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ACROPOLIS

Aggregate and Cumulative Risk Of Pesticides: an On-Line Integrated Strategy

SEVENTH FRAMEWORK PROGRAMME

Deliverable 3.4 Validation of the model

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Validation of a cumulative and aggregate exposure model using biomonitoring studies and dietary records for Italian vineyard spray operators.

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Abstract

Risk assessments for exposures to plant protection products (PPPs) have used single sources, such as food or individual occupational sources, rather than consider exposure to multiple sources. The need for improved tools to estimate the cumulative and aggregate exposure to compounds such as PPPs is recognised. Such risk assessments are now required to be considered according to the EU Regulation 1107/2009. A new model has been developed to estimate the exposure of individuals within a population to single compounds or compounds with a Cumulative Action Group, considering both dietary and non dietary sources. As an exercise to validate the model outputs a field study was carried out in Italy with operators applying tebuconazole fungicides, with measurements made for the dermal exposure. Whole urine samples were collected and analysed to provide values for the absorbed dose of tebuconzole, with duplicate diet samples collected and analysed as a measure of dietary exposures. The Acropolis model provided predicted values of exposure for the combined dietary and non-dietary routes of exposures which were compared to the measured absorbed dose values. The Acropolis model outputs provided mean daily exposure values of 1.76 (± 1.96) µg a.s. /kg BW which compare favourably to measured mean values from the biomonitoring field study of 1.71 (± 1.31) µg a.s./kg BW. Exposures can be calculated for multiple compounds, routes and sources of exposure. The aggregate model links to the cumulative dietary exposure model developed in parallel and is implemented in the web-based software tool MCRA.

Keywords: common assessment group, probabilistic modelling, occupational exposure, consumer exposure

Running title: Validation of aggregate model for pesticide exposure assessment

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1. Introduction

The regulation of plant protection products (PPP) in the European Union (EU) now requires the cumulative risk to be considered according to the regulation 1107/2009. Historically the risk assessments for human and environmental safety have been performed by considering the active substances within a single PPP, which is often a single active substance (a.s.). Rather than restricting the risk assessment on a single PPP the combined exposure to compounds within a cumulative action group (CAG) from various sources and routes needs to be considered. The aggregate model developed as part of the EU Acropolis project allows such exposures to be estimated, taking into account exposures from the use of several product types and use scenarios. A key element of the Acropolis project involved the use of case studies of aggregate exposure to triazole compounds and a biomonitoring field study with spray operators using tebuconazole products in vineyards in the Lombardy region of Italy to evaluate model predictions. Biomonitoring techniques to measure the absorbed dose were used together with operator dermal dosimetry and duplicate diet sampling to provide data for external and absorbed dose of tebuconazole in volunteers.

Previous studies have been reported which have measured urinary levels of pesticide parent compounds and metabolites particularly for children of farmers and farm workers (Bradman et al 2007). The early work to evaluate exposures to compounds within a CAG focussed on the organophosphate pesticides. Urinary levels of dialkyl phosphates (DAP) for the population have been reported (Heudorf et al 2001; Duggan et al 2003) to assess exposures from all routes. Occupational exposure to organophosphate pesticides have also been reported, with Ueyama et al (2012) reported that urinary DAP levels for a range of workers in Japan, including pesticide applicators, being similar to those reported previously. Exposure to pesticides as part of a total diet study has been performed by analysing community food samples (Gimou at al 2008; Nougadère et al 2012) and from duplicate diet samples (Melnyk et al 1997).

For risk assessment it is important to be able to quantify the contribution of the different sources and routes of exposure. Spot urine samples provide limited information in terms of exposure, due to the variable time interval between exposure and sampling (Bradman et al 2013). It is more informative to determine exposure in terms of the absorbed dose by conducting biomonitoring studies in which the whole urine sample is collected over the time period during which the parent compounds and metabolites would be eliminated from the body. With knowledge of the pharmacokinetics of the compounds under study, the mass of parent compounds and metabolites collected in the urine can be related to the absorbed dose of the compound by all routes. To allow an estimate of the contribution by the different routes of exposure, monitoring of residues in the diet during the exposure period under investigation need to be collected. Therefore the biomonitoring field study in the Acropolis project was designed to compare the absorbed dose of a triazole compound with the measured intake in the diet and the estimated absorption via the dermal route by measuring the actual dermal exposure (ADE). The inhalation route of exposure was not measured, as this is considered to be a minor route of exposure, particularly when respiratory personal protection (RPE) is worn by the operator. The individual values for dermal and dietary exposures can be further compared to model estimates with MCRA and the German Model or EUROPOEM database, and ultimately with aggregate exposure predictions from the Acropolis model as part of a validation exercise.

