

This is a repository copy of *Assessment of exposure of professional operators to pesticides*.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/124799/>

Version: Accepted Version

Article:

Wong, Hie Ling, Garthwaite, Dave, Ramwell, Carmel et al. (1 more author) (2018) Assessment of exposure of professional operators to pesticides. *Science of the Total Environment*. pp. 874-882. ISSN 0048-9697

<https://doi.org/10.1016/j.scitotenv.2017.11.127>

Reuse

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can't change the article in any way or use it commercially. More information and the full terms of the licence here: <https://creativecommons.org/licenses/>

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

Assessment of exposure of professional agricultural operators to pesticides

Hie Ling Wong^{a,c}, David G. Garthwaite^b, Carmel T. Ramwell^b, Colin D. Brown^a

^a Environment Department, University of York, York, YO10 5NG, United Kingdom

^b Fera Science Ltd (Fera), Sand Hutton, York, YO41 1LZ, United Kingdom

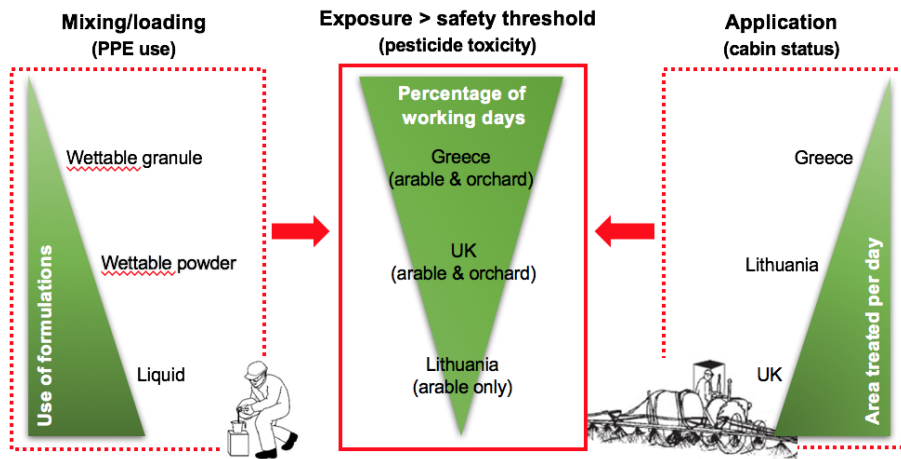
^c Faculty of Earth Science, University Malaysia Kelantan, Locked Bag 100, Jeli, 17600,
Kelantan, Malaysia

Corresponding author: Hie Ling Wong

e-mail: hw1166@york.ac.uk

telephone number: +44(0) 1904 322999

Graphical abstract



Highlights

- First use of comprehensive dataset for activities of professional pesticide operators
- Operator exposures compared for three countries and arable and orchard systems
- Small number of applications in all systems with estimated exposure > safety level
- Risks in Greece driven by use of wettable powder formulations
- Risks in the UK driven by large areas of land treated per day

Abstract

This study investigates how field practices in handling and applying pesticides influence the long-term patterns of professional agricultural operators' exposure to pesticides. It presents the first use of a comprehensive pesticide application dataset collected on behalf of the European Food Safety Authority with 50 operators selected to cover arable and orchard cropping systems in Greece, Lithuania and the UK. Exposure was predicted based on the harmonised Agricultural Operator Exposure Model (AOEM) and compared with Acceptable Operator Exposure Levels (AOELs). The amount of pesticides handled by individual operators across a cropping season was largest in the UK arable and orchard systems (median 580 and 437 kg active substance, respectively), intermediate for the arable systems in Greece and Lithuania (151 and 77 kg, respectively), and smallest in the Greek orchard system (22 kg). Overall, 30 of the 50 operators made at least one application within a day with predicted exposure greater than the AOEL. The rate of AOEL exceedance was greatest in the Greek cropping systems (8 orchard operators, 2.8-16% of total applications; 7 arable operators, 1.1-14% of total applications), and least for the Lithuanian arable system (2 operators, 2.9-4.5% of total applications). Instances in Greece when predicted exposure exceed the AOEL were strongly influenced by the widespread use of wettable powder formulations (>40% of the total pesticide active substance handled for 11 of the 20 Greek operators). In contrast, the total area of land treated with an active substance on a single day was more important in the UK and Lithuania (95th percentile observed value was 132 and 19 ha day⁻¹ for UK arable and orchard systems, respectively). Study findings can be used to evaluate current assumptions in regulatory exposure calculations and to identify situations with potential risk that require further analysis including measurements of exposure to validate model estimations.

Keywords: Plant protection product, mixing/loading, formulation, PPE, AOEM, operator exposure

1. Introduction

Pesticides are widely used in agriculture to increase crop productivity and quality in order to meet the increasing demand for food from the world's growing population. Off-target movement of pesticides, however, may pose a risk to human health and the environment due to the intrinsic toxicity of this class of chemicals. Three major categories of human exposure to pesticides are identified, namely occupational, environmental, and dietary exposures (Mehrpour et al., 2014). Occupational exposure to pesticides is of particular interest in epidemiology because the exposure could be at levels hundreds of times greater than that for the general population (Sacchetti et al., 2015), and because this may cause excess risk for some diseases (Brouwer et al., 2016). For example, an association between occupational exposure and cancer was first reported around 50 years ago with higher prevalence of lung and skin cancers among farmers who used insecticides in vineyards (Mostafalou and Abdollahi, 2013). A review on the consequences of occupational exposure to pesticides on the male reproductive system proposed that the majority of pesticides could affect the system by mechanisms including reduction of sperm counts and density, inhibition of spermatogenesis, sperm DNA damage, and increasing abnormal sperm morphology (Mehrpour et al., 2014). Agricultural operators are mainly exposed to pesticides during the preparation and application of the spray solution (Damalas and Abdollahzadeh, 2016). Due to spills and splashes, direct spray contact, or even drift, they are potentially exposed to pesticides via two routes of exposure, namely dermal absorption and respiratory inhalation (Gao et al., 2013; Moon et al., 2013; Ye et al., 2013; Damalas and Koutroubas, 2016). Whilst the dermal route is usually considered to constitute the major route of exposure to pesticides

for agricultural operators (Zhao et al., 2015; Atabila et al., 2017), the inhalation route should not be neglected because of the presence of airborne spray droplets or vapour resulting from the spray preparation; the application could be dangerous as the lungs can rapidly absorb the dissolved pesticides into the bloodstream (Ogg et al., 2012; Choi et al., 2013). Generally, the operator is expected to engage in both mixing/loading and application tasks, and exposures via the dermal and inhalation routes arising from these tasks are summed to give the total potential exposure (EFSA, 2014).

The exposure of agricultural operators to pesticides could be influenced by a range of factors including the properties of the compound, agricultural factors (e.g. crop height, application equipment and technique), environmental factors (e.g. wind velocity and direction, temperature and relative humidity), protection measures, working behaviour, experience, and training (Aprea, 2012; Gao et al., 2013; Tsakirakis et al., 2014; Zhao et al., 2016). Generally, the levels of exposure during typical activities are predicted rather than measured due to complexities in measuring dose via different routes and limitations in biological monitoring together with the very wide range in climatic and working conditions that need to be considered (Colosio et al., 2012). Conventionally, the potential risk from human exposure to pesticide is expressed with a risk quotient which is the ratio of predicted exposure to a toxicological reference value that combines the risk with the amount and conditions of pesticide use (Cunha et al., 2012). Several predictive models are available to estimate operator exposure to pesticides including the EUROpean Predictive Operator Exposure Model (EUROPOEM), the UK Predictive Operator Exposure Model (UK POEM), the German Operator Exposure Model (German model), and the Bystanders, Residents, Operators, and WorkerS Exposure models (BROWSE) (Lammoglia et al., 2017).

