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# Comparison of residents' pesticide exposure with predictions obtained using the UK regulatory exposure assessment approach

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ABSTRACT

The UK regulatory methods currently used for estimating residents' potential pesticide exposure were assessed to determine whether they provide sufficiently conservative estimates. A non-random sample of 149 residents living within 100 m of fields where pesticides were sprayed provided first morning void urine samples one and/or two days after spraying. Using farmers' spray information, regulatory exposure assessment (REA) models were applied to estimate potential pesticide intake among residents, with a toxicokinetic (TK) model used to estimate urinary biomarker concentrations in the mornings of the two days following the spray. These were compared with actual measured urinary biomarker concentrations obtained following the spray applications. The study focused on five pesticides (cypermethrin, penconazole, captan, chlorpyrifos and chlormequat). All measured cypermethrin urinary biomarker levels were lower than the REA-predicted concentrations. Over 98% and 97% of the measured urinary biomarker concentrations for penconazole and captan respectively were lower than the REA-predicted exposures. Although a number of the chlorpyrifos and chlormequat spray-related urinary biomarker concentrations were greater than the predictions, investigation of the background urinary biomarker concentrations suggests these were not significantly different from the levels expected had no pesticide spraying occurred. The majority of measured concentrations being well below the REA-predicted concentrations indicate that, in these cases, the REA is sufficiently conservative.



## 1. Introduction

Government Ministers must approve all pesticides, including those used in agriculture, horticulture, forestry, food storage and the home or garden, before they can be marketed or used in Great Britain. The regulatory health risk assessment underpinning the approval of pesticides involves the comparison of estimates of potential human exposure with toxicological reference levels; for example, Acceptable Operator Exposure Level (AOEL) or Acceptable Daily Intake (ADI), below which there is considered to be high confidence that there will be no adverse health effects.

The Chemicals Regulation Directorate (CRD) of the British Health and Safety Executive (HSE) acts as the Regulator for pesticide products and authorises their sale, supply, use and storage in Great Britain. For residents, the exposure assessment submitted to support approval must consider three scenarios; exposure at the time of application (e.g. from spray drift), exposure after the application (e.g. spray vapour) and exposure through entry into areas where spray drift fallout has occurred (e.g. children's exposure whilst playing in garden where drift has landed). Applicants for pesticide approval may provide their own assessments based on measurements made during application, other analogous measurement data or exposure models to estimate exposure, provided these produce an appropriate exposure assessment for each of these exposure scenarios (HSE, 2012).

There is a general paucity of exposure measurements, in particular for residents. Therefore the exposure assessment usually relies on simple exposure assessment tools. Due to the inherent nature of these tools, there is uncertainty associated with estimates

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obtained. To account for this uncertainty and also the true variability that will occur in individual exposures, the tools are designed to provide conservative estimates; however, they have not been comprehensively evaluated to determine if they are truly conservative, in particular for residents. Work undertaken in previous studies of pesticide exposure suggests that the current REA methods are sufficiently conservative for farm workers and pesticide applicators (Cooper and Dobson, 2007; Sleeuwenhoek et al., 2007; Colosio et al., 2011). However, there is a lack of information on the potential exposures experienced by non-occupational groups, such as bystanders and residents. Sleeuwenhoek et al. (2007) reported that the REA model in use for Great Britain at the time, may sometimes underestimate exposure for bystanders; however, they did not collect data for residents.

The research project 'Biological monitoring of pesticide exposure in residents' funded by the Department of Environment, Food and Rural Affairs (DEFRA) aimed to assess whether the exposure assessment tools used for the REA produce sufficiently conservative estimates. Galea et al. (2015a) reported on residents' exposure to captan, chlormequat, chlorpyrifos and cypermethrin in three geographical areas of Great Britain, whilst a separate manuscript is planned reporting on residents' exposure to penconazole.

In this manuscript, we compare the biomarker concentrations in urine obtained from residents following spray events, with the estimates obtained for residents using the exposure assessment models applied in the pesticide approval process. These exposure estimates were generated using spray event information provided by participating farmers to estimate intake for our adult and child participants residing within 100 m of the treated fields. The model outputs were converted into estimated urinary biomarkers by applying a toxicokinetic model, based on that of Rigas et al. (2001).