2. Material and methods

The process of estimating aggregate exposure brings together various model and data components, each of which is described below. Many different comparisons could potentially be made in order to validate the final estimate or intermediate calculations. Figure 1 shows how the estimation is constructed, and which comparisons are presented in this paper for validation.

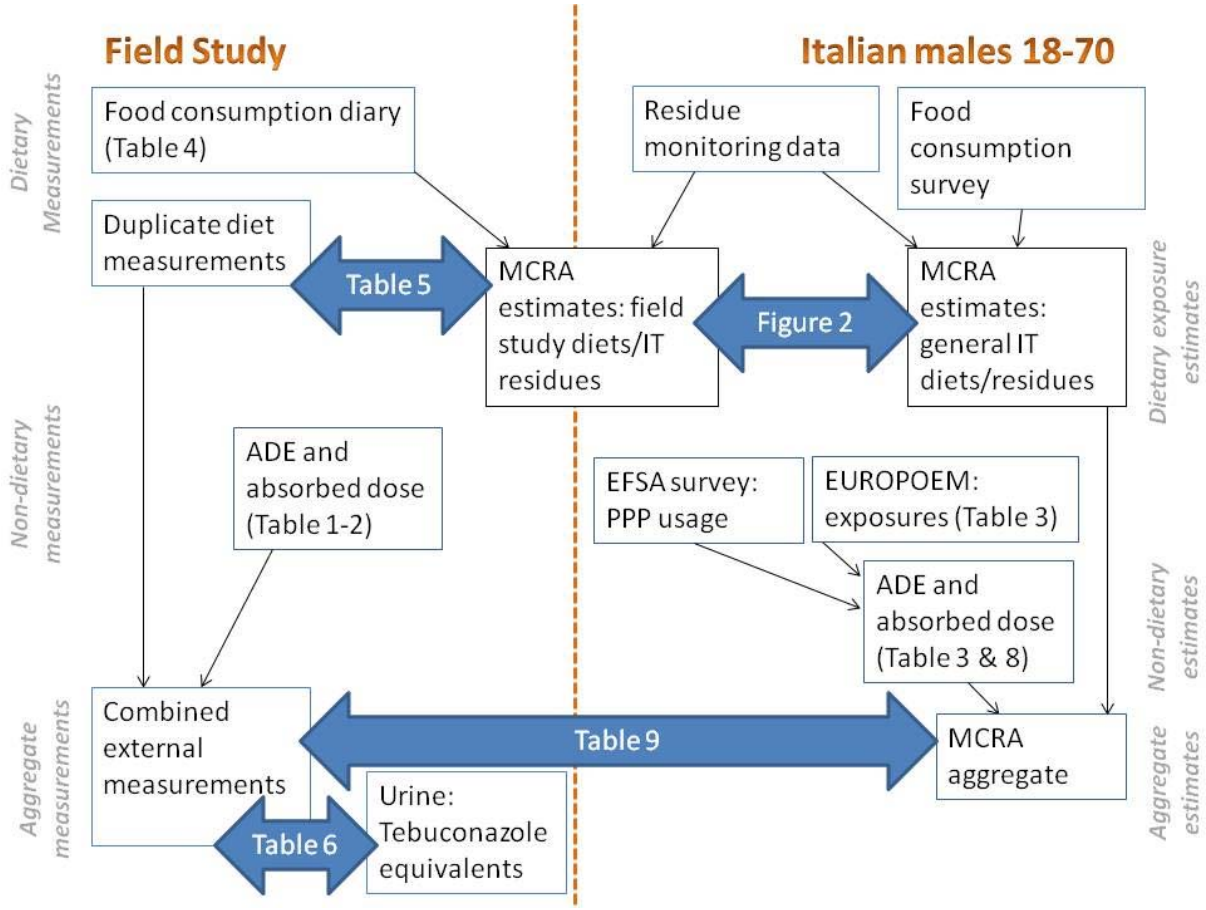


Figure 1. Aggregate model data sources, derived estimates. Blue arrows indicate where direct comparisons can be made to assess the model