Operator exposure must be estimated in the risk assessment for pesticides in accordance with EU Regulation (EC) 1107/2009 (Thouvenin et al., 2016). The exposure is normally

estimated separately for mixing/loading and application tasks and for the recommended conditions of use (EFSA, 2014). Two operator exposure models were officially recommended by Regulation 1107/2009 for lower-tier risk assessment of agricultural operators to pesticides in the EU, namely the UK POEM (UK MAFF, 1992) and the German model (Lundehn et al., 1992) (NASDA, 2013). These are deterministic models derived from statistical analysis of data from exposure studies conducted before 1990. They have been superseded by the newly developed Agricultural Operator Exposure Model (AOEM; Großkopf et al., 2013a). The AOEM is the first harmonised European operator exposure model, relying on empirical data from 34 exposure studies (1994-2009) to reflect agricultural practices and scientific knowledge. Despite the large database used for model development, the AOEM has some data gaps including the lack of exposure data for knapsack mixing/loading and hand-held applications in low crops (Großkopf et al., 2013b).

European Union Directive 91/414/EEC concerning the placement of plant protection products on the market required that application of plant protection products following good practice should have no harmful effects on human health and no unacceptable influence on the environment. Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures ensures that the intrinsic toxicological potential of hazardous products is clearly communicated to users in the EU for the necessity of protection measures (Lichtenberg et al., 2015). In performing risk assessments of exposure to plant protection products in the EU, the zonal approach has been introduced by Regulation (EC) 1107/2009 for the evaluation and registration of plant protection products by taking into account national agronomics and regional differences (i.e. environmental conditions and application techniques) (Tsakirakis et al., 2014). The wide diversity of agriculture throughout the EU including farming practices

and farm size incurs some challenges for European policy-makers in making decisions (EPRS, 2016).

This study investigates how field practice in handling and applying pesticides influences exposure for professional agricultural operators. To do this we apply information from a European database of pesticide application practices where, for the first time, all pesticide handling activities across individual working days were quantified for a large number of individuals and over protracted periods of up to a full year (Garthwaite et al., 2015). We select individuals from different cropping systems and different regulatory zones (northern, central, southern) of the EU and applied the AOEM (Großkopf et al., 2013a) to assess levels of exposure for professional operators. We analyse results to determine differences in behaviours and patterns of exposure with cropping, region and working practices and compare exposures with Acceptable Operator Exposure Levels (AOELs) to investigate any implications for operator assessments within regulatory procedures.

2. Methodology

2.1. Pesticide application data

We used a dataset for pesticide application collected on behalf of the European Food Safety Authority (EFSA) in view of performing environmental risk assessments for pesticides in response to Regulation 1107/2009 (Garthwaite et al., 2015). The data were collected based on specifically designed survey forms in eight EU member states that together represent the three regulatory zones comprising Northern (Lithuania), Central (Belgium, Netherlands, Poland and United Kingdom) and Southern (Greece, Italy and Spain). Overall, the surveys collected information regarding >36,000 individual application events for operators on over 400 farms, with 645 sprayers used on nine different crops. A minimum of twenty fields were surveyed for each crop for between

two and five crops in each member state, with at least two member states collecting information on each crop (Garthwaite et al., 2015).

We assessed the long-term patterns of professional agricultural operators' exposure to pesticides handled for Lithuania, the UK, and Greece to represent the three regulatory zones. These three member states were also the only ones that met the data quality requirements of our study with respect to finalised quality checking and data entry (Garthwaite et al., 2015). The temporal unit of assessment was whole working days in 2012-2013; the periods of data collection were selected to quantify application practice across a cropping season, and up to one year where available (Garthwaite et al., 2015). Whilst the main thrust of the survey was to investigate the extent of a professional operator's exposure over a 12-month period, the period of data collection varied between cropping systems for various reasons; these included an unusually late spring and short growing season in Lithuania in 2013 and late contact with the operators in Greece whereby pesticide applications had already commenced (Garthwaite et al., 2015). Ten professional operators were chosen randomly whilst ensuring representation of different sizes of arable and orchard holdings in the UK (sum of area for all crops for arable system: 28-1040; orchard system: 16-121 ha) and Greece (arable system: 9-106 ha; orchard system: 1-9 ha) (Table S1). There are no data for orchards in Lithuania as no survey was carried out and this country was analysed for arable operators only (sum of area for all crops: 10-483 ha) (Table S1). The dataset for a single operator combined applications to all crops on the holding. The major crops were wheat, potatoes, and oilseed rape in Lithuania, citrus, grapes, and vegetables in Greece, and wheat, oilseed rape, sugar beet and apples in the UK (Garthwaite et al., 2015). Individual holdings comprised of different numbers of fields from 1 up to 70. The selected operators had spraying experience ranging from 3 to 54 years and differing levels of training in handling pesticides (Table S1). Overall, data were extracted for 50 randomly selected

operators; the information for each application event comprised pesticide active substance, total amount of active substance handled, date of application, application technique, pesticide formulation, content of active substance in pesticide product, area treated per application, and PPE used.

2.2. Agricultural Operator Exposure Model (AOEM)

We employed the AOEM to estimate the levels of exposure during mixing/loading and application tasks because it reflects the latest scientific knowledge and application practices in the EU (Großkopf et al., 2013a). The AOEM is developed to generate 75th- and 95th-percentile exposure based on the empirical data of 34 unpublished exposure studies that were conducted to Good Laboratory Practice standards between 1994 and 2009. In regulatory risk assessment, the 75th percentile is used for assessing longer-term operator exposure to pesticides to provide a realistic upper estimate of daily exposure that will be exceeded very rarely over the course of a spraying season (EFSA, 2010). The 95th percentile is designed to support acute risk assessment as methodologies develop (EFSA, 2014).

The AOEM is usually applied to single active substances whereas here we applied it to all applications across a season; hence, we adopted algorithms from the AOEM to estimate the median exposure for all pesticides handled during each working day and over periods up to one year. The algorithms (Table 1) describe the dependency of exposure on the amount of pesticides handled. One constraint in these empirical equations is that any exponent greater than 1 ($\alpha > 1$) may result in a superlinear dependency on the amount of active substance handled and needs to be forced to 1 (Großkopf et al., 2013a). Thus, we selected the algorithms with an exponent smaller than or equal to 1 where available ($\alpha \leq 1$) for four identified exposure situations, namely tank mixing/loading for vehicle-mounted/-trailed or hand-held spray equipment (tank

ML), low crop application using vehicle-mounted/-trailed boom sprayers (LCTM AP), high crop application using vehicle-mounted/-trailed broadcast air-assisted sprayers (HCTM), and high crop application using hand-held spray equipment directed upwards (HCHH AP). Each exposure calculation comprised total exposures via dermal and inhalation routes. Dermal exposure was further segregated into protected or total exposure via hands and body dependent on whether PPE was used or not (Table 1). Here, total exposure refers to that without PPE use and protected exposure includes any PPE use (e.g. gloves and coveralls). The equation to calculate exposure to the head has a different structure that incorporates various types of PPE that modify exposure to differing extents.

