Research on exposure of residents to pesticides in the Netherlands

OBO flower bulbs

Onderzoek Bestrijdingsmiddelen en Omwonenden

(Onderzoek Bestrijdingsmiddelen en Omwonenden)

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Prof. dr. ir. R.C.H. Vermeulen, principal investigator

Authors:

CLM Advies en Onderzoek
Ir. Y.M. Gooijer
Drs. G.W. Hoftijser
Ir. L.C.C. Lageschaar

Radboudumc
Drs. A. Oerlemans
Dr. ir. P.T.J. Scheepers

Schuttelaar & Partners
Ir. C.M. Kivits

TNO
Dr. J. Duyzer
Drs. M.G. Gerritsen-Ebben

Utrecht University
Ir. D.M. Figueiredo
Dr. A. Huss
Dr. E.J.M. Krop
Prof. dr. ir. R.C.H. Vermeulen

Wageningen University and Research
Dr. ir. F. van den Berg
Dr. ir. H.J. Holterman
Dr. ir. C.J.M. Jacobs
Ir. R. Kruijne
Dr. J.G.J. Mol
Dr. ir. M. Wenneker
Ir. J.C. van de Zande

Personal contribution
Prof. dr. P.J.J. Sauer

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Summary

Residents have raised concerns regarding possible health effects of applications of pesticides in the vicinity of homes. The Health Council of the Netherlands concluded in 2014 that there were sufficient reasons to initiate an exposure assessment study among residents living close to agricultural land. The "Onderzoek Bestrijdingsmiddelen en Omwonenden" (OBO) study was initiated to clarify the extent to which agricultural use of pesticides in the vicinity of homes contributes to exposure of residents to pesticides. This report describes the results of the exposure assessment study of residents living nearby agricultural land cultivated with flower bulbs (OBO flower bulbs). It should be noted that human exposure is the focus and that health effects were not investigated in this study.

The research questions were:

i) What are concentrations of pesticides in the environment of residents living near agricultural land with the cultivation of flower bulbs compared to residents living further away?
ii) What is the personal exposure to pesticides of residents living near agricultural land with the cultivation of flower bulbs compared to residents living further away?
iii) What are the exposure sources and routes contributing to personal and environmental exposure to pesticides in areas with the cultivation of flower bulbs?

To answer the research questions, an exposure assessment strategy was developed that included environmental sampling, biomonitoring, and the collection of contextual information. Homes within 250 m of selected agricultural fields with cultivation of flower bulbs and residents living in these homes were included. Growers and their families, living in the selected area, were also eligible for participation in the study but were treated separately in the statistical analyses. Environmental samples collected from homes were analyzed for a large number of pesticides used in bulb growing and other cultures and personal samples from the residents were analyzed for five selected pesticides. Results were compared to the results from samples collected from control locations located at least 500 m away from any agricultural fields. This yielded a vast amount of data that was analyzed carefully using various methods including statistical and deterministic models to answer the research questions.

Existing deterministic exposure models for pesticides, representing different exposure routes, were coupled and verified using measurement results from OBO experimental studies on spray drift and volatilization and the field study. This provided insights into the relative importance of the different exposure routes for residential pesticide exposures.

1. Higher concentrations of several pesticides were found in environmental samples collected from inside and outside the homes of people (residents) living close to bulb fields compared to concentrations in homes further away from the fields (controls).
2. These higher concentrations of pesticides were observed in the homes of people living close to bulb fields, both in the use and non-use period.
3. Biomarkers of two out of the five analyzed pesticides were found in more than half of the urine samples from persons, including (young) children, in both residents and controls. This was observed inside as well as outside periods of pesticide use. Relationships between the concentrations of these two pesticides in urine and distance to sprayed fields or periods of pesticide use were not consistently observed. However, concentrations found in urine correlated with the concentrations of pesticides inside and outside the homes.
4. Concentrations of pesticides inside and outside the homes of growers were generally higher than those found for residents living near agricultural land.
5. Calculations showed that volatilization of pesticides from the field after spraying and pesticides in house dust are likely the most important routes for exposure to pesticides of residents living close to bulb fields in our study. Because wind during spraying was not directed towards the homes of residents, drift was not observed in the field study. From experimental studies within OBO flower bulbs we conclude that drift can reach higher altitudes and larger distances than thought before.
6. The research has generated tools for a time-resolved predictive model to estimate exposure of residents of bulb fields and other crops with downward spraying, via both air and house dust, for all pesticides, locations and moments. However, important knowledge and information gaps still remain precluding estimates on a national scale.

Some pesticides were found in urine samples among participants as well as controls, including (young) children. At the same time correlations were found between environmental and urinary concentrations of these pesticides. These outcomes need to be explored in relation to possible health implications. Such an evaluation should take into account more factors influencing pesticide concentrations, including different pesticides used, varying distances to agricultural fields, different soil types, varying weather conditions and different susceptible subgroups (e.g. unborn or young children and individuals with co-morbidities).

Glossary

2,4,6-TCP	2,4,6-trichlorophenoxyacetic acid, biomarker for prochloraz in human urine
4-HSA	4-hydroxychlorpropham-O-sulphonic acid, biomarker for chlorpropham in human urine
5-HBC	methyl 5-hydroxy-2-benzimidazole carbamate (or hydroxycarbendazim), biomarker for carbendazim in human urine
Additional field	Field in the OBO study that is situated within 250 m of a location home
ADI	Acceptable daily intake, a measure of the amount of a specific substance in food or drinking water that can be ingested (orally) on a daily basis over a lifetime without an appreciable health risk (WHO, 1987)
AOEL	Acceptable Operator Exposure Level. It is a health based limit-value that represents the internal (absorbed) dose available for systemic distribution from any route of absorption (Heer, 2007)
Aerosol	Suspension of fine particles or liquid droplets in air
ARfD	Acute Reference Dose
ASE	Accelerated Solvent Extraction
BAG	Basisregistraties adressen en gebouwen: building registration
Biokinetics	The process of absorption, distribution, metabolism and excretion
Biomarker of exposure	Parent substance or metabolite in a biological medium (i.e. urine) that reflects exposure integrated over time and different uptake routes and sources.
BMI	Body Mass Index
BREAM	Bystander and Resident Exposure Assessment Model
BROWSE	Bystanders, Residents, Operators and Workers Exposure models for plant protection products
BRP	Basisregistratie Personen
$CaCl_2$	Calcium chloride
CLM	Centrum Voor Landbouw En Milieu
Control homes	Homes in the residents' field study of controls, situated in rural areas, further than 500 m away from any agricultural field
Controls	Participants of the residents' field study, living in a control home

Conversion factor	Factor to calculate back from the biomarker concentration or amount in urine to the original administered dose
Ctgb	Dutch Board for the Authorisation of Plant Protection Products and Biocides (College voor de toelating van gewas-beschermingsmiddelen en biociden)
DDM	Dust from doormat
Deterministic model	Mathematical model in which all parameters can have one unique value only and in which one parameter set results in one unique output.
DRN	Drift Reducing Nozzle
DRT	Drift Reducing Technique
EFSA	European Food Safety Authority
EU-MRL	Maximum Residue Level of a pesticide in food in the European Union (Level that should not be exceeded when using pesticides according to good agricultural practice. This is not necessarily a toxicological related maximum level).
Excretion rate	The amount of metabolite which is excreted in urine per unit of time (e.g. nmol/h).
External exposure	Exposure of a resident to external sources, such as pesticides concentration in air and dust, before these enter the body
Farm homes	Homes in the residents' field study with at least one resident reporting to work in agriculture
GC-MS/MS	Gas Chromatography - Tandem Mass Spectrometry
Growers' family	Participants of the residents' field study, living in a farm home
GSM	Global System for Mobile communications
h	Hours
Half-life	Time required to decrease the concentration of the metabolite in the urine by half
IDEFICS	IMAG (Institute of Environmental and Agricultural Engineering, Wageningen, the Netherlands) program for Drift Evaluation for Field sprayers by Computer Simulation
Infant	Very young child or baby, under the age of 12 months
Internal exposure	Exposure to the fraction of the initial pesticide dose that is absorbed and distributed through the body
IS	Internal standard (substance added to a sample(extract) to aid in the quantification in an analysis method.
KAVB	Koninklijke Algemene Vereeniging voor Bloembollencultuur
kg	Kilograms
KNMI	Koninklijk Nederlands Meteorologisch Instituut

LC-MS/MS	Liquid Chromatography - Tandem Mass Spectrometry
LC-HRMS	Liquid Chromatography – High Resolution Mass Spectrometry
Location homes	Homes in the residents' field study, situated within 250 m of a target field
LOD	Limit of detection, lowest concentration of pesticide that can be detected (not accurately quantified) in a sample
LOQ	Limit of quantification, lowest concentration of a pesticide that can be quantified in a sample
LDS-system	Low dosage system
m	Meters
Measuring campaign	Collection of measurements, performed at a home and by participants, started after a target field applied one or more selected pesticides (seven days) or in a control period (two days)
mg	Milligram (1 mg = 0.001 gram)
mL	Milliliters
mol	Mole
mPa	Millipascal
MRL	Maximum Residue Level
ng	Nanogram (1 ng = 0.000 000 001 gram)
NICE	National Institute for Health Care Excellence
Non-toilet trained children	Young children (e.g. infants and toddlers in the diaper study and toddlers in the residents' field study) who are wearing a diaper
Non-use period	Period in the residents' field study in which a pesticide is not used
NVWA	Nederlandse Voedsel- en Warenautoriteit, in English: Netherlands Food and Consumer Product Safety Authority
OBO	OBO study / Onderzoek Bestrijdingsmiddelen en Omwoneden
OPEX	Model for assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products.
OPS-st	Operational Priority Substances – Short term
PEARL	Pesticide Emission Assessment at Regional and Local scales
Pesticides	In this report when mentioned in the context of the product used by the grower: the plant protection product. in all other cases, e.g. analysis, emission to the environment, exposure of residents, the active substance of a plant protection product.

pg	Picogram (1 pg = 0.000 000 000 001 gram)
PM	Particulate matter
PUF	Polyurethane foam
Recovery	in analytical methods: amount of pesticide added to a QC sample divided by the amount of pesticide found during analysis, x 100% in volunteer studies: amount of biomarker (in mole) excreted through urine divided by the amount of pesticide (in mole) administered
REML	Restricted maximum likelihood
Residents	Participants of the residents' field study, living in a location home
RH	Relative humidity
RIVM	National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu)
RSD	Relative standard deviation (measure for precision)
RSD_{wl}	within laboratory relative standard deviation (intermediate precision of analytical measurements)within-
Spray drift	Quantity of plant protection product that is carried out of the sprayed (treated) area by the action of air currents during the application process (ISO22866).
Spray event	A single application of a pesticide or mixture of pesticides in an agricultural field using a boom sprayer.
Statistical model	Mathematical model which accounts for variability in one or more input parameters and expresses outputs as probability density functions.
Target field	Field in the OBO study on which an application started a measuring campaign
Target location	Location, including the target field, the surrounding participating homes and the surrounding additional fields.
TEB-OH	Hydroxy-tebuconazole, biomarker for tebuconazole in human urine
TNO	Toegepast Natuurwetenschappelijk Onderzoek
Toddler	A young child, between 2 to 4 years
Toxicokinetics	Biokinetics of toxic substances
Trueness	(in analytical methods) closeness of the measured values to the actual (true) value
Uncertainty	Refers to a lack of data or an incomplete understanding of the context of the risk assessment decision. It can be either qualitative or quantitative (U.S. EPA, 2011).

US-EPA	United States Environmental Protection Agency
Use period	Period in the residents' field study in which a pesticide is used
UTC	Coordinated Universal Time
µg	Microgram (1 µg = 0.000 001 gram)
µmol	micromole
Variability	Refers to the inherent heterogeneity or diversity of data in an assessment. It is "a quantitative description of the range or spread of a set of values" (U.S. EPA, 2011).
VFD	Vacuumed floor dust
Volatilization	The transfer of condensed pesticide residues from surfaces (e.g. leaves, soil water) into the atmosphere after application or from spray droplets during application
XAD-2	Polyaromatic adsorbent resin for hydrophobic compounds

1. Introduction and study design

1.1 Introduction

1.1.1 Background

The application of pesticides on agricultural land (see Box 1.1) in the vicinity of homes has raised concerns from local residents living near agricultural land. These concerns are related to the adverse health effects that may be associated with exposure to the active substances of these pesticides.

At the time the present study started (2015), the authorization procedures of the Dutch Board for the Authorization of Plant Protection Products and Biocides (College voor de toelating van gewasbeschermingsmiddelen en biociden, Ctgb) did not include a separate assessment of risks for residents, except for residents living near greenhouses[1]. The safety of residents was assumed to be covered by the authorization procedures that apply to operators, workers, and professional bystanders. However, it is not clear if this assumption is valid. Due to spray drift and volatilization of pesticides from nearby agricultural land, residents are likely to be exposed to lower levels but for a longer duration. Also, other populations are exposed such as children and the elderly, who may be more vulnerable. The possible accumulation of pesticides in the home environment may also contribute to the duration of exposure. The previously used environmental exposure assessment models for operators, workers and professional bystanders did not take into account this longer duration of exposure and were therefore not suitable to estimate actual exposure of residents.

The concerns regarding resident pesticide exposure and possible associated health effects have resulted in a request by the Dutch government for advice on the issue. In response, the Health Council of the Netherlands published its advice in 2014, with the main conclusion that there were sufficient reasons to initiate an exposure assessment study among residents living close to agricultural land. The reasons included the observed health effects in farmers and growers coupled with some evidence of health effects in residents from international studies, and very limited knowledge about the actual exposure of Dutch residents. In its report, the Council proposed that an exposure study should cover multiple years, multiple application techniques, as well as multiple crops and pesticides. In addition, the study should involve measurements of both the environment and of residents to investigate the contribution of various exposure sources to personal exposure (Health Council of the Netherlands, 2014). Figure 1.1 indicates possible exposure sources and routes as identified by the Health Council of the Netherlands.

[1] Since 2016, shortly after the OBO-study started, a new assessment methodology is used by the Ctgb, based on the OPEX model developed by the European Food Safety Authority (EFSA, 2014), which includes exposure of residents in the authorization procedures.

Box 1.1 Pesticides

In Dutch, several terms can describe the chemicals used on agricultural land, which may reflect the thoughts of different groups. In the OBO study we therefore agreed on the Dutch term "bestrijdingsmiddelen" as the most neutral way to describe the substances from the perspective of residents.

In this report, the English word 'pesticides' is used. When mentioned in the context of the product used by the grower, it refers to the plant protection product. In all other cases, e.g. analysis, emission to the environment, exposure of residents, it refers to the active substance(s) of the plant protection product."

Following the advice of the Health Council, the Dutch Ministries of Infrastructure & Water Management and Economic Affairs & Climate Policy commissioned the National Institute for Public Health and the Environment (RIVM) to coordinate an exposure assessment study with the objective of 'acquiring data on the (potential) exposure of residents in agricultural areas in which pesticides are used intensively'. To clarify the extent to which the agricultural use of pesticides in the vicinity of homes contributes to total exposure of residents to pesticides, the "Onderzoek Bestrijdingsmiddelen en Omwonenden" (OBO) study was developed. Because of the different fields of expertise that are necessary to conduct such a study, it was designed and performed by a broad consortium of research institutes. Its goals and design are guided by input from international scientists and stakeholder groups such as the residents, growers, and manufacturers of pesticides. The study objective is to investigate residents' exposure to pesticides.

In the OBO study, carefully designed field measurements, detailed auxiliary data collection, experimental studies, and modelling efforts are combined. The obtained integrated model frameworks can then potentially be applied to extrapolate exposure assessment to a broader range of crops and substances used in agriculture, as well as to a larger population. Information about sources, routes, and levels of exposure can ultimately be used to provide input in authorization procedures for pesticides, health studies and, if applicable, to estimate the effect of existing and future mitigation strategies on population exposures. Although their importance is recognized, authorization procedures and mitigation strategies fall outside the scope of the current study. It should be noted that human exposure is the principal endpoint and that health effects were not investigated in this study. In 2018, an initial health survey of people living in the direct vicinity of agricultural plots in the Netherlands has been carried out. Box 1.2 summarizes the main findings of this survey.

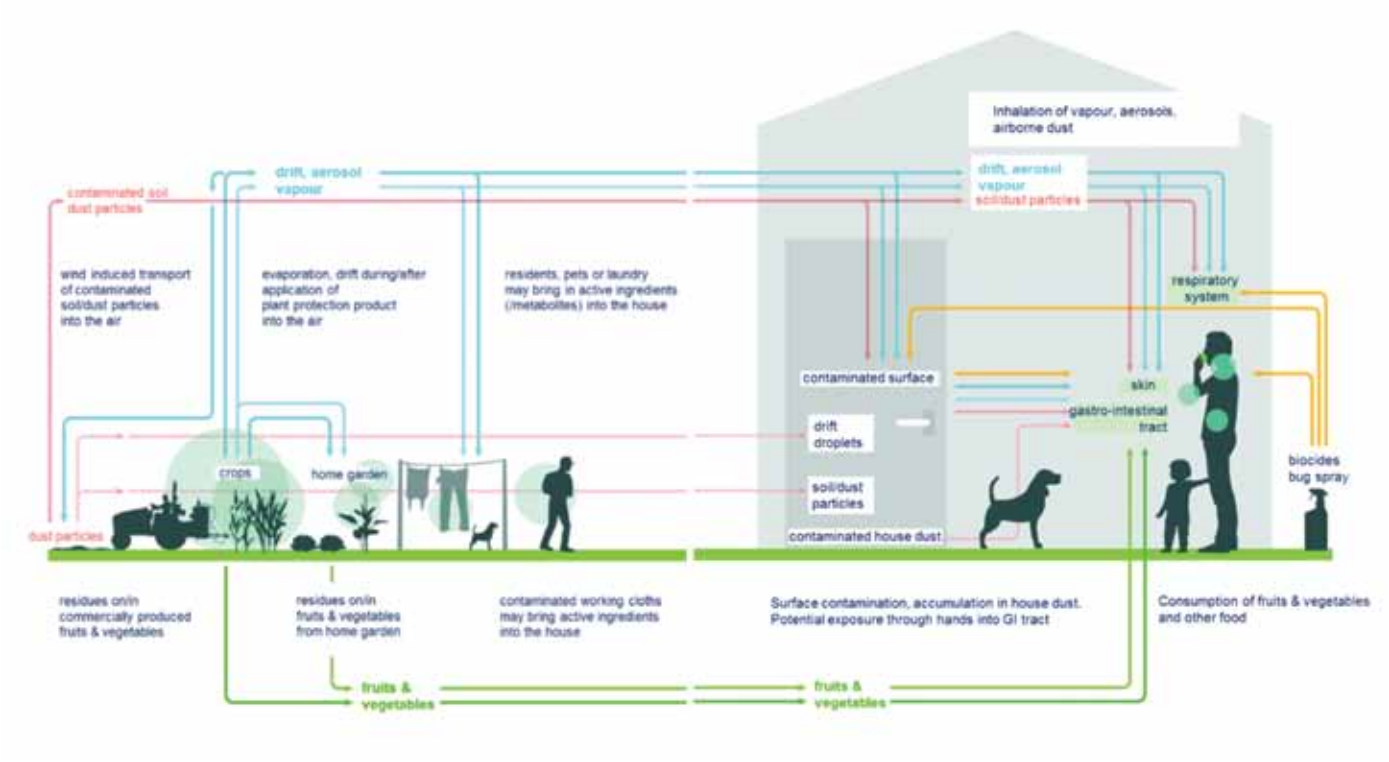


Figure 1.1: Exposure sources and routes.

Different suggested sources and routes of for outdoor (left panel) and indoor (right panel) exposure to pesticides. Colored arrows represent different types of routes: blue: direct exposure; red: indirect exposure via particles; green: indirect exposure via food; yellow: direct and indirect exposure from products used at home. Figure is adapted from the report of the Health Council of the Netherlands (2014).

Box 1.2: Health survey

RIVM, Utrecht University and the Netherlands Institute for Health Services Research (NIVEL) have performed a survey on the health of people living in the direct vicinity of agricultural plots ("Gezondheidsverkenning"). The survey results were published in a report in July 2018 (RIVM Rapport 2018-0068).

Data on the actual exposure to pesticides of people living in the direct vicinity of agricultural plots were not available. The researchers used the distance of homes from agricultural plots and the surface area of nearby plots as exposure proxies and investigated whether they were linked to diseases and conditions observed in nearby residents. In general, no clear links were found. People who lived nearer to agricultural plots did not have more diseases and conditions than people who lived further away. Some conditions did even occur less frequent, although lifestyle factors may have contributed to this finding. In contrast with the general results, a higher mortality rate due to airway conditions was found among people living in the proximity to fields where maize was cultivated.

The survey also found some noteworthy associations for people living in proximity to agricultural plots. These did not show a consistent link with the quantity or proximity of specific crops. Conditions included a higher birth weight among babies born to people living near summer barley fields, Parkinson's disease and eye irritation among people living near fruit orchards, and leukemia among people living near plots with cereals, beets and potatoes (crops that are rotated).

1.1.2 Aim of OBO

The OBO study aimed to assess pesticide exposure for residents living close (< 250 meters) to agricultural fields and to better understand the possible routes of environmental exposure. Because it is infeasible to measure exposure levels to all pesticides for all residents living close to agricultural land, a study design was developed that combined environmental and personal measurements with exposure models in order to estimate pesticides exposure for the Dutch population.

The OBO-study aimed to address the following main research questions:

i) What is the personal exposure to pesticides for residents living near agricultural land?
ii) What are concentrations of pesticides in the environment for residents living near agricultural land?
iii) What sources and routes of exposure contribute to environmental exposure to pesticides for residents?
iv) What is the exposure for residents to pesticides through different seasons and in different regions in the Netherlands?

For the OBO study, the characterization and quantification of human exposure was the central aim. In discussions with residents, it became clear that their concerns were not limited to their personal exposure, but also include concerns regarding the impact of pesticides on the environment. Although the current study monitored environmental pesticide concentrations as a means to estimate human exposure, it was not the aim of the study to present a comprehensive overview of environmental pesticide concentrations or to evaluate the impact of pesticides on the environment.

1.1.3 Phasing of the study

The original design of the OBO study included measurements in areas with flower bulb cultivation and downward spraying techniques as well as areas with orchards and sideways/upward spraying techniques. With that design, residents in one area could serve as controls for the other area as applied pesticides differ in these cultivations. For budgetary reasons, the OBO study was divided in two phases, with each phase focusing on a different method of pesticide application. As commissioned by the aforementioned Dutch ministries, pesticide exposure after using downward spraying techniques in areas with cultivation of flower bulbs was addressed in phase 1. Sideways/upward spraying is intended to be (part of) the focus of phase 2. The results of phase 1, OBO flower bulbs, are described in this report. With phasing of the study, inclusion of a separate control population became necessary.

1.1.4 Aim of OBO flower bulbs

The aim for OBO flower bulbs is the assessment of pesticide exposure among residents living within 250 m of an agricultural field where pesticides are applied using the downward spray technique. The main research questions for OBO flower bulbs were:

i) What are concentrations of pesticides in the environment of residents living near agricultural land with the cultivation of flower bulbs compared to residents living further away?
ii) What is the personal exposure to pesticides of residents living near agricultural land with the cultivation of flower bulbs compared to residents living further away?
iii) What are the exposure sources and routes contributing to personal and environmental exposure to pesticides in areas with the cultivation of flower bulbs?

Phase 1 only focused on the downward spray pesticide application technique. Therefore it was impossible to address the research question regarding pesticide exposure through different seasons and regions in the Netherlands. This issue can only be addressed when data on exposure related to the sideways/upward pesticide application techniques is gathered.

1.2 Study design

To answer the research questions, an exposure assessment strategy was developed to include personal biomonitoring, environmental sampling, and the collection of contextual information. In a selected subset of study locations, additional biomonitoring measurements were collected. Supplementary experiments were also included to generate complementary information on methods of urine collection from diapers, biomarker excretion, as well as pesticide spray drift and volatilization. This information was necessary for optimal sampling and analytical protocols and generating data suitable for exposure modelling.

Measurements

Environmental samples were collected from homes of residents living in the vicinity of crops (< 250 m). The samples provided information regarding the residents' exposure levels, as well as factors that influence exposure, including home distance to agricultural land, pesticide chemical characteristics, pesticide application techniques, and meteorological conditions. For comparison, environmental samples were collected from homes of control participants living > 500 m from agricultural fields in a non-urban environment. Urine samples were used to assess the internal exposure of residents because they are a well-established matrix in human biomonitoring of non-persistent compounds and relatively easy to collect.

Modelling

Existing exposure models were used to predict environmental pesticide concentrations. The models were calibrated with results from measurements from the experimental studies during the study and verified using measurement results from the residential field study.

The design of OBO flower bulbs is illustrated in Figure 1.2. Measurements were conducted in 4 main protocols (A, B, C and D) and results provided input for modelling. The individual protocols of the study are outlined below. Detailed methodology is further explained in chapters 2 (Methodological studies), 3 (Residents' field study), 5 (Experimental studies and field studies) and 6 (Modelling).

1.2.1 Residents' field study (protocols A and B)

For the residents' field study, flower bulb fields with sufficient homes within 250 m in at least 2 main wind directions were selected as target fields (see figure 1.3). If owners and growers of these fields consented, these fields were included in the study as "target fields". All residents living within 250 m of the perimeter of the target fields were invited to participate in the residents' field study.

Growers informed the researchers if any of the selected pesticides (see chapter 3) were applied on target fields, which triggered a series of measurements at the homes of participating residents (defined as measurement campaign).

