry exposure measurements were performed on the same crop at the same location. Therefore, leaf wall height information is not required to justify any mismatch between sites.

The overall crop height at each site was reported in the study. Mean measurements of leaf wall height at each site were recorded in the raw data as field notes. These measurements are summarised in Table C7 together with representative photographs.

Table C7: Reported leaf wall height.

Site	Location	Variety	Row width (m)	Reported crop height (m)	Recorded leaf wall height (m)	Representative photograph
1	Veneto, IT	Moscato - Merlot	2.5	1.8	1.2	
2	Charente, FR	Ugni blanc	3.0	2.0	1.5	
3	Champagne, FR	Chardonnay, Pinot noir, Pineau Meunier	1.1	1.5	1.5	

Site	Location	Variety	Row width (m)	Reported crop height (m)	Recorded leaf wall height (m)	Representative photograph
4	Alsace, FR	Pinot Auxerrois, Muscat, Pinot Gris, Pinot Noir Gewurztraminer	1.6	1.9	1.5	

Dose expression in terms of leaf wall area

Published information[8] describes the following relationship between leaf wall area (LWA) and leaf wall height (LWH):

LWA (m^2) = 2 x LWH (m) x (ground area (m^2) ÷ row spacing (m))

Using this approach, the application rates per hectare of the active substances in the studies can be expressed as a dose per LWA as in Table C8.

Table C8: Dose per unit LWA.

Study	Site	LWA (m^2/ha)	Analyte	Application rate (mg a.s./m^2 LWA)				
				T 1	T 2	T 3	T 4	Total
1	1	11200	Iprovalicarb	9.643	12.054	14.464	19.286	55.446
	2	9333	Iprovalicarb	16.682	16.586	17.839	16.971	68.079
	3	10000	Iprovalicarb	11.970	11.970	-	-	23.940
	4	14400	Iprovalicarb	3.438	6.875	10.313	-	20.625
	5	15000	Iprovalicarb	9.900	13.200	13.200	13.200	49.500
	6	10400	Iprovalicarb	8.654	11.250	-	-	19.904
2	1	9600	Dimethomorph	23.438	23.438	23.438	-	70.313
			Dithianon	54.688	54.688	54.688	-	164.063
	2	12222	Dimethomorph	18.409	18.409	18.409	-	55.227
			Dithianon	42.955	42.955	42.955	-	128.864
	3	12000	Dimethomorph	12.000	15.000	18.000	-	45.000
			Dithianon	28.000	35.000	42.000	-	105.000

Study	Site	LWA (m^2/ha)	Analyte	Application rate (mg a.s./m^2 LWA)				
3	1	8800	Dimethomorph	23.693	25.278	23.301	-	72.273
			Dithianon	55.284	58.983	54.369	-	168.636
	2	10000	Dimethomorph	23.985	25.365	21.375	-	70.725
			Dithianon	55.965	59.185	49.875	-	165.025
	3	12000	Dimethomorph	17.438	18.988	18.513	-	54.938
			Dithianon	40.688	44.304	43.196	-	128.188
4 [2]	1	10000	Pyrimethanil	102.925	-	-	-	102.925
	2	15556	Pyrimethanil	52.933	-	-	-	52.933
	3	15000	Pyrimethanil	54.893	-	-	-	54.893
5 [2]	1	11000	Pyrimethanil	93.156	-	-	-	93.156
	2	14444	Pyrimethanil	59.228	-	-	-	59.228
	3	10000	Pyrimethanil	80.487	-	-	-	80.487
6/7 [3]	1	-	Fenbuconazole	No data				
	2	-	Fenbuconazole	No data				
	3	-	Fenbuconazole	No data				

Study	Site	LWA (m^2/ha)	Analyte	Application rate (mg a.s./m^2 LWA)				
8	1	9600	Iprovalicarb	10.969	-	-	-	10.969
	2	10000	Iprovalicarb	11.700	-	-	-	11.700
	3	27273	Iprovalicarb	4.059	-	-	-	4.059
	4	18750	Iprovalicarb	6.192	-	-	-	6.192

For the paired studies which had one or more mismatches between the exposure and DFR parts (as described earlier in this report), the LWA results are examined in Table C9.

Table C9: Comparison of dose per LWA for mismatched studies.