2.3. Exposure calculation

Total exposure of an operator to individual active substances handled across a whole working day ($\text{mg kg bw}^{-1} \text{d}^{-1}$) comprised of dermal (DE , $\text{mg kg bw}^{-1} \text{d}^{-1}$) and inhalation (IE , $\text{mg kg bw}^{-1} \text{d}^{-1}$) routes for both mixing/loading (ML) and application (AP) tasks:

$$\text{Exposure}_{ML} = \frac{((DE_{ML(H \text{ or } Hp)} + DE_{ML(B \text{ or } Bp)} + DE_{ML(C)}) \times DA_{ML}) + (IE_{ML} \times IA_{ML})}{BW \times UF} \quad \text{(Eqn. 1)}$$

$$\text{Exposure}_{AP} = \frac{((DE_{AP(H \text{ or } Hp)} + DE_{AP(B \text{ or } Bp)} + DE_{AP(C)}) \times DA_{AP}) + (IE_{AP} \times IA_{AP})}{BW \times UF} \quad \text{(Eqn. 2)}$$

$$\text{Total exposure} = \text{Exposure}_{ML} + \text{Exposure}_{AP} \quad \text{(Eqn. 3)}$$

where subscripts H and Hp are exposures via total hands and protected hands respectively, B and Bp are exposures via total body and protected body respectively, and C is exposure to the head. BW is the body weight of an operator (75 kg as a default), and UF is the unit conversion factor from μg to mg (1000). Dermal absorption (DA , %) defines absorption of pesticide via skin surfaces and is a function of the percentage of active substance(s) in the product (EFSA, 2012; So et al., 2014); DA_{ML} is assumed to be 25 and 75% for formulated products that contain proportions of active substances $>5\%$ and $\leq 5\%$, respectively; DA_{AP} is 75% with active substance $\leq 5\%$ in the spray solution;

and DA is 10% during both tasks for active substances with log octanol-water coefficient (P_{ow}) <-1 or >4 together with molecular weight greater than 500 g mol^{-1} . Inhalation absorption (IA , %) refers to the adjustment of inhalation uptake for the use of respirators based on protection factors reported by EFSA (2010); values are 10% for a power-assisted respirator, 25% for a valved filtering half mask, reusable half mask with filters, disposable filtering half mask, or full-face mask, and 100% for no respirator use for both IA_{ML} and IA_{AP} , separately. IA_{AP} is 100% for all LCTM and HCTM sprayers independent of the cabin status.

All handled pesticides were classified into three major formulation types to determine potential exposure during tank mixing/loading (Table 2), namely wettable powders which have relatively larger exposure, liquid formulations which have intermediate exposure, and wettable granules which have relatively smaller exposure (Großkopf et al., 2013b). Two formulation categories were removed from the analyses, namely rodenticide bait (ready for use) and others (unknown). All LCTM and HCTM applications were grouped into two classes for sprayers with the presence of a cabin (i.e. cab with no filter, cab with carbon filter and closed cab) and sprayers with no cabin (open and no cab). Exposure to pesticides during application in a cabin and/or with PPE use was calculated using the equation for protected exposure, and with no cabin and no PPE use was calculated based on the equation for total exposure.

Several assumptions were made during the study. We assumed that the listed PPE were worn continuously during the mixing/loading and/or application tasks because no data were collected for individual applications. For a number of holdings where there was no information collected on the use of PPE for an individual application method, we assumed that the operators used the same types of PPE as used for other application methods on the same holdings. Where the use of specific types of PPE were not listed in the survey, we assumed that the operators did not wear PPE during either

mixing/loading or application tasks. For a small number of applications in the UK where dates of application were not recorded, the summed exposure to the same active substance on the same working day could not be calculated and these remained as separate applications.

2.4. Comparison between predicted exposure and the respective AOELs

Exposure was combined for all applications of a single active substance on a single working day and this value was compared with the respective Acceptable Operator Exposure Level (AOEL, $\text{mg kg bw}^{-1} \text{d}^{-1}$) established during EU regulatory assessment. The AOEL is the maximum amount of an active substance to which an operator may be exposed internally without causing any adverse health effects (Marrs and Ballantyne, 2004). It is usually derived from the no observed adverse effect level based on the most relevant sub-acute or sub-chronic toxicity study divided by a safety factor (100) to account for differences in sensitivity between test animals and humans, and the variation in sensitivity between individuals (Matthews, 2002). We extracted the AOELs for a total of 180 substances from the EU Pesticides Database (2016), Pesticide Properties Database (PPDB, 2017), and Bio-Pesticides Database (BPDB, 2017). Three active substances where AOELs were not available were removed from the analyses, namely calcium and derivatives, sulphur, and paraffin oil.

3. Results

3.1. Pesticide application data

Table 3 summarises application data for the 50 professional operators from different cropping systems in Lithuania, the UK and Greece. The total number of active substances handled by the selected operators was larger in the arable system of the UK (24-66 compounds) and smaller for those in Lithuania (4-24 compounds). Operators in

the cropping systems of Greece and the orchard system of the UK generally handled around 20 different active substances over the cropping season. The total mass of pesticides handled over the survey period was largest in the UK arable (median: 580 kg a.s.) and orchard system (437 kg a.s.), intermediate for the arable systems in Greece (151 kg a.s.) and Lithuania (77 kg a.s.), and smallest in the Greek orchard system (22 kg a.s.).

Fig. 1 shows cumulative frequency distributions of the area treated with a single active substance on single working days. The percentage of days when at least one treatment occurred varied across the selected operators, with some operators in the Greek arable system and the UK orchard system applying pesticides on ca. 40% of all days covered by the survey period (Table S1); more commonly, operators carried out spraying on ca. 20% of days. EFSA (2014) proposed representative values of 50 and 10 ha for the area of arable and orchard crop, respectively, treated with an individual active substance in a single day using vehicle-mounted equipment (EFSA, 2014). Median values for area treated with an individual active substance in one day were below the EFSA values in all cropping systems. However, the EFSA values were exceeded at the 95th percentile in UK arable and orchard systems (132 and 19 ha day⁻¹, respectively) and in the Lithuanian arable system (103 ha day⁻¹) (Table 4). The absolute maximum area treated by a single operator on one day was 199 ha on one of the UK arable holdings, necessitating 11 separate mixing/loading procedures across the day.

3.2. Estimated total exposure for professional operators

Fig. 2 shows that the total exposure per working day for the selected operators estimated for the full study period varied across the different cropping systems. Here, the exposure is expressed for all days with applications to correct for differences in the cropping period with applications across different operators. Overall, the medians of total daily

exposure were largest in the Greek arable system (9.7×10^{-3} mg kg bw⁻¹ day⁻¹) and orchard system (7.7×10^{-3} mg kg bw⁻¹ day⁻¹), intermediate for the UK orchard system (6.9×10^{-3} mg kg bw⁻¹ day⁻¹) and arable system (1.8×10^{-3} mg kg bw⁻¹ day⁻¹), and smallest for the Lithuanian arable system (1.1×10^{-3} mg kg bw⁻¹ day⁻¹). For individual cropping systems, the variance around the mean daily exposure for the 10 operators was largest in the UK cropping systems (coefficients of variation 116% and 105% for arable and orchard systems, respectively), intermediate for the arable systems in Lithuania (93%) and Greece (73%), and smallest in the Greek orchard system (43%).