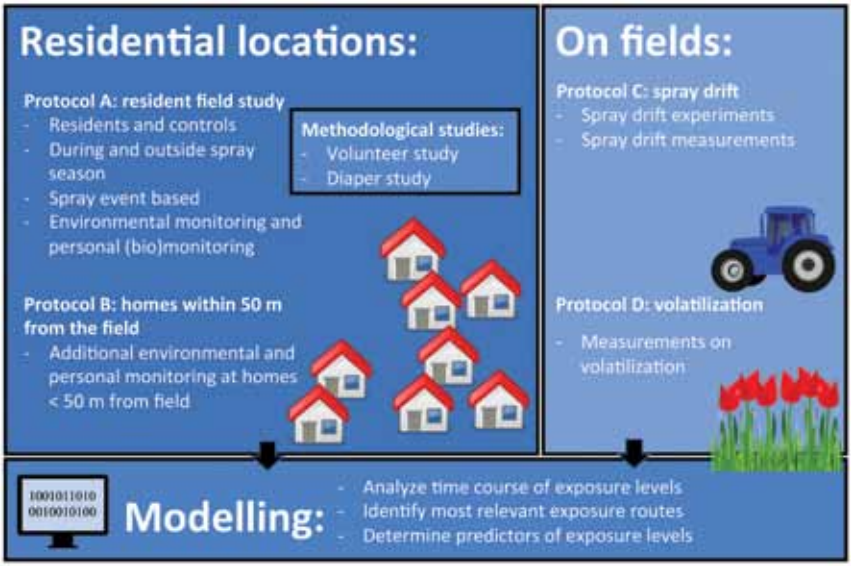


Figure 1.2: study design.
The OBO flower bulb study consists of a residents' field study (protocol A and B), and agricultural field measurements (protocol C and D). Additional methodological studies were imbedded in protocol A. Exposure modelling uses results from all protocols.

Protocol A

Protocol A samples were collected from the residents and their homes during the spray season and in the off-season. During the spray season, immediately after a reported spray event, environmental and urine samples were collected from the residents and their homes. The same sampling protocol was used to collect "off-season" samples outside of the spray season. Environmental samples included outdoor air (7 times 24h for spray season; 2 times 24h for off-season), indoor dust, soil in residential gardens, and, if applicable, home grown fruits and vegetables. During the spray season, first morning urine samples were collected from the residents for seven consecutive days following pesticide application. For off-season sampling, first morning urine samples were collected from residents for two consecutive days. At least one spray event on a target field was followed and if possible, 2 events with one of the selected pesticides were followed. Households situated more than 500 m away from any agricultural field but within the general vicinity of the selected locations were included as controls for this part of the study.

For reasons of cost effectiveness, not all collected samples were analyzed. The subset of samples for analysis was selected based on expected exposure levels. This is described in detail in chapter 3.

Protocol B

Protocol B was completely nested within protocol A and the goal was to gather detailed information about pesticide propagation and exposure pathways. Since protocol B involved more elaborate environmental and urine sampling than protocol A, protocol B was employed only in residential homes that were within 50 m from the perimeter of the target fields. Environmental sample collection procedures in protocol B homes were identical to those in protocol A homes, with the addition of an indoor air sample collection during the first 24h following the spraying event. In addition to collecting urine samples as described in protocol A, protocol B residents collected all urine samples from the time of pesticide application until the morning of the following day. To measure dermal exposure, hand wipe samples were collected from protocol B residents within 24 h of the spray event.

1.2.2 Methodological studies

Two methodological studies were carried out to determine the best method for urine collection in non-toilet trained infants and the conversion factor between pesticide exposure and urine metabolite excretion (volunteer studies).

Urine collection in non-toilet trained infants

For urine collection in non-toilet trained infants, four methods were evaluated in a pilot study. The study examined the success scores of sample collection by parents/caretakers and acceptance scores by infant and parents/caretakers. The most successful and accepted method was used for urine collection in infants.

Volunteer studies

For most pesticides the metabolism in humans is unknown and the only available metabolic data is derived from animal studies. As animal metabolism might be different from humans, the volunteer studies aimed to identify the most suitable urinary biomarkers of pesticide exposure in humans. A second aim was to generate data on biokinetics such as urinary excretion rates. This was achieved by controlled oral or dermal administration of each of the selected pesticides in independent tests. Conversion factors derived from these tests were used in conjunction with urinary biomarker concentrations to calculate pesticide uptake.

1.2.3 Spray drift (protocol C)

Spray drift experiments

Spray drift models have previously been developed to assess drift of droplets and evaporation drift to the environment. These models have been developed to estimate the environmental fate of pesticides near application areas, such as deposition on surface water. Because residential exposure was not considered during the development of these models, there are knowledge gaps in predicting residential

exposure, especially at larger distances (> 5 m) from the field and at greater heights (> 3 m). Targeted experimental studies on experimental fields were carried out to study spray drift at longer distances (5 to 50 m) and greater heights (up to 10 m). Results from these studies helped to calibrate the spray drift models, which provided output for use in subsequent environmental fate models. Additionally, the amount of spray drift differs between spraying with standard versus drift reducing nozzle types as well as between applications in a cropped versus a bare soil field. The magnitudes of these differences were investigated in the experiments.

Spray drift field measurements

Spray drift measurements, quantifying spray deposition on ground surfaces and airborne spray drifts downwind of the treated field were performed by spraying a 'flower bulb' field to approximate the real-life situation, including homes and fences. The spray technique was as used in practice and the application was done under real-life conditions (including field and weather). For practical reasons, measurements were performed using a fluorescent tracer instead of a pesticide. Initially, these measurements were planned on target fields. In spring 2017 it was no longer possible to perform spray drift experiments on a target field and instead experiments were performed on fields of the experimental farm "Unifarm" at WageningenUR. Spray drift field measurements were performed by spraying a bare soil surface alongside different types of 'gardens' and 'houses' to quantify the different types of barriers at the edge of the field and their effect on ground deposition and airborne spray drift in the garden. The gardens mimicked an open garden, a half open garden with a 30% wind-closed windbreak shield, and a closed garden with a 100% wind-closed anti-root cloth mimicking a closed fence in front of a greenhouse tunnel (the 'house').

1.2.4 Volatilization (protocol D)

Pesticide volatilization experiments were conducted at two different locations: an OBO-study target field with hyacinth and an experimental field at the Wageningen University research station with a surrogate crop. A surrogate crop, onions, was used for the second location because no field with flower bulbs was available and onion cultivations share similarities with flower bulb cultivations.

At both locations, the rates of pesticide volatilization from the treated crops and influencing factors were measured on the day of pesticide application and several times during the first week after application. This was achieved by a combination of measurements of concentration gradients and on-site meteorological observations, including measurements of turbulence intensity and leaf wetness. The meteorological observations can also be used to test and improve volatilization models.

In addition to the volatilization measurements, the residue of the pesticide on the leaves was determined. The results of such measurements can be used to relate the

strength of volatilization to the remaining mass of the pesticide on the leaves. This also helps to determine to which extent and for how long volatilization could continue.

1.2.5 Modelling

In order to select models suitable for assessing the exposure of residents living near fields where pesticides are intensively used, a screening of different models was conducted. The most suitable models were then combined into a deterministic modelling framework. To verify model estimates in the OBO flower bulb study setting, model predicted exposure concentrations in different media (e.g. air, dust, soil) were compared to concentrations measured in and outside households. Once verified, the deterministic models were used to estimate pesticide exposure of residents living within 250m of the target fields. The contributions of different exposure routes to total internal exposure and different factors that might influence the concentrations of pesticides in urine were also investigated with the use of statistical modelling techniques.

1.2.6 Add-ons

Although not part of its primary aim, the OBO flower bulb study provided an opportunity for the development of new methods in environmental and personal exposure assessment. Three pilot studies, referred to as add-on studies, were conducted within the OBO study framework:

- Personal sampling of pesticide exposure using silicone wristbands
- Environmental sampling with polyurethane foam (PUF) disk-based passive air samplers
- Measuring personal exposure to pesticides through hair analysis

Although these methods were not applied to assess exposure in the main OBO flower bulb study, results of the pilot studies are included in Appendix 27-29 of this report.

1.3 Definitions of location, fields, homes and participants

1.3.1 Location

In the context of this study, a “location” was defined as a geographic area that includes the target field, location homes and additional fields (all explained below).

1.3.2 Fields

A “target field” is defined as the central field in a location where a spray event on that field triggers the start of the measurements. The selection of possible target fields within a location is described in detail in chapter 3. The growers of target fields shared with the OBO consortium information on types of pesticides that would potentially

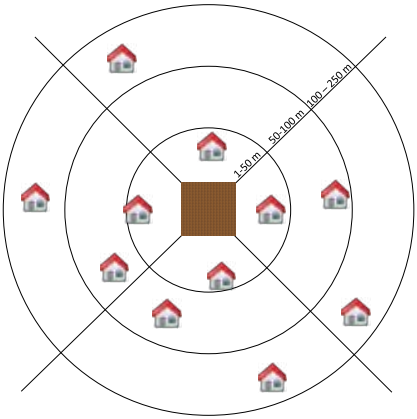


Figure 1.3: Theoretical location with target field and homes within pre-defined proximity zones.
The black circles represent distances.

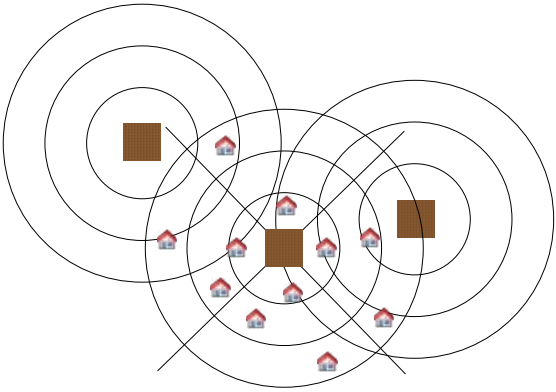


Figure 1.4: Theoretical location with multiple fields.
A target field (center) is shown with surrounding homes at different distances. Additional fields at the location and within 250 m of homes are shown. In theory, some additional fields can be closer to a participating home than the target field.

be applied on the fields, application method, and planned application schedule. The growers also informed the OBO researchers once a scheduled pesticide application on the target field was confirmed. Participating homes and residents were invited to participate in the study based on proximity to target fields. Ideally, recruited homes would be situated at different distances around a target field (Figure 1.3). However, such situations were rare and different distributions were explored (see chapter 3).

"Additional fields" are defined as all agricultural fields within 250 m of a participating home that were not target fields (Figure 1.4). As all fields near a home could potentially influence exposure, growers of additional fields were also asked to share their spraying schemes.

1.3.3 Homes

Location homes

Homes up to 250 m from the perimeter of a target field were recruited as potential study participants. Proximity categories were set at <50 m, 50 – 100 m, and 100 -250 m from the target field. These distance categories were chosen with the assumption that direct droplet and vapor drift are the most important factors influencing exposure concentrations within 50 m of a target field where the pesticide was applied with the downward[2] spraying method. In the proximity zone of 50 - 250 m, volatilization and air dispersion could play a role in exposure concentrations. Note that a participating household could be situated closer to an additional field than to the target field, as explained in Figure 1.4. In the study, homes within 250 m of a target field will be referred to as "location homes". All location homes participated in protocol A. Location homes situated in the <50 m proximity zone were also invited to participate in protocol B.

Farm homes

Participation was open to growers and their family living within 250 m of a target field. In the residents' field study we defined a "farm home" as a residential home where at least one resident reported to be working in agriculture or related industries. Results from location homes and farm homes are shown separately in this report because scientific literature has indicated that occupational exposure to different types of chemicals or pesticides can influence residential exposure (Coronado 2006; Thompson et al, 2003; Thompson et al, 2014).

Control homes

Control homes were selected to study regional background pesticide exposure patterns and were situated at least 500 m from any agricultural field. They must also be situated in a non-urban area (< 1500 addresses per km^2) and within 20 km from a target field. Control homes participated only in protocol A.

1.3.4 Participants

Residents

All persons living in a location home were invited to participate in the study. It is important to select study participants who, due to different home locations and personal time activity patterns, had different levels and routes of exposure. For example, toddlers may have more contact with indoor surfaces than adults. Similarly, young children may have more contact with outdoor surfaces (e.g. soil) while playing. In practice however, there was limited opportunity to specifically enroll residents from all age groups in equal numbers as study participants.

[2]Together with sideways/upwards spraying the main techniques in the Netherlands

Growers' families

Growers' families may represent the most exposed group of residents. Additionally, other exposure routes may be relevant for this group (e.g. contaminated work clothes). In this study, we recruited growers' families with similar method as other families: if a grower lived in an eligible home in proximity to a target field, the grower and other family members were invited to participate. Like for farm homes, results of growers' families are analyzed and presented separately.

Controls

Controls are participants in control homes.

1.4 Outline of the report

This report describes the results of phase 1 of the OBO study, OBO flower bulbs. Chapter 2 describes the methods development study for urine collection in infants (the "diaper study"), and the study of pesticides biokinetics and urinary metabolites (the "volunteer study").

Chapter 3 describes the methods of the residents' field study, including the selection of target fields, selection of pesticides to be measured in environmental and personal sampling, recruitment of participants, and methodology for exposure assessment.

Chapter 4 describes the results of protocol A and B of the residents' field study. Chapter 5 discusses both the methods and results of the field experiments for the study of pesticide spray drift and volatilization.

Chapter 6 describes the calibration, verification, and results of exposure models, which used the results from chapters 2 to 5 as model inputs. Exposure model results include the routes, levels, and determinants of exposure.

Chapter 7 summarizes and discusses the results OBO flower bulbs. The report ends with conclusions based on the study findings and recommendations.

2. Methodological sub-studies

This chapter describes two studies that relate to the determination of pesticide biomarkers in urine (i.e. biomonitoring). More specifically, in the first part the selection and validation of a method to collect urine samples from non-toilet trained children was addressed in order to be able to determine their exposure of pesticides (paragraph 2.1). The second part (paragraph 2.2) describes a study in adult human volunteers aiming at the identification of biomarkers of exposure to five pesticides. In addition, the absorption, distribution, metabolism and excretion (ADME) of selected urinary metabolites following administration of a small quantity of a pesticide by oral intake or skin application are described. The contribution of this work to the overall project is to be able to relate the residents' external pesticide exposure to the biomarker concentration measured in urine.

2.1 Urine collection in non-toilet trained children

This paragraph describes the context and the aims for urine collection from non-toilet trained children. The design of a pilot study is described, and the materials and methods used are specified. The results are presented and discussed in view of the study aims, i.e. to determine the pesticide exposure in young children.

2.1.1 Background

In the main study design, it was decided to invite all residents living in homes located close to agricultural land where pesticides are applied. In addition, residents at reference locations were invited to participate in the study (see paragraph 1.2 study design). Urine samples would be collected during normal toilet visits. Written instructions were prepared for adolescents and adults, but collecting urine samples from young, non-toilet trained children, is more challenging as these study participants will not be able to follow instructions. Urine collection in non-toilet trained children requires involvement of their parents or caretakers and the use of some technical solutions.

Collection methods should not introduce contamination or affect the integrity of the urine sample, should be convenient for young children and their parents, and should be cost-beneficial in this large-scale biological monitoring study. In addition, the minimum sample volume for analysis, the timing of collection, and the sample success rate should be considered (Lee and Arbuckle, 2009). Various methods have been used for urine collection in children, such as urine bags, the free catch, cotton diapers, gel diapers and absorbent pads (e.g. gauze or cotton pads). According to the National Institute for Health Care Excellence (NICE), the free catch is considered as the gold standard in a clinical setting (NICE, 2007). It is well known that the extraction of urine from a gel-absorbent polyacrylate diaper is complex. At the same time, these diapers are commonly used, and are therefore potentially an attractive collection device. Urine

collection from an absorbent diaper insert or a urine bag has been used and validated in the clinic for the diagnosis of urinary tract infections. Each method has its own advantages and limitations and it depends on the situation which method is preferred (Lee and Arbuckle, 2009; Liaw et al., 2000).

2.1.2 Aim

For the subgroup of non-toilet trained children different methods for urine collection with a sufficient success and acceptance rate were considered. The role of the parent/caretaker in the urine collection procedure was also evaluated as their involvement is crucial to obtain a urine sample. The objective for this sub-study is to evaluate different urine collection methods for non-toilet trained children with criteria to collect a sufficient urine volume (>5 mL) to allow biomarker analyses and sufficient appreciation (score of 6 or higher on a 10-point scale) of the collection methods for parents/caretakers.

2.1.3 Methods

Four commonly applied methods to collect urine from non-toilet trained children were studied for feasibility to collect urine samples from young children (age 0-3 y) in a non-clinical setting. The selected methods were: a urine collection pad (Hessels+Grob, Apeldoorn, the Netherlands), a urine bag (Urinocol Pediatric, Braun), the free catch and a disposable polyacrylate diaper (Pampers Baby Dry size 3, Procter & Gamble). A brief description of each of the four methods will be given below (Table 2.1).

An *absorbent pad* can be inserted in a diaper and urine can be extracted from the pad in the laboratory. The insert is relatively easy to install, as well as removal of the pad with absorbed urine in it and urine extraction. Obtaining sufficient volume for urine analysis is a limitation of this method, especially when a relatively large volume (>5 mL) is required for performing multiple analyses on one sample. We evaluated a relatively new type of collection pad, the PeeSpot, which has been validated for the diagnosis of urinary tract infections and electrolyte disturbances in a clinical setting. It consists of a felt material containing a dried hygroscopic polymer that can absorb up to 1.2 mL of urine. The standard size is 0.5 x 2.4 x 1.0 cm (h x l x w). For this study, the PeeSpot size was enlarged to 0.5 x 10.0 x 3.0 cm (h x l x w) with a capacity to absorb up to 15 mL of urine.

The *urine bag* has been commonly used in hospitals and is relatively easy to use but needs more efforts from the parents compared to the PeeSpot. The bag should be attached to the skin in the correct position (by use of adhesive tape) and after removal, the urine should be transferred to a urine container. The parents have to monitor whether the adhesive tape detaches or causes skin reactions.

Table 2.1: Overview of urine collection methods for non-toilet trained children tested in this study.

Code	Method	Product name	Description
A	Absorbent pad	PeeSpot	New method developed for pediatrics; absorption pad is placed in the diaper
B	Collection bag	Braun Urinocol	Solution most routinely used in hospitals
C	Free catch	-	Urine collection in a regular container; reported as a method in research
D	Diaper	Pampers Baby-Dry	Obvious solution but not much used because of difficulty to extract substances of interest from the gel

The *free catch* method is considered the gold standard for non-toilet trained children. A void is collected by placing a container into the urine stream, e.g. during a regular diaper change or before/after bathing. This method might be time consuming, not always successful and it requires the involvement of preferably two adults, one to hold the child upright and one to catch the urine in the collection cup.

The *diaper* is a urine collection method that comes closest to the normal routine for the parents or care-givers. The Pampers Baby Dry diaper was selected as this type is generally available in many countries and consists of a separate polyacrylate gel compartment, which can be easily separated. Collection and storage of a wetted diaper in a sealed bag is easy and can be part of a normal routine for most parents or care takers. However, extraction of the urine from the diaper in the laboratory is challenging (Hu et al., 2004).

The pre-selected urine collection methods were compared in a pilot study involving volunteers. The study protocol (NL51952.091.14) was submitted to the Medical Ethical Board Arnhem-Nijmegen and approval was obtained before the participants were recruited. Participants were recruited in and around Nijmegen by poster announcements. Written informed consent of the parents was obtained after verification of inclusion and exclusion criteria of the child. Inclusion criteria were: the child has to wear a diaper and the infant body-weight should be above 2.5 kg. Exclusion criteria were: bladder infection or other illness or unwellness, pre-existing skin problems such as diaper dermatitis, and a history of an allergic reaction to adhesive tape. The study population in this pilot consisted of parents of eight non-toilet trained children with a mean age of 22 months for the boys (n=4) and a mean age of 14 months for the girls (n=4). All four methods were used in 24 attempts (three attempts per method and per child), and the sequence of the method application was randomly assigned.
The urine bag and the PeeSpot were installed during a normal diaper refreshment to decrease participant burden. Parents were asked to check the diaper every 30 min

after installation. According to the provided instructions, the parents had to place the PeeSpot in the area of the urethra. The free catch method was performed during a regular diaper change. Regarding the diaper method, one pre-weighted diaper per day was collected and the difference in weight was used to calculate the voided urine volume. Parents were also asked to complete a short questionnaire regarding information on leakage, displacement, user experiences, and the overall convenience for the child and the parents, based on a user acceptance score on a 0 - 10 scale where 0 was inconvenient and 10 was convenient. A successful sample was defined as a yielded volume of at least 5 mL available for urine analysis and free of faeces contamination. The success rate was calculated from the number of successful collected samples and the total amount of attempts.

2.1.4 Results

From the results in Table 2.2 it becomes clear that the diaper method is the most convenient method for urine collection with a mean acceptance score of 9 on a scale from 0 to 10. The success rate for diapers was 67 % (16 out of 24 attempts) and the urine volume yielded (mean of 120 mL) was well above the threshold of 5 mL. A limitation of the diaper method is that faeces may make the urine sample unsuitable for analysis (33% of the attempts). The performance of the other tested methods was much lower compared to the diaper method (Table 2.2). The acceptance score of the absorption pad was sufficient, but the mean yielded urine volume was below our criterion of 5 mL (mean of 4.1 mL). Based on the results the diaper was selected as the most convenient and best performing method of urine collection in non-toilet trained children.

Different techniques for urine extraction from a diaper have been described, e.g. using a syringe to aspirate the sample, immersing the gel layer in an organic solvent or by applying hydraulic pressure (Lee and Arbuckle, 2009). For the polyacrylate or gel diaper, the addition of a calcium salts solution effectively collapses the polymer to release the urine. Hu et al. (2004) concluded that diapers containing a separate compartment with the gel material are most suitable for urine extraction, however they also stated that the brand of the diaper could affect the recovery efficacy. In this pilot-study we adopted and modified the method of Hu et al. (2004), which has been developed for the analysis of urinary pyrethroid metabolites. The modified method in short: the polyacrylate granules are coiled when dry and become uncoiled when the material comes in contact with water or urine. The polymer continues to uncoil, absorbs more water and forms a gel-like material. Upon addition of solid CaCl2 the polymer collapses due to ion exchange, and most of the absorbed urine is released with the analytes remaining in solution. A modification to the method of Hu is the addition of solid $CaCl_2$ (0.1 g of $CaCl_2$ per 1 g of gel material) compared to the addition of a 100 mL of 150 g/L $CaCl_2$ solution to prevent loss of sensitivity by diluting of the sample.
The materials used in the selected type of diaper were evaluated for pesticide residues or any other components that might interfere with extraction and analysis of the target

Table 2.2: Comparison of the methods for urine collection by different criteria (%).

Scoring criterion	Absorbent pad	Collection bag	Free catch	Diaper
Success rate (%)	17	21	4	67
Missing sample (%)	42	67	96	33
Faeces contamination (%)	17	12	0	33
Acceptance score[1]	7.3 ± 1.8	4.7 ± 2.2	2.8 ± 3.0	9.0 ± 1.3
Urine volume (mL)[1]	4.1 ± 2.5	10 ± 10	152[2]	120 ± 80[3]

[1]Arithmetic mean ± standard deviation; [2]Only one attempt was successful; [3]Based on weight increase of the diaper.

metabolites. The blank extracts showed that the diapers were free of contamination. For the urinary biomarker of tebuconazole (TEB-OH) and for creatinine, the recovery of the extraction method was determined. To test this, known quantities of the analytes were dissolved in urine and added on the diaper. The mean recovery was on average 106 ± 3% for TEB-OH corrected with an internal standard (IS) with an relative standard deviation (RSD) of 3%. The mean recovery of creatinine was 87% with an RSD of 3% (Oerlemans et al., 2018).

2.1.5 Discussion

This study evaluated four methods for collection of urine from non-toilet trained children for pesticide exposure characterization. The method should be suitable for urine collection at home, the collection material must be acceptable for the participants and the urine collection itself should impose a low burden on both parents and child. A minimum sample volume of 5 mL is required for multiple laboratory analysis.

The diaper method demonstrated to be most successful and the participant scores were the highest of all four methods tested. Collection of urine with the diaper succeeded in 67% of the total number of attempts, and faeces in the diaper caused all missed samples. Using a validated diaper brand and type is essential to ensure high recoveries, but some parents may still not want to use the selected study diaper (Liaw et al. 2000).

In our study, the success rate of the clean catch method was rather low compared to previous reports. A success rate of 88% has been reported by Alam et al. compared to 4% in our study. However, all of the children in the study of Alam et al. (2005) were admitted to the hospital, whereas in our study urine was collected at home. Nurses might be more successful in applying clean catch urine collection compared to the parents of the child (Alam et al. 2005).

The success rate of the PeeSpot method was only 17%, while the device was found to be reliable in clinical applications (Roelofs-Thijssen et al. 2013). Our low success rate could be partly explained by the relatively low volume yield; 64% of the received samples yielded a volume below the required 5 mL. Despite the clear instructions, it

might be that the position of the pad in the diaper was not optimal, resulting in a lower volume absorbed, or that the pad was presumably displaced as a result of crawling/ walking.
Urine bags are frequently used in hospitals and are often applied in clinical studies. The risk of contamination is low, which makes it a suitable method for the determination of urinary tract infections (NICE 2007). Although it is reported that the use of urine bags is relatively simple and reliable, the participants reported various outcomes with an overall high number of missings (67%), compared to only 4% in a previous study in a clinical setting of Alam et al. (2005).

2.1.6 Conclusion

In this study, four methods to collect urine from non-toilet trained children were evaluated for biomonitoring purposes in a non-clinical setting. Use of a commercially available disposable diaper was the most suitable and convenient method for the parents and the child. A previously described diaper urine extraction procedure was adopted and the extraction method resulted in high recoveries of TEB-OH and creatinine.