Paired studies	Site	a.s.*	LWA application rate					
			Final treatment			Total dose		
			mg/m^2 LWA		% difference	mg/m^2 LWA		% difference
			Exposure	DFR		Exposure	DFR	
2 Exposure 3 DFR	1	Dim	23.4	23.3	0.4%	70.3	72.3	2.8%
		Dit	54.7	54.4	0.5%	164.1	168.6	2.7%
	2	Dim	18.4	21.4	15.1%	55.2	70.7	24.6%
		Dit	42.9	49.9	15.1%	128.9	165.0	24.6%
	3	Dim	18.0	18.5	2.7%	45.0	54.9	19.8%
		Dit	42.0	43.2	2.8%	105.0	128.2	19.9%
4 Exposure 5 DFR	1		Single treatment only			102.9	93.2	9.9%
	2		Single treatment only			52.9	59.2	11.2%
	3		Single treatment only			54.9	80.5	37.8%
* for studies with more than one analyte: Dim = dimethomorph, Dit = dithianon								

As discussed earlier, as the aim of the project is to calculate TC values, a mismatch in application rates is of most concern when the higher rate is used in the DFR study (a higher rate in the corresponding exposure study would result in a more precautionary TC).

For paired studies 2 and 3, a higher rate in terms of LWA is in the DFR part of the study at sites 2 and 3 only. This difference is considerably lower (negligible for site 3) when only the final treatment before re-entry and DFR sampling is considered.

For paired studies 4 and 5, although the application rates expressed per ha at each site were almost identical in the exposure and DFR studies, differences are predicted when the application rates are expressed in terms of LWA. In these studies, a higher application rate in terms of LWA is predicted in the DFR part of the study at sites 2 and 3, especially the latter.

Appendix D: TC calculations with and without mismatched studies

The report above describes and discusses the likely significance of the various mismatches between the exposure and DFR parts of the paired studies 2 and 3 and the paired studies 4 and 5. These differences are also considered in terms of the database description in Appendix B and in terms of the predicted dose per LWA in Appendix C.

To determine how the mismatched studies influence the final TC values, TC calculations excluding the mismatched studies have been compared to those based on the full dataset.

Table D1: TC comparison for potential exposure.

Transfer Coefficient for Potential Exposure (cm^2/h)						
Task	**Complete Dataset**			**Excluding Studies 2, 3, 4 and 5**		
	Body	**Hands**	**Total [1]**	**Body**	**Hands**	**Total [1]**
Harvesting 75th centile	560	800	1500	560	800	1500
Harvesting 95th centile	910	1300	1800	910	1300	1800
Pruning/training 75th centile	2900	1900	3800	1600	800	2500
Pruning/training 95th centile	5900	2600	6500	1900	1100	2900
Pruning/shoot lifting 75th centile	3400	3200	6100	3400	3200	6100
Pruning/shoot lifting 95th centile	4900	3900	9000	4900	3900	9000

[1] The percentile TC values for the body and hands may not add up to the corresponding total TC values because the latter are calculated from the sum of all relevant dosimeters for each individual study subject, whereas a given percentile value for body exposure and hand exposure will not necessarily relate to the same individual study subject.

Table D2: TC comparison for actual exposure.

Transfer Coefficient for Actual Exposure (cm^2/h)						
Task	**Complete Dataset**			**Excluding Studies 2, 3, 4 and 5**		
	Body [2]	**Hands [3]**	**Total [1]**	**Body [2]**	**Hands [3]**	**Total [1]**
Harvesting 75th centile	60	-	-	60	-	-
Harvesting 95th centile	130	-	-	130	-	-
Pruning/training 75th centile	340	250	980	-	-	-
Pruning/training 95th centile	720	310	1000	-	-	-
Pruning/shoot lifting 75th centile	140	220	350	140	220	350
Pruning/shoot lifting 95th centile	200	230	420	200	230	420

[1] The percentile TC values for the body and hands may not add up to the corresponding total TC values because the latter are calculated from the sum of all relevant dosimeters for each individual study subject, whereas a given percentile value for body exposure and hand exposure will not necessarily relate to the same individual study subject.
[2] Body exposure beneath a single layer of long-sleeved and long-legged clothing.
[3] Actual hand exposure under work gloves (partial nitrile).

The TC values for the 'harvesting' and 'pruning/shoot-lifting' tasks are derived from studies 1 and 8, respectively, and these values remain the same irrespective of whether studies 2, 3, 4 and 5 are included or excluded.

The mismatched studies covered the 'pruning/training' task. For this task, by excluding studies 2, 3, 4 and 5, the TC values for potential body exposure, potential hand exposure and total potential exposure decrease. These decreased potential exposure TC values for the 'pruning/training' task rely on a single study pair (studies 6 and 7) and this study pair does not have any data for the calculation of actual exposure TCs for the body or hands.

Therefore, the exclusion of studies 2, 3, 4 and 5 would result in less precautionary (i.e. lower) TC values for potential exposure to the body and hands and would not allow the derivation of TC values for actual body and hand exposure. Also, by excluding these data, the TC values

for the pruning/training' task would be based on limited data (a single study pair). For this reason, and based on the evidence presented elsewhere in this report, exclusion of the mismatched studies would increase, rather than decrease, uncertainly and detract from the usefulness and robustness of the database.