3.3. Comparison of levels of exposure with the respective AOEL

Fig. 3 categorises all applications made by each individual operator according to ratios between the predicted exposure and the respective AOEL for each active substance handled on a single working day. Here, the same substance applied several times on the same working day is considered as one application whereas the same active substance applied on successive days counts as two applications. Overall, Greek cropping systems had the largest number of applications with AOELs exceeded (estimated exposure: AOEL >1.0) and the Lithuanian arable system had the least. There were seven arable and eight orchard operators in the Greek cropping systems where at least one application exceeded the AOEL, four arable and nine orchard operators in the UK cropping systems, and two operators in the Lithuanian arable system. Table 5 shows that the percentage of applications with AOEL exceeded were larger in Greek cropping systems compared to the UK and Lithuania. Generally, most of the applications had exposure estimates that were at least a factor of 10 smaller than the respective AOELs.

4. Discussion

The structure of agriculture varies across the EU due to differences in topography, geology, climate, natural resources, infrastructure, and social customs. In this study, the

size of farm holding was largest in the UK (median areas of 165 and 38 ha for arable and orchard systems, respectively), intermediate for the Lithuanian arable system (44 ha), and smallest for Greece (arable 32 ha; orchard 3 ha) (Table S1). Individuals spent different amounts of time spraying crops with an absolute range across all holdings of 1 to 418 hours over the period investigated (Table S2). Cumulative time spent spraying was longest in the UK orchard system (median 306 hours; 95th percentile 412 hours) and arable system (median 75 hours; 95th percentile 308 hours). The total amount of active substance handled during each working day is the dominant input parameter for estimating operator exposure within the AOEM (Großkopf et al., 2013a).

Fig. 3 indicates the potential risk of exposure to pesticides handled amongst the selected professional operators with some applications generating predicted exposures where the AOEL was exceeded. Exposures during mixing/loading tasks were larger than those during application (Fig. S1), and varied by formulation type (Table 1) with wettable powder > liquid > wettable granule formulations. Moon et al. (2013) undertook a risk assessment of operator exposure to pesticides in apple orchards and proposed a greater dermal exposure during mixing/loading of wettable powders (0.003-0.007% of total prepared amount) when compared to liquid formulations (0.001-0.002%) due to direct contact with fine pesticide powders when tearing the pouch and pouring into the mixing tank. In comparison, wettable granules are formulated to be non-dusty and have relatively lower potential for exposure (Zhao et al., 2015). The exposure calculations for mixing/loading of wettable powders in AOEM rely on just two exposure studies for hand-held applications to citrus in Spain with similar application conditions and equipment (Großkopf et al., 2013b). Given the dominance of wettable powders in the exposure estimates, priority should be given to improving the statistical power of the AOEM model with more studies on the exposure to different formulations using tractor-mounted and hand-held equipment (Großkopf et al., 2013a).

A dramatic shift from wettable powder formulations to wettable granules was identified previously in a study on advances in agrochemical formulation (Mulqueen, 2003). Nevertheless, the current study indicates significant use of wettable powder pesticides in Greece, whilst liquid formulations were more commonly used in the UK and Lithuania, and there was relatively little use of wettable granules in any of the cropping systems. There is a range of potential factors that could influence the physical forms (solid/liquid) of a pesticide product including the application technique, customer acceptability and business need, and the regional market requirements (Mulqueen, 2003; Green and Beestman, 2007).

Generally, the predicted exposures for the HCTM applications in orchard systems were high compared to LCTM applications in arable systems. Whereas cabin status was identified previously as having no great impact on the operator's exposure to pesticides and was therefore excluded from the LCTM scenario of the AOEM, it was identified as an important influence in the HCTM scenario (Großkopf et al., 2013a). In the present study, we classified the HCTM sprayers into two major groups for sprayers with and without cabins. This classification contributes significantly to those exposures with AOELs exceeded amongst the orchard operators, particularly amongst the Greek operators where none of the HCTM sprayers in our sample set were fitted with cabins (Table S1). Eight out of ten cabins in both UK cropping systems and a smaller proportion in the Lithuanian and Greek arable systems were fitted with carbon filters (Table S1); this exposure reduction measure is not included into the AOEM so it is likely that exposure during application is overestimated for these operators.

Occupational exposure to pesticides is affected significantly by working practices relating to the use of PPE. Agricultural operators are protected by the requirements on PPE as proposed by regulations to reduce the exposure to levels deemed acceptable (Woodruff et al., 1994). The requirements are usually determined based on the intrinsic

toxicological properties and exposure profile of the products (e.g. formulation types and application scenarios) (Lichtenberg et al., 2015). Whilst the use of PPE is considered in the AOEM, there are some limitations in the exposure calculations due to the lack of data for inhalation routes both during mixing/loading and application tasks and for exposure to the head during application when protected by PPE (Großkopf et al., 2013a). Overall, the EFSA dataset indicates that the selected professional operators generally wore gloves and protective clothing during mixing/loading activities with less PPE used during applications (Table S3). During mixing/loading activities, there was slightly higher use of face shields for liquid pesticides and respirators for solid pesticides (i.e. wettable powders and wettable granules). For the application tasks, there was less implementation of PPE in the UK and Lithuania due to the presence of cabins as compared to Greece where open tractors are more common (Table S1). Lichtenberg et al. (2015) proposed that the use of respirators for inhalable droplets during mixing/loading of liquid pesticides is less relevant compared to use for powder/dust pesticides and that the assigned PPE can be omitted when spraying occurs from a closed cabin. In practice, the use of PPE could be affected by other factors including personal preference, availability in the workplace, toxicity of pesticide, and thermal comfort (MacFarlane et al., 2013).

In the regulatory risk assessment, predicted total absorbed doses (sum of skin and respiratory absorbed doses) of agricultural operators to pesticides should not be greater than the AOEL for an individual active substance or combination of active substances formulated into a single product. EFSA (2014) proposed default assumptions that the total area treated with each substance per day using vehicle-mounted equipment be taken as 50 and 10 ha for arable and orchard crops, respectively. However, these values were exceeded relatively frequently for at least one compound per working day for some operators from the UK and Lithuanian cropping systems (Fig. 1). It is known that the

area treated is influenced by the type of equipment used (for example, newer sprayers may allow spraying with a stable boom at faster ground speeds) and EFSA (2014) states that values were derived based on “relatively simple and older models”. Equipment used by the operators ranged from 1 to 43 years old, but nearly 50% of operators from the orchard systems used equipment that was at least 20 years old (Table S4). The representative values for area treated from EFSA guidance are intended to be towards the upper end of the range in values occurring in the field and not the absolute maxima. Nevertheless, the analysis presented here suggests a need to review how representative these values are for spraying practice across the whole of the EU.

According to Regulation (EC) No 1107/2009, the AOEL is used as a limit in the authorisation process of the use of any active substances, and further work or ultimately no authorisation is triggered if the exposure estimate exceeds the AOEL (Aprea et al., 2016; Thouvenin et al., 2016). The AOEL is generally derived from the most sensitive no observed adverse effect level for relevant endpoints based on an oral short-term toxicity study as a default procedure (i.e. 90-day study or occasionally 1-year study) (European Commission, 2006). In practice, an agricultural operator’s exposure to pesticides occurs mainly through the dermal route, and to a lesser extent through the inhalation route (CTGB, 2016). Route-to-route extrapolation is only appropriate if the type and extent of effects of a substance are independent of the route of exposure (European Commission, 2006). We did not adjust the AOEL for route of exposure, so uncertainties are introduced because of the lack of information on any association between adverse effect and route of exposure, as well as by the repeated dose that is used in most toxicity studies to determine the no observed adverse effect level.