2.2 Volunteer study

This paragraph describes the context and the study on the identification of urinary biomarkers and provides information on the biokinetics of selected pesticides in human volunteers. The design of the volunteer study is described, and the materials and methods used are specified. The results are presented and discussed in the light of the study aims.

2.2.1 Background

This study will provide an identification of metabolites in human urine which reveals candidate biomarkers of exposure to pesticides. The urine collection and analysis will result in urinary metabolite concentrations of the selected biomarker in each analyzed urine sample. The question to be answered is how this biomarker concentration in urine can be converted to the exposure of the corresponding pesticide. For back-calculation to the exposure, a conversion factor is required for each pesticide. To derive this conversion factor, controlled administration of each of the selected pesticides (see chapter 3, and Table 2.3) was performed in human volunteers. Volunteer studies were performed after both oral or dermal exposure, separately.

2.2.2 Aim

The following objectives apply for the human volunteer study:

1. *Identification of human biotransformation products*
   For the selected pesticides the biotransformation products were not studied after controlled administration in humans, but carried out and reported in animal studies (EFSA draft assessment reports). These data cannot be readily adopted for biomonitoring purposes due to interspecies differences and should therefore be verified in humans.

2. *Selection of the most suitable biomarker following oral or dermal uptake*
   Pesticide exposure leads to excretion of one or multiple metabolites in urine. The choice of a metabolite as a biomarker of exposure should be made before the OBO field samples can be analyzed. The most abundant metabolite may not necessarily be the best choice. The metabolite should be unique for the pesticide of interest to safeguard selectivity of the method; any endogenous formation or occurrence of the same metabolite due to other exposures could result in bias. Sufficient sensitivity should be obtained in the chemical analysis of the biomarkers.

3. *Estimation of conversion factors to calculate-back from the biomarker concentration to uptake*
   Depending on the route of exposure, the excretion pattern of metabolites may differ. This is related to the liver as the most prominent organ that changes the chemical properties of the substance by enzymatic metabolism. Other organs than the liver may also have metabolizing capacity, but this may involve different enzymes and the capacity is usually much lower. Following ingestion, the parent substance (i.e. the pesticide) will be absorbed from the intestine and will first pass the liver before reaching other organs. In the liver the parent substance will be metabolized before entering the blood circulation, resulting in exposure of internal organs to the metabolites instead of the parent substance. When the parent substance enters the body by inhalation or by skin absorption, the parent substance may be distributed and reach potential target organs, even before it is metabolized in the liver. Because of this 'first pass' effect, conversion factors will be estimated separately for oral and skin exposure. Uptake by inhalation was not studied in volunteers because of the difficulty to predict the safety for the model compounds in an inhalation setting and of technical limitations to perform safe inhalation experiments for humans.

4. *Evaluation of the biokinetics and differences between human subjects*
   The kinetics of uptake, distribution, metabolism and excretion (also called biokinetics or toxicokinetics) may be different from one individual to the other. Differences could be explained by age, sex, medication use, but other unknown factors may also be involved, for example genetic differences that may affect metabolism. For the interpretation of the biomarkers of exposure it is useful to be able to estimate the inter-individual variability.

2.2.3 Methods

The study protocol (NL56428.091.16) was submitted to the Medical Ethical Review Board Arnhem-Nijmegen and approval of the protocol was obtained before the participants were recruited. Participants were recruited in the area of Nijmegen by poster announcements and advertisements on diverse websites (e.g. Proefbunny). Written informed consent of the participants was obtained after verification of inclusion and exclusion criteria. The inclusion criteria were: age between 18 and 40 y, BMI between 20 and 25, alcohol consumption less than two standard glasses per day, and Caucasian. The exclusion criteria were: use of prescribed medication (except oral contraceptives), intension to become pregnant during the study period, breastfeeding at the time of the study, skin disorders, smoking and direct contact or working with pesticides. For each pesticide, three male and three female adults received a fixed single dose in a random order on two occasions for oral and dermal administration, separated by at least two weeks. A fixed oral dose was predefined for all participants and did not exceed the acceptable daily intake (ADI) for a person with a body weight of 50 kg. Dermal dose was also fixed and predefined for all volunteers and the amount absorbed in the body was estimated with IH SkinPerm (AIHA, 2011) and did not exceed the ADI. Dosages of the five pesticides are provided in Table 2.3, and the characteristics of the volunteers are provided in Table 2.4.

Table 2.3: Oral and dermal doses of the five selected pesticides for the volunteer studies.

Pesticide	Oral dose (mg)	Dermal dose (mg)	Modelled skin uptake[1] (mg)	ADI (mg/kg bw/day)
Tebuconazole	1.5	2.5	0.0186	0.03
Chlorpropham	2.5	1.0	0.2768	0.05
Prochloraz	0.5	0.5	0.0471	0.01
Asulam	5	5	0.1135	0.36
Carbendazim	1.5	1.5	0.0026	0.03

[1]Estimated total amount absorbed after 1 h using IH-SkinPerm v1.21.

Table 2.4: Characteristics of the participants.

	Mean age (yr)		Mean height (cm)		Mean weight (kg)	
Pesticide	F (n=3)	M (n=3)	F (n=3)	M (n=3)	F (n=3)	M (n=3)
Tebuconazole	23	24	171	186	61	71
Chlorpropham	25	22	174	188	67	79
Prochloraz	21	23	173	179	62	76
Asulam	21	22	179	184	72	83
Carbendazim	21	24	173	182	63	69

Yr: years; cm: centimeters; kg: kilograms; F: female; M: male.

For oral administration, the pesticide was dissolved in 200 mL of tap-water. The solution was ingested within 5 min. For the dermal administration, the pesticide was dissolved in acetone and 100 µL was and applied on a marked rectangular surface of 100 cm^2 on the non-dominant forearm. Directly after application the volunteer was seated with his/her arm placed in a fume hood to prevent inhalation of the pesticide evaporating from the skin surface.

After one hour, the exposure was stopped by cleaning of the skin surface with a wipe immersed in a solution of water and ethanol (50:50 v/v). The subsequent modelled skin uptake in that hour was calculated by using IH-SkinPerm v1.21 (Table 2.3). This calculated skin uptake does not account for the amount stored in the stratum corneum, as that amount could be taken up into the body over a relative long time after stopping the external exposure (Rom and Markowitz 2007).
All volunteers were made aware of food items which might contain residues of the administered pesticide and were asked to refrain from the use of these products from 48 hours before and during the urine collection period. A pre-exposure urine sample was obtained before each administration to verify any recent uptake of the pesticide of interest. Levels in pre-exposure urine samples were low or below the limit of quantification, with maximum levels <2 µmol/mol creatinine for asulam, <5 µmol/mol creatinine for carbendazim, <0.2 µmol/mol creatinine for prochloraz, <6 µmol/mol creatinine for tebuconazole, and <15 µmol/mol creatinine for chlorpropham. Urine was collected in separate portions at predefined time intervals for the first 12 h, and further without time restriction up to 48 h after administration. The clock time of each urine micturition was recorded by the participant on a registration form.
For biomarker identification, 24 h post-exposure pooled urine samples were prepared by taking 1% of the volume of each of the voids collected by each volunteer during the first 24 h post-exposure. All samples were analyzed using liquid chromatography with full scan high resolution mass spectrometry (LC-HRMS). This was done with and without enzymatic deconjugation by Helix Pomatia enzymes. The data were evaluated using a dedicated 'suspect' lists of biomarkers known from animal studies (based on EFSA Draft Assessment Reports). In addition, for detection of unknown biomarkers, a dedicated software tool (Thermo Scientific Compound Discoverer 2.0) was used for metabolite discovery by comparing the measurement results of the pre-exposure and post-exposure pooled urine samples. The metabolites with the highest relative detectability (RD) were selected as the candidate exposure biomarkers.

The RD was calculated based on the detection signal of the metabolite and the absence of noise and interferences. For the candidate biomarkers, analytical standards were acquired either from commercial suppliers of analytical references standards, from agrochemical companies or through custom synthesis. A number of tentatively identified biomarkers were fully identified using these analytical reference standards.

Table 2.5. Biomarkers (tentatively) identified in human urine after oral and dermal exposure, including the relative detectability (RD).

Pesticide	Selected biomarker of exposure in urine (RD)	Other biomarkers (RD)
Tebuconazole	tebuconazole-1-hydroxy (TEB-OH) (1.00)	M10: M03 SO3 (0.01) M11: M03 gluc (0.26) M04 (0.22) M04 isomer (0.16) M12: M04-gluc (0.03) M12: M04-gluc isomer (0.05) M06 (0.72) M06-gluc (0.16) M07 (0.08)
Chlorpropham	4-hydroxychlorpropham-O-sulphonic acid (4-HSA) (1.00)	M2 4-aryl OH (0.315) M2-GlcA (0.043) M6 (aniline) (0.001) M6-SO3 (0.140) M9 (acetanilide) (0.078) M9-GlcA (0.001) M9-SO3 (0.011) M4 di-OH (aryl/alkyl?) (0.013) M4-SO3 (1) (0.007)
Prochloraz	2,4,6-trichlorophenoxyacetic acid (2,4,6-TCP)*	M2 BTS3037-gluc BTS45186 / M3 BTS54908
Asulam	Asulam (1.00)	Acetylasulam (0.06)
Carbendazim	methyl 5-hydroxy-2-benzimidazole carbamate (5-HBC) (1.00)	5-HBC-G (0.01) 5-HBC-SO3 (0.53) 5,6-DHBC-G (<0.01) 5,6-DHBC-SO3 (0.53)

* for Prochloraz, the indicated metabolites were close to the LOD in LC-HRMS analysis. Relative responses varied between the different subjects. Therefore, no relative detectabilities were provided.

After the biomarker selection, a dedicated method for the quantification of the biomarkers was developed, based on liquid chromatography tandem mass spectrometry (LC-MS/MS). The methods were validated and used for the quantification of the biomarker in the individual urine samples for the evaluation of the biokinetics and to establish the conversion factors.

2.2.4 Results and discussion

1. *Identification of human biotransformation products and 2. selection of the most suitable biomarker following oral or dermal exposure*

The results from the biomarker verification revealed that the identified biomarkers in human urine (Table 2.5) corresponded to the main metabolites found in animal studies (based on EFSA draft assessment reports). However, the ratios of excretion in urine were different in comparison to the ratios in animals. No differences were observed in the identified main biomarkers between oral and dermal exposure or between individuals. Asulam was mainly excreted unmetabolized in urine. Other biomarkers tentatively identified with a lower RD are also presented in Table 2.5.

2. *Estimation of conversion factors to calculate the uptake from the biomarker excretion observed in urine*

For the estimation of the conversion factors the recoveries were determined, i.e. the total excreted amounts (in µmol) of the metabolites in the first 48 h after administration were calculated and divided by the dose (in µmol). Calculations were performed in molar fractions to correct for differences in molecular weight between the primary compound and the metabolite. The conversion factors for oral and dermal exposure are provided in Table 2.6. For example, for tebuconazole it means that on average 38% of the oral administered dose is excreted in urine as TEB-OH. For prochloraz, the oral conversion factor was relatively low (2.0%), probably due to: (a) limited uptake in the gastro-intestinal tract, and (b) main excretion pathway of metabolites is via the faeces. Standard deviations give an indication of the inter-individual variability and the uncertainty in the conversion factor.

For the use of the conversion factors in the back-calculation of exposure we would like to address three potential sources of bias. The first potential source of bias results from the observation period of 48 h which was too short to fully account for the urinary excretion, which continued after this timepoint, after dermal exposure. If the follow-up time would have been longer the recoveries would have been higher and the conversion

Table 2.6: Oral and dermal conversion factors.

Pesticide	Oral conversion factor mean ± SD	Dermal conversion factor mean ± SD
Tebuconazole	0.38 ± 0.16	0.010 ± 0.0045
Chlorpropham	0.37 ± 0.14	0.027 ± 0.010
Prochloraz	0.020 ± 0.017	0.0010 ± 0.00076
Asulam	0.35 ± 0.051	0.00062 ± 0.00038
Carbendazim	0.40 ± 0.18	0.015 ± 0.0059

SD: standard deviation.

factors lower. With the presented conversion factors, we tend to overestimate in the back-calculation. This bias is larger for skin compared to oral route of exposure because of the much slower uptake via the dermal route which results in a more gradual (slower) excretion. A more accurate value could be determined by a longer observation period or by making a model prediction of the elimination pattern after 48 h.
Secondly, after stopping skin exposure, we could not quantify the exact amount taken up. Potential losses of substance unaccounted for may also have resulted in a lower conversion factor. Again, our calculation leads to potential overestimation in the back-calculated skin exposure.

The third source of bias concerns the back-calculation of inhalation uptake from the amount of excreted urinary metabolite. We did not study inhalation exposure and therefore we were not able to estimate a factor for conversion of inhalation exposure. If the oral conversion factor would be used instead, inhalation exposure would be underestimated: after oral administration a higher fraction of the pesticide would be expected to appear in urine (compared to inhalation) due to liver passage following absorption from the gastrointestinal tract before reaching other internal organs (the so-called first pass effect). After inhalation exposure the pesticide would reach internal organs via the blood circulation without first passing the liver, which would have resulted in a higher value of the conversion factor. By using the much higher oral conversion factor we would underestimate the contribution from inhalation exposure. Regarding the influence of the first pass effect, inhalation is more similar to skin absorption: for both routes of uptake the pesticide would be distributed to internal organs before reaching the liver. If the dermal conversion factor would be used for back-calculation of the inhalation exposure our back-calculation would likely overestimate because of the first source of bias (see above).

3. Evaluation of the biokinetics and differences between human subjects

For the evaluation of the biokinetics, for each pesticide, the time course of the urinary excretion rates in nmol/h was calculated and corrected for body weight (Figures 2.1-2.5). It is shown that for all pesticides the excretion of the metabolite was nearly complete within 48 h after oral exposure. The peak excretion rates were found between 1 and 6 h post administration.

After dermal administration, the excretion rates were much slower than the rates observed after oral uptake, probably due to the relative slow dermal uptake. Peak excretion rates were found, ranging from 6 to 28 h post application. For all pesticides, except chlorpropham, the excretion was not complete within 48 h. The pesticides will probably remain in the stratum corneum of the skin and will very slowly diffuse to the blood circulation. This skin absorption process was probably not completed up to 48 h after wiping the skin as there can be uptake into the body over a relative long time after external exposure was stopped (Rom and Markowitz 2007).

The mean ± standard deviation of the elimination half-lives after oral and dermal administration of the compounds are given in Table 2.7. Separate values for males and females were not provided as the half-lives were not significantly different. Asulam has the shortest oral half-life with 2.9 h ± 0.5 h, most likely due to its high polarity and being excreted unmetabolized. Prochloraz has the longest oral half-life with 25 h ± 13 h. The dermal half-lives were substantially longer than the oral ones, probably as a result of a much slower uptake. It was not possible to derive a dermal half-life for prochloraz because the metabolite levels in urine were very low or below the LOD, and there was no clear excretion phase observable in the first 48 h.

The time courses of the urinary excretion rates are presented in Figures 2.1-2.5, and show that the urinary elimination patterns for the biomarker vary between individuals within a factor of 10. The y-axis represents the excretion rate in nmol/h/kg bw on a logarithmic scale, and the x-axis represents the relative time after administration on a linear scale.

When the percentage of excretion of the biomarker in relation to the administered dose is relatively high, such as following oral administration, the comparability between individuals increases. The inter-individual variability of the excretion rates after dermal exposure is larger, probably because of the low skin absorption rates resulting in lower excretion rates. The uptake route itself may also introduce variability as the skin properties and conditions can vary between individuals.

In some individuals an unexpected increase or decrease of the excretion rate can be observed (e.g. Figure 2.1a-M2 and 2.2b-F2), probably as a result of an additional exposure to an external source (e.g. via food), incorrect registration of the time of urine collection, incorrect urine collection or excessive or low water intake. For example, when a study participant collects only a fraction of the urine instead of the complete void, the excretion rate will change. When drinking large amounts of liquid, the kidneys will excrete more water and thus the process of metabolite excretion might be altered as well, resulting in changed elimination rates (Anastasio et al. 2001).

Table 2.7: Oral and dermal half-lives of excretion.

Pesticide	Oral half-life (h) mean ± SD	Dermal half-life (h) mean ± SD
Tebuconazole	7.9 ± 1.1	15 ± 4.0
Chlorpropham	4.6 ± 0.3	10 ± 2.7
Prochloraz	25 ± 13	Unable to determine
Asulam	2.9 ± 0.5	13 ± 3.9
Carbendazim	5.3 ± 1.4	14 ± 6.2

h: hours; SD: standard deviation.

The relatively short half-lives of the pesticides, especially after oral exposure can be used to determine a urine sampling strategy corresponding to the biokinetics of the compounds of interest. In addition, when dermal exposure is expected, the samples should preferably be collected on the day after the day of potential exposure. For oral exposure, sample collection can be the same day or the next day after potential exposure, preferably within five half-lives of the pesticide.

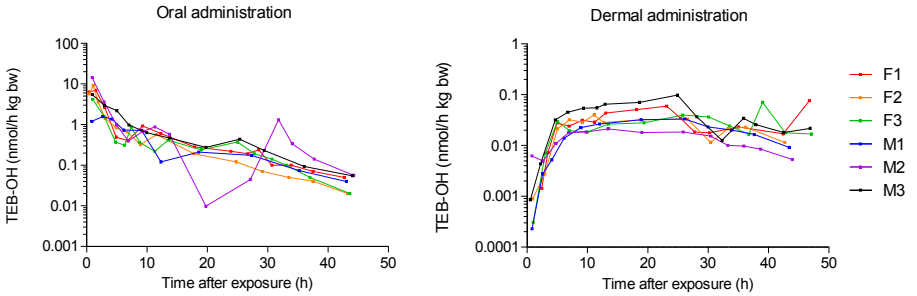


Figure 2.1: Time courses of the urinary excretion rate of TEB-OH after oral (left panel) and dermal (right panel) administration of tebuconazole in six human volunteers.

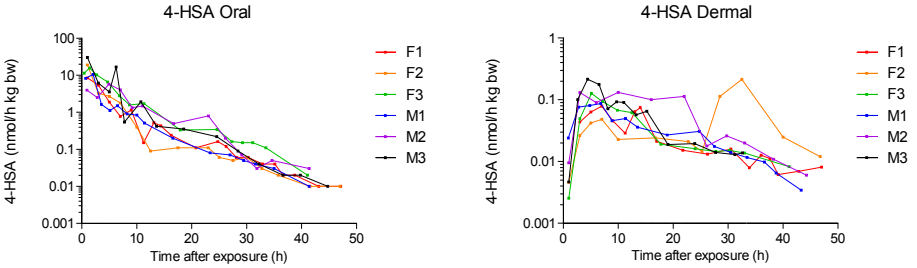


Figure 2.2: Time courses of the urinary excretion rate of 4-HSA after oral (left panel) and dermal (right panel) administration of chlorpropham in six human volunteers.

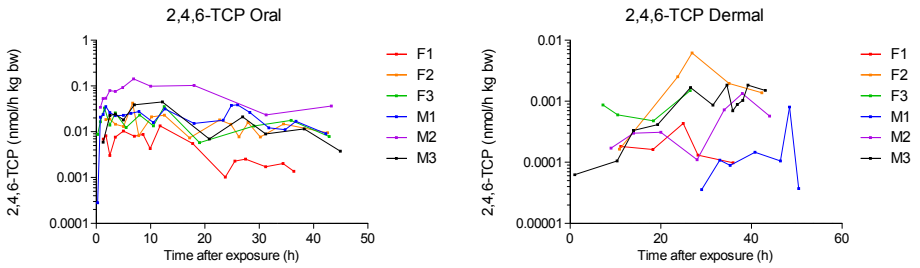


Figure 2.3: Time courses of the urinary excretion rate of 2,4,6-TCP after oral (left panel) and dermal (right panel) administration of prochloraz in six human volunteers.

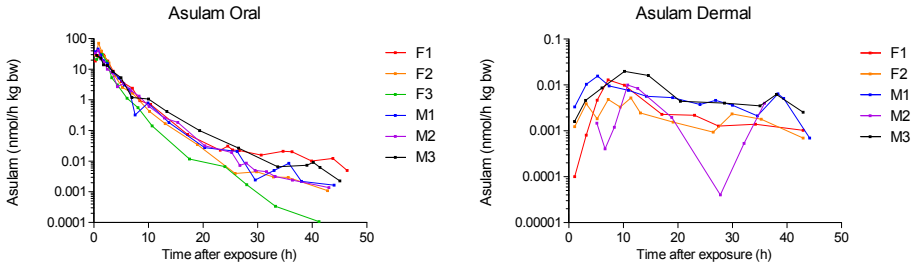


Figure 2.4: Time courses of the urinary excretion rate of asulam after oral (left panel) and dermal (right panel) administration of asulam in six human volunteers.

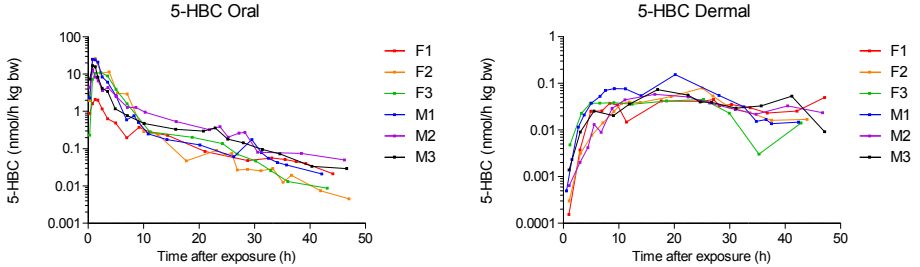


Figure 2.5: Time courses of the urinary excretion rate of 5-HBC after oral (left panel) and dermal (right panel) administration of carbendazim in six human volunteers.

2.2.5 Conclusion

Based on the results obtained after oral and dermal administration of the five pesticides to human volunteers on separate experiments, five specific urinary biomarkers of exposure were proposed. The identified metabolites corresponded to the major metabolites observed in animal studies. Conversion factors based on molar fractions were calculated for the individual pesticides and can be used to evaluate and quantify the exposure in biomonitoring studies. When the fraction excreted within 48 hours was very low, the inter-individual variability was relatively high. Furthermore, the study demonstrated that metabolites are readily excreted after oral exposure but excretion rates were much lower after dermal exposure. Uptake by the skin is a comparatively slow process resulting in slow availability in the blood circulation and a continued excretion that may continue after 48 h following exposure.

3. Design and methods of the residents' field study

Collection of measurements and data in the residents' field study required selection of field locations and study areas, identification of eligible participants, selection of pesticides to be measured, selection of sampling techniques and selection of methods for chemical analyses of pesticides and biomarkers. This chapter describes selection procedures as well as methods used in the residents' field study, starting with the selection of pesticides to be studied and techniques to measure concentrations of these in the field in chapter 3.1, followed by the selection of locations and fields (chapter 3.2). In chapter 3.3, the selection procedure of participants is described, followed by the methods of the resident field study in chapter 3.4.

3.1 Selection of pesticides

3.1.1 Product use and pesticide properties

First, an inventory of the pesticides (see Box 1.1) available in 2015 to tulip and lily growers was conducted. The inventory resulted in a list of pesticides (active substances) to be monitored in environmental samples and in a shortlist of pesticides which are considered to be the most suitable for biomonitoring. OBO flower bulbs initially focused on pesticides used in cultivation of tulip and lily but later included other flower bulb cultivations that use selected pesticides.

The method to select relevant pesticides considered information about registration and usage of pesticides on tulip and lily farms, availability of analytical methods, estimated deposition and source strength of emissions from plant and from soil, estimated dermal exposure and skin penetration, possible exposure originating from other, and non-agricultural pesticide use (Kruijne et al., 2019).

The authorization registry of the Ctgb was searched for the pesticides with an authorized use in one or both flower bulb crops tulip and lily; as at the end of 2015. The focus was on pesticides which were authorized for spraying applications. The pesticides selected for environmental monitoring and biomonitoring in humans had to be registered for tulip and/or lily farming during the field phase of the project (between 2016 and 2017). In case the expiration date of the registration of a pesticide was before the end of this period, the notifier was asked for his plans to submit a request for a new registration. The inventory resulted in a total of 30 pesticides (Appendix 1, Table 1 and Kruijne et al., 2019).

The list of pesticides with a registration for spraying application in tulip and/or lily was combined with the estimated number of growers that use a pesticide (market share in % of the growers) and with pesticide formulation data. This resulted in a list of prioritized pesticides to be further assessed for possibilities for inclusion in the chemical analysis of personal samples (Appendix 1, Table 2). For environmental analysis, the list of prioritized pesticides was extended with their environmental breakdown products as far as they are also known to be human metabolites. A further extension was made with pesticides that were found in soil and plant material from flower bulbs by RIKILT in 2014. These analyses had been done in the frame of regular surveillance of pesticide use in bulb flowers by the NVWA.

For biomonitoring, due to budgetary constraints (see also 3.1.2, personal samples), only 5 pesticides could be selected for urine analyses. The pesticides suited for the proposed method of analysis and commonly used by tulip and lily growers were arranged by product type (herbicide, insecticide and fungicide). The relevance of the pesticide for tulip cultivation and for lily cultivation was estimated considering the following five indices and/or aspects:

1. The maximum dose rate, actual application frequency, and market share: pesticides applied with high rates, frequencies and pesticides with large market shares were preferred.
2. The saturated vapor pressure was an indicator for the source strength of volatilization processes; high saturated vapor pressure indicates more volatilization.
3. The calculated skin penetration flux; high values indicate high potential for dermal uptake.
4. Possible exposure through food; pesticides which are commonly present in/on fruits and vegetables were considered less favorable because this might interfere with assessment of environmental exposure.
5. Analytical aspects; knowledge on urinary excretion, main mammalian metabolites, availability of analytical reference standards.