Appendix E: Further consideration of the relationship between applied dose and DFR

This dataset demonstrates a relatively wide range of DFR values observed after the application of a similarly wide range of doses. Therefore, these data provide an opportunity to explore the relationship between applied dose and resulting DFR levels, although this not required for the derivation of the TC values in this report.

Several sources of additional variation within the studies should be considered when comparing the data in the different studies: the number of applications prior to the DFR sampling date varied; the interval between the final application and the sampling date varied; different active substances were applied (so decline rates varied); and there was some variation in the crop structures (as measured by Leaf Wall Area).

The following figures show the observed DFR levels plotted against the applied dose. Each figure shows a linear trend line for mean DFR with a range (grey-shaded) to show the corresponding 95% confidence interval, fitted by linear regression.

Figures E1 - E4 show plots of DFR against dose expressed per unit ground area for: the whole dataset against the total amount of active substance applied (which accounts for multiple applications but ignores any decline between applications and will therefore over estimate the amount present contributing to the DFR); those cases where only one application was made (to remove the effect of multiple applications); the dose in the final application (for the whole dataset); and the estimated dose after accounting for decline after applications. For these cases, the estimated dose present was calculated assuming exponential decline, using the indicative DT50s (given in Section 4, page 8) and the time (days) between applications and sampling. Visual comparison of the fit, and consideration of the adjusted R-squared value, suggests that the model which accounts for decline of active substances after application (Figure A10, adj. $R^2 = 0.74$) provides a better fit to the data than the other comparisons.

Two figures show the data with the dose expressed per unit leaf wall area. Figure E5 shows a plot of DFR against total dose applied expressed as the quantity per leaf wall area for the whole dataset. Again, from visual comparison and based on the adjusted R^2 value (0.75) this appears to be a slightly better model than the fit against total dose per unit area (Figure E4). Finally, figure E6 shows the DFR values against the estimated dose remaining at the time of DFR sampling after taking account of multiple applications. Visually this appears to be a similar fit to where the application rate is expressed per unit area, but it has the highest (by a small margin) adjusted R^2 value of 0.77.

Therefore, within this dataset the best estimate[1] of the mean trend between applied dose and DFR is:

> DFR µg/cm^2 = 0.015 x dose active substance mg/m^2 leaf wall area + 0.046, or where the leaf wall area expression is not known,
> DFR µg/cm^2 = 1.43 x dose active substance kg/ha + 0.026.