## 2. Materials and methods

### 2.1. Overview

The study received full ethical approval by the NHS South East Scotland Research Ethics Committee (SESREC) 3 (study number 10/S1103/63). Galea et al. (2011) describes the overall study design, which is discussed in more detail in Galea et al. (2015b). In brief, sample and data collection took place in three major arable crop growing and orchard areas in Great Britain: East Lothian, Kent, and Norfolk. Farmers were recruited into the study if they were likely to spray their agricultural crops with relevant pesticides (captan, chlormequat, chlorpyrifos, cypermethrin and penconazole) and there were residential areas within 100 m of the fields being sprayed. The farmers provided details of their pesticide usage throughout the spray season. Residents (adults aged 18 years and over and children in their care aged 4–12 years) living within 100 m of the edge of a field belonging to a recruited farm were approached to participate in the study. Participants provided informed written consent. First morning void urine samples on one and/or two days after a spray event were collected from participating residents, as well as a number of first morning void samples that were not associated with spray events (background samples collected during and outwith the spray season, with the spray season being taken to be March–August). These urine samples were frozen as soon as possible, being stored at −15 to −20 °C prior to analysis.

Urine samples collected within 2 days of a relevant spraying event were analysed only for the relevant pesticide(s) sprayed during the event. Background samples, both within and outwith the spray season, were analysed for all the relevant pesticides of interest to the study. The analytical method for chlormequat was based on that reported by Lindh et al. (2011) measuring chlormequat itself. The analytical method for captan was based on that reported by Berthet et al. (2011) measuring cis-1,2,3,6-tetrahydrophthalimide (THPI). The analytical method for chlorpyrifos was based on that reported by Sams and Jones (2011) measuring 3,5,6-trichlorpyridinol (TCP). The analytical method for cypermethrin measured cis- and trans- 2,2-dichlorovinyl-3,3-dimethylcyclopropane-1-carboxylic acid (DCVA) (Jones et al., 2009). A novel method was developed during the study for penconazole biomarkers and this was based on earlier work to develop a method based on a major animal biomarker (Pen-COOH) (Jones et al., 2009). More information on analytical methods is given in Galea et al. (2015b).

The laboratory that analysed the urine samples participates in external quality assurance schemes for chlorpyrifos and cypermethrin (G-EQUAS, www.g-equas.de). The analysts were blind to whether the urine samples were related to spray events or were background samples. All analytes were quantified using multipoint matrix-matched calibration curves (including a blank) and quality control samples (matrix spikes) were run every five samples (coefficient of variation <20% for all analytes). Samples were analysed in duplicate and the mean value reported. Aliquots of positive samples were reanalysed throughout the project to evaluate sample stability. There was no evidence of sample degradation for any biomarker studied throughout the assessment period.

### 2.2. Pesticides of interest and spray event information collected

Table 1 provides details of the pesticides considered in the study, along with a summary of participants measured urinary biomarker concentrations following the pesticide spray events. These spray event related samples were obtained from 149 eligible participants (125 adults and 24 children). Participants were considered eligible if, after excluding samples with low (below 2 mmol/L) or high (greater than 30 mmol/L) creatinine concentrations (Cocker et al., 2011; EWDTS, 2002), they provided at least one spray event related and at least one background urine sample.

Farmers were asked to provide details of their pesticide usage throughout the spray season for the fields within 100 m of participating households. This information included the start and finish times of the spray event, product and active ingredients used, quantities applied (weight of active substance/ha), dose rate, spray method as well as the size of the field, crop and weather conditions. In instances where farmers already maintained comprehensive records of their pesticide usage, the researcher requested copies of these. Where detailed records were not already maintained, participating farmers were asked to record the relevant information using an adaptation of the spray record form recommended by DEFRA (DEFRA, 2006).

### 2.3. Predicting residents' exposures using regulatory exposure assessment (REA) approach

Data for all spray events that involved products containing the relevant pesticides and for which urine samples were collected from participants were entered into a Microsoft Excel file in an anonymous format. This file was then forwarded to a representative of the CRD who used this information to predict the residents' exposures using the model applied in the regulatory process as described below (HSE, 2012). These independent predictions were made without any knowledge of the urinary biomarker concentrations obtained from the participants.

The REA models considered three pathways of exposure (HSE, 2012). The first of these was direct exposure to spray drift at the time of application. Based on values derived from generic field trials, estimates using the REA models were made of the amount of pesticide that might be deposited on the skin and enter the