Ideally, the five pesticides to be selected for biomonitoring would represent the three product types (herbicide, insecticide, fungicide), the different physicochemical properties of the pesticide, and both tulip and lily cultivation. At the early stage of the project, a proposal for selection was made per product type. Although the representation of three product groups was not a requirement by itself, it was expected to increase the length of the period of application and therefore to enlarge the time window to plan the experiments. In the initial selection of candidates for biomonitoring the emphasis was on aspects 1 and 2. When multiple candidates were obtained, then the other aspects were considered.

Herbicides

Most of the herbicides in Appendix 1 (Table 2) were applied only once. The herbicide substances asulam and chlorpropham were applied twice. Note that higher application

frequencies (with lower maximum dose rates) were allowed when the product “Certis Chloor IPC 40% Vloeibaar” was applied with an LDS system, or in combination with other specific pesticides (all according to the label text). The herbicide metamitron had the highest recommended dose rate and the herbicide S-metolachlor the lowest. The highest market shares were reported for chlorpropham and pendimethalin (tulip and lily) and for metamitron (tulip); all growers used a pesticide based on these active substances. Other herbicides with high market share were asulam and S-metolachlor.

The pesticide chloridazon has the lowest vapor pressure and can only be applied once every three years. Therefore, this pesticide was not selected for biomonitoring. The other pesticides within the herbicide group with low vapor pressure were asulam and metamitron. The pesticides pendimethalin, dimethenamide-P, S-metolachlor, and chlorpropham had the highest vapor pressures within the herbicide group. All pesticides in this group had a systemic mode of action, or the pesticide enters the plant through the leaves and roots (pendimethalin).

Within this group of pesticides, the highest calculated dermal absorption rates were for chlorpropham, S-metolachlor, and dimethenamide-P.

In general, exposure to herbicides through food is very unlikely. The only exception could be chlorpropham through potatoes treated with this pesticide as sprout inhibitor. Dermal (most of the residue is present on the potato skin) and dietary exposure may occur. However, the beneficial indices for the other selection properties were considered to outweigh a potential issue with background exposure through routes other than use in bulb fields.

Based on these indices for the group of herbicides, chlorpropham and asulam were considered the most relevant candidates for inclusion in the biomonitoring. Chlorpropham representing a volatile, low to moderate dose rate pesticide, and asulam representing a non-volatile, high dose rate pesticide.

Insecticides

The insecticides in Appendix 1 (Table 2) were applied 2, 3 or 4 times, with the exception of lambda-cyhalothrin which was applied 11 times in tulip and 20 times in lilies. The insecticide thiacloprid had the highest recommended dose rate whereas lambda-cyhalothrin had the lowest recommended dose rate. Compared to the group of herbicides, the recommended dose rate in the group of insecticides was approximately one order of magnitude lower. The market shares of these insecticides were generally lower than the market shares of the investigated herbicides. One reason for this difference was that most of the lily growers choose an insecticide that is based either on flonicamid, acetamiprid, or thiacloprid. An insecticide with relatively high market share in tulip was spirotetramat.

The pesticides deltamethrin and spirotetramat had the lowest vapor pressures within the group of insecticides. In addition, these two pesticides have very high sorption coefficients (Kruijne et al., 2019). These properties made these pesticides less suitable candidates for biomonitoring. The five other pesticides within the group of insecticides have considerably higher vapor pressures. The pesticides deltamethrin and spirotetramat have a non-systemic mode of action; the other pesticides within the group of insecticides have a systemic mode of action.

Within this group of insecticides the highest dermal absorption rates were calculated for acetamiprid, flonicamid, thiacloprid, and pymetrozine.

Based on these indices for the group of seven insecticides, it was proposed to select either flonicamid, acetamiprid, or thiacloprid for biomonitoring in the vicinity of the selected experimental fields used for lily cultivation. The choice depended on the product used by the participating grower. For tulip, spirotetramat would be the most obvious candidate based on its market share within the insecticides. However, the low vapor pressure and short degradation half-life indicate that significant emission by volatilization is unlikely.

Fungicides

The fungicides in Appendix 1 (Table 2) were applied 3 to 5 times in tulip, and up to 6 times in lily. The pesticide prochloraz had the highest recommended dose rate in the group of fungicides. The pesticide fluopyram had the lowest recommended dose rates in the group of fungicides. The market shares of these fungicides were generally lower than the market shares of the herbicides proposed and were comparable with the market shares of the insecticides. Fungicides with relatively high market share were prochloraz, fluopyram, and trifloxystrobin (80%; in lily). The fungicides with the highest market share in tulips were boscalid (55%), and tebuconazole (50%).

The fungicides with the lowest vapor pressures within the group were prothioconazole and boscalid. Except for prochloraz and trifloxystrobin, the pesticides within the group of fungicides have a systemic mode of action.

Within this group the highest dermal absorption rates were calculated for tebuconazole, prochloraz, and prothioconazole.

The risk of background exposure from food intake was high for boscalid and was also relatively high for tebuconazole, fluopyram, and to a lesser extent for trifloxystrobin and prochloraz.

Based on these indices for the seven identified fungicides, it was proposed to select prochloraz for the biomonitoring in the vicinity of the selected experimental fields used for lily cultivation. For tulip, tebuconazole was proposed. Trifloxystrobin would be a

third candidate because it was used both in tulips and lilies. Similar to the insecticides, the choice will depend on the pesticides used by the participating growers.

In summary, the eight pesticides in Table 3.1 were proposed for biomonitoring based on this inventory. In addition; one pesticide, spirotetramat, was proposed because it was the only insecticide with a high market share in tulip cultivation (100%). However, this pesticide has physicochemical properties which makes it unlikely to volatilize. Therefore it was not on the final list.

The field study focused on applications of the eight selected pesticides on target fields for onset of the measurements. After collection of all urine samples, the final selection for biomonitoring of five pesticides biomarkers was made based on application and/or measured levels in environmental samples. It was decided that biomonitoring focuses on four applied pesticides: chlorpropham, asulam, prochloraz and tebuconazole. Based on the results of the environmental samples in the first stage of the field measurements, the fungicide carbendazim was included in the biomonitoring. Carbendazim had no authorization for field use in 2015 (or after) but arose as degradation (secondary) product from thiophanate-methyl, which is used in bulb disinfection. We therefore refer to the biomarker of carbendazim as the biomarker of thiophanate-methyl/carbendazim.

3.1.2 Chemical analysis

The possibility to detect a pesticide in chemical analysis was taken into consideration in the selection of the pesticides to be studied. For this, two types of samples are

Table 3.1: Pesticides pre-selected for biomonitoring.

Product use	Pesticide	Product(s)	Remarks
Herbicide	chlorpropham	Intruder, Certis Chloor IPC 40% Vloeibaar	
	asulam	Asulox	
Insecticide	flonicamid	Teppeki	Used both in lily and in tulip. Most growers use one of these three insecticides.
	acetamiprid	Gazelle	
	thiacloprid	Calypso	
Fungicide	prochloraz	Mirage plus 570 SC Allure vloeibaar	Used in lily and occasionally used for late season applications in tulip
	trifloxystrobin	Luna sensation (also contains fluopyram); Flint	Most used in lily, also used in tulip
	tebuconazole	Spirit (also contains folpet) Luna experience (also contains fluopyram)	Used in tulip and in lily.

distinguished: environmental samples (air, dust, soil and homegrown vegetables) and personal samples (urine samples and handwipes).

Environmental samples

Target pesticides for the analysis of environmental samples were the ones mentioned in 3.1.1 (Appendix 1; Table 1 and Table 2), environmental breakdown products of these and pesticides that had been found before in soil and plant material from bulb flowers by RIKILT in 2014. Many of the target pesticides can be measured simultaneously in multi-residue methods based on liquid chromatography with tandem mass spectrometry (LC-MS/MS) and/or gas chromatography with tandem mass spectrometry (GC-MS/MS). Nevertheless some pesticides (e.g. glyphosate, mancozeb, mineral oil) would each need a separate dedicated method. For reasons of budgetary constraints, the decision was made to restrict the number of methods to be used for analysis of the environmental samples to one multi-residue method. Comparing LC-MS/MS and GC-MS/MS multi-residue methods, LC-MS/MS covered a larger number of the target pesticides and was therefore selected. The consequence was that certain pesticides that can only be determined by GC-based multi-methods (e.g. chlorothalonil, esfenvalerate, folpet) were excluded from the scope of analysis. The total number of pesticides covered in the environmental analysis was 46[1] (Appendices 2 and 3).

Personal samples

To assess the internal exposure of residents, urine was selected as the biological matrix because of ease of collection and well-established methods for non-persistent compounds. For most pesticides selected for environmental analysis, it would not be meaningful to determine them in urine as such, because upon uptake they are fully metabolized and the original pesticide would not be detectable in urine. Consequently, the target compounds in urine are typically urinary metabolites (biomarkers of exposure).

Compared to the measurement of pesticides in environmental samples, the possibilities for simultaneous quantitative analysis of pesticides biomarkers in residents' urine are limited, for the following reasons:

- Analytical reference standards of the biomarkers, and their isotopically labeled analogues (required for optimum quantitative analysis) are often not available and need to be custom synthesized;
- Optimum measurement of a biomarker typically requires a dedicated analysis method, limiting the options for multi-biomarker analysis;
- For interpretation of the biomarker concentrations in the residents' urine, data on biokinetics are needed which require additional methodologic studies for each individual pesticide (see chapter 2).

[1] This number is larger than the number of pesticide mentioned in Appendix 1, because pesticides previously found in soil/crops from bulb flowers, and metabolites that might also occur as human metabolites in personal monitoring were also included.

According to these three reasons, the number of pesticides for which urinary biomarkers were included was restricted to five. The five were selected from a prioritized short list of eight pesticides expected to be frequently used by the bulb growers, representing different physicochemical properties, and with low(er) likelihood of dietary exposure (Table 3.1). The final selection was an informed decision based on pesticides actually applied in the fields, and findings in the environmental samples in the first stage of the field measurements and included: asulam, chlorpropham, prochloraz, tebuconazole, and carbendazim (note: with the inclusion of carbendazim, also its precursor thiophanate-methyl is included since this compound is converted to carbendazim both in the environment and in the human body). Measured urinary biomarkers of these pesticides were metabolites, except for asulam.

The handwipes, included in the personal monitoring to assess dermal exposure, were analyzed for the same pesticides (parent compounds in this case) as selected for urinary pesticides.

3.2 Locations and fields

3.2.1 Selection of locations and target fields

This section describes the method used to pre-select appropriate measuring locations by using spatial analysis. Spray applications at a field may expose residents to pesticides through spray drift and through volatilization. Houses located within 50 m distance at the lee side of the treated field are assumed directly exposed to spray drift. The pesticide deposited on the crop and/or soil may volatilize and this process is assumed to affect houses within 250 m distance in each direction.

A method was developed to obtain a pre-selection of appropriate measuring locations in a fixed, objective and systematic way (Kruijne et al., 2019). Homes and people can be exposed to pesticides that disperse from several fields and therefore the geographic location of homes in relation to the flower bulb field was considered. The final selection of locations and fields depended on the willingness of the growers and residents to participate in the experiments, the conditions at the field and the field borders, and cultivation plans of the grower.

The flower bulb crops tulip and lily were chosen because these are the largest flower bulb crops with respect to area grown and pesticide use in the Netherlands (Kruijne et al., 2019). The first selection procedure used criteria for the number of homes in four wind directions and within two distances (<25 m and 25-50 m) from a flower bulb parcel and some additional criteria regarding the presence of buildings, trees, hedges which affect the wind and deposition pattern. The method involved the spatial analysis and ranking of the results, followed by a review and visual desk-inspection of the flower bulb parcels with the highest suitability scores.

Due to the spatial structure of residences in the surroundings of the flower bulb parcels in The Netherlands as a whole, the number of potentially appropriate locations was limited. The appropriate locations which met the criteria were situated in the flower bulb growing areas in the provinces of Noord-Holland and Zuid-Holland. This was explained by the regional distribution of flower bulb fields in The Netherlands, and by the different spatial distribution of houses in these flower bulb regions compared to the entire population.

Because of the limited number of appropriate measuring locations, the procedure was repeated with a stepwise relaxation of criteria, like including field cultivating other types of flower bulbs (Kruijne et al., 2019). An evaluation by visiting the location and the growers resulted in the final selection of study locations.

3.2.2 Inclusion of target fields and additional fields

Recruitment of flower bulb growers

The first step in the recruitment of flower bulb growers was to place an article about OBO in 'Bloembollenvisie', a journal of the Bulb Growers' Association KAVB. Then the growers were contacted by phone. Depending on their response, we either directly scheduled a visit or we sent them an information package and called later. When a visit was scheduled during the first phone call, the growers received the information package during our visit.

The information package contained:

- An invitation drafted by the RIVM to participate in the study
- A brochure about the OBO flower bulb study
- A letter of recommendation from KAVB (Royal General Bulb Growers' Association)
- A copy of an article about OBO that appeared in 'Bloembollenvisie' (now called Greenity)

Support from the KAVB proved to be very helpful in gaining trust amongst flower bulb growers. Most growers indicated that after the first contact they would consult the KAVB to discuss if they should participate or not.

During the visit the purpose of the study was explained and growers were stimulated to participate. If the grower was positive about participation, the location of their fields, as well as the grown crops, were mapped. The use of the selected pesticides was also inventoried.

Finding growers willing to participate proved to be more difficult than expected. One of the main reasons was that the information used on grown crops and land ownership was outdated (from 2014). Fields are frequently leased to colleagues and some had changed ownership in the meantime. Because of crop rotation, there were no flower

bulbs on some selected fields, while other fields that did have flower bulbs were not selected. To overcome this, a map was brought to each visit in which the fields belonging to each individual grower were highlighted. Current and future crops, if already known, were also noted.

During the period of field visits an information meeting for growers was organized to explain the OBO flower bulb study and answer growers' questions. KAVB also participated in this meeting.

Results of recruitment

The selection of eligible fields resulted in 70 potential locations. 56 locations were dropped because there were no flower bulbs present at the time, growers did not want to participate or none of the selected pesticides were going to be applied. Eventually, twelve growers were willing to participate of which ten growers had fields that matched the criteria, which resulted in fourteen eligible target fields. Nine target fields were selected for the residents' field study, owned by eight different flower bulb growers.

3.2.3 Field monitoring and data collection

Field monitoring

Most of the contact with the growers was done by phone and email. During the spraying season, growers contacted CLM if they planned to use a selected pesticide. CLM informed other parties to start the environmental monitoring. Prior to the spraying event, a tank sample was taken.

Collecting spray registration

At the end of 2016 and 2017, information on spray registration of the eight participating flower bulb growers was requested. This information was anonymized, coded and sent to the OBO data manager.

In addition, growers that grew crops on other fields within 250 meters of participating residents were contacted and asked to share their spray registration pertaining to these fields. These are referred to as additional fields. Not all growers were willing to share their spray registration. In these cases, standard spray schemes were used. Some additional fields were near multiple target fields. Of the 135 individual fields of which the spray registration was required, registrations from 58 parcels were received. Registrations of five of these fields lacked important data and were therefore not included in the results shown in chapter 4 and the modeling in chapter 6. Standard spray schemes were used for 74 fields. For the three remaining fields CLM could not create standard spray schemes for the specific crop types.

3.3 Selection of homes and residents

Sample size calculation

Before the project started, a power calculation was performed to assess how many participants should be included. Based on NHANES data (Center of Disease Control, USA), taking urinary 3-Phenoxybenzoic acid, a metabolite of pyrethroid pesticides, it was estimated that 80% power at an alpha of 0.05 to detect a 40 to 100% difference between exposed subjects and background levels (mean 0.292 µg/l; SD 0.26) assuming an exposure prevalence of 100% and 50%, respectively, would be reached with 200 residents.

Selection of addresses and participants

After selection of a target field, all residential addresses within 250 m of the perimeter of the target field were identified using the Dutch cadastral data "Basisregistraties adressen en gebouwen" (BAG). Potential control homes were also selected using the cadastral data to identify homes in medium to low urbanized areas (i.e. <1500 addresses/km^2), situated within 20 km from a target field, and not having agricultural fields within 500 m of the home.
Invitation letters and a brochure were sent to all selected addresses. Interested invitees were interviewed by phone using a structured interview script to check if they fulfilled the inclusion criteria.

Inclusion criteria for the residents' field study were:

- Having his/her primary place of residence at the pre-selected (target/control) location;
- Ability to complete the administered questionnaires or communicate with the study assistant (sufficient knowledge of the Dutch language and no cognitive impairment);
- No doctor diagnosed kidney or liver disease as these could change metabolite formation.

Study participants were asked about availability and willingness of further household members to participate in the study. If available, children (aged < 18 years) were also asked to participate. Inclusion criteria were also applied to these potential additional study participants.

Response rate

The OBO flower bulb study initially aimed to include 100 homes with 200 residents. In total, 1778 residential addresses at target locations and 482 addresses at control locations were selected. At the target locations, 80 homes were included corresponding to a response rate of 4.5% and a range in response rate from 2.1% to 33.3% by target location. Sixteen control homes were included (response rate: 3.3%). The number of people participating in a home ranged from one to six and in total 164 residents from location homes and 28 controls were included in the study. In total, 96 homes

and 192 residents were included. This is slightly under the aimed numbers. Not all homes participated in all measurement campaigns as three homes missed one of the two seven-day measurement campaigns due to holidays and four homes ended their participation before the end of the study.

3.4 Materials and methods of the resident field study

The resident's field study was approved by the Medical Ethical Committee of the Utrecht Medical Center of Utrecht University. The study took place from May 2016 to December 2017. Measurements in the spraying season were conducted per location for seven consecutive days, with a spray event on the target field as starting point. Two-day measurements were performed in a period without spray events with the selected pesticides on the target field (October - February). In this report we refer to all conducted measurements at one location during a seven- or two-day period as "measurement campaign". In Figure 3.1 the infographic of all residential measurements is shown.

3.4.1 Questionnaires and diaries

Data on house characteristics, participants demographic, and lifestyle information were collected using questionnaires, field forms and diaries. Per home, a questionnaire on home characteristics was filled out by one of the adult participants. At the first home visit the research assistant completed a field form on building characteristics.

Each participant also completed a questionnaire on personal characteristics, socio-economical position, presence of pets, use of medication, educational level, type of work/education and contact with pesticides. Parents were asked to fill in the questionnaires for their children. Questionnaires were completed before the measurement campaign started. If a second measurement week was performed in a home, all participants filled in a short questionnaire on characteristics that changed since they completed the first questionnaire.

During the measurement campaigns, participants filled out a daily diary on food intake, hours spent at home and/or elsewhere and personal use of chemicals or pesticides.

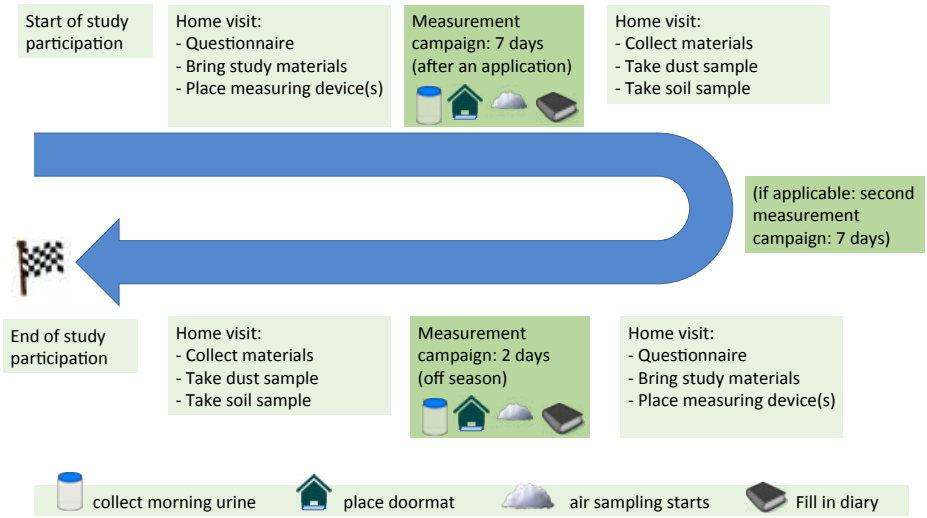


Figure 3.1: Infographic on the residents' field study.
The flow of participation as a resident to the measurement campaigns.

Figure 3.2: Outdoor air sampling.
Air sampling set up for outdoor sampling with the air pump in its housing on the ground and the seven PM10 sample inlets above. All samplers are switched on at the same time remotely through GSM links.

3.4.2 Air monitoring

Air samples were taken outside participating homes and inside the homes participating in protocol B (within 50 m of the edge of the field). Here we describe our procedures concerning sampling and siting of samplers in the field.

Outdoor air sampling

According to protocol A, sampling started at the time the grower notified that he/she planned to carry out an application (spray event). At that time, sampling was started remotely via GSM connection with the pumps. Figure 3.2 shows the air sampling setup with the pump in its housing on the ground. A protocol was drafted dealing with the positioning of the air samplers. This was a tradeoff between practical options and scientific demand. The scientific demand is described as: sampling should take place on a location where the flow of air coming from the target field was not hindered by obstacles, yet at the same time as close to the house that a sample representative of the exposure of the residents could be taken. Similar demands were valid for in house sampling. Here the sampling should be representative of in-house exposure of residents. For measurement protocol A the air sampling unit was positioned according to the following guidelines:

- The site is not accessible to the public
- The site has main power supply within 20 m
- The site is not so close to a house that the sound of the pump may be a burden to the residents or neighbors,
- The site has a free flow of air coming from the target field

Finding suitable locations appeared to be difficult and the ideal solution was not possible in all cases. Pumps were usually placed in the backyard of the homes. This could mean that a building (e.g. the residents' home) could stand in between the sprayed target field and the sampling unit.

Air was sampled through a standard PM10[2] inlet and drawn through a glass fiber filter and a tube containing XAD-2 absorbent (Amberlite XAD-2). The filter/XAD-2 combination absorbs both gaseous and particle bound pesticides. Because of the PM10 inlet only pesticides absorbed to particles smaller than 10 µm are sampled. Sampling by all samplers positioned at the homes in the study (and inside the homes in the B protocol) was started at the same time. Sampling rate was controlled at 60-70 l/min. After the start of the protocol, sampling was continued for a 24-hour period using the first inlet, filter/ XAD-2 set. After that 24 h period, sampling was started using the second inlet and filter set, and so on. At the end of the seven-day period, the filter/ XAD-2 samples were collected and transported to the laboratory for extraction of the filters and XAD-2 followed by chemical analysis by LC-MS/MS.

[2] PM10 Particulate Matter with a diameter less than 10 µm. This inlet is meant to prevent particles larger than this size to enter the sampler and reach filters.

Indoor air sampling

Protocol B sampling indoors started at the same time as protocol A sampling.

For the environmental monitoring indoors, a pump (placed in a box) with a lower capacity (drawing 25 L air/min) was used. Air was drawn through a filter holder equivalent to the outside sampler, described above, containing a glass fiber filter and XAD-2 absorbent tubes. The device contained one filter holder as only one 24-hour sample was taken. It was switched on and off remotely. The location of in-house sampling devices according to protocol B had similar guidelines as the outdoor pumps:

- No burden to the residents
- Free flow of air from the rest of the house to the room where the sampling takes place
- A suitable power supply.

Figure 3.3 illustrates a typical set up.

Figure 3.3: Indoor air sampling.
Air sampling setup used indoor with the air pump in its housing on the floor in an acoustically well insulated box and one PM10 sample inlet above. The pump drawing approx. 25 L/min is connected to the filter holders. The whole system is placed inside the home (often the kitchen) All samplers are switched on at the same time using a GSM link remotely.

Analyses of air samples

The samples were transported to the TNO laboratories and treated as follows:
TNO laboratories transferred the XAD-2 and the glass filter from the sampling filter holder into a metal extracting cell. A mix of Deuterium labelled pesticides was added to the samples to act as an internal standard.
The samples were extracted using low temperature *Accelerated Solvent Extraction* (ASE) and concentrated to a fixed volume of 1000 µl. With each batch of samples, a reagent blank and a quality control sample were included. The quality control consists of 5 ng/pesticides mixture added to 10 g blank XAD-2.

The pesticide concentration in the concentrated extracts was determined using liquid chromatograph coupled to a Mass spectrometer LC-MS/MS. Details on the analysis are given in Appendix 2. LODs were 0.003 ng/m^3 for most pesticides, 0.006-0.03 ng/m^3 for six pesticides (see Appendix 2) based upon the average sample volume of air used and from validation. The average recoveries of the pesticides were typically in the range 50-150%. Within laboratory reproducibility (relative standard deviation, RSD_{wl}) was generally around 20% at the 0.05 ng/ m^3 level.
The concentrations in the samples were calculated in ng/m^3. The actual, measured, volume of air that was used to load the filter/XAD-2 combination was used to calculate these concentrations. The results included a quantification of the LOQ (limit of quantification) and the LOD for each pesticide in each sample. The LOD (limit of detection in ng/m^3) was determined based upon the average sample volume of air used and from validation studies. Here the LOQ was estimated as 10 times the standard deviation of the lowest concentration measured. The LOD was derived as three times this standard deviation.

3.4.3 Indoor environment

Sampling of two types of indoor dust was performed in all homes in protocol A.

Vacuumed Floor Dust (VFD)

In all participating homes, vacuumed floor dust (VFD) was collected from the living room by the research assistant after the sampling week. For this, a sample sock (Allied Filter Fabrics, Hornsby, Australia) was attached to the hose of a vacuum cleaner. Initially, the research assistant vacuumed 2 m^2 of carpet or 4 m^2 of smooth floor for two minutes. After the first samples were analyzed, this was increased to 4 m^2 of carpet or 6-8 m^2 of smooth floor, depending on available free floor space, to increase the amount of dust collected. Sampling time was increased to five minutes. Sampling duration and area were recorded. The sample amount varied from 0.02 to 28 grams, with a median value of 0.37 gram. Samples were stored at -18°C until sample selection and analysis.