2.1 Occupational Exposure

Field studies were performed in the Lombardy region of Italy with application of triazole fungicides to wine grape vineyards to determine the potential dermal exposure (PDE) and actual dermal exposure (ADE) using whole body and patch dosimetry methods. The dermal dosimetry methodology followed a modified version of the OECD Guideline protocol (OECD 1997) and is described in detail by Fustinoni et al (submitted/in press, 2013) .
Urine samples were collected for the 24 hour period prior to the start of the pesticide application and for periods of between 24 and 48 hours following the end of the application. Two specific metabolites of tebuconazle had been identified for analysis in the urine samples, TEB-OH (4-chlorophenyl)-2,2-dimethyl-3-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-pentanediol and TEB-COOH 5-(4-chlorophenyl)-2,2-dimethyl-3-(1H-1,2,4-triazol-1ylmethyl)-3-olpentanoic acid

The field studies were done during 2011 with pesticides containing the active substance (a.s.) tebuconazole. Further field studies in 2012 were only done with pesticides containing the a.s. penconazole, due to a change in local practice by famers, who were no longer using pesticides containing tebuconazole. For the validation described here it was decided to focus on tebuconazole and to use only the 2011 data.

2.2 Dietary Exposure

2.2.1 Collection of duplicate diet samples

The volunteers in the field studies were asked to provide duplicate diet samples and a detailed diary of food items consumed during the two day period, starting the day before the pesticide application and dermal exposure measurements. Supervising scientists provided instructions for the monitoring period and explained the objectives of the study. For each monitoring day a short interview was carried out when collecting the diary and the containers with the duplicate diet to check the completeness of the information and gain an understanding of whether the diet of the volunteers on the sample day was typical or if there were foods usually eaten but not consumed in the sample day. This check for completeness included the list of food items provided and the description of recipes. Duplicate portions were collected in four categories based on the likelihood of the food containing residues of a conazole compound, using information from residue surveillance programmes. In this way possible dilution of pesticides present by food items that do not contain the conazole compounds was minimised. The four categories of food types were:

- All fresh vegetables and fruits, including fruit juice
- All food containing cereal products
- All liquids
- All meat products

Each duplicate food sample was stored by the volunteer either in a small plastic bag (solid foods) or in a bottle (beverages and liquids). A fridge box was provided to store the duplicates prior to collection. Following the duplicate diet protocol, the mass and constitution of each of the individual categories of food collected was the same as that consumed by the volunteer. Moreover, they were asked to handle and manage the duplicate food in the same manner as the food consumed (i.e., if the lunch box was opened during the lunch break close to the field of application, the box with the duplicate sample was opened too. This procedure was followed for all the beverages and foods. An evaluation of any leftover food was performed, with the duplicate sample reduced in size as appropriate.

Details about where the food was purchased or sourced (shop, home garden, etc.) and the type of food (packed, fresh) were collected in order to enhance the interpretation of the results.

The duplicate food samples were collected at the end of each monitoring day, weighed, described in the most detailed way, if possible the ingredient were separated and put into the most suitable container size, usually 500g/ml. The samples were collected at the end of each monitoring day then stored in a freezer below -18˚C .The samples were comminuted in the presence of dry ice (Fussell et al 2007) or liquid nitrogen to minimise degradation of analytes and then transported in dry ice to the UK where they were analysed by Fera

2.2.2 Analytical technique

Sample extraction was carried out using QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) citrate buffered acetonitrile extraction in combination with dispersive solid phase extraction Payá et al 2007). Residues of the conazole pesticides present in sample extracts were quantified using Ultra High Performance Liquid Chromatography tandem quadrupole mass spectrometry (UHPLC-MS/MS). Quantification was made by the use of calibration standards prepared in matrix. Since different samples can produce different matrix effects each sample was analysed with and without spiking (single point standard addition at 1 µg/kg) to minimise the possibility of false negative results. Method performance was assessed by calculating the recovery of tebuconazole spiked into those samples that were shown not to contain detectable residues. The mean recovery and (%RSD) for different samples types were; 101 (9) for cereal samples (n=11), 101 (20) for vegetable samples (n=27), 90 (12) for liquids (n=20) and 83 (25) for other samples (n=25) including wine. The overall mean recovery for all samples (n=92) was 91 with an associated %RSD of 21 demonstrating that the analytical method was under control and fit for purpose around the 1 µg/kg concentration.