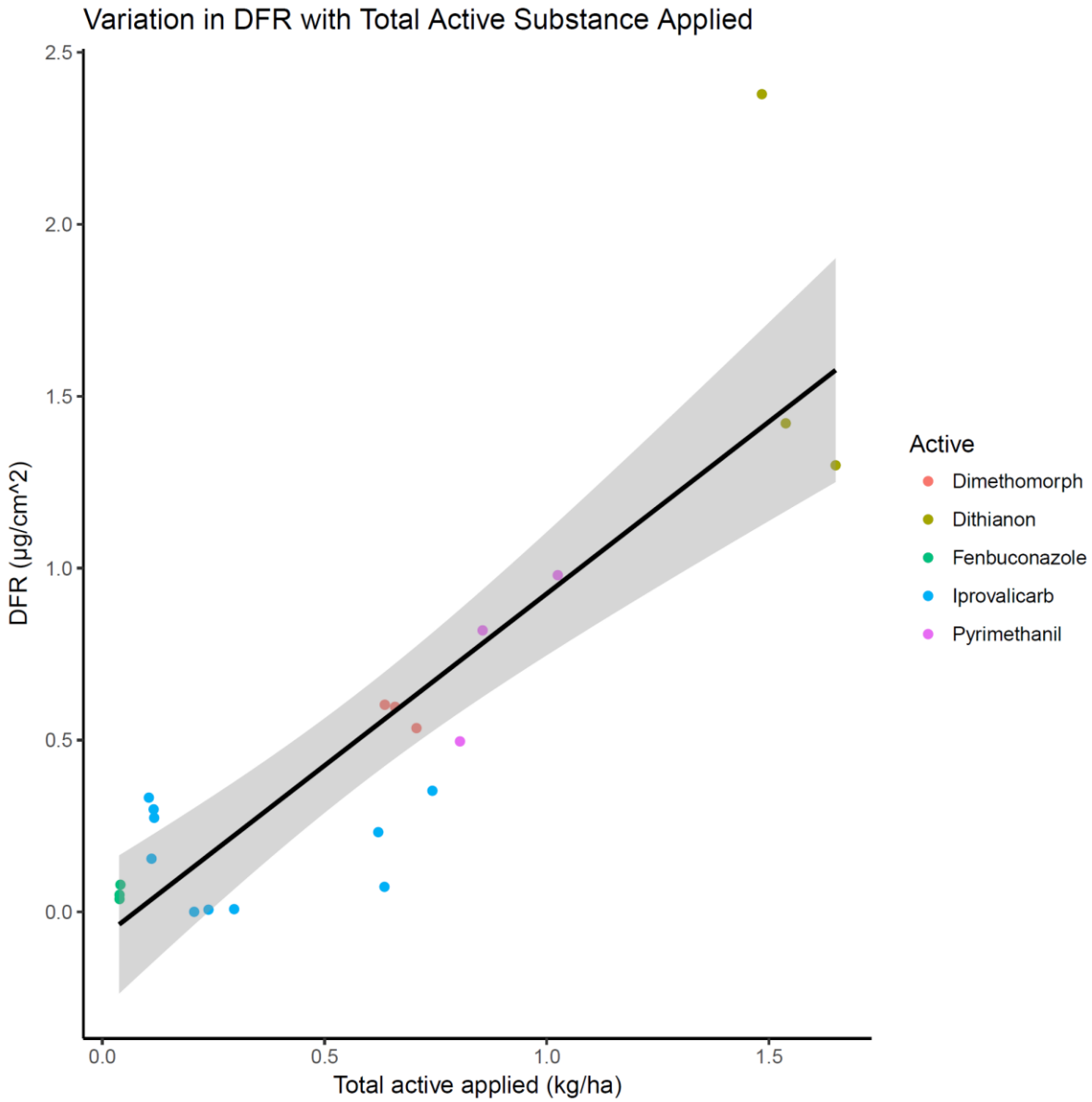


Figure E1: Variation in DFR with total dose of active substance applied per unit area

[1] Regression diagnostics are limited for small data sets, but generally residual vs fitted values support a linear assumption. Normal Q-Q plots showed residues to be normally distributed with the exception of the highest dithianon DFR data point. A scale location plot indicated some issues with heteroscedasticity. Residues vs leverage indicates the highest DFR datapoint is clearly influential to the regressions.

Summary of regression model for Figure E1:

Model	Adj. R^2	Estimate	Std. Error	t value	p or Pr(>|t|)
DFR ~ total kg/ha	0.729				2.644e-07
Constant		-0.07439	0.10000	-0.744	0.466
Total kg/ha		1.00013	0.13191	7.582	2.64e-07 ***