Determination of pesticides

For determination of pesticides in the dust samples, a multi-residue method was used based on QuEChERS extraction (Lehotay 2007) and LC-MS/MS. This way, all 46 selected pesticides and relevant metabolites could be measured simultaneously in one analysis run.

In brief, the entire dust sample was extracted with water and acetonitrile/1% acetic acid by mechanical shaking. Salts were added to induce phase partitioning. An aliquot of the organic phase containing the pesticides was evaporated to dryness and reconstituted in water/acetonitrile. The extract was analyzed by LC-MS/MS. Pesticides were quantified by 1-point standard addition. A more detailed description of the method can be found in Appendix 3.

With each batch of samples, a reagent blank and a quality control were included. The positive control was prepared by spiking a 1 g subsample from a batch of control dust at 10 or 50 µg/kg.

In-house validation and on-going analytical quality control were done according to EU guidance document SANTE/11945/2015 (currently SANTE/11813/2017). LOQs, here defined as the lowest successfully validated concentration, were 1 µg/kg for most pesticides, 3-20 µg/kg for nine pesticides (see Appendix 3, Table 2). Trueness was assessed through recovery. The average recoveries of the pesticides were typically in the range 70-110%. Within laboratory reproducibility RSD_{wl} was generally around 20% at the 10µg/kg level, and <20% at the 50 µg/kg level.

Dust doormat dust (DDM)

In each home, a clean doormat was cut to applicable size and placed at the main entrance by a participant on the day of the spray event (Figure 3.1). The doormat was collected by the research assistant within 5 days after the end of the measurement campaign and transported in a clean box to the laboratory. The size of the doormat and start and end date of collection were recorded. In the laboratory, all dust material was collected from the doormat by vacuum cleaning with a sample sock (Figure 3.4). The amount of dust material retrieved from the doormat varied from 0.55 to 196 grams, with a median of 6.0 grams. Samples were stored at -18°C until sample selection and analysis.

The analysis of the dust material was done as described for vacuumed floor dust above.

Both vacuumed floor dust and dust material from doormats were highly heterogeneous, containing sand, dirt, hair, fibers, and dust (see Figure 3.5). In all cases, the entire dust sample was extracted, using a fixed ratio of g dust: ml extraction solvent.

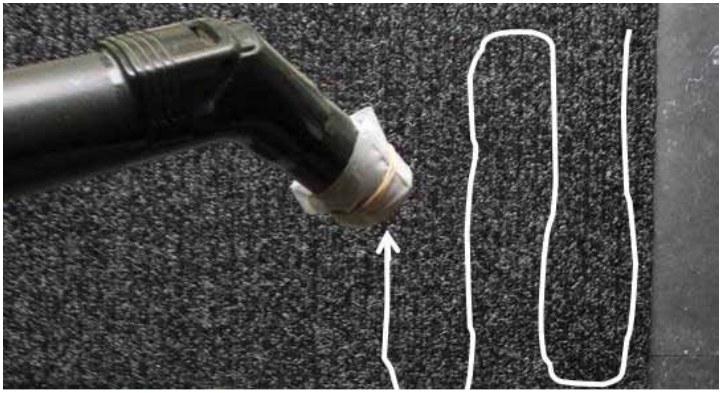


Figure 3.4: Collection of dust material from doormat by vacuum cleaning with sample sock.

3.4.4 Outdoor environment

From the garden of participating homes, a soil sample was taken. Five uncovered areas of soil were randomly selected in the garden and approximately 150 – 250 grams of top soil were collected per area and combined into a single soil sample. Upon receipt in the laboratory, samples were thoroughly mixed and stored at -18°C until sample selection and analysis.

If participants had homegrown fruits or vegetables, the research assistant requested a 'harvest ready' sample for analysis. If not available, unripe crops or leaves were sampled in some cases. Upon receipt in the laboratory, the samples were homogenized in a food cutter or blender and stored at -18°C until and analysis.

Determination of pesticides in soil and crops

For determination of pesticides in the soil and plant material, a multi-residue method was used based on QuEChERS extraction (Lehotay 2007) and LC-MS/MS. This way, all selected pesticides and relevant metabolites (total of 46) could be measured simultaneously in one analysis. In brief, 5 grams of homogenized soil or plant material was extracted with acetonitrile/1% acetic acid by mechanical shaking. Salts were added to induce phase partitioning. An aliquot of the upper acetonitrile layer was diluted with water. The extract was analyzed by LC-MS/MS. Pesticides were quantified using 1-point bracketing matrix-matched calibration. A more detailed description of the method can be found in Appendix 3.

With each batch of samples, a reagent blank and a quality control were included. The positive control was prepared by spiking 5 g of a blank soil or plant material sample at 10 µg/kg.

In-house validation and on-going analytical quality control were done according to EU guidance document SANTE/11945/2015 (currently SANTE/11813/2017). LOQs, here

Figure 3.5: Examples of dust samples.

defined as the lowest validated concentration, were 1 µg/kg for most pesticides, 3-10 µg/kg for some pesticides (see Appendix 3). Trueness was assessed through recovery. The average recoveries of the pesticides were typically in the range 70 - 110%. Within laboratory reproducibility (relative standard deviation) was generally <20% at the 10 µg/kg level.

3.4.5 Personal monitoring

Personal monitoring consisted of the collection of two types of samples by the participants themselves: urine samples and hand wipes (part of protocol B). The urine collection was subdivided into morning urine (part of protocol A) and in first day urine (part of protocol B) collection. All collection materials were provided by the research assistant and samples were collected according to the provided written instruction materials.

3.4.5.1 Urine samples

Morning urine (protocol A)

Participants collected morning urine on seven consecutive days, starting the morning after a spray event. Time of urine collection and the time of the previous toilet visit was registered in the diary. Samples were stored at 4°C until picked up by the research assistant. Subsequently, the samples were aliquoted in the laboratory. Aliquots were stored at -18°C until selection and analyses. Morning urine was also collected by the control subjects and in the two-day measurement campaign.

For toddlers who were non-toilet trained at the time of the study, a diaper was collected at the same time-periods as the adults. The diapers were stored in a sealed bag at 4°C, and stored at -18°C upon arrival in the laboratory until analysis. For a detailed description, see chapter 2.

First day urines (protocol B)

Residents in protocol B, living closer than 50 m to the edge of the field, collected all urine voids from the start of the spraying event until the next morning, if they were at home. Times of urine collection and urine samples that were not collected when they were not at home were registered in the diary. Urine samples were also stored at 4°C until picked up by the research assistant, aliquoted and stored at -18°C until selection and analyses. After collection of a urine sample on the next morning after the spray event, the participants continued to collect their morning urine (only) on days 2 – 7. All diapers from non-toilet trained toddlers were collected until the following morning.

Table 3.2: Target biomarkers and additional biomarkers.

Target biomarker	Additional biomarkers
tebuconazole-1-hydroxy (TEB-OH)	metolachlor mercapturate, trifloxystrobin-acid, boscalid-OH, spirotetramat-enol
4-hydroxychlorpropham-O-sulphonic acid (4-HSA)	boscalid-OH, flonicamid, imidacloprid, metamitron, metamitron-desamino, spirotetramat-enol, trifloxystrobin-acid
2,4,6-trichlorophenoxyacetic acid (2,4,6-TCP)	No additional biomarkers
Asulam	boscalid-OH, flonicamid, imidacloprid, metamitron, metamitron-desamino, spirotetramat-enol, trifloxystrobin acid
methyl 5-hydroxy-2-benzimidazole carbamate (5-HBC, hydroxy-carbendazim)	acetamiprid, boscalid-OH, flonicamid, fluopyrambenzamide, imidacloprid, metamitron, metamitron-desamino, metolachlor-mercapturate, propamocarb, prothioconazole-desthio, thiacloprid, trifloxystrobin-acid

Analyses of urines

The urine samples were analyzed for the target biomarker of exposure according to the sample selection. The selection process is described in chapter 3.4.7. The target biomarker was determined using a validated analytical method. Some of the methods also included the detection or semi-quantitative determination of additional pesticide biomarkers. For these additional biomarkers, the method was either not validated or it was validated but the performance characteristics did not meet the criteria for quantitative analysis. Therefore, concentrations reported for these additional biomarkers should be considered as indicative. Table 3.2 provides an overview of the target biomarker and the additional biomarkers.

Analysis of TEB-OH (biomarker for tebuconazole)

For sample analysis, samples were thawed at room temperature prior to sample preparation. An aliquot of 5 mL of urine was transferred to an Erlenmeyer, and 50 µL of the internal standard working solution was added, resulting in a final concentration of 1 ng/mL of D6-TEB-OH in urine. For deconjugation, 5 µL of *Helix pomatia* β-glucuronidase/arylsulfatase was dissolved per 2.5 mL acetic acid solution in milliQ water (0.25 M, pH 4.75), and 2.5 mL of this mixture was added to each sample. The samples were incubated overnight for at least 16 h at 37 °C, and then a subzero-temperature liquid-liquid extraction was performed as previously described by Yoshida and Akane (1999). One mL of the acetonitrile layer was transferred to a vial for subsequent LC-MS/MS analysis. A more detailed description of the method can be found in Appendix 4.

With each batch of samples, the calibration curves, and blank acetonitrile and milliQ water were freshly prepared and measured three times during the batch analysis for quality control purposes.

In-house validation and on-going analytical quality control was done according to SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for TEB-OH was 0.05 ng/ml in urine. For the other pesticides/biomarkers quantification was matrix-matched based on the calibration curve, and if matrix-effects were found to vary considerable for different urine samples, these biomarker levels could only be determined semi-quantitatively. Moreover, no labelled standards were included for these compounds. Estimated LOQs were 0.05 ng/ml for metamitron-desamino, spirotetramat-enol, trifloxystrobin-acid and boscalid-OH (M150F01).

Determination of 4-HSA (biomarker for chlorpropham)

4-HSA is a sulfate-conjugate of chlorpropham and most sensitively detected as such, so without deconjugation.

For sample analysis, urine was thawed and re-homogenized by vortex mixing. A 0.9 ml aliquot was mixed with 0.1 ml of internal standard solution and transferred into an Amicon 30kDa Ultra-centrifuge filter (10 min, 3500xg). The filtrate was analyzed by

LC-MS/MS without further clean-up. The response of 4-HSA in samples and calibrants in blank urine was normalized to the response of the D7-4-HSA internal standard. Quantification was done using 1-point bracketing matrix-matched calibration. A more detailed description of the method can be found in Appendix 4.

With each batch of samples, a reagent blank (milliQ) and a positive control were included. The positive control was prepared by spiking one of the samples from the batch with the pesticide/biomarker mix at 2 ng/ml urine.

In-house validation and on-going analytical quality control was done according to SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for 4-HSA was 0.1 ng/ml urine. With this method, asulam could also be quantitatively determined, with an LOQ of 1 ng/ml (for more sensitive determination of asulam see the dedicated method described below). Semi-quantitative determination with estimated LODs for additional pesticide biomarkers were as follows: 0.1 ng/ml for imidacloprid, flonicamid, metamitron-desamino, trifloxystrobin-acid, spirotetramat-enol; 0.5 ng/ml for metamitron, boscalid-OH (M150F01), 5-HBC.

The average RSD_{wl} as obtained for 2 ng/ml 4-HSA spikes analyzed together with the field samples were 97% and 11%, respectively.

Note: since this method does not include a deconjugation step, it only determines non-conjugated forms of pesticides metabolites, which in certain cases (especially for boscalid-OH (M150F01) and 5-HBC) are minor urinary metabolites.

Analysis of 2,4,6-TCP (biomarker for prochloraz)

For sample analysis, samples were thawed at room temperature prior to sample preparation. An aliquot of 5 mL of urine was transferred to an Erlenmeyer, and 5 µL of the internal standard working solution was added, resulting in a 1 ng/mL concentration of 6C13-2,4,6-TCP in urine. For deconjugation purposes, 5 µL of Helix pomatia β-glucuronidase/arylsulfatase was dissolved per 2.5 mL acetic acid solution in milliQ water (0.25 M, pH 4.75), and 2.5 mL of this mixture was added to each sample. The samples were incubated overnight for at least 16 h at 37 °C under gentle agitation, and then a solid phase extraction (SPE) clean-up/concentration step was performed. The SPE eluent was evaporated to dryness and reconstituted in 1 mL of 50% water, 50% acetonitrile and 0.1% formic acid and transferred to a vial for subsequent LC-MS/MS analysis. A more detailed description of the method can be found in Appendix 4.

With each batch of samples, the calibration curves, and blank acetonitrile and milliQ water were freshly prepared and measured three times during the batch analysis for quality control purposes.

In-house validation and on-going analytical quality control was done according to

SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for 2,4,6-TCP was 0.25 ng/ml in urine. Other pesticides/biomarkers could not be determined with this method as the SPE washing steps, buffers and LC conditions were fully optimized for 2,4,6-TCP to reach an acceptable LOQ.

Determination of asulam (biomarker for asulam)
Asulam is mainly excreted through urine unmetabolized. Therefore, similar as for 4-HSA, no deconjugation step is required. The 4-HSA method turned out to be less sensitive and lacked robustness for determination of asulam, and therefore a separate method needed to be developed.

For sample analysis, urine was thawed and homogenized by vortex mixing. The extraction method was based on the QuEChERS approach (Lehotay 2007). In brief, to 1.8 ml of urine, 0.2 ml of a D3-asulam internal standard solution was added after which extraction was done with acetonitrile/1% acetic acid. Then, salts were added to induce phase separation. The acetonitrile phase was analyzed by LC-MS/MS. The response of asulam in samples and calibrants was normalized to the response of the D3-asulam internal standard. Quantification was done using 1-point bracketing calibration. A more detailed description of the method can be found in Appendix 4.

With each batch of samples, two reagent blanks (milliQ) and two positive controls were included. The positive control was prepared by spiking two samples from the batch with the pesticide/biomarker mix at 2 ng/ml urine.

In-house validation and on-going analytical quality control was done according to SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for asulam was 0.1 ng/ml urine. Semi-quantitative determination with estimated LODs for additional pesticide biomarkers were as follows: 0.1 ng/ml for 4-HSA, imidacloprid, flonicamid, metamitron-desamino, trifloxystrobin-acid, and 0.5 ng/ml for 5-HBC, spirotetramat-enol, metamitron, and boscalid-OH (M150F01).

The average RSD_{wl} as obtained for asulam 2 ng/ml analyzed together with the field samples were 104% and 13%, respectively.

Note: since this method does not include a deconjugation step, it only determines non-conjugated forms of pesticides metabolites, which in certain cases (especially for boscalid-OH (M150F01) and 5-HBC) are minor urinary metabolites.

Determination of 5-HBC (biomarker for carbendazim and thiophanate-methyl)
Thiophanate-methyl is used for bulb disinfection and degrades into carbendazim in the environment. 5-HBC is a urinary biomarker for both thiophanate-methyl and carbendazim. Hence, 5-HBC found in urine may come from either thiophanate-methyl or carbendazim exposure. In urine, 5-HBC is (partially) excreted as conjugates. For the

determination of total 5-HBC, a method involving an enzymatic deconjugation step was developed.

For sample analysis, urine was thawed and homogenized by vortex mixing. An aliquot of 3 ml of urine, after addition of $^{13}C^{-15}N$-5-HBC internal standard, was enzymatically deconjugated overnight. The biomarkers were extracted with 6 ml acetonitrile/1% acetic acid by shaking. Then, salts were added to induce phase separation. An aliquot of the acetonitrile extract was evaporated to dryness and reconstituted in methanol/water. The concentrated extract was analyzed by LC-MS/MS. The response of 5-HBC in samples and calibrants was normalized to the response of the $^{13}C^{-15}N$-5-HBC internal standard. Quantification was done using 1-point bracketing calibration. A more detailed description of the method can be found in Appendix 4.

With each batch of samples, one reagent blank (milliQ) and two positive controls were included. The positive control was prepared by spiking two samples from the batch with the pesticide/biomarker mix at 2 ng/ml urine.

In-house validation and on-going analytical quality control was done according to EU guidance document SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for 5-HBC was 0.05 ng/ml urine. Semi-quantitative determination with estimated LODs for additional pesticide biomarkers were as follows: 0.05 ng/ml for acetamiprid, carbendazim, flonicamid, metolachlor-mercapturate, prothioconazole-desthio, thiacloprid, and trifloxystrobin-acid (CGA321113); 0.1 ng/ml for boscalid-hydroxy M510F01 and tebuconazole-OH; 0.5 ng/ml for asulam, fluopyram-benzamide, imidacloprid, metamitron, metamitron-desamino, propamocarb.
The average RSD_{wl} as obtained for 5-HBC 2 ng/ml analyzed together with the field samples were 102% and 11%, respectively.

Creatinine

Creatinine was analyzed after centrifuging the sample but prior to further pre-treatment of the samples by the laboratory for clinical chemistry of Radboud university medical center according to the Jaffe method (Slot, 1965). Urine samples were corrected for creatinine by dividing the urine results (ng/mL) by the creatinine values (mol/mL) and adjusting for creatinine molar mass (113.12 g/mol). The results in chapter 4 are therefore presented in ng/ug creatinine.

3.4.5.2 Handwipes (protocol B)

For dermal exposure assessment, hand wipes were collected from participants in protocol B. The wipe material consisted of a pre-wetted (3 mL 50% water and 50% ethanol) paper tissue (art no. 8382, Kimtech Science, Irving, Texas, USA) stored in an air-tight plastic container (art no. 2114-0006, Thermo Scientific, Rochester, USA). Both hands on both sides were wiped in the evening (preferably before dinner) on day of the spray event by the participant themselves according to provided instructions. The day and time of collection of the wipe sample was recorded in the diary and the wipe sample was stored at 4°C until collected by the research assistant. Afterwards it was stored at -18°C until analysis.

Analysis of hand wipes

The hand wipes were analyzed in a multi-method for the five target substances, i.e. tebuconazole, chlorpropham, prochloraz, asulam and carbendazim. The sample extraction was performed in the plastic container in which the wipe was stored. This reduces the extraction losses. A detailed description of the sample extraction and analysis is described in Appendix 5.

For sample extraction, specimens were thawed at room temperature prior to sample preparation. The wipes were cut in 64 small pieces and these were put back in the same container. 80 mL of methanol was added, and the container was placed in an ultrasonic bath for 1 h, followed by 10 min on a mechanical shaker. 8 mL of methanol extract was transferred to a test tube and dried at 40°C under a gentle flow of nitrogen. The dried extract was dissolved in 1 mL of 50% methanol and 50% water and was centrifuged at 2000 RCF to remove remaining fibers. The supernatant was transferred to a vial for subsequent LC-MS/MS analysis.

With each batch of samples, the calibration curves, and blank wipe extract, methanol and milliQ water were freshly prepared and measured three times during the batch analysis for quality control purposes. The LOQs for the target compounds were as follows: 0.25 ng/wipe for tebuconazole, 2.5 ng/wipe for chlorpropham, 1.0 ng/wipe for prochloraz and 0.5 ng/wipe for asulam and carbendazim.

3.4.6 Tank samples from target field

Collection of tank samples

Spray parameters, such as driving speed and nozzle type, were registered in the field. Duplicate tank samples of the spraying liquid were taken directly before and directly after the spray event. Aliquots of the tank samples were stabilized with methanol, transported under cooled conditions and delivered to RIKILT for further processing and analysis.

Analysis of tank samples

Tank mix samples were taken in the field and processed in a dedicated laboratory room, i.e. separated from the trace analysis samples. The content of the vial containing the tank mix was weighted, mixed and then sequentially diluted in methanol to reach concentrations within the linear range of LC-MS/MS analysis (typically 10,000x). Analysis of the diluted mixtures was done by LC-MS/MS (instrument conditions, see environmental samples (soil/plant material) in Appendix 3, Table 1). For this purpose, analysis was restricted to pesticides applied/registered during the spray event. Quantification was done against solvent standards. With the strong dilution factor employed, matrix effects were considered negligible.

3.4.7 Selection of samples for analysis

After collection of all samples, due to budgetary constraints, not all collected environmental and personal samples were analyzed. The objective of the selection procedure for the location homes was to maximize contrast in exposure. For this aim, a simplified approach using a Gaussian plume dispersion model was applied. The model took different factors into account that influence the dispersion of pesticides starting from the moment of application on the crop. These factors included:

- Distance between the target field and the home;
- Wind conditions (wind direction and speed);
- Climatic conditions (cloud cover);
- Relative position of the house to the field (angle to midpoint of field);
- Difference in source strength between the moment of spraying and volatilization in the following days.

Estimates from the model were used to select approximately 40-50% of the location homes for analysis of the outdoor air samples, including at least one low exposed home. In the selection of the exposed homes the distance to the field and the area of other agricultural fields surrounding the home were also considered to select samples from different distances. Selections were done per seven-days measurement campaign, meaning that if a home participated in two seven-day measurement campaigns, it could be included in neither selection, both selections or only one. If a home was selected for inclusion of a seven-day measurement campaign, the samples from the two-days measurement campaign were also analyzed. All control homes were selected for analyses.

From the selected homes, all collected environmental samples were analyzed. As air samples were not always available due to pump failure, an additional selection for air samples was performed to include more outdoor air samples and also all indoor samples. This selection included all homes participating in protocol B that were not yet selected in the initial selection procedure. Here, only air samples were analyzed.

Similar to the procedure for environmental samples, a selection was made for urine samples. For the analyses of urine samples, selection of residents was based on the selection of homes:

- All children (under 18 years) living in a selected home were included in the analyses of urine samples and one adult per selected home was selected.
- If no children were living in a selected home, maximal 2 adults were included. Of adult samples, the adult(s) with the most complete set of urine samples was selected for analysis.

Urine samples from day 1, 2, 4 and 7 of a seven-day measurement campaign were selected for analyses together with both samples of the two-day measurement campaign.

Hand wipes were only collected from residents participating in protocol B. All hand wipes of selected individuals were included in the analysis.

Homes were selected based on distance to field and contrast of possible exposure due to spraying, therefore these cannot be seen as a population mean. Although proper randomization was not achieved, this selection was imperative to study influence of distance and to have a set of homes that differ between each other.

It has to be noted that a few environmental samples were lost in the procedure due to pump failure or lost during collection. That means that the number of samples in the result section may not always correspond to the expected number of samples.

3.4.8 Data handling and statistical methods

Data collection

All data collected from the residents' field study were transferred to the OBO data manager at Utrecht University. Meteorological data was obtained from the closest weather station of the Royal Netherlands Meteorological Institute (KNMI).

Results below the LOD

The LC-MS/MS technique has pesticide-specific limits of detection (LOD) and limits of quantification (LOQ). In the OBO flower bulb study we use the LOD as cut-off for detection as levels above the LOD but below the LOQ may be more accurate than imputed values (Succop, 2004). For levels below the LOD, imputation was done when the pesticide (biomarker) was detected (>LOD) in at least 40% of the measured samples. Imputation was performed using the method proposed by Lubin et al. (2004). This consists of imputing the values below LOD based on the maximum likelihood estimation, while accounting for the distribution of the data and correlation between different compounds in the same medium.

Period

Environmental samples (air and dust) were grouped according to the period of sampling: during the period the pesticide was used (use period) or outside the period the pesticide was used (non-use period). Periods of application of each pesticide based on reported applications were summarized. Based on this descriptive summary, shown in Appendix 6, for each pesticide the collected samples were grouped by use period and non-use period.

Statistical methods

All data analyses were performed using R, version 3.5. For statistical tests ANOVA, Student's t-Test and Wilcoxon test were used. To test for association between paired samples, Pearson's product moment correlation coefficient was used. Spearman's rank correlation coefficient was used to study the relationship between two variables. P-values below 0.05 were considered statistically significant. In chapter 6 a brief explanation is given on the statistical methods used for statistical model selection. The models in question were built by fitting a linear mixed-effects model to the data, via Restricted Maximum Likelihood Estimation (REML). Selection of parameters was done using an automatic backward elimination procedure.

4. Results from the residents field study

4.1 Fields, homes, participants and measurement campaigns

4.1.1 Fields

Target locations and control locations

Nine target fields were included in our study. A target location (or "location") is defined as a target field, the surrounding participating homes and the surrounding additional fields. Additional fields can overlap between locations. Table 4.1 shows the locations, the size of the target field at each location, the type of flower bulbs cultivated in the period that our measurements were performed, the conducted measurement campaigns, and the applied pesticides with their concentrations. As outlined in chapter 1.2.1, measurements were also taken at control locations. Control locations were at least 500 m away from any agricultural field, had a similar urbanization grade as the locations and were within 20 km of a target field.

Measurement campaigns

Measurement campaigns were seven-day or two-day periods of sample collection at a location. We aimed to follow two spray events on each target field. In total 14 seven-day measurement campaigns following a spray event were completed (Table 4.1). Also two-day measurement campaigns outside the spraying season at both target and control locations were completed (Table 4.1). Eleven spray events included one or more of our selected pesticides in a mixture while three of the spray events were performed with only a selected pesticide (Table 4.1). Self-reported dosage and measured dosage of the used pesticides are also presented in Table 4.1. The sprayed substances folpet, mancozeb, chlorothalonil, esfenvarelate, quinmerac and mineral oil were outside the scope of the LC-MS/MS multi-methods used (see chapter 3). Differences between self-reported and measured dosages are small. For the modelling in chapter 6 we used the self-reported dosages because those were available for all used pesticides.

Table 4.1: Characteristics of spray events in the resident field study (part 1).