2.3 Availability of data from existing models

A range of models and databases were used to compare against the measured and predicted dietary and non-dietary exposures, in particular the EUROPOEM database (EUROPOEM, 1996, 2002) and German Model (Lundehn et al) for non-dietary exposure and MCRA (2013) for dietary exposure. The data from the field biomonitoring study can therefore be used to make the following comparisons for the dietary and non-dietary routes to validate the aggregate exposure model within Acropolis.

i) *Dietary exposure*
Actual food item consumption from individual food diaries vs Predicted food item consumption from Italian population survey data (MCRA)

ii) *Dermal exposure*
Individual ADE measured in the field study vs Predicted ADE from EUROPOEM and German operator exposure model at the population level

iii) *Absorbed dose*

- Measured absorbed dose vs predicted absorbed dose using duplicate diet and dermal exposure data (on the same individuals)
- Measured absorbed dose vs predicted absorbed dose using aggregate Acropolis model (on the same individuals)

3. Results

3.1 Operator exposure data from the biomonitoring field study

A summary of all the data from the operator exposure field study is presented in Table 1 to illustrate the relationship between measured ADE and absorbed dose. The ADE for the field study described by Fustinoni (in press) is summarised separately in Table 2 for all eight operators and for the six operators which only used tractor mounted application equipment. The data are expressed as a proportion of the amount handled in the same format as with current exposure models, namely the UK Predictive Operator Exposure Model (Martin 1986) and the German model (Lundehn et al 1992).

Table 1. Details from the 2011 field study for operator dermal exposure and absorbed dose equivalent of tebuconazole

Individual ID	Age	Body Weight (kg)	Duplicate Diet Day	PDE (µg a.s.)	ADE (µg a.s.)	TEB equivalents in 24h post-exposure urine sample (µg)	Quantity of a.s. used (g)	ADE mg a.s/kg a.s. used	Absorbed dose ug TEB/kgBW
S01	51	92	2	15913	3650	180.6	99.0	36.9	2.0
S01	51	92	3	22496	1296	299.2	67.5	19.2	3.3
S02	49	100	2	1877	251	28.2	198.0	1.3	0.3
S02B	50	100	2	5829	558	41.3	594.0	0.9	0.4
S03	52	93	2	8657	2970	79.7	594.0	5.0	0.9
S04	41	57	2	6582	428	8.8	148.5	2.9	0.2
S04	41	57	3	4570	390	29.9	148.5	2.6	0.5
S04	41	57	4	6637	1152	32.9	148.5	7.8	0.6
S05	40	90	3	12585	2331	155.0	1530.0	1.5	1.7
S05	40	90	ns	15014	1503	341.8	900.0	1.7	3.8

ns = not sampled. Note that this final value is excluded from some later comparisons, where duplicate diet data is required

There are 5 individual volunteers used in the study, some of which were used for 2 days to give a total of 9 replicate data sets for dermal exposure. However on one of the days there was no duplicate diet sampling, giving a total of 8 data sets with both dermal and dietary exposure data The ratio between ADE and PDE is interesting and provides some information relating to the protective factor of the cotton coveralls worn as external dosimeters. The ratio of ADE/PDE has an average of 0.147, with a range 0.058-0.343. This variation reinforces the usefulness of ADE data, rather than relying on PDE which is measured only on the outer clothing worn by the operator.

Table 2. Measured actual dermal exposure to tebuconazole for operators during vine spraying (ug a.s./kg a.s. applied)

	All operators	Only tractor mounted application technique
Mean	7.19	5.75
Median	2.48	1.92
75th percentile	5.57	3.96

The German Model predicts an ADE value of 1.51 ug a.s./kg a.s. applied assuming use of appropriate PPE for mixing and loading and application and 2.44 ug a.s./kg a.s. applied assuming no use of gloves during the application. The use scenario selected for the German Model was tractor mounted/trailed broadcast air assisted sprayer. The product selected was a WP (wettable powder) formulation containing 250 g/kg a.s. applied at a dose rate of 1 kg/ha to treat a total of 8 ha. The outputs from this model are 75th percentile values from the underlying database, which is not visible to the user.