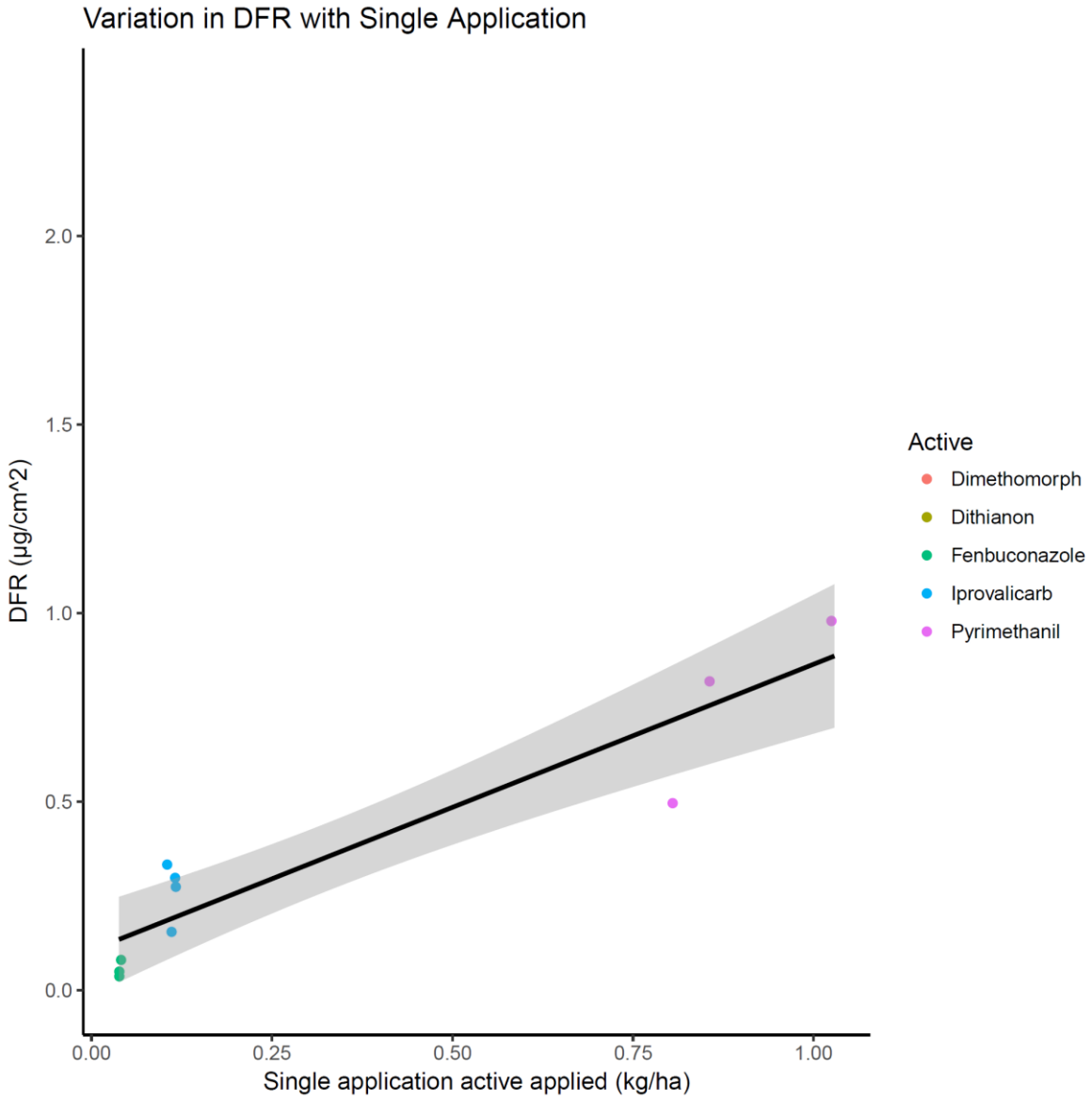


Figure E2: Variation in DFR with dose of active substance per area where only a single application was made

Summary of regression model for Figure E2:

Model	Adj. R^2	Estimate	Std. Error	t value	p or Pr(>|t|)
DFR ~ single application kg/ha	0.8548				8.006e-05
Constant		0.10572	0.05148	2.054	0.0741
Single application kg/ha		0.75861	0.10323	7.348	8.01e-05 ***