Our study indicates that a few relatively hazardous substances contributed significantly to the working days with estimated exposures greater than the AOELs (Table S3); these included diquat, glufosinate-ammonium, prosulfocarb, chlorothalonil, and chlorpyrifos,

all of which have AOEL $<0.1 \text{ mg kg bw}^{-1} \text{ d}^{-1}$. Chlorpyrifos made a significant contribution to those exposures where AOELs were exceeded in the UK orchard system, but all uses in the UK were withdrawn with effect from April 2016 except use as a drench for brassica seedlings. Besides this restriction on use of chlorpyrifos, several other active substances have been restricted or removed from the market in one or more of the member states since the period of data collection including amitrole, carbendazim, flusilazole, ioxynil, and tepraloxydim. However, only amitrole was associated with a single exceedance of the AOEL in the UK orchard cropping system (Table S3).

Limitations within the current study include the reliance on the assumptions and underpinning data embedded into the AOEM and the derivation of regulatory AOEL values. A particular constraint within the AOEM is the relatively simple treatment of protection factors to incorporate efficiency of personal protective equipment and the influence of cabin design on exposure under different field conditions. There is a clear need for validation of exposure predictions against field measurements and biological monitoring, and this should include generation of data for modern spray machinery and in a range of countries with different cropping, environmental and cultural conditions. Three active substances where AOELs were not available were removed from the analyses, namely calcium and derivatives, sulphur, and paraffin oil. The data collection was designed to make broad comparisons across cropping systems and countries and did not allow direct comparison of individual crop types because a particular crop may only have been grown on a small number of holdings. A direct comparison of pesticide usage and application practice between individual crops would be useful to add into any future study.

5. Conclusion

This study allows an evaluation of the European regulatory exposure assessment against a high-quality dataset on operator practices across three member states and two cropping systems. The dominant influences on estimated exposure were the extensive use of wettable powder formulations in Greece and multiple mixing and loading activities associated with large areas of crop treated with a pesticide product each day in the UK and Lithuania. The model predicted clear differences in exposure across the different systems, driven by variations in agricultural practices and working behaviours, and there were some applications that generated predicted daily exposures that exceeded the AOEL, particularly for more hazardous active substances. Study results can be used to evaluate current assumptions in regulatory exposure calculations and to identify situations with potential risk that require further analysis including measurements of exposure to validate model estimations.

Acknowledgements The authors gratefully acknowledge sponsorship of this research by the Ministry of Education, Malaysia and the University Malaysia Kelantan (UMK).

References

- Apra, M.C., 2012. Environmental and biological monitoring in the estimation of absorbed doses of pesticides. *Toxicology Letters* 210, 110-118.
- Apra, M.C., Bosi, A., Manara, M., et al., 2016. Assessment of exposure to pesticides during mixing/loading and spraying of tomatoes in the open field. *Journal of Occupational and Environmental Hygiene* 13, 476-489.
- Atabila, A., Phung, D.T., Hogarh, J.N., et al., 2017. Dermal exposure of applicators to chlorpyrifos on rice farms in Ghana. *Chemosphere* 178, 350-358.

- BPDB, 2017. The Bio-Pesticide Database developed by the Agriculture & Environment Research Unit (AERY), University of Hertfordshire. <http://sitem.herts.ac.uk/aeru/bpdb/atoz.htm> (Last accessed: February 2017).
- Brouwer, M., Schinasi, L., Freeman, L.E.B., et al., 2016. Assessment of occupational exposure to pesticides in a pooled analysis of agricultural cohorts within the AGRICOH consortium. *Occup. Environ. Med.* 73, 359-367.
- Colosio, C., Rubino, F.M., Alegakis. A., et al., 2012. Integration of biological monitoring, environmental monitoring and computational modelling into the interpretation of pesticide exposure data: introduction to a proposed approach. *Toxicology Letters* 213, 49-56.
- CTGB, 2016. Board for the authorisation of plant protection products and biocides: Evaluation for the authorisation of plant protection products and biocides according to Regulation (EC) No 1107/2009. Chapter 4 Human toxicology; mammalian toxicity dossier version 2.1. <http://ctgb.nl/docs/default-source/gewas.-toetsingskader/evaluation-manual-v2.1/eu-part-v2.1/g-4-human-toxicology-dossier-eu-eu-2-1-alg.pdf?sfvrsn=2> (Last accessed: April 2017).
- Cunha, J.P., Chueca, P., Garcera, C., Molto E., 2012. Risk assessment of pesticide spray drift from citrus applications with air-blast sprayers in Spain. *Crop Protection* 42, 116-123.
- Choi, H., Moon, J.K., Kim J.H., 2013. Assessment of the exposure of workers to the insecticide imidacloprid during application on various field crops by a hand-held power sprayer. *Journal of Agricultural and Food Chemistry* 61, 10642-10648.
- Damalas, C.A., Abdollahzadeh, G., 2016. Farmers' use of personal protective equipment during handling of plant protection products: determinants of implementation. *Science of the Total Environment* 571, 730-736.

- Damalas, C.A., Koutroubas, S.D., 2016. Farmers' exposure to pesticides: toxicity types and ways of prevention. *Toxics* 4, 1-10.
- EFSA, 2010. Scientific opinion on preparation of guidance document on pesticide exposure assessment for workers, operators, bystanders and residents. *EFSA Journal* 8(2):1501.
- EFSA, 2012. Guidance on dermal absorption EFSA panel on plant protection products and their residues (PPR). *EFSA Journal* 10(4): 2665.
- EFSA, 2014. EFSA guidance on the assessment of exposure for operators, workers, residents and bystanders in risk assessment for plant protection product. *EFSA Journal* 12(10):3874.
- EPRS, 2016. European Parliamentary Research Service: Precision agriculture and the future of farming in Europe. Scientific Foresight Unit, European Parliament. doi:10.2861/020809.
- EU Pesticide Database, 2016. European Commission – Plants. <http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN> (Last accessed: April 2017).
- European Commission, 2006. Draft: guidance for the setting and application of acceptable operator exposure levels (AOELs). Commission Working Document SANCO 7531 rev.10.
- Gao, B.B., Tao, C.J., Ye, J.M., et al., 2013. Measurement of operator exposure to chlorpyrifos. *Pest Manag. Sci.* 70, 636-641.
- Garthwaite, D., Sinclair, C., Glass, R., et al., 2015. External scientific report: collection of pesticide application data in view of performing Environmental Risk Assessments for pesticides. EFSA supporting publication 2015:EN-846.