Within the ACROPOLIS model a subset of data from the EUROPOEM database was selected relating to a study involving the application scenario most similar to that used in the field study, i.e. broadcast air assisted spraying of grape vines. The data for ADE from the EUROPOEM database have been used with data on PPP usage for grape vines in Italy collected in EFSA funded surveys (Glass et al 2012) to generate a distribution of exposures based on the areas treated on a daily basis. The use of such a distribution is demonstrated in case studies within ACROPOLIS (Kennedy et al 2014) to estimate ADE and absorbed dose of triazole PPPs, providing an example of non-dietary exposure within the aggregate model. Using exposure data from the EUROPOEM model represented as ug a.s./kg a.s. applied and survey data in the form of typical areas sprayed on a daily basis the following data were generated for exposure to tebuconazole, assuming a dose rate of 1 kg/ha.

Table 3. Predicted actual dermal exposure to tebuconazole for operators during vine spraying (ug a.s./kg a.s. applied) using EUROPOEM

Parameter	ADE ug a.s./kg a.s. applied
Mean	6.24
Median	5.38
P75	8.59

3.2 Data for dietary exposure

The collection of duplicate diet samples and a diary of food intake allow a comparison to be made of the tebuconazole intake on a daily basis for each of the volunteers. An example of the food diary information is shown in Table 4, which was used with MCRA to estimate the intake of tebuconazole for each of the coded food items

Table 4. Example of data information collected for the dietary diary of volunteer S01

Individual	Day Of Survey	Food item consumed	Amount Consumed (g)	FoodEx1 name
S01	1	100073	12.00	L4.Wheat flour, white
S01	1	100083	36.50	L3.Other bread
S01	1	100084	194.00	L4.Wheat bread, white

S01	1	100122	50.00	L3.Pasta, wheat flour, filled
S01	1	100124	100.00	L3.Pasta, wheat flour, without eggs
S01	1	100321	171.00	L3.Tomatoes (Lycopersicum esculentum)
S01	1	100332	5.30	L3.Garlic, bulb (Allium sativum)
S01	1	100362	2.00	L3.Salt
S01	1	100365	21.45	L3.Basil, herb (Ocimum basilicum)
S01	1	100476	70.00	L3.Beef liver
S01	1	100493	18.25	L3.Ham, pork
S01	1	100542	64.84	L4.Salsiccia
S01	1	100632	10.00	L3.Cheese, Parmigiano Reggiano
S01	1	100644	80.00	L3.Cheese, processed spreadable

Analysis of the duplicate diet samples provides data for measured intake of tebuconazole by the volunteers in the field study. A total of 25% of the 64 samples analysed resulted in values for tebuconazole below the limit of quantification (LOQ) which was 0.25ng/g, therefore the data have been collated in Table 4 using half the LOQ value to represent values <LOQ for individual sample types. Total residue values for the food consumed have also been shown assuming zero for samples <LOQ, and also an estimate of tebuconazole residues based on the diary information for the volunteers and residue data for Italy within MCRA.