Location	Target field size [ha]	Type of bulbs on target field	Measur-ment campaign	Sprayed #	Self reported dosage [kg/ha]	Mean measured dosage [kg/ha]	Additional fields			
							Nr of fields	(%) spray reg.	(%) assumed reg. (scheme)	(%) no usable reg. or scheme
A	2.45	Hyacinthus and fritillaria	1	Folpet	0.23	n.d.	18	50%	44%	6%
				Mancozeb	1.50	n.d.				
				Tebuconazole	0.05	0.06				
				Thiacloprid	0.12	0.11				
			Outside season	n.a.	n.a.	n.a.				
B	2.29	Lilium	2	**Flonicamid**	0.07	0.06	18	50%	44%	6%
				Fluopyram	0.08	0.07				
				Trifloxystrobin	0.08	0.06				
			Outside season	n.a.	n.a.	n.a.				
C	2.00	Fritillaria	3	**Chlorpropham**	0.80	0.76	18	17%	67%	16%
				Pendimethalin	0.80	n.d.				
			4	Mancozeb	1.88	n.d.				
				Tebuconazole	0.15	0.15				
			Outside season	n.a.	n.a.	n.a.				
D	0.43 0.66	Allium Narcissus	5	**Chlorpropham**	0.80	0.88	23	22%	65%	13%
				Pendimethalin	0.80	0.69				
			6	Chlorothalonil	0.50	n.d.				
				Esfenvarelate	0.01	n.d.				
				Mancozeb*	1.24	n.d.				
				Prochloraz*	0.16	0.10				
			Outside season	n.a.	n.a.	n.a.				
E	4.58	Tulip	7	**Acetamiprid**	0.05	0.07	18	67%	33%	0%
				Esfenvarelate	0.01	n.d.				
				Mancozeb	1.50	n.d.				
				Mepanipyrim	0.15	0.20				
			8	**Cyhalotrin-Lambda**	0.01	n.d.				
				Mancozeb	1.50	n.d.				
				Flonicamid	0.07	0.07				
				Tebuconazole	0.08	0.07				
			Outside season	n.a.	n.a.	n.a.				
F	1.83	Hyacinthus and fritillaria	9	Folpet	0.15	n.d.	16	56%	31%	13%
				Tebuconazole	0.15	0.17				
			10	**Acetamiprid**	0.05	0.08				
			Outside season	n.a.	n.a.	n.a.				

(Table 4.1 continues on the next page.)

Table 4.1: Characteristics of spray events in the resident field study (part 2).

Location	Target field size [ha]	Type of bulbs on target field	Measur-ment campaign	Sprayed #	Self reported dosage [kg/ha]	Mean measured dosage [kg/ha]	Additional fields			
							Nr of fields	(%) spray reg.	(%) assumed reg. (scheme)	(%) no usable reg. or scheme
G	3.64	Lilium	11	**Asulam**	0.20	0.21	13	38%	62%	0%
				Cyhalotrin-Lambda	0.01	0.05				
				Metamitron	0.37	0.53				
				Mineral oil	4.80	n.d.				
				Quinmerac	0.03	n.d.				
			12	**Asulam**	0.20	0.21				
				Cyhalotrin-Lambda	0.01	0.05				
				Mancozeb	1.28	n.d.				
				Metamitron	0.37	0.24				
				Mineral oil	4.80	n.d.				
				Pymetrozine	0.10	0.07				
				Quinmerac	0.03	n.d.				
			Outside season	n.a.	n.a.	n.a.				
H	8.40	Tulip	13	Esfenvarelate	0.01	n.d.	14	21%	71%	8%
				Fluopyram	0.08	0.07				
				Trifloxystrobin	0.08	0.07				
			Outside season	n.a.	n.a.	n.a.				
I	1.47	Allium	14	**Trifloxystrobin**	0.13	0.09	12	42%	58%	0%
			Outside season	n.a.	n.a.	n.a.				
Control locations			In season	n.a.	n.a.	n.a.	n.a	n.a	n.a.	n.a.
			Outside season	n.a.	n.a.	n.a.				

reg. = registration.
# Pesticides in our analyses are in bold.
* Only applied on narcissus.
n.a.: not applicable; n.d.: not determined.

Additional fields

Additional fields are all fields within 250 m of participating homes, excluding the target field. The number of additional fields per location and corresponding spray information are provided in Table 4.1. Flower bulbs were cultivated on 90% of the additional fields. The owners of the additional fields were contacted to share their spraying registration. Growers of 36% of the additional fields did so (percentage per location in Table 4.1). If the spray registration was not made available, we identified the type of flower bulbs or crop on that field by asking growers, by visual identification or via the *"Basisregistratie Percelen"* (BRP). Using the flower bulb or crop type, a standardized spray scheme for fields with these flower bulbs or crops was provided by CLM. These schemes were based on crop/bulb type, location, applications in additional fields and expert opinion. However, these schemes may have been inaccurate for both the used pesticide and the spray dates. Schemes were overall available for 59% of the additional fields, (percentage per location in Table 4.1). From 6% of the additional fields, no general spraying scheme could be obtained for the flower bulb or crop type or the received registration was not accurate enough to use and these fields were therefore not included in the study.

4.1.2 Homes

Location homes

Location homes are situated within 250 m of a target field and participated in Protocol A (Figure 1.2). Table 4.2 shows the included location homes and Appendix 21 shows the characteristics of these homes. Of the included homes, 18 homes were also included in Protocol B (Figure 1.2), corresponding to 86% of the homes within 50 m of the edge of a target field.

After a spray event, location homes were selected for analyses of the environmental samples as described in chapter 3.4.7. There were 115 seven-day measurements in a location home and 58 (50%) of these were selected for analyzes. Due to pump failure, not all outdoor air samples from selected homes could be analyzed and samples from other location homes were also selected for analysis of outdoor air samples (Table 4.2). If a home was selected for analyses during the use period, its samples were also included for analysis in the non-use period. A flow diagram on inclusion and selection of homes is in Appendix 7.

Farm homes

Seven of the included location homes were defined as farm homes (see chapter 1.3). The results of these seven homes were excluded from the main analyses but can be found in Appendix 8.

Control homes

In addition to location homes, control homes were included in the study to evaluate background exposure at homes in the same region. Measurements at control homes

Table 4.2: Homes included in the study and homes selected for analyses.

Location	Measuring campaign	Participating homes	Analyzed Homes Air concentration				Analyzed Homes Dust			
			Protocol A		Protocol B		Protocol A		Protocol B	
			Homes $	Farm homes	Homes $	Farm homes	Homes $	Farm homes	Homes $	Farm homes
A *#	1	10	1	1	1	1	6	2	2	2
	Outside season	9	4	1	1	1	6	2	2	2
B	2	5	3	2	2	2	2	2	2	2
	Outside season	5	5	2	2	2	3	2	2	2
C#	3	11	6	0	4	0	4	0	2	0
	4	10	5	0	2	0	4	0	3	0
	Outside season	11	8	0	4	0	4	0	3	0
D	5	10	8	2	4	2	5	2	3	2
	6	10	7	1	3	1	4	1	3	1
	Outside season	11	9	2	4	2	5	2	3	2
E	7	3	3	1	2	1	2	1	2	1
	8	4	2	1	2	1	2	1	2	1
	Outside season	4	4	1	2	1	2	1	2	1
F	9	12	5	1	1	1	6	1	3	1
	10	4	3	0	0	0	3	0	1	0
	Outside season	9	6	1	1	1	6	1	3	1
G	11	7	5	0	0	0	4	0	1	0
	12	7	4	0	0	0	4	0	1	0
	Outside season	7	6	0	0	0	4	0	1	0
H	13	8	6	0	2	0	5	0	2	0
	Outside season	8	6	0	2	0	5	0	2	0
I	14	14	5	0	2	0	5	0	2	0
	Outside season	14	7	0	2	0	5	0	2	0
Controls	In season (1)	11	8	n.a	n.a	n.a	9	n.a	n.a	n.a
	In season (2)	6	4	n.a	n.a	n.a	3	n.a	n.a	n.a
	Outside season	15**	12	n.a	n.a	n.a	15**	n.a	n.a	n.a

* Most pumps failed during spray event 1.
# One house participated in both location A and location B (was situated within 250 m of both fields).
** One home participated twice: 16 measurements in 15 homes off season.
$ Number of homes, including farm homes, of which the collected samples were analyzed.

were performed at approximately the same time as at the locations. We included 16 control homes in the study, of which six participated in all three measurement campaigns, five only in one seven day measuring campaign, two in one seven-day and one two-day measuring campaign, one in one seven-day and two two-day measuring campaigns and two ended their participation after one seven-day measurement campaign (Appendix 7).

All environmental samples collected in control homes, both in and off season, were selected to be analyzed.

4.1.3 Personal sampling

Residents

Everybody living in a participating home at a target location was eligible for participation in the personal monitoring protocol as "resident". Of the eligible persons, 164 were included in the study (see Table 4.3) of which 39 were children (under the age of 18 years).

Fifty-seven residents living in homes participating in protocol B collected a hand wipe and all urine voided during the day of the spray event. Urine was collected from the start of the spray event until the following day, which included a morning urine sample. The number of adults and children in protocol B are provided in Table 4.3.

Controls

28 controls were included of which four were under the age of 18 years. Controls participated in protocol A. Not all controls participated in all measurement campaigns (see 4.1.2, Control homes). Details are listed in Table 4.3. Samples from all control children and one adult per control home were selected for analyses.

Growers' families

Among the selected residents, 17 adults and nine children were living in a home that was classified as farm home. The results from these residents were excluded from the main results but are described in Appendix 8.

4.1.4 Outline of the result section

Both environmental and personal samples were collected during and following a spray event or outside the season. This chapter shows the results of both types of samples. Possible influences of home characteristics on environmental pesticide levels, personal characteristics and food intake on urine levels will be explored in chapter 6.

Paragraph 4.2 – 4.4 outline the results of the selected environmental samples, focusing on outdoor air, vacuumed floor dust (VFD), dust collected from doormats (DDM) and soil collected from the gardens. Results from indoor air, collected in homes within Protocol B, are provided in paragraph 4.5. The study protocol included collection of homegrown fruits and vegetables. Results from these analyses are presented in Appendix 9.

From the personal samples collected in the residents' field study, results from the selected morning urine samples are given in paragraph 4.6 and results from first day urine samples in paragraph 4.7. Hand wipe results are shown in paragraph 4.8. Paragraph 4.9 describes the three pilot studies that were added to the OBO flower bulb study (add-on studies). The results from chapter 4 are summarized and discussed in paragraph 4.10. The general discussion of the results from the OBO flower bulb study can be found in chapter 7.

Table 4.3: Participants included and selected for urine analyses.

Location	Measurement campaign	Participating homes	Participating residents		Selected for analyses			
					Adults		Children (0-17 yrs)	
			Adults	Children (0-17 yrs)	All	Prot. B	All	Prot. B
A*	1	10	21	5	11	7	5	3
	Outside season	8	21	3	9	7	3	0
B	2	5	10	0	1	1	0	0
	Outside season	4	10	0	1	1	0	0
C **	3	10	17	3	11	6	2	2
	4	11	19	3	9	5	2	2
	Outside season	11	19	3	11	5	2	2
D	5	10	17	7	11	6	7	5
	6	10	15	5	10	5	3	3
	Outside season	11	19	7	12	5	3	3
E	7	3	6	9	1	1	2	2
	8	4	7	9	4	3	7	4
	Outside season	4	7	9	4	3	8	5
F	9	12	16	5	15	5	4	0
	10	4	6	0	5	2	0	0
	Outside season	9	14	3	11	2	4	0
G	11	7	9	3	7	1	2	0
	12	7	9	3	7	1	3	0
	Outside season	7	9	3	7	1	3	0
H	13	8	9	2	3	1	1	1
	Outside season	8	9	2	3	1	1	1
I	14	14	21	4	6	3	3	3
	Outside season	14	21	4	6	3	3	3
Control locations	In season (1)	11	18	2	15	n.a.	2	n.a.
	In season (2)	6	8	2	5	n.a.	0	n.a.
	Outside season	15#	26	2	19	n.a.	1	n.a.

* 2 residents from location A also participated in location B.
** 2 residents from location C, campaign 3 participated in location B.
# One control home with 1 control participated twice in the off season.
Prot. B: participating in protocol B.

4.2 Environmental samples: sample selection and data treatment

4.2.1 Sample selection

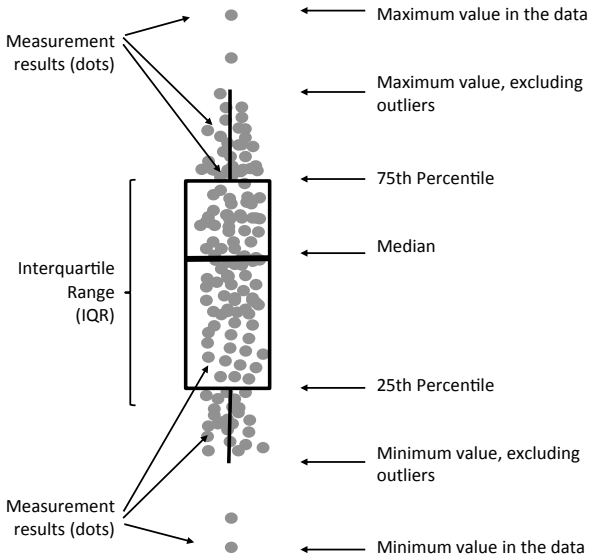
During all measurement campaigns, over 2000 environmental samples were collected. From both types of dust samples, 56% were selected for analysis as were 74% of the outdoor air samples (Appendix 7). The levels of 46 different pesticides were determined in each selected environmental sample.

4.2.2 LOD and imputation

As described in chapter 3.4, the LOD was determined for each pesticide for each type of sample. If more than 40% of the results were above the LOD, values were imputed (see chapter 3.4.8) and medians, interquartile ranges (IQR) and a minimum/maximum are expressed in boxplots. Box 4.1 explains how a boxplot should be interpreted. If imputation was possible for one medium (for example outdoor air) but not for the others, graphs show boxplots for the imputed results and dot-plots with the percentage below LOD for the non-imputed results. If for none of the media imputation was possible, no graphs are shown, and instead, results are expressed in tables as percentage (%) of samples with levels above the LOD. The pesticide-specific LODs are listed in Table 4.5.

Box 4.1: Explanation of a boxplot

Results from this study are often expressed in boxplots. The figure below explains how boxplots should be interpreted. In our figures, the measured values, shown as dots, are also added to the figure to show the individual observations.



Box 4.2 explains the use of logarithmic scales and Box 4.3 explains the units that are used.

Box 4.2: Logarithmic notation

A logarithmic scale is a nonlinear scale used when there is a large range of quantities. In this report we show Log10 scales in several graphs. The explanation for numbers on the log10 scale is:

Numeric notation	0.00001	0.0001	0.001	0.01	0.1	1	10	100	1000	10000	100000
Logarithmic notation	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-1}	10^{0}	10^{1}	10^{2}	10^{3}	10^{4}	10^{5}

Box 4.3: Metric units of mass (weight)

Below we show the relation between different units of mass (weight):

1 kg	=	1000 gram
1 gram		
1 mg	=	0.001 gram
1 µg	=	0.000 001 gram
1 ng	=	0.000 000 001 gram
1 pg	=	0.000 000 000 001 gram

4.3 Environmental samples: outdoor air within measurement campaigns

4.3.1 Outdoor air sampling

This paragraph presents concentrations of applied pesticides in ambient (outdoor) air near participating homes across days. Table 4.4 summarizes the applications of 28 pesticides on our target fields during measurement campaigns and the percentage of the results with levels above the LOD. Overall, 54% of the 28 applied pesticides were detected in the air samples. For 13 pesticides, the percentage of samples above the LOD was too low to be imputed while imputation was possible for 15 pesticides.

Table 4.4: Percentage of outdoor air samples collected at a location with pesticide values above the LOD, ordered by measurement campaign and per day following the spray event.

Measurement campaign	Pesticide	Nr homes analysed (outdoor air)	Days (% houses > LOD)						
			1	2	3	4	5	6	7
1	Tebuconazole	1	0	0	0	0	0	0	0
	Thiacloprid		0	0	0	0	0	0	0
2	Flonicamid	3	100	100	67	100	100	100	67
	Fluopyram		100	100	100	100	100	100	100
	Trifloxystrobin		100	100	100	100	100	100	100
3	Chlorpropham	6	100	100	100	100	100	100	100
	Pendimethalin		100	100	100	100	100	100	100
4	Tebuconazole	5	100	100	100	100	100	100	100
5	Chlorpropham	8	100	100	100	100	100	100	100
	Pendimethalin		100	100	100	100	100	100	100
6	Prochloraz	7	100	100	100	100	100	100	100
7	Acetamiprid	3	0	33	100	0	0	0	0
	Mepanipyrim		100	100	100	67	67	67	33
8	Cyhalotrin-Lambda	2	50	50	0	100	0	50	50
	Flonicamid		100	100	100	100	100	100	100
	Tebuconazole		100	100	100	100	100	100	100
9	Tebuconazole	5	100	100	100	100	80	80	100
10	Acetamiprid	3	0	100	67	33	0	0	0
11	Asulam	5	0	0	0	0	0	0	0
	Cyhalotrin-Lambda		40	20	60	40	20	40	60
	Metamitron		100	100	100	100	80	80	100
12	Asulam	4	50	0	25	0	0	0	25
	Cyhalotrin-Lambda		50	25	25	0	25	0	0
	Metamitron		100	50	100	100	50	0	25
	Pymetrozine		25	0	25	0	0	0	0
13	Fluopyram	6	100	100	100	100	100	100	100
	Trifloxystrobin		67	67	33	33	33	33	33
14	Trifloxystrobin	5	40	60	20	0	0	20	20

Percentage of homes with pesticide levels above the LOD is indicated in gray bars.
LOD: Limit of detection.

To present the results in a comprehensive manner, this paragraph first presents the concentrations in outdoor air shown for each spray event during the consecutive seven days of measurements. Next, this paragraph evaluates wind direction and drift as a potential predictor of concentration levels. In the next paragraph we evaluated other potential predictors namely:

- Use period vs Non-use period;
- Location vs control locations;
- Distance to the applying field.

In these paragraphs the results from VFD and DDM will also be described. Results from soil collected from the gardens of participating homes are in paragraph 4.4.6.

Indoor air concentration levels, collected in Protocol B homes, and the relation between outdoor and indoor air levels, as well as correlations between the different types of samples are presented and discussed in paragraph 4.5.

4.3.2 Outdoor air levels across sampling days

In Figure 4.1 the results are shown grouped per spray event to visualize patterns in concentration levels per location. If an additional field reported an application with the same pesticide, or the schemes indicated the possibility of such an application, we indicated this in the graph. Each line (color) in Figure 4.1 represents the results of outdoor air pesticide concentrations across days and per home. Concentrations of different pesticides follow patterns over time that are similar for most homes while patterns between individual homes can differ. For example, in measurement campaign 3, chlorpropham and pendimethalin show similar patterns within the same homes but patterns differ between homes. It should be noted that parameters such as wind direction and wind speed, background levels and additional spray events can all have a large impact on air concentrations.

4.3.3 The effect of wind, drift and volatilization

Wind is a transportation route for both drift and volatilization of pesticides. Here the effect of wind was evaluated on day 1 (including possibly drift and volatilization) and on days 2-7 (volatilization). None of the included locations had homes situated in all possible wind directions but in seven of the nine locations, homes were situated in at least two wind directions around the field. The effect of wind on exposure of residential homes depends on many factors, including wind direction as well as wind speed. The wind speed varied between 2 and 6 m/s during the spray events and went up to maximal 12 m/s during the first 24h of all measurement campaigns. More data on the meteorological conditions during the measurement campaigns is shown in chapter 6, Table 6.2. Drift during or shortly after spraying can contribute to the exposure during the first 24h as does the volatilization of pesticides. If no other spray events with the same pesticide occurred in the area, volatilization is most likely the main contributor of air concentrations in the following 6 days.

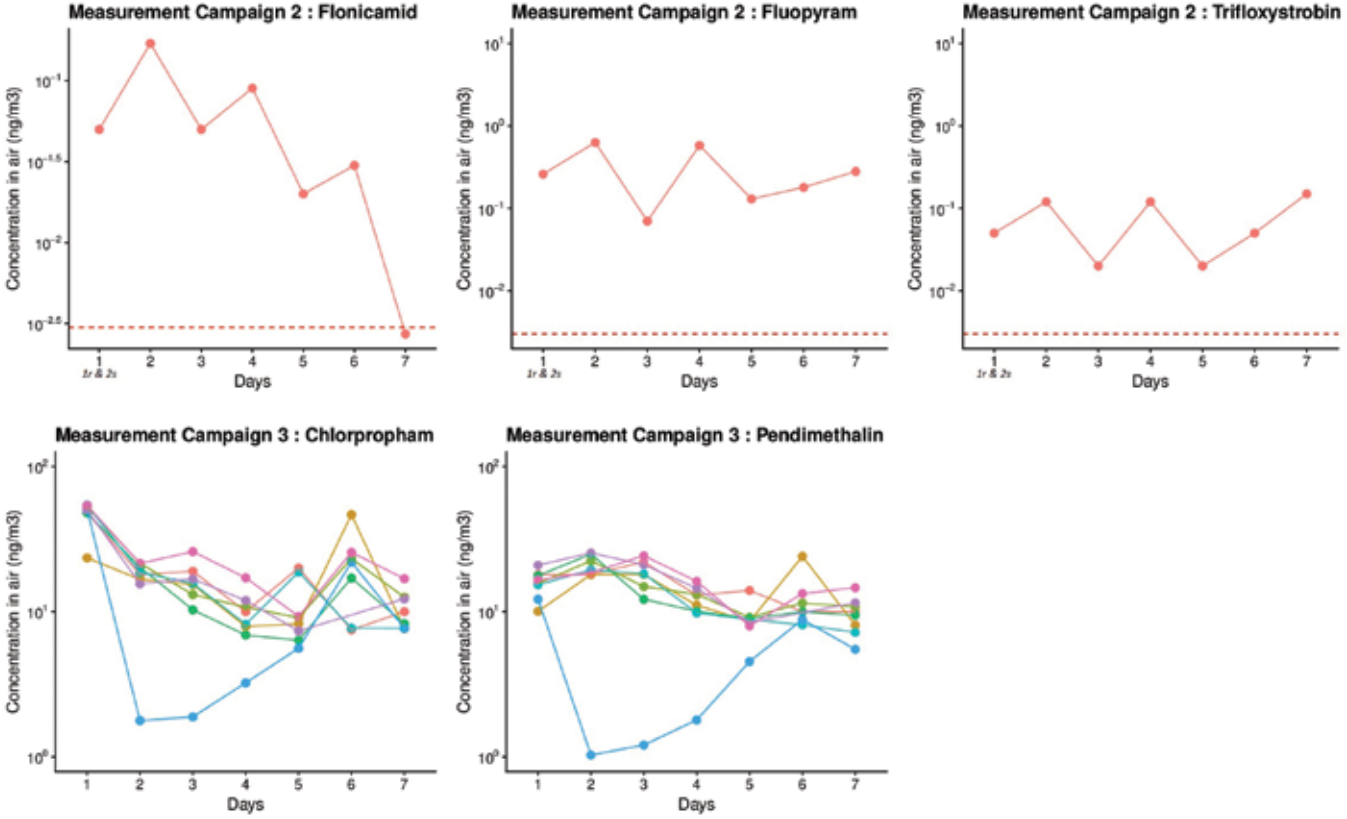


Figure 4.1: Concentrations in outdoor air for the 7 days after a spray event.
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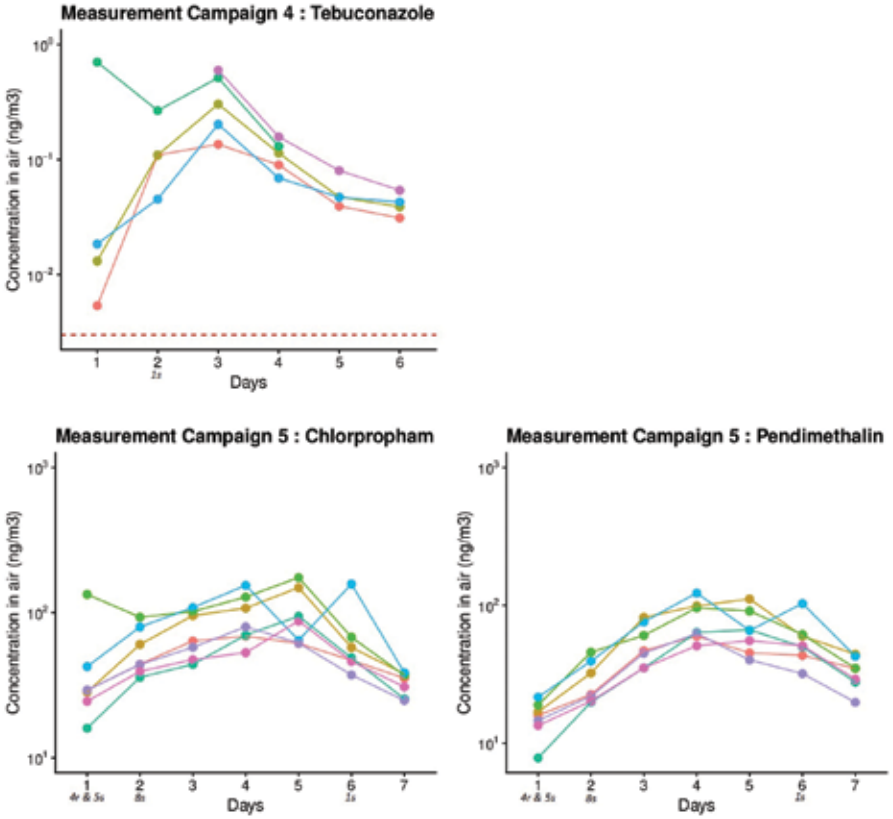

Figure 4.1: Concentrations in outdoor air for the 7 days after a spray event.