- Green, J.M., Beestman, G.B., 2007. Recently patented and commercialised formulation and adjuvant technology. *Crop Protection* 26, 320-327.
- Großkopf, C., Martin, S., Mielke, H., et al., 2013a. Joint development of a new agricultural operator exposure model. BfR Wissenschaft, Germany.
- Großkopf, C., Mielke, H., Westphal, D., et al., 2013b. A new model for the prediction of agricultural operator exposure during professional application of plant protection products in outdoor crops. *Journal of Consumer Protection and Food Safety* 8, 143-153.
- Lammoglia, S.K., Kennedy, M.C., Barriuso, E., et al., 2017. Assessing human health risks from pesticide use in conventional and innovative cropping systems with the BROWSE model. *Environment International* 105, 66-78.
- Lichtenberg, B., Mischke, U., Scherf, S., Rover, M., Martin, S., 2015. Hazard and risk based allocation of safety instructions to operators handling pesticides. *Journal of Consumer Protection and Food Safety* 10, 373-384.
- Lundehn, J.R., Westphal, D., Kieczka, H., et al., 1992. Uniform principles for safeguarding the health of applicators of plant protection products. *Mitteilungen aus der Biologischen Bundesanstalt für Land und Forstwirtschaft, Heft 277*, Berlin, Germany.
- MacFarlane, E., Carey, R., Keegel, T., et al., 2013. Dermal exposure associated with occupational end use of pesticides and the role of protective measures. *Safety and Health at Work* 4, 136-141.
- Matthews, G., 2002. Operator exposure to pesticides. *Pesticide Outlook* 2002. doi:10.1039/b211168n.
- Marrs, T.C., Ballantyne, B., 2004. *Pesticide toxicology and international regulation*. John Wiley & Sons Ltd, West Sussex.

- Mehrpour, O., Karrari, P., Zamani, N., Tsatsakis, A.M., Abdollahi, M., 2014. Occupational exposure to pesticides and consequences on male semen and fertility: a review. *Toxicology Letters* 230, 146-156.
- Moon, J.K., Park, S., Kim, E., Lee, H., Kim, J.H., 2013. Risk assessment of the exposure of insecticide operators to fenvalerate during treatment in apple orchards. *J. Agric. Food Chem.* 61, 307-311.
- Mostafalou, S., Abdollahi, M., 2013. Pesticides and human chronic diseases: evidences, mechanisms, and perspectives. *Toxicology and Applied Pharmacology* 268, 157-177.
- Mulqueen, P., 2003. Recent advances in agrochemical formulation. *Advances in Colloid and Interface Science* 106, 83-107.
- NASDA, 2013. National Association of the State Departments of Agriculture Research Foundation: personal protective equipment for agricultural pesticide operators: policies, process, and standards/certifications required in the United States, European Union, and Brazil. <http://www.nasda.org/File.aspx?id=19751> (Last accessed: February 2017).
- Ogg, C.L., Hygnstrom, J.R., Bauer, E.C., Hansen, P.J., 2012. Managing the risk of pesticide poisoning and understanding the signs and symptoms. Institute of Agriculture and Natural Resources, University of Nebraska-Lincoln Extension.
- PPDB, 2017. The Pesticide Properties Database (PPDB) developed by the Agriculture & Environment Research Unit (AERY), University of Hertfordshire. <http://sitem.herts.ac.uk/aeru/ppdb/en/atoz.htm> (Last accessed: May 2017).
- Sacchetti, G., Calliera, M., Marchis, A., et al., 2015. New risk indicator approach for operators, workers, bystanders and residents for a sustainable use of plant production products. *Environ. Sci. Pollut. Res.* 22, 17586-17595.

- So, J., Ahn, J., Lee, T.H., et al., 2014. Comparison of international guidelines of dermal absorption tests used in pesticides exposure assessment for operators. *Toxicological Research* 30, 251-260.
- Thouvenin, I., Bouneb, F., Mercier, T., 2016. Operator dermal exposure and individual protection provided by personal protective equipment during application using a backpack sprayer in vineyards. *J. Verbr. Lebensm.* 11, 325-336.
- Tsakirakis, A.N., Kasiotis, K.M., Charistou, A.N., et al., 2014. Dermal & inhalation exposure of operators during fungicide application in vineyards. Evaluation of overall performance. *Science of the Total Environment* 470-471, 282-289.
- UK MAFF, 1992. Scientific Subcommittee on Pesticides and British Agrochemicals Joint Medical Panel: estimation of exposure and absorption of pesticides by spray operators (UK MAFF) 1986 and the Predictive Operator Exposure Model (POEM-UK MAFF).
- Woodruff, T.J., Kyle, A.D., Bois, F.Y., 1994. Evaluating health risks from occupational exposure to pesticides and the regulatory response. *Environmental Health Perspectives* 102, 1088-1096.
- Ye, M., Beach, J., Martin, J.W., Senthilselvan, A., 2013. Review: occupational pesticide exposures and respiratory health. *Int. J. Environ. Res. Public Health* 10, 6442-6471.
- Zhao, M.A., Yu, A., Zhu, Y.Z., Kim, J.H., 2015. Potential dermal exposure to flonicamid and risk assessment of applicators during treatment in apple orchards. *Journal of Occupational and Environmental Hygiene* 12:D147-D152.
- Zhao, M.A., Yu, A., Zhu, Y.Z., Wu, S.Q., Kim, J.H., 2016. Human exposure and risk assessment of chromafenozide during treatment in rice fields. *Human and Ecological Risk Assessment* 22, 116-125.

Table 1 Equations to predict median exposure to pesticides on a daily basis; the total amount of active substance (TA) is the major parameter for exposure, the slope α was set to 1 in case $\alpha > 1$; exposure is given in $\mu\text{g}/\text{person}$ (Großkopf et al., 2013a).

Tank ML	$\log \text{exposure} = \alpha \cdot \log TA + [\text{formulation type}] + \text{constant}$
Total hands	$\log DE_{ML(H)} = 0.71$ $\cdot \log TA + 0.57 [\text{liquid}] + 1.55 [\text{WP}] - 0.34 [\text{glove wash}] + 2.73$
Protected hands	$\log DE_{ML(Hp)} = 0.39 \cdot \log TA + 0.17 [\text{liquid}] + 1.74 [\text{WP}] + 1.02$
Total body	$\log DE_{ML(B)} = 0.71 \cdot \log TA + 0.24 [\text{liquid}] + 1.69 [\text{WP}] + 2.87$
Protected body	$\log DE_{ML(Bp)} = 0.95 \cdot \log TA - 0.05 [\text{liquid}] + 1.99 [\text{WP}] + 0.87$
Head	$\log DE_{ML(C)} = \log TA + 0.55 [\text{liquid}] + 1.31 [\text{WP}] + 1.52 [\text{no face shield}] - 1.07$
Inhalation	$\log IE_{ML} = 0.53 \cdot \log TA - 0.73 [\text{liquid}] + 2.26 [\text{WP}] + 0.61$
LCTM AP¹⁾	$\log \text{exposure} = \alpha \cdot \log TA + [\text{droplet}] + [\text{equipment}] + \text{constant}$
Total hands	$\log DE_{AP(H)} = \log TA + 1.43 [\text{normal droplet}] - 1.41 [\text{normal equipment}] + 1.30$
Protected hands	$\log DE_{AP(Hp)} = \log TA + 1.46 [\text{normal droplet}] - 0.61 [\text{normal equipment}] - 0.67$
Total body	$\log DE_{AP(B)} = \log TA + 0.56 [\text{normal droplet}] - 1.62 [\text{normal equipment}] + 2.52$
Protected body	$\log DE_{AP(Bp)} = \log TA + 0.34 [\text{normal droplet}] - 0.94 [\text{normal equipment}] + 0.49$
Head	$\log DE_{AP(C)} = \log TA + 0.32 [\text{normal droplet}] - 0.22 [\text{normal equipment}] - 0.22$
Inhalation	$\log IE_{AP} = 0.46 \cdot \log TA + 0.13 [\text{normal droplet}] + 0.65 [\text{normal equipment}] - 0.89$
HCTM AP	$\log \text{exposure} = \alpha \cdot \log TA + [\text{cabin}] + \text{constant}$
Total hands	$\log DE_{AP(H)} = 0.49 \cdot \log TA + 0.89 [\text{no cabin}] + 2.29$
Protected hands	$\log DE_{AP(Hp)} = 0.88 \cdot \log TA + 1.18^3)$
Total body	$\log DE_{AP(B)} = \log TA + 0.86 [\text{no cabin}] + 2.86$
Protected body	$\log DE_{AP(Bp)} = \log TA + 0.50 [\text{no cabin}] + 1.30$
Head	$\log DE_{AP(C)} = \log TA + 1.46 [\text{no cabin}] + 0.82$
Inhalation	$\log IE_{AP} = 0.63 \cdot \log TA + 1.00 [\text{no cabin}] + 0.51$
HCHH AP²⁾	$\log \text{exposure} = \alpha \cdot \log TA + [\text{culture}] + \text{constant}$
Total hands	$\log DE_{AP(H)} = \log TA - 0.94 [\text{normal culture}] + 4.02$
Protected hands	$\log DE_{AP(Hp)} = \log TA - 1.26 [\text{normal culture}] + 1.90$
Total body	$\log DE_{AP(B)} = 0.32 \cdot \log TA - 1.50 [\text{normal culture}] + 5.75$
Protected	$\log DE_{AP(Bp)} = \log TA - 1.48 [\text{normal culture}] + 3.72$