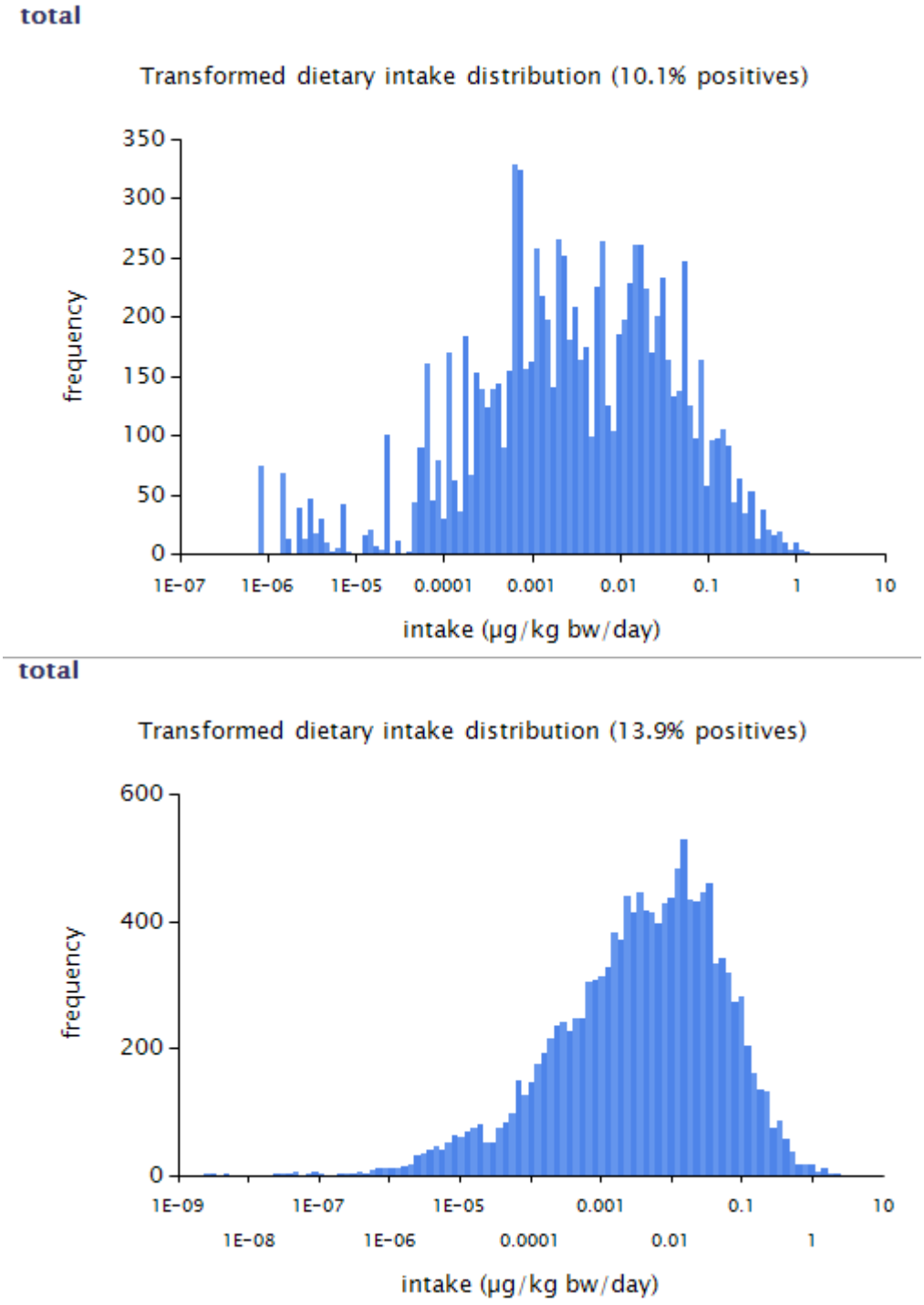
Table 5 .Values for measured residues of tebuconazole (ug/day) in duplicate diet samples and estimated values based on diet diary and MCRA. Lines in bold are those carried forward in subsequent comparisons of aggregate exposure

Sample ref	Cereals[1]	Vegetables[1]	Other[1]	Liquids[1]	Total[1]	Total[2]	MCRA Diary[3]
S1D1	0.095	0.009	0.031	0.063	0.198	0.127	0.222
S1D2	**0.159**	**0.055**	**0.083**	**0.063**	**0.359**	**0.297**	**0.159**
S1D3	**0.140**	**0.059**	**0.112**	**0.063**	**0.374**	**0.312**	**0.165**
S2B*D1	0.035	0.031	0.039	0.063	0.167	0.039	0.168
S2B*D2	**0.035**	**0.028**	**0.015**	**0.063**	**0.140**	**0.000**	**0.098**
S2D1	0.089	0.015	0.009	0.063	0.176	0.089	2.090
S2D2	**0.039**	**0.013**	**0.014**	**0.063**	**0.128**	**0.000**	**0.492**
S3D1	0.074	0.013	0.013	0.063	0.161	0.074	0.319
S3D2	**0.038**	**0.013**	**0.102**	**0.151**	**0.303**	**0.253**	**0.496**
S4D1	0.028	0.010	0.015	0.063	0.115	0.000	0.196
S4D2	**0.053**	**0.008**	**0.030**	**0.063**	**0.153**	**0.053**	**0.701**
S4D3	**0.047**	**0.015**	**0.016**	**0.063**	**0.141**	**0.047**	**0.219**
S4D4	**0.028**	**0.016**	**0.026**	**0.168**	**0.237**	**0.168**	**0.218**
S5D1	0.033	0.009	0.006	0.063	0.109	0.000	0.034
S5D2	0.048	0.021	0.013	0.063	0.143	0.000	0.216
S5D3	**0.033**	**0.018**	**0.005**	**0.063**	**0.118**	**0.000**	**0.174**