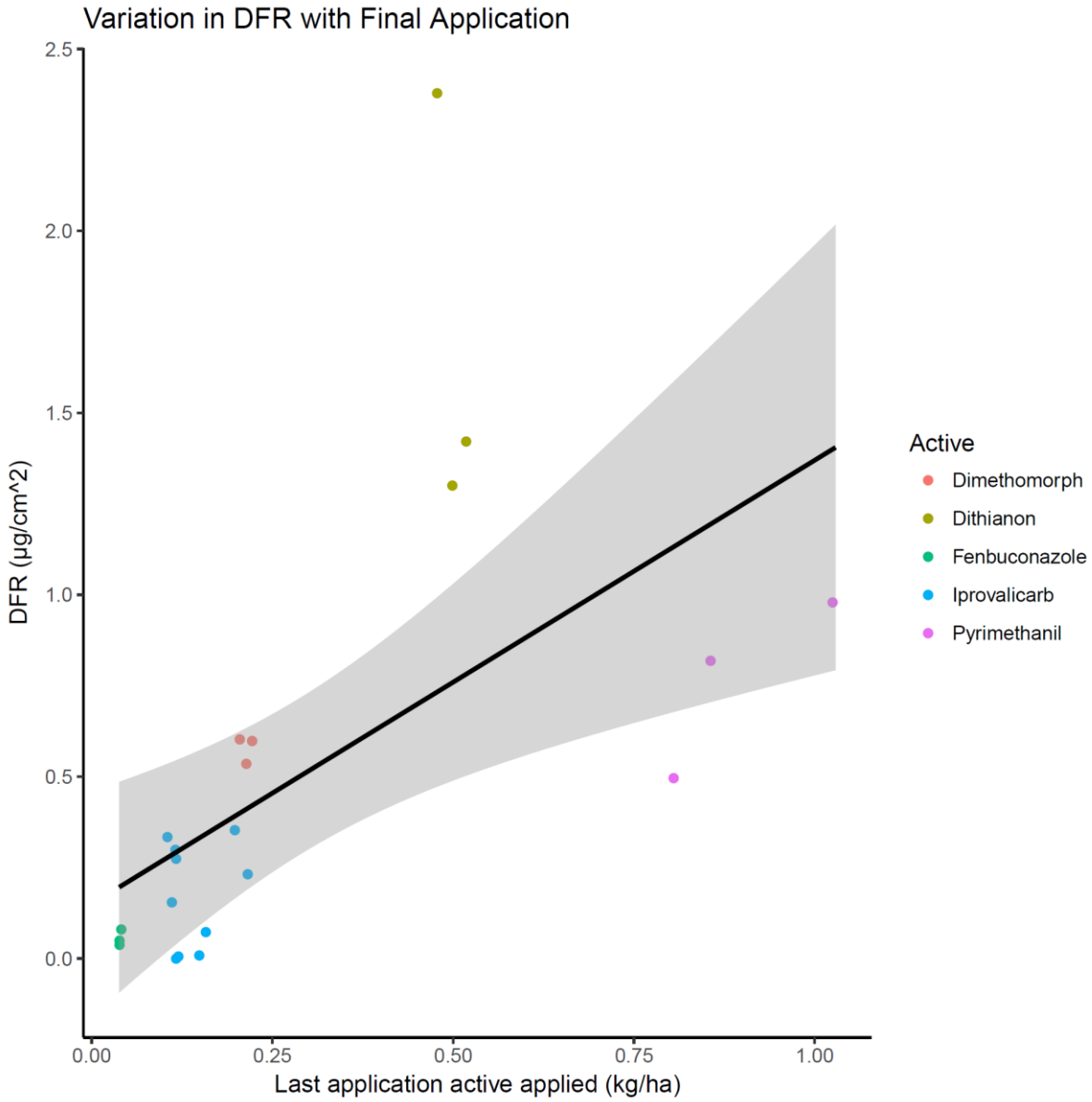


Figure E3: Variation in DFR with dose active substance applied per area in last application before DFR sampling

Summary of regression model for Figure E3:

Model	Adj. R^2	Estimate	Std. Error	t value	p or Pr(>|t|)
DFR ~ Final application kg/ha	0.3183				0.003682
Constant		0.1496	1.006	1.006	0.32637
Final application kg/ha		1.2200	3.287	3.287	0.00368 **

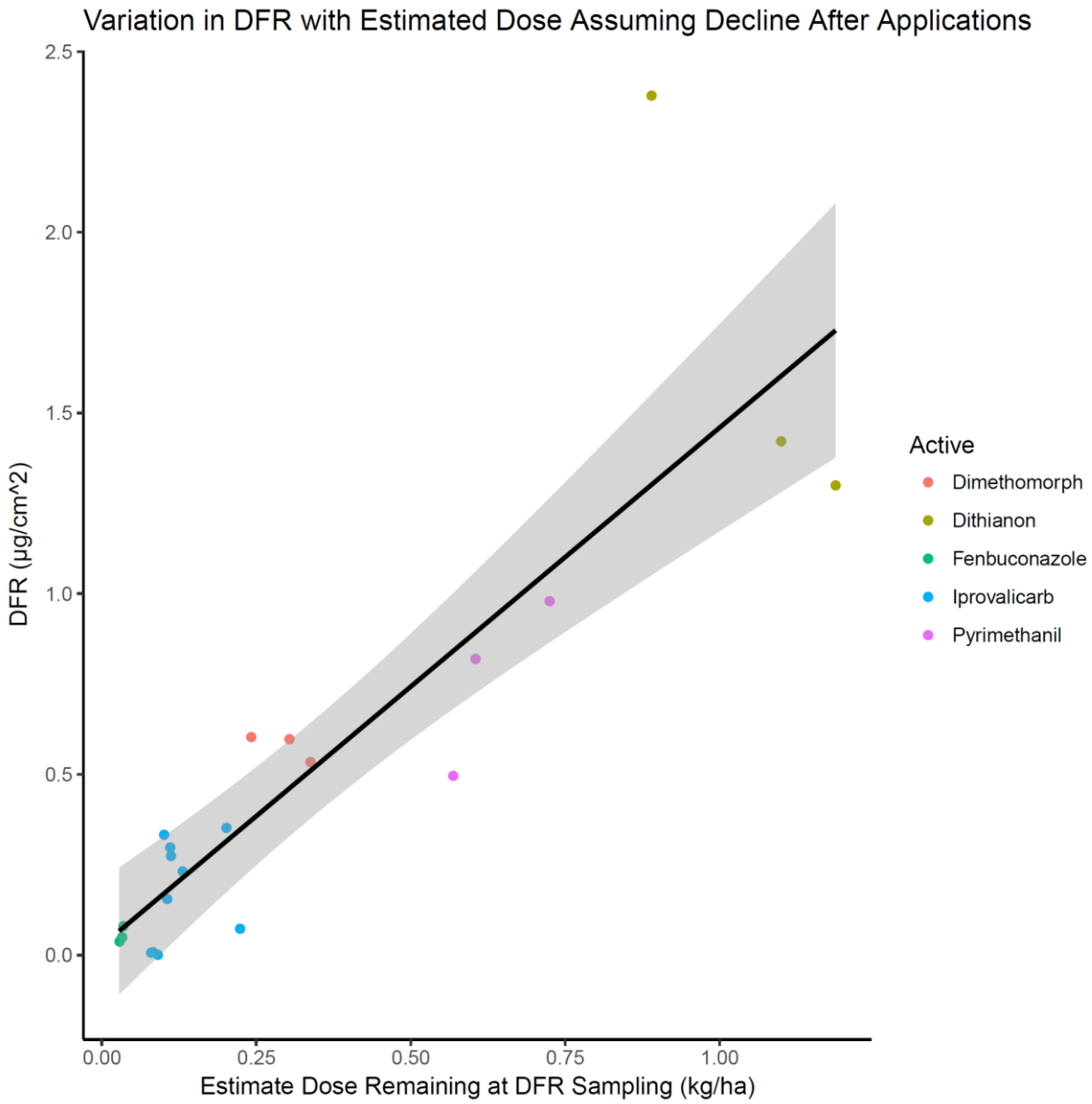


Figure E4: Variation in DFR with estimated dose per unit area remaining at DFR sampling (assuming exponential decline after application and indicative decline DT50s given in Section 4, page 8)