body

Head $\log DE_{AP(C)} = 0.34 \cdot \log TA - 1.18 [normal\ culture] + 2.87$

Inhalation $\log IE_{AP} = 0.74 \cdot \log TA - 0.57 [normal\ culture] + 2.13$

¹⁾ For LCTM AP, the droplet sizes are grouped into 'normal' and 'coarse' subsets with the latter size being chosen when drift reducing nozzles are used; the 'normal' and 'small' equipment subsets are used with the small equipment for treatment in small areas/high crops.

²⁾ For HCHH AP, the 'normal' and 'dense' culture subsets with the dense culture refers to unavoidable direct contact with sprayed crop during applications.

³⁾ The dependency of the factor [cabin] was not significant.

AP, application; ML, mixing/loading; DE, dermal exposure; IE, inhalation exposure; H, total hands; Hp: protected hands; B, total body; Bp, protected body; C, head; WP, wetttable powder formulation

Table 2 Classification of pesticide formulations into wettable powder, liquid and wettable granule groups included in the AOEM model.

Wettable Powder	Liquid	Wettable Granule
dustable powder (DP), wettable powder (WP), water-soluble powder (SP)	capsule suspension (CS), emulsifiable concentrate (EC), emulsion-oil in water (EW), microemulsion (ME), oil dispersion (OD), oil miscible flowable (OF), oil miscible liquid (OL), soluble concentrate (SL), suspension concentrate (SC), suspo-emulsion (SE)	Granule (GR), tablet (TB), water dispersible (WG), water soluble granules (SG)

Table 3 Summary of application data for 50 selected professional operators showing the total number and total mass of active substances handled during the survey period.

Holding code	LTAB	UKAB	GRAB	UKOR	GROR
Total number of active substances handled					
01	15	33	19	6	20
02	7	29	20	30	3
03	24	34	20	23	33
04	7	24	13	17	16
05	15	27	17	23	32
06	18	48	13	25	14
07	9	49	21	41	23
08	7	55	19	18	15
09	4	30	8	12	19
10	18	66	12	26	14
Median	12	34	18	23	18
Total mass of active substances handled					
01	166.0	103.5	268.5	131.4	21.1
02	27.8	184.3	191.4	275.6	1.9
03	808.7	926.1	122.6	557.4	69.8
04	7.3	64.1	11.6	452.0	16.9
05	431.6	249.2	148.2	422.2	68.9
06	410.2	911.6	153.1	876.7	17.6
07	53.1	3128.8	423.7	1051.5	35.3
08	18.1	2547.4	188.2	819.7	21.8
09	3.2	93.8	67.4	331.0	10.4
10	99.9	2088.8	38.8	380.2	25.3
Median	76.5	580.4	150.7	437.1	21.5

Table 4 Comparison between areas treated with individual active substances on a single spray day expressed as 50th, 75th and 95th percentiles, and the EFSA default values (EFSA, 2014).

Cropping system	Area treated per active substance per day (ha)					EFSA value ¹⁾
	Summary of database information (percentile)					
	25 th	50 th	75 th	95 th	Maximum	
Lithuania arable	7.8	29.8	47.0	102.9	129.6	50.0
UK arable	14.5	26.2	58.6	132.2	198.7	50.0
Greek arable	2.8	5.0	9.3	19.6	30.7	50.0
UK orchard	4.0	6.9	10.1	18.5	42.8	10.0
Greek orchard	1.5	2.7	3.2	5.0	5.0	10.0

¹⁾ For vehicle-mounted equipment

Table 5 Summary of instances in the different cropping systems when predicted exposure exceeded the AOEL.

Cropping system	No. of operators with any instance of exposure > AOEL	Applications with AOEL exceeded (% of total number of applications)
Lithuania arable	2	2.9-4.5
UK arable	4	1.1-5.6
Greece arable	7	1.1-14.3
UK orchard	9	0.8-6.5
Greece orchard	8	2.8-16.0