Key. [1] half LOQ value used for <LOQ, [2] zero value used for <LOQ samples, [3]Analysis using MCRA with individual diary-based consumption amount and corresponding average tebuconazole levels in Italian monitoring data 2007-10

Alternative estimates of the daily intake of tebuconazole have also been calculated within MCRA using the adult males for the general Italian population. The comparison shown in Figure 2 gives an indication of how representative the dietary intake of the volunteers in the study is.

Figure 2. Estimates of the distribution of tebuconazole for the 6 individuals in the field trial (top) and the whole Italian male population (bottom). Simulations were carried out in MCRA using randomly sampled residue concentrations from Italian monitoring data from 2007-2010.



3.3 Combination of measured dermal exposure, dietary intake and urinary metabolite data for tebuconazole

Combining the data for the dietary and non-dietary exposure routes provides an indication of the contribution of each of the routes, and how the measured "external" dose compared to the

measured internal dose from the biomonitoring study. The data for the urinary metabolites of tebuconazole are presented in Table 6 together with the data for estimated dietary intake based on measured residues of tebuconazole in the duplicate diet and non dietary exposure based on the measured ADE from the biomonitoring field study

Table 6. Summary of measured dietary and non-dietary (external) exposure for selected individual days of the biomonitoring study

Individual ID	Body Weight (kg)	Sampling Day	Dietary Intake (DD) µg/kgBW	Non dietary µg /kgBW	Urine TEBeq (µg)	**Urine µg/kgBW**	**Aggregate (µg/kgBW)**	Percentage non dietary
S01	92	2	0.00390	39.67	180.6	**1.963**	**39.68**	100.00%
S01	92	3	0.00407	14.09	299.2	**3.252**	**14.09**	99.99%
S02	100	2	0.00128	2.51	28.2	**0.282**	**2.51**	99.96%
S02B	100	2	0.00140	5.58	41.3	**0.413**	**5.58**	99.91%
S03	93	2	0.00326	31.94	79.7	**0.857**	**31.94**	99.98%
S04	57	2	0.00268	7.51	8.8	**0.154**	**7.52**	99.84%
S04	57	3	0.00247	6.84	29.9	**0.525**	**6.85**	99.94%
S04	57	4	0.00416	20.21	32.9	**0.577**	**20.21**	99.98%
S05	90	3	0.00131	25.90	155	**1.722**	**25.90**	99.99%

3.4 Outputs from the ACROPOLIS model.

The ACROPOLIS model combines dietary and non-dietary exposures using MCRA to estimate the daily intake of compounds of interest in the selected population, which in this case is the Italian male population. The non-dietary exposure is taken from the EUROPOEM database in this case to represent the exposure of operators applying PPPs to grape vine. The MCRA summary estimates of daily dietary intakes of tebuconazole are shown in Table 7.

Table 7. Output from MCRA for dietary intake of tebuconazole for Italian male population

	Compound name	Compound code	Contribution	Median (µg/kg bw/day)	Mean (µg/kg bw/day)	p25-p75 (µg/kg bw/day)
Total	Tebuconazole	RF-0403-001-PPP	97.50%	0.0403	0.335	(0 - 0.312)
Upper tail individuals > P97.5	Tebuconazole	RF-0403-001-PPP	95.10%	0.0702	2.24	(0 - 4.1)

The non-dietary data for exposure to tebuconazole are presented in EUROPOEM as µg a.s. /kg a.s. used which need to be converted into daily exposure values based on typical usage rates of tebuconazole in Italian grape vine. The non-dietary files generated as input to the ACROPOLIS model should use PPP usage data where available. In our case Italian data from the EFSA project (Glass et al. 2012) have been used. To illustrate the scale of dermal exposures, and as input for the MCRA aggregate model run for the general Italian operator population, 1000 simulations were generated by combining random draws with replacement from 31 sampled usage points (daily total kg a.s. applied) and 12 observed dermal (hand + body) concentration values from EUROPOEM. Details of this process are explained in Kennedy *et al* (in prep). In this, for the first set of summaries presented

in Table 8 the value for dermal absorption of 75% as proposed as a default in EFSA (2010) is used. These values appear to be above the measured values from the field study, indicating that the German model estimates with a less conservative 10% dermal absorption value are more appropriate.