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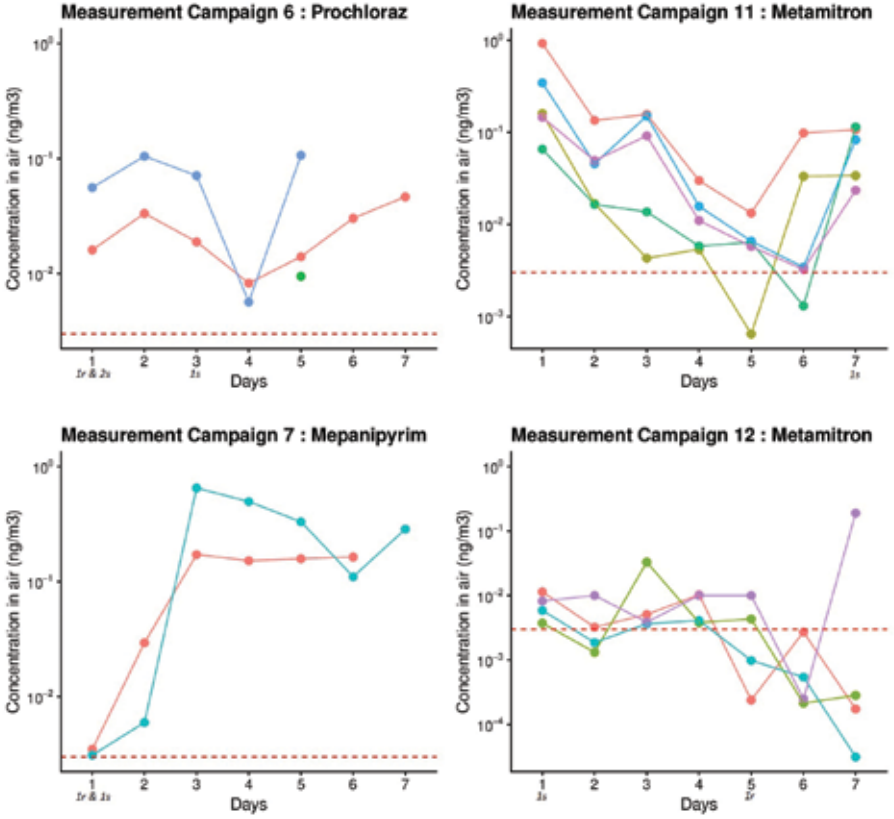

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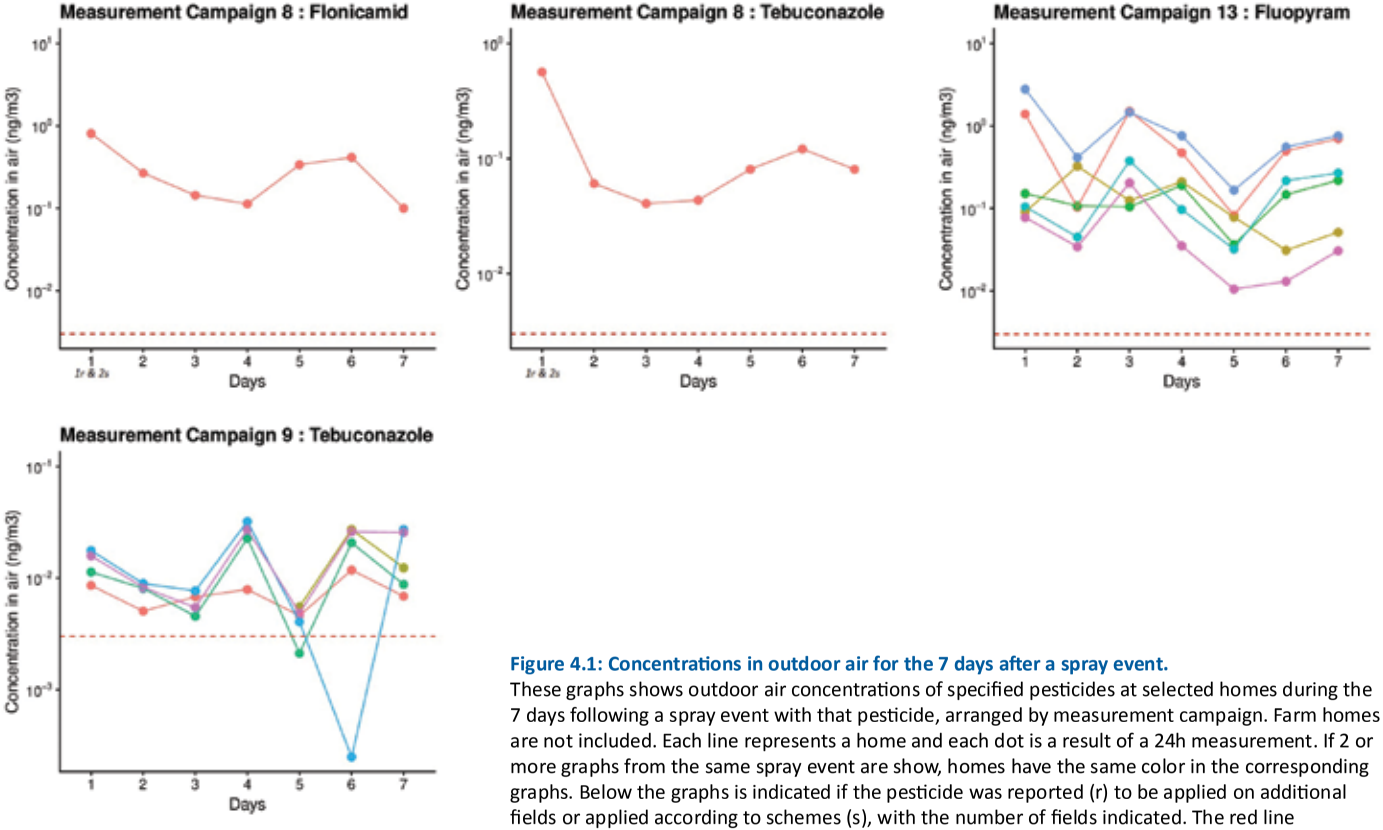

Figure 4.1: Concentrations in outdoor air for the 7 days after a spray event.
These graphs shows outdoor air concentrations of specified pesticides at selected homes during the 7 days following a spray event with that pesticide, arranged by measurement campaign. Farm homes are not included. Each line represents a home and each dot is a result of a 24h measurement. If 2 or more graphs from the same spray event are show, homes have the same color in the corresponding graphs. Below the graphs is indicated if the pesticide was reported (r) to be applied on additional fields or applied according to schemes (s), with the number of fields indicated. The red line represents the LOD. For chlorpropham (0.01 ng/m3) and pendimethalin (0.003 ng/m3) in spray event 3 and 5 the LOD is not indicated as it is far below the lowest observation. Due to pump failure, no results from measurement campaign 1 are shown.

First 24 hours after spraying

Figure 4.2 shows plots of three measurement campaigns with the target field indicated with a dashed box, the additional fields shown in green, and the selected homes as black dots. Dot size is proportional to measured outdoor air concentration within the first 24 hours after a spray event of a specific pesticide (shown as quintile). In addition, wind direction and speed are indicated. Plots for all other campaigns are shown in Appendix 10. Overall, concentrations of applied pesticides do not appear to be higher in homes situated downwind. This is unexpected, as the wind is seen as the primary transportation route for both drift and volatilization and the concentrations are normally highest near the source[1]. An explanation could be the use of the pesticide on nearby or further away fields or relatively large background contributions. Unfortunately, we cannot exclude that other fields in the vicinity may have applied the specific pesticides.

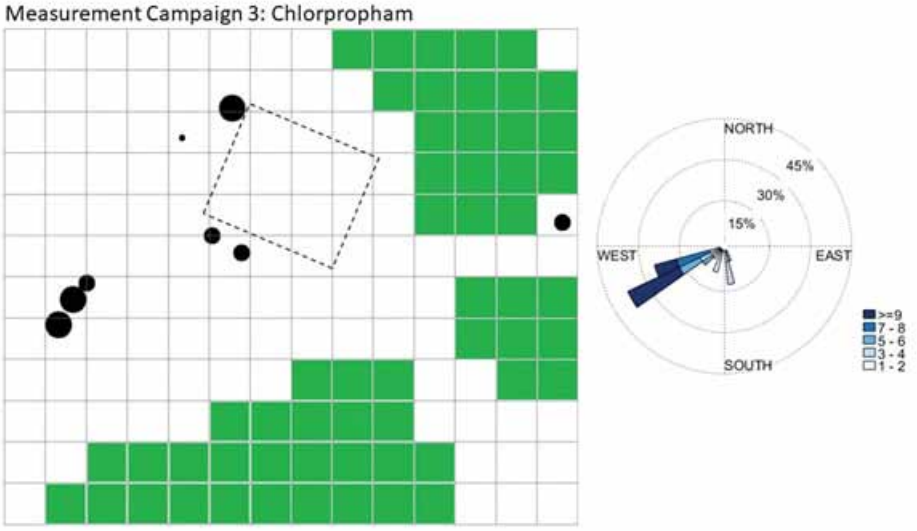

Figure 4.2: Panel A Wind and chlorpropham concentrations in air during the first 24h.
(continues on the next page, text below panel C on the next page.)

[1] For normal sources with emissions near ground level.

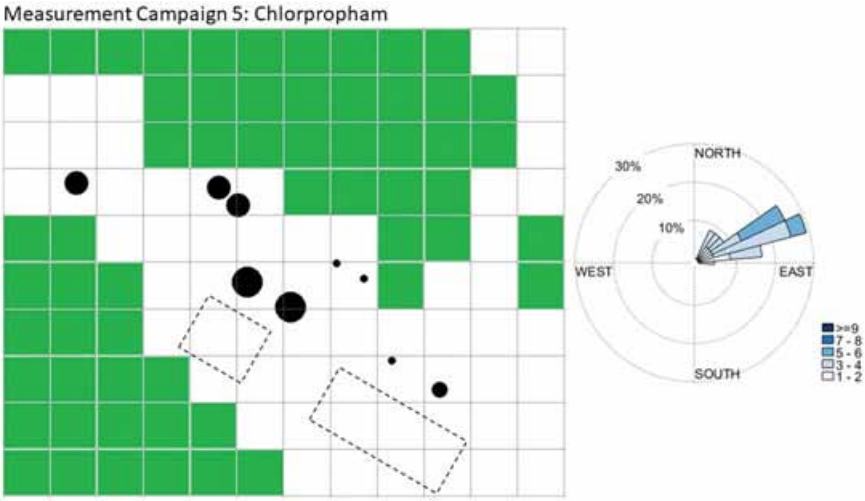

Figure 4.2: Panel B. Wind and chlorpropham concentrations in air during the first 24h after a spray event on the target fields.
(text below panel C.)

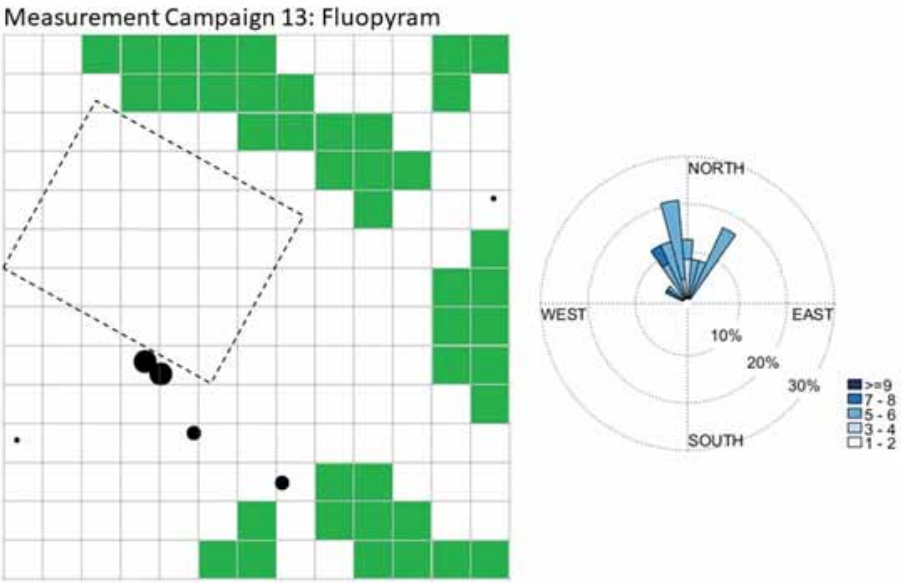

Figure 4.2: Panel C. Wind and fluopyram concentrations in air during the first 24h.
Graphic display of the location of a specified measurement campaign. Each cell is 50 by 50 meters. The target field is represented by the dotted box. The wind rose next to the display represents wind direction and wind speed (colored by category) during the first 24h after application. Wind direction is represented as the direction the wind originates from. Legends for wind speed are given on the right side of the display. Green cells are cells with additional fields. Dots are location homes (farm homes excluded) and the dot size represents the measured concentration in outdoor air of the specified pesticide, in quantiles of the exposure. Here we show three representative plots, all plots are in Appendix 10.

Day 1 vs days 2 to 7

A difference between concentrations on day 1 and days 2 – 7 is expected as drift only occurs on day 1 and volatilization is highest on the first day. Regarding measured concentrations at day 1 versus day 2 to 7, results were included if only a target field, but no additional fields, reported (both registration and schemes) an application of the same pesticide during the whole measurement campaign. For campaigns 3, 9 and 13, no other fields in the area reported such an application (see Figure 4.1). Figure 4.3 shows outdoor air concentrations comparing day 1 with days 2 – 7. Overall, concentrations on day 1 were higher compared to the other days. Only for chlorpropham and pendimethalin in measurement campaign 3, the number of observations in both groups were considered large enough to statistically test for differences. Statistically significant group differences were found for chlorpropham ($p<0.001$) and pendimethalin ($p<0.05$).

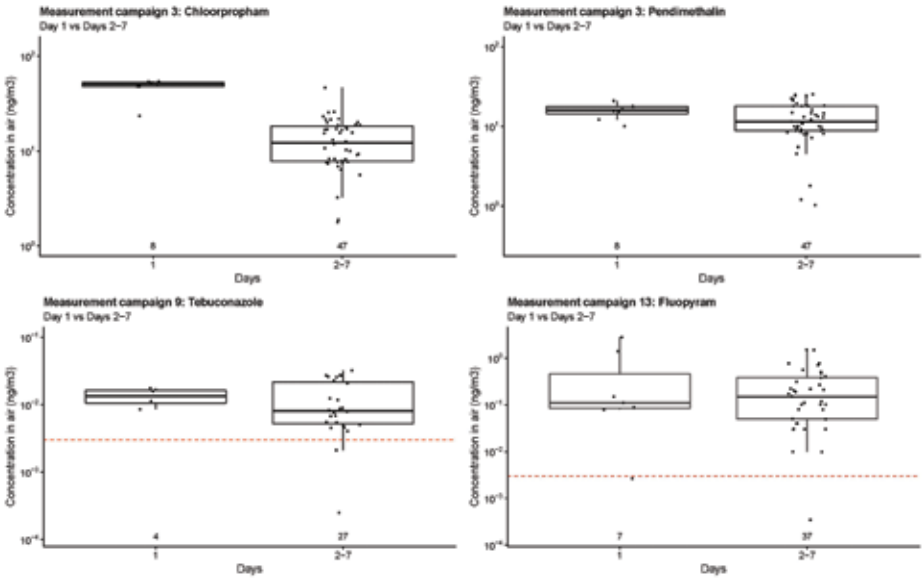

Figure 4.3: Effect of days after application.

For each specified pesticide the outdoor air concentrations during day 1 compared to day 2 – 7 of that measurement campaign.

Results are shown in boxplots. The red dotted line is the LOD for the specified pesticide. The number of filters (24 h measurement) per category is shown above the x-axes.

4.4 Environmental samples: measured pesticide levels

4.4.1 Period, location, distance and sample type

In this part we explore different determinants of the levels of pesticides in samples collected from the homes, independent of the measurement campaigns.

Use period

A possible determinant of exposure is the period of pesticide use (use period). Per pesticide, the use and non-use periods were determined using the provided registration or schemes (details are provided in Appendix 6). If a pesticide was not reported to be applied on any of the target or additional fields, measurements were considered to fall in the non-use period and all other moments were considered the use period. We subsequently compared concentration levels in the use period to non-use period. This was done for all 46 determined pesticides, not only for pesticides applied on the target fields. Results are grouped per pesticide, depending on application on the target field, on additional fields or no reported application on our target and/or additional fields.

Location

Another possible determinant of exposure is the location, comparing homes at the target location to homes from control locations. For this, concentrations measured at control homes were added to the comparison between use and non-use periods.

Distance

Close proximity to a field may lead to higher exposure due to both drift and volatilization. To evaluate the effect of distance, the distance of a home to the applying target field was determined. Next, per applied pesticide on day 1, it was checked if the specific pesticide had been applied on the target field or possibly also on an additional field (only reported applications, not from schemes). If a home was closer to a registered sprayed additional field than the target field, the distance to the additional field was used as closest distance to an applying field. If there was no application of a specific pesticide within 250 m of the home on day 1, the home was categorized as > 250 m from a field. Homes were grouped in four categories based on the closest distance to an applying field: up to 50 m, 50-150 m, 150 - 250 m, and > 250 m. Control homes were evaluated separately.

Sample types

Pesticide levels were determined in extracts of VFD and DDM. As dust samples were collected once per sampling campaign, they reflect the exposure during the whole week. Pesticide levels in samples of outdoor air and dust are determined in different types of assays, with their own LOD. These are indicated in Table 4.5.

In the garden of each location home and control home, soil samples were collected for analyses of the 46 pesticides. Results of soil samples are given in paragraph 4.4.6.

Table 4.5: Percentage of environmental samples above the LOD for all tested pesticides, grouped by application in target fields, additional fields or not applied during measurement campaign.

	Vapor	Air	Outdoor Air (% > LOD)				Dust	VFD (% > LOD)				DDM (% > LOD)			
	pressure**	LOD	Location homes		Control homes		LOD	Location homes		Control homes		Location homes		Control homes	
Active Ingredient*	(mPa at 20°C)	(ng/m3)	U	N	U	N	(ng/g)	U	N	U	N	U	N	U	N
Applied in the target field(s)															
acetamiprid	1.7E-04	0.003	10	3	0	0	1	14	16	19	6	6	0	0	0
asulam	5.0E-04	0.003	11	11	13	9	1	37	2	8	0	38	15	0	0
chlorpropham	2.4E+01	0.01	100	99	100	88	20	39	12	18	5	55	20	29	4
cyhalotrin-lambda	2.0E-04	0.03	25	23	13	17	10	2	0	0	0	0	0	0	0
flonicamid	9.4E-04	0.003	71	65	69	41	3	68	46	15	42	22	13	0	5
fluopyram	1.2E-03	0.003	74	56	68	47	1	52	38	25	12	56	61	14	11
floupyram-benzamide	1.2E-03	0.003	80	76	76	76	1	2	0	0	0	0	0	0	0
mepanipyrim	2.3E-02	0.003	54	1	22	11	1	9	0	0	0	24	7	0	0
metamitron	7.4E-04	0.003	75	11	36	29	3	46	10	0	0	28	8	0	0
metamitron-desamino	7.4E-04	0.003	51	19	31	16	1	37	10	8	11	25	3	0	0
pendimethalin	9.9E-01	0.003	100	100	100	99	1	79	43	27	33	97	78	43	8
prochloraz	1.5E-01	0.003	89	89	49	71	1	80	83	15	58	90	92	18	57
prothioconazole	7.4E-03	0.003	0	0	0	0	NA	0	0	0	0	0	0	0	0
prothioconazole-desthio	1.3E+04	0.003	96	91	95	75	3	80	56	55	33	76	52	11	17
pymetrozine	2.2E-03	0.003	5	3	0	1	1	14	6	0	0	18	18	0	0
tebuconazole	1.3E-03	0.003	94	31	69	47	1	88	78	69	63	88	59	91	43
thiacloprid	3.0E-07	0.003	18	10	5	8	1	31	21	9	0	3	2	11	4
trifloxystrobin	5.5E-03	0.003	63	15	49	12	1	14	4	18	0	12	7	11	4
trifloxystrobin-acid	3.4E-03	0.003	48	35	0	28	1	0	0	0	0	0	0	0	0
Applied in the additional fields															
boscalid	7.2E-05	0.003	90	46	65	41	1	90	90	54	58	98	87	91	67
chloridazon	1.0E-06	0.003	32	18	26	10	1	27	5	7	0	11	6	0	0
dimethenamidP	2.5E+00	0.003	95	59	63	42	1	12	6	0	0	0	9	0	0
kresoxim-methyl	2.3E-03	0.003	91	31	35	28	3	15	18	9	10	3	4	0	0
S-metolachlor	3.7E+00	0.006	100	75	100	48	1	43	21	22	4	57	41	20	63
spirotetramat	5.9E-06	0.01	40	2	30	6	1	5	2	0	8	10	2	0	0
spirotetramat-enol	*3.6E-07*	0.003	1	0	0	0	1	0	3	0	4	5	2	0	0
Not applied during measuring week															
azoxystrobin	1.1E-07	0.003	33	38	29	18	1	67	59	73	43	58	61	29	20
cyprodinil	5.1E-01	0.003	35	15	30	4	1	21	18	0	12	17	13	12	0
deltamethrin	1.2E-05	0.003	35	38	21	18	10	0	7	0	13	10	3	0	4
difenoconazole	3.3E-05	0.003	31	46	31	17	1	27	18	12	12	6	13	6	6
dimethomorph	9.9E-04	0.003	7	0	1	0	1	27	21	12	12	19	10	6	19
fludioxonil	3.9E-04	0.01	7	1	7	0	1	50	50	19	31	33	16	25	6
fluopicolide	3.0E-04	0.003	20	0	12	0	1	10	9	6	6	2	3	0	0
flutolanil	4.1E-04	0.003	12	29	17	4	1	33	26	19	0	42	39	12	0
fosthiazate	5.6E-01	0.003	28	0	8	0	1	0	0	0	0	0	0	0	0
imidacloprid	4.0E-07	0.003	30	21	28	17	1	81	65	94	88	25	35	75	44
linuron	5.1E-02	0.003	87	90	64	50	1	19	30	0	0	26	50	0	6
oxamyl	5.1E-02	0.003	22	4	4	0	1	15	7	0	0	8	2	0	4
primicarb	4.3E-01	0.003	3	6	10	12	1	10	9	12	6	8	6	0	0
propamocarb	8.0E-01	0.003	50	38	48	38	1	62	41	56	44	29	29	6	25
pyraclostrobin	2.6E-05	0.003	90	73	51	49	1	93	85	18	38	93	90	67	61
sulcotrione	5.0E-03	0.003	0	0	0	0	3	0	0	6	0	0	0	0	0
terbuthylazine	1.2E-01	0.003	59	4	60	12	1	4	0	6	0	0	0	0	0
thiophanate-methyl	9.0E-03	0.003	0	0	0	0	1	48	71	31	56	71	84	19	12
carbendazim#	*9.0E-05*	0.003	95	88	49	62	1	94	91	56	50	73	84	81	38
toclofos-methyl	8.8E-01	0.003	97	95	83	88	10	25	18	0	6	17	29	0	0

VFD: vacuumed floor dust; LOD: Limit of Detection; U: During pesticides usage period; N: Outside pesticides usage period.

Underlined: same vapor pressure of parent compound was used.

* secondary products/metabolites are under their parent compound, outline to the right.

** source: Pubchem; EPA/CompTox; IUPAC.

Carbendazim is a secondary product of thiophanate-methyl but also a pesticide as such.

4.4.2 Effect of use period and location on outdoor air concentrations

Table 4.5 shows the percentage of outdoor air measurements that were found to be above the LOD, per pesticide and by use and non-use period. The percentage of control homes with pesticide levels above the LOD are also shown in Table 4.5. For pesticides with <40% of measurements above the LOD, results indicate overall higher percentages of samples above the LOD in outdoor air samples in the use period compared to the non-use period. The number of samples above the LOD is also higher in when location homes then to control homes. This suggests an overall higher concentrations in the location homes. Means and ranges of all measurements can be found in Appendix 11.

Results (including concentrations) of samples which were > 40% detected above the LOD (imputation threshold, table 4.5) are shown in Figures 4.4 to 4.6. Figure 4.4 shows results of pesticides applied on target fields, Figure 4.5 pesticides used on additional fields, and Figure 4.6 pesticides that were not applied on target or additional fields during the measurement week. Outdoor air sample results are shown in Panels A of these figures. Plots show concentrations in the use period and the non-use period for location homes and control homes.

All results from outdoor air filters of all selected location homes and during all seven measured days were combined, independent of the spray events, the wind direction or the distance to the field. Levels were tested for significant differences using t-tests, results and p-values are reported in Table 4.6. For all pesticides except for prochloraz, levels are significantly higher for location homes in the use period compared to location homes in the non-use period. For most pesticides, a significant difference between location homes and control homes in the use period was observed while differences between location homes and control homes in the non-use period, or between control homes in the use and non-use period are less frequently statistically significant.

Of the pesticides sprayed on additional fields, outdoor air concentrations of four pesticides are shown in Figure 4.5: boscalid, dimethenamid-P, kresoxim-methyl, and S-metolachlor. The remaining pesticides sprayed on additional fields had levels with less than 40% above LOD (see Table 4.5). Overall, there is a tendency for location homes to have higher air concentrations than control homes, independently of period. Additionally, for some pesticides a pattern of higher concentrations in the use period compared to the non-use period in location homes could be seen. Differences between locations and periods were often statistically significant (Table 4.6).
Concentrations of pesticides not applied on target or additional fields during our measurement campaigns are shown in Figure 4.6. These pesticides could have been sprayed elsewhere, prior to our campaign and/or could be used in bulb disinfection. While clear differences between location homes and control homes could be observed in both periods, patterns differ between the different pesticides. For two of these pesticides, samples from the non-use period show higher levels compared to those from the use period. P-values of t-tests are provided in Table 4.6.