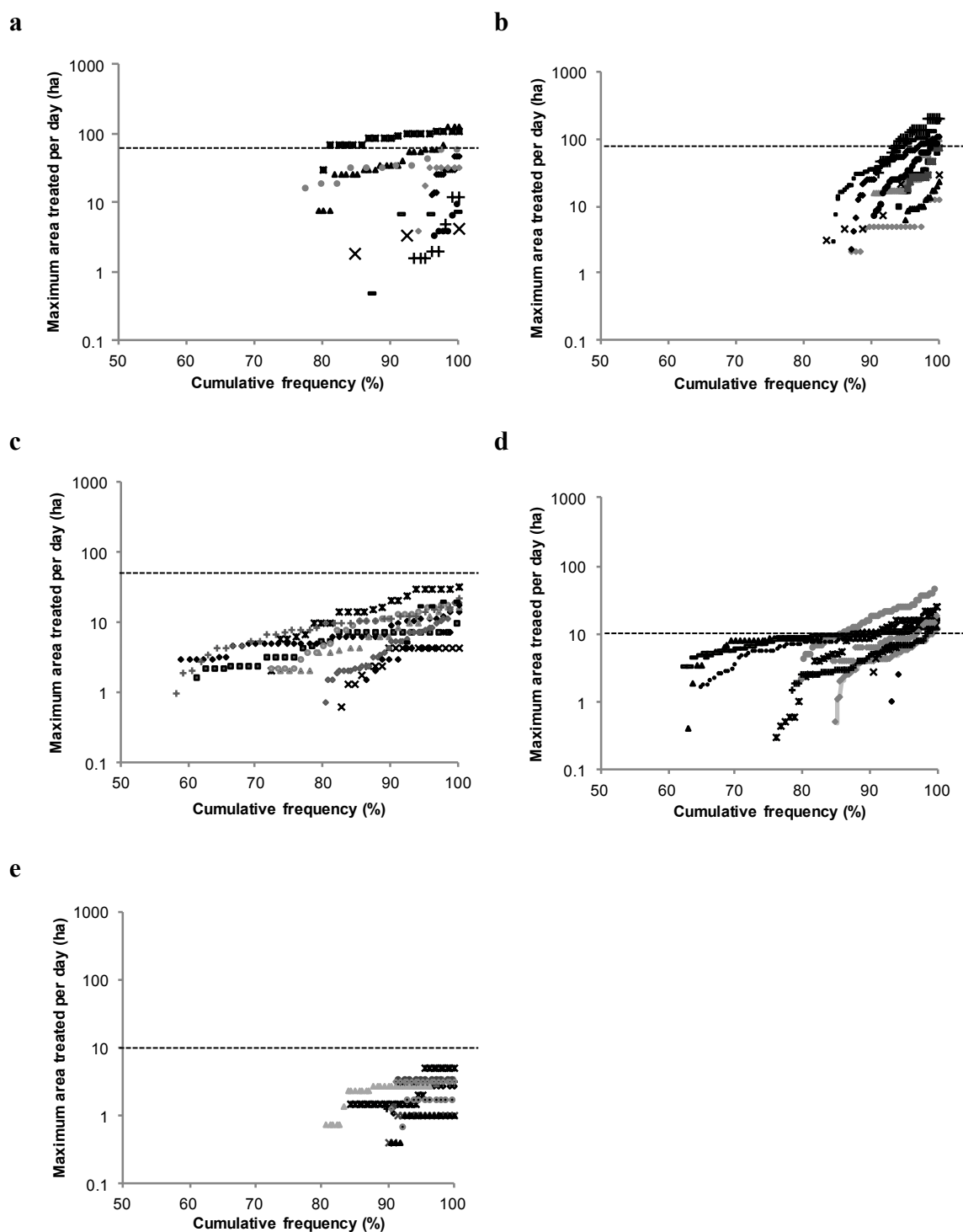


Fig. 1. Cumulative frequency distributions of maximum areas treated with a single active substance on a single working day for arable operators in Lithuania (a), the UK (b) and Greece (c), and orchard operators in the UK (d) and Greece (e). The EFSA default values for total area treated per day with individual substances (50 and 10 ha day^{-1} in arable and orchard systems, respectively) is indicated by the dashed lines. Different symbols represent individual operators and each value shown is one substance applied on a single working day.

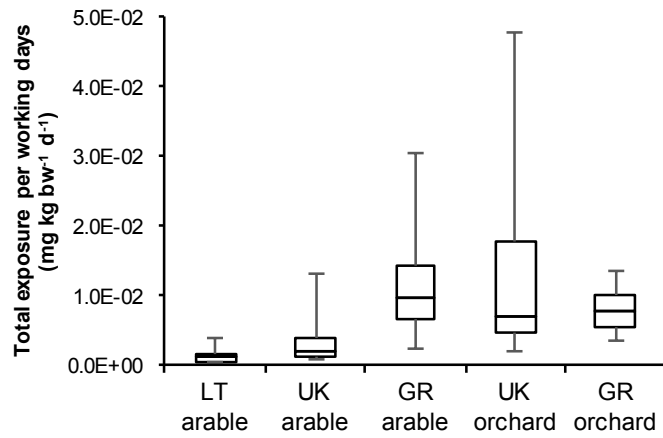


Fig. 2. Estimated exposures for 10 randomly selected professional operators from the cropping systems in Lithuania, the UK and Greece. Values are calculated for individual operators based on the respective total number of working days. Boxes show the median and quartiles, and whiskers show the range.

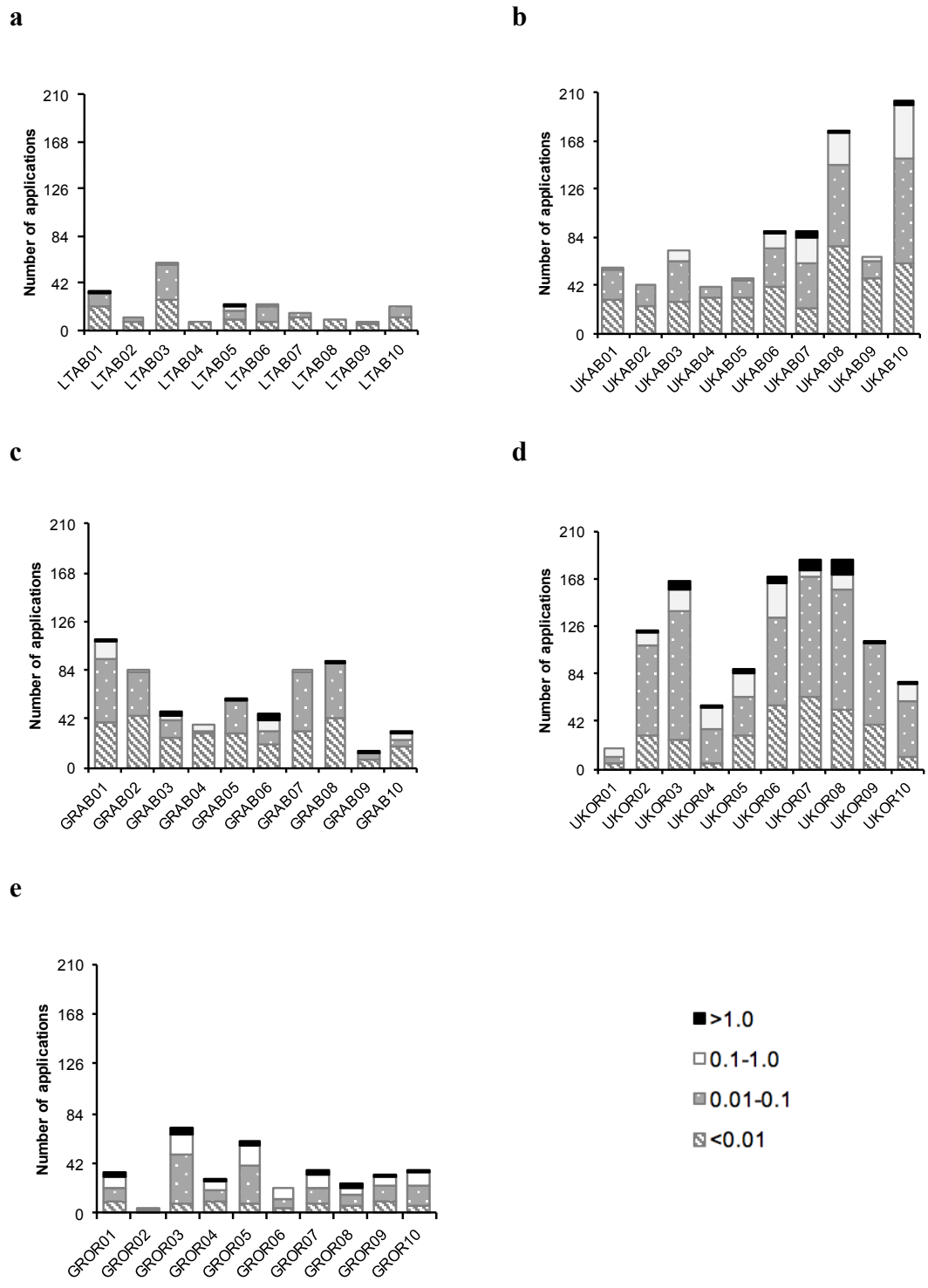


Fig. 3. Bar charts showing the total number of applications made by a single operator (each bar is one operator) and how these applications classify into instances where predicted exposure:AOEL was >1.0, 0.1-1.0, 0.01-0.1, or <0.01. Separate charts show the data for the arable systems of Lithuania (a), the UK (b), Greece (c), and the orchard systems of the UK (d) and Greece (e). Each individual application refers to one active substance applied on a single working day.