Table 8. Estimated absorbed dose from actual dermal exposure to tebuconazole for Italian male operators during vine spraying (µg a.s./day) using EUROPOEM concentrations and typical usage amounts, for 75% and 10% dermal absorption values.

Parameter	Estimated absorbed dose µg a.s./day (75% dermal absorption)	Estimated absorbed dose µg a.s./day (10% dermal absorption)	Measured absorbed dose µg a.s./day (based on urinary analysis)
Mean	492	66	95
Median	223	30	41
P75	543	72	155

Considering the comparison of measured exposure with predicted exposure using the aggregate model there appears to be some agreement in the levels of exposure as shown in Table 9. The mean exposure from 9 individual-day measurements is 1.71 (± 1.31) µg tebuconazole/kg BW, and the mean aggregate model prediction is 1.76 (± 1.96) µg tebuconazole/kg BW. With such a small dataset the correlation was poor, although given the range and magnitude of uncertainties associated with the data and model outputs the agreement between predicted and measured exposure is encouraging.

Table 9. Summary of predicted and measured exposure to tebuconazole (ug a.s./kg BW)

Volunteer ID	Predicted aggregate ACROPOLIS model exposure (µg /kg BW)	Measured aggregate exposure (µg/kgBW)
S01	0.418	3.971
S01	0.286	1.413
S02	0.768	0.252
S02B	2.305	0.559
S03	2.478	3.197
S04	1.021	0.754
S04	1.013	0.687
S04	1.013	2.025
S05	6.584	2.591
Mean	1.765	1.717
SD	1.959	1.309

5. Discussion

A validation exercise has been described, involving the use of a biomonitoring field study to generate data for the absorbed dose of tebuconazole with volunteer pesticide operators in Italy. Sources of exposure during the monitoring period which included the pesticide handling tasks have been determined for the different routes. The models developed within Acropolis have also been used to estimate the exposure for dietary and non dietary exposure for a sample population representative of the volunteers in the study, which in this case is the Italian male population. In addition the

outputs available from the aggregate model have been compared to individual elements of the model and the measured values from the biomonitoring study. The approach described relates to aggregate exposure, defined as exposure to a single compound from multiple sources and routes. However this technique can be expanded to consider the aggregate and cumulative exposure to a range of compounds within a CAG, which would provide the risk assessor the complete exposure information. Such data for individual compounds and routes of exposure are required to enable appropriate action to be proposed by risk managers should there be exposures which are considered to have a potential human health impact.

The non-dietary exposure data use exposure estimates from the EUROPOEM database and typical usage rates of tebuconazole in Italian grape vine based on recent survey data to provide a distribution of exposures. In the initial data comparison the proposed EFSA default for dermal absorption of 75% was used. In the final comparison values of 10% for dermal absorption were used as this resulted in the measured values from the field study being closer to the German model estimates. In considering the dietary exposure measurements and predictions, there is some agreement between modelled and measured exposures. The final step of the validation exercise of the Acropolis model compares the measured exposure with predicted exposure using the aggregate mode. Chronic (daily average) or acute exposure (individual-days combined across all individuals) can be predicted by the Acropolis model, therefore in this validation exercise the acute daily exposures have been used for comparison. There does appear to be some agreement in the levels of exposure as shown in Table 9 with mean exposures of 1.71 (± 1.31) µg tebuconazole/kg BW for the measured exposure and 1.76 (± 1.96) µg tebuconazole/kg BW for the predicted exposure using the Acropolis model . The correlation between the two datasets was poor, as would be expected from using a small sample size with exposure data and scenarios known to have an inherent high variability. However, the level of agreement between measured and predicted exposure values is encouraging and should provide the basis for future work to be undertaken building upon this initial study.

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