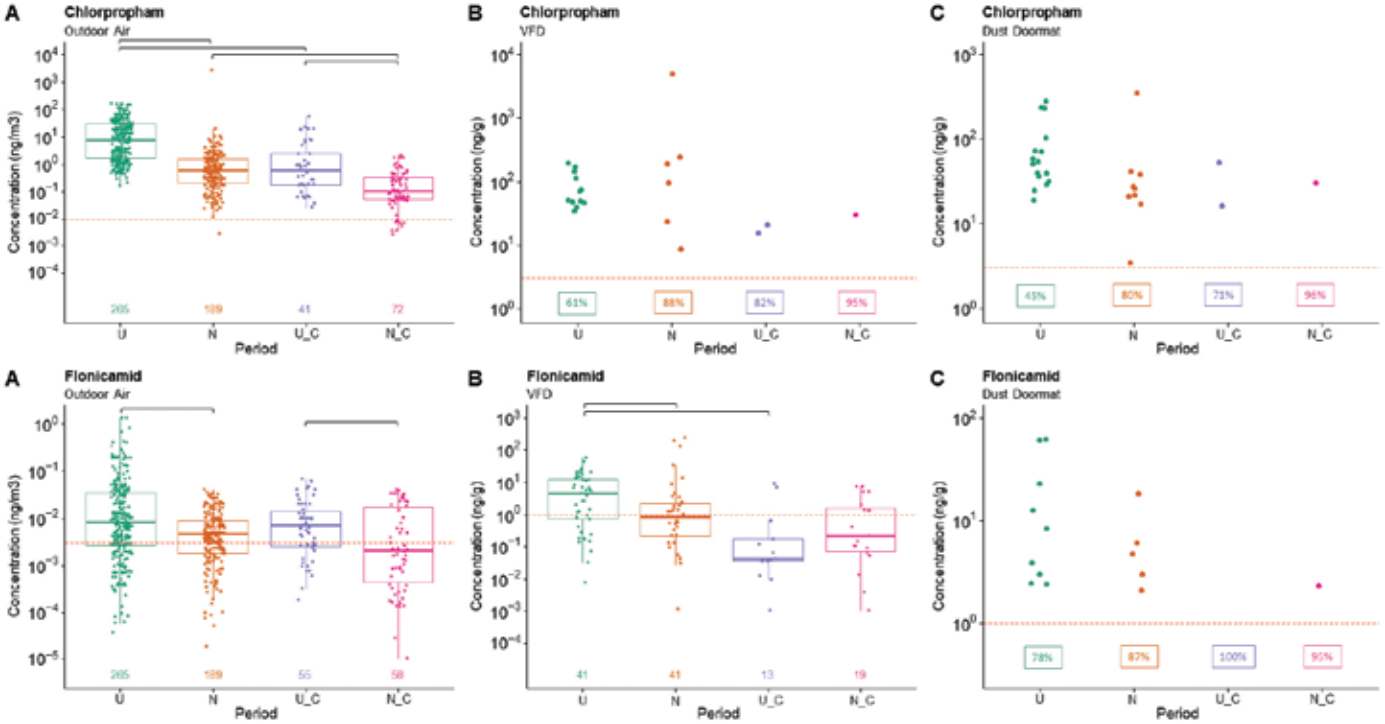

Figure 4.4: Measured concentrations of pesticides applied on the target fields at location homes and control homes in the use and non-use periods.
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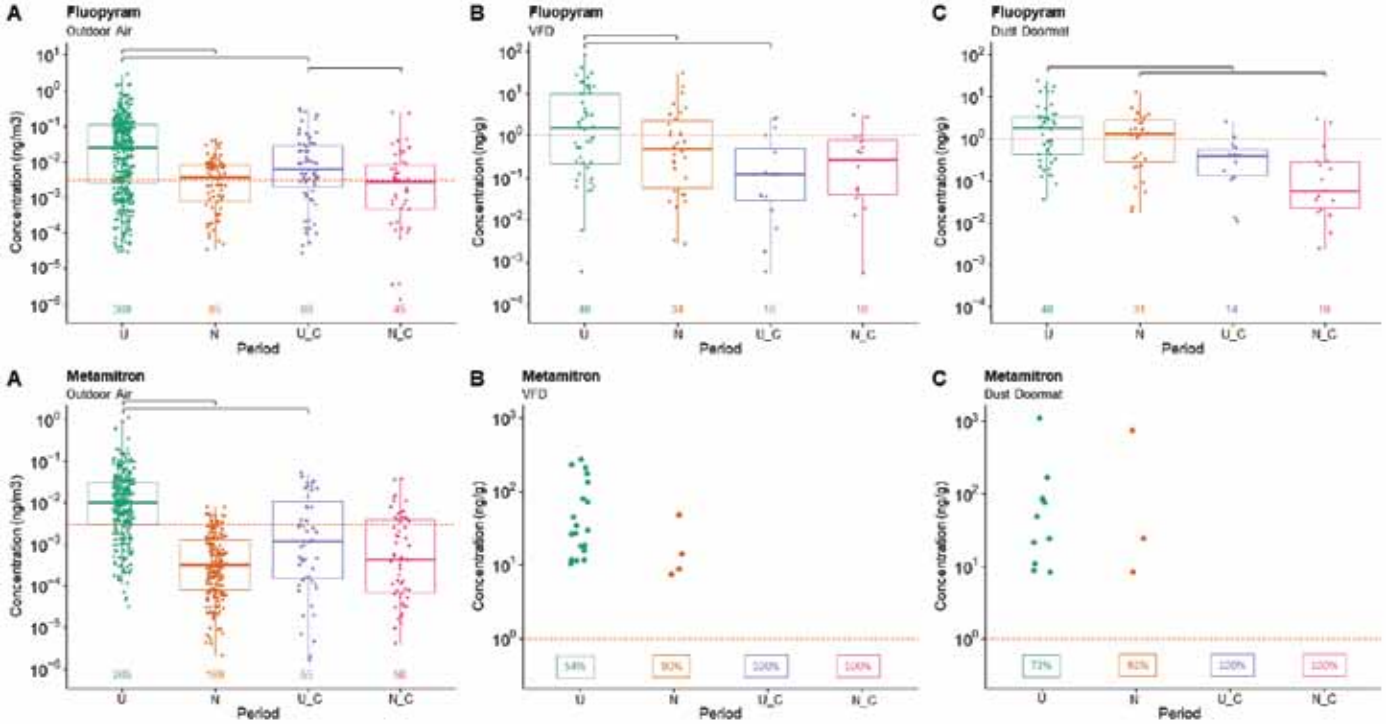

Figure 4.4: Measured concentrations of pesticides applied on the target fields at location homes and control homes in the use and non-use periods.
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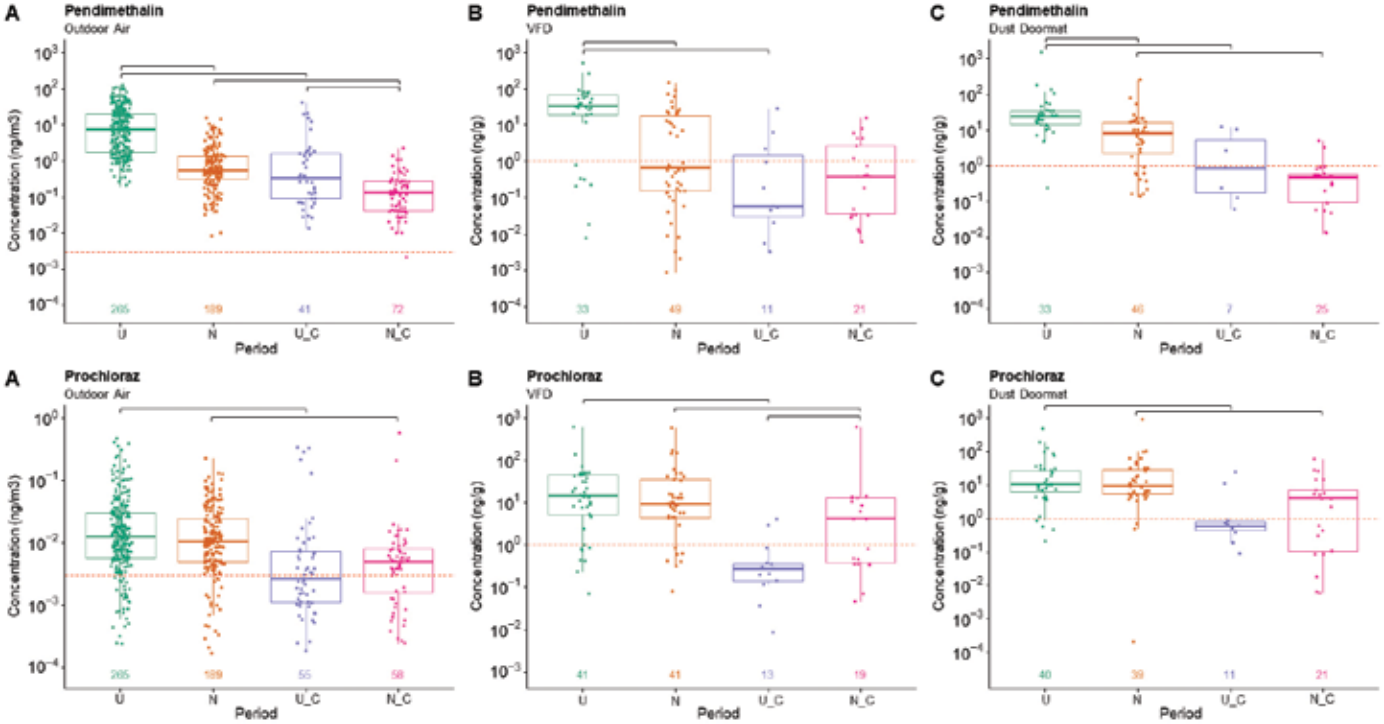

Figure 4.4: Measured concentrations of pesticides applied on the target fields at location homes and control homes in the use and non-use periods.
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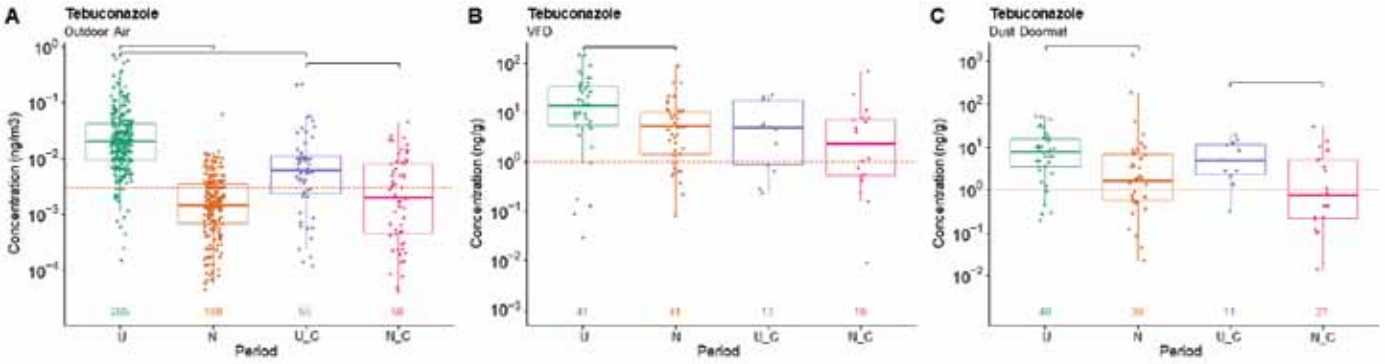

Figure 4.4: Measured concentrations of pesticides applied on the target fields at location homes and control homes in the use and non-use periods.
On the x-axis is the period. U: location homes, use period; N: location homes, non-use period; U_C: Controls in use period; N_C: controls in the non-use period. In the box plot Figures the number of observations is shown. If imputation of results below the LOD was not possible, dotplots with percentage below the LOD are shown. The red line represents the LOD. (A) Results for outdoor air; (B) results for vacuumed floor dust (VFD); (C) results from dust from the door mat. The black line(s) above the boxplots inform on statistically significant difference between group means (t-test: $\alpha < 0.05$). The exact p-values are shown in table 4.6.

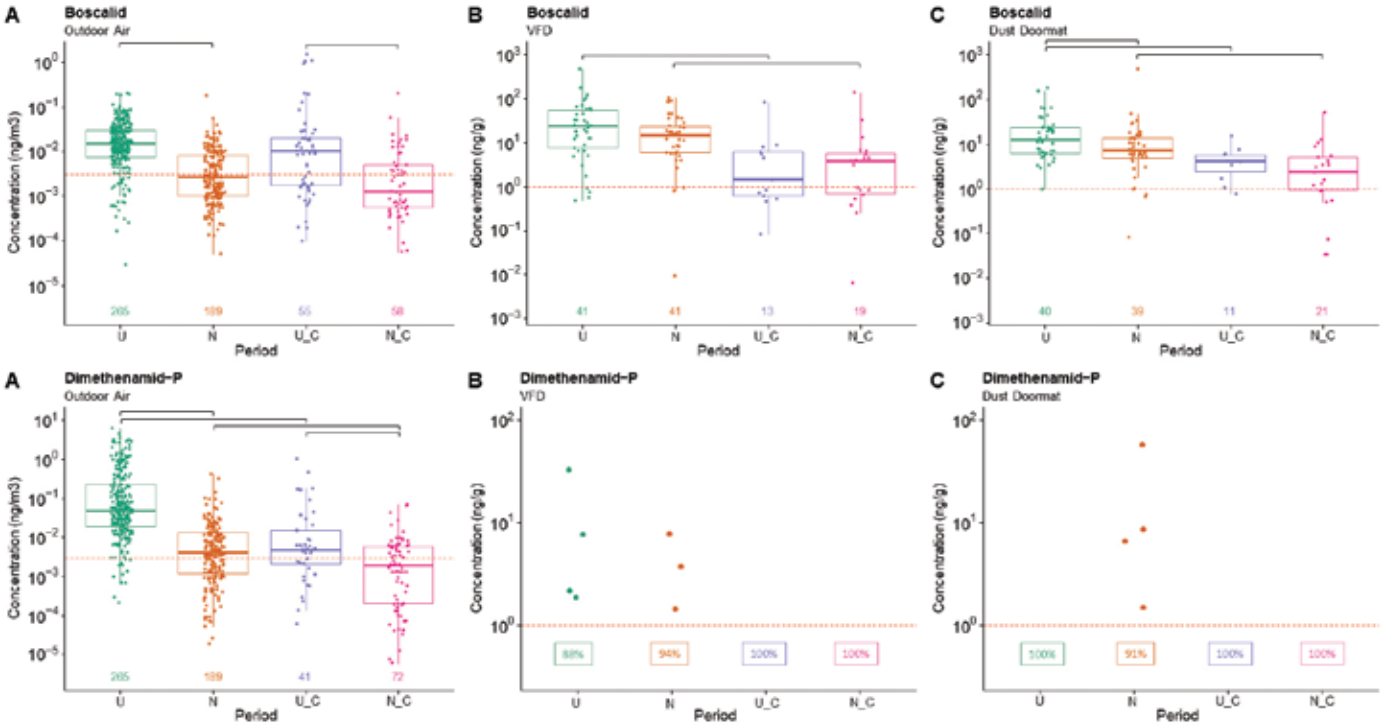

Figure 4.5: Measured concentrations of pesticides applied on additional fields at location homes and control homes in the use and non-use periods.
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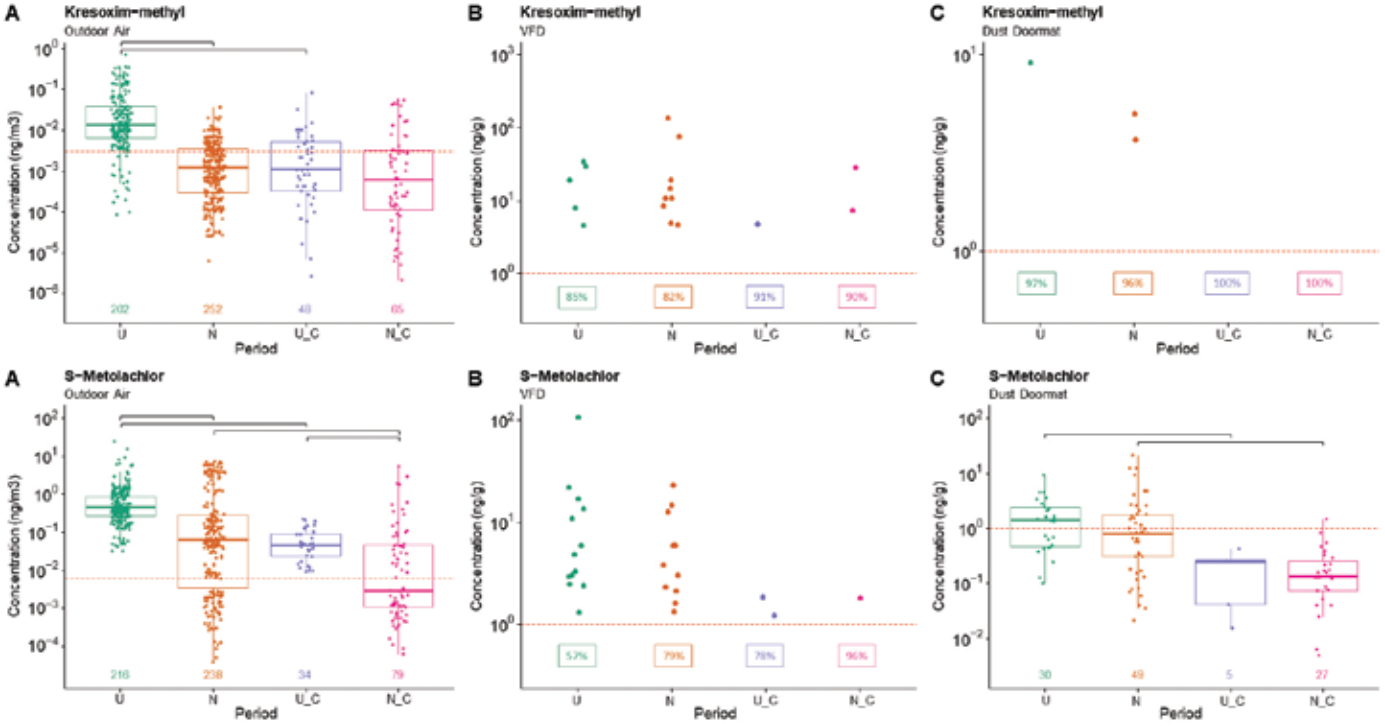

Figure 4.5: Measured concentrations of pesticides applied on additional fields at location homes and control homes in the use and non-use periods.
On the x-axis is the period. U: location homes, use period; N: location homes, non-use period; U_C: Controls in use period; N_C: controls in the non-use period. In the box plot Figures are the numbers of observations. The red line represents the LOD. If imputation was not possible, the box below the LOD contains the percentage of samples below the LOD. (A) Results for outdoor air; (B) results for vacuumed floor dust (VFD); (c) results from dust from the door mat. The black line(s) above the boxplots inform on statistically significant difference between group means (t-test: $\alpha < 0.05$). The exact p-values are shown in table 4.6.

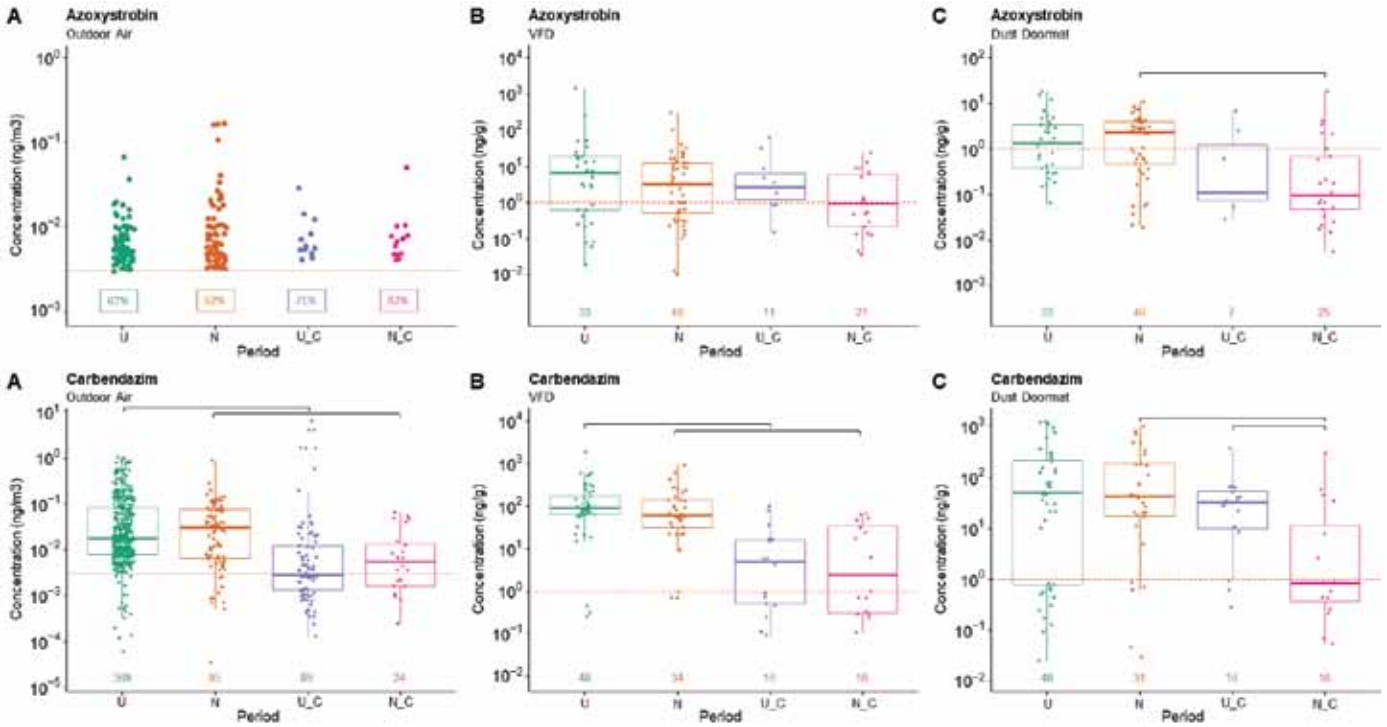

Figure 4.6: Measured concentrations of pesticides not applied during the measuring week or secondary products at location homes and control homes in the use and non-use periods.

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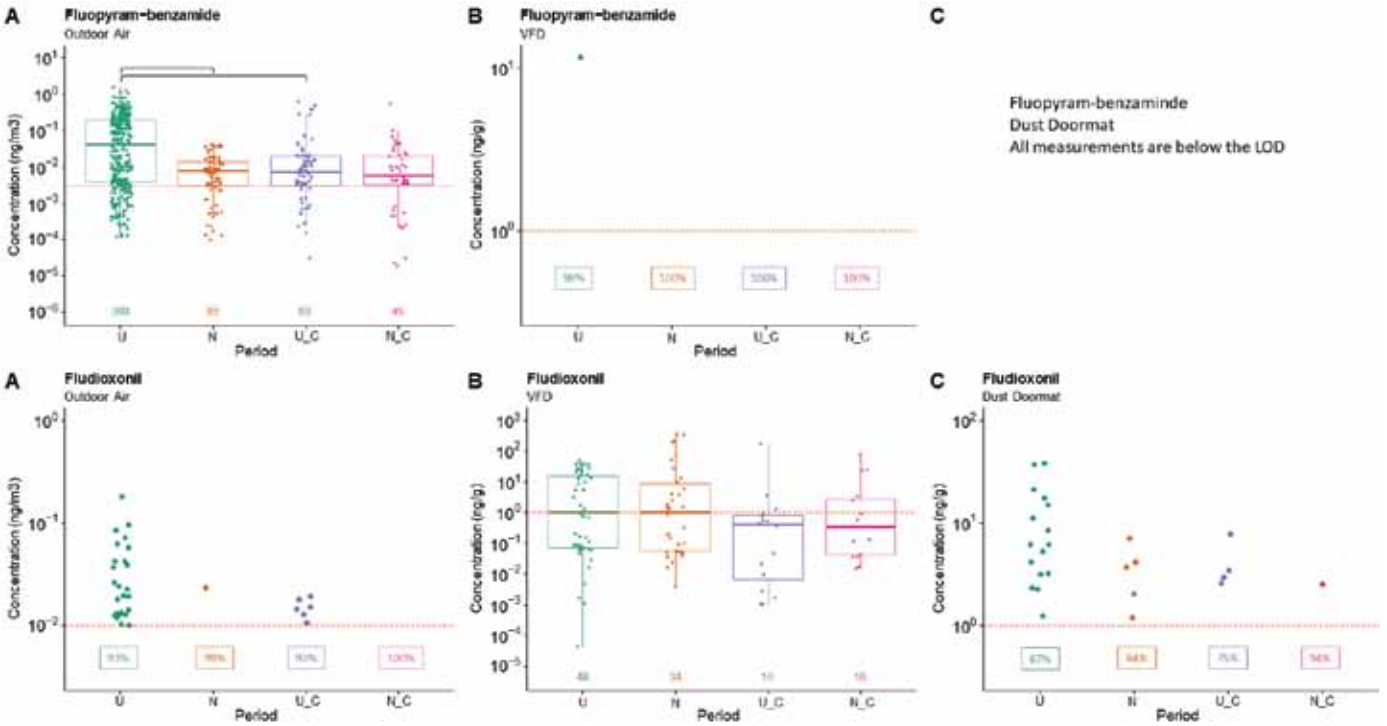

Figure 4.6: Measured concentrations of pesticides not applied during the measuring week or secondary products at location homes and control homes in the use and non-use periods.

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