Summary of regression model for Figure E4:

Model	Adj. R^2	Estimate	Std. Error	t value	p or Pr(>|t|)
DFR ~ Est remaining dose kg/ha	0.7427				1.56e-07
Constant		0.02617	0.08766	0.299	0.768
Est remaining dose kg/ha		1.43291	0.18254	7.850	1.56e-07 ***

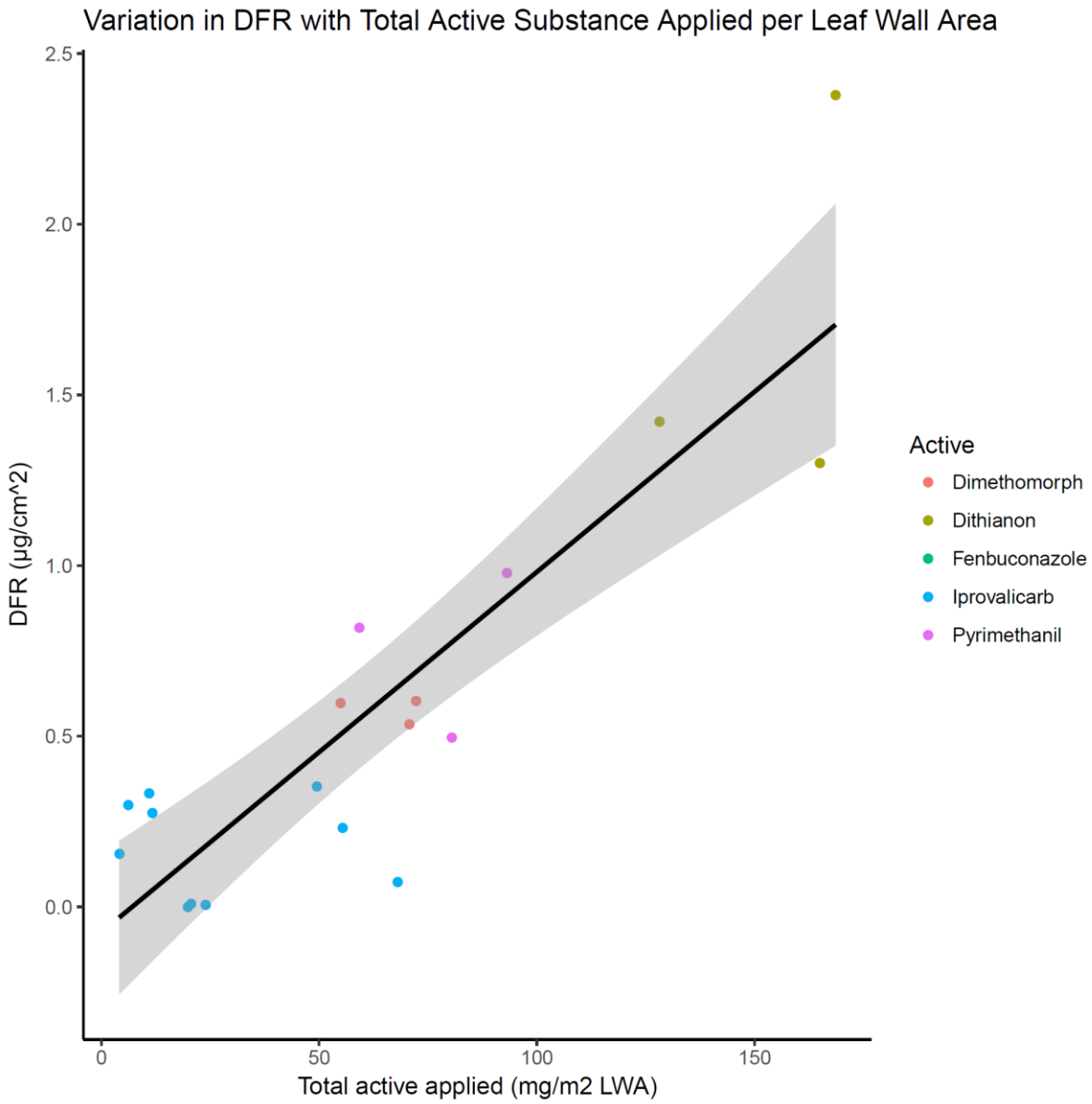


Figure E5: Variation in DFR with total dose applied per Leaf Wall Area

Summary of regression model for Figure E5:

Model	Adj. R^2	Estimate	Std. Error	t value	p or Pr(>|t|)
DFR ~ Total dose per LWA	0.7496				1.022e-06
Constant		-0.074404	0.111286	-0.669	0.513
Total dose per LWA		0.010557	0.001425	7.409	1.02e-06 ***

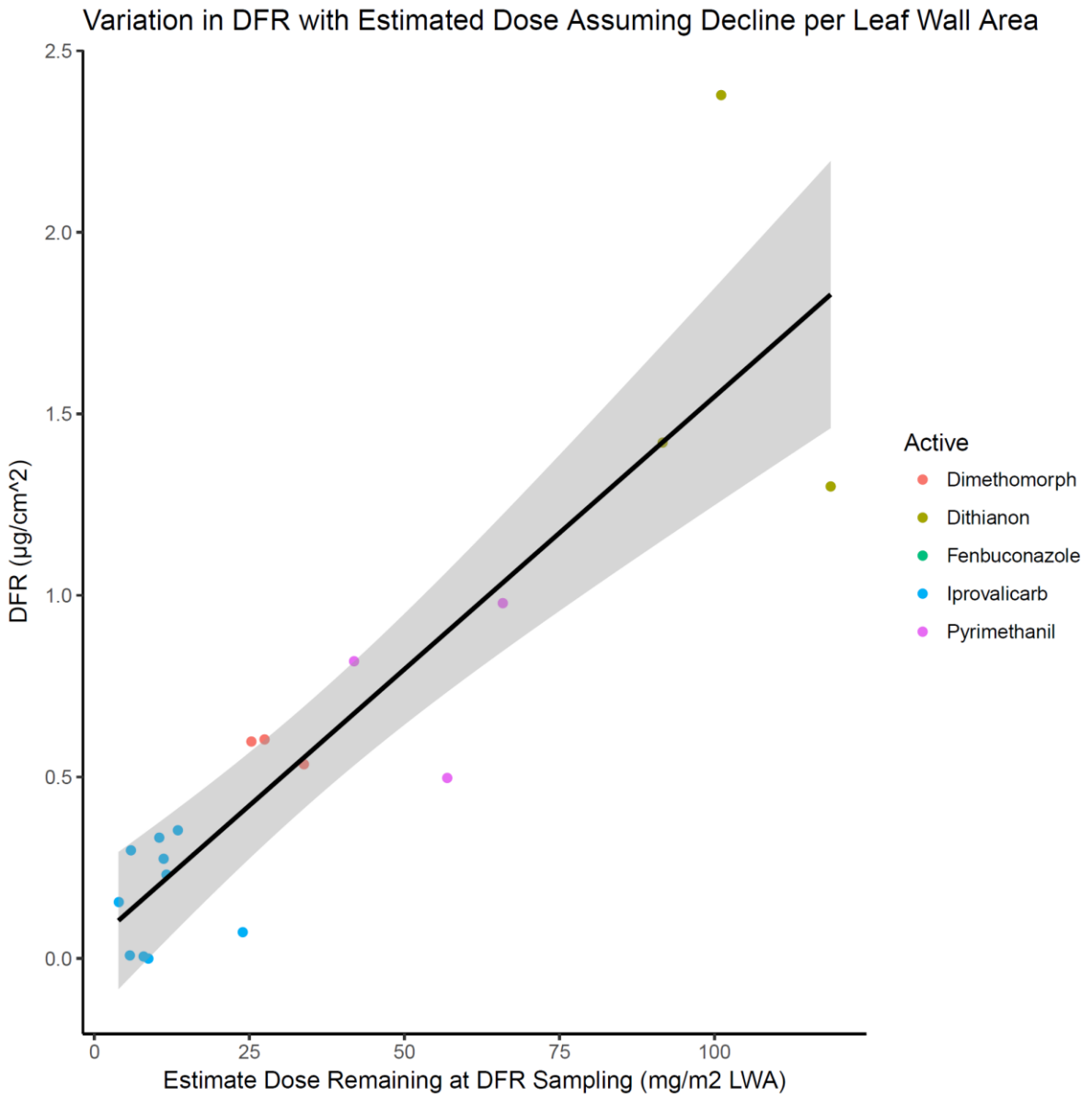


Figure E6: Variation in DFR with estimated remaining dose at DFR sampling (assuming exponential decline after application and indicative decline DT50s given in Section 4, page 8) per Leaf Wall Area

Summary of regression model for Figure E6:

Model	Adj. R^2	Estimate	Std. Error	t value	p or Pr(>|t|)
DFR ~ Est remaining dose per LWA	0.7687				5.155e-07
Constant		0.045846	0.094661	0.484	0.634
Est remaining dose per LWA		0.015014	0.001925	7.799	5.15e-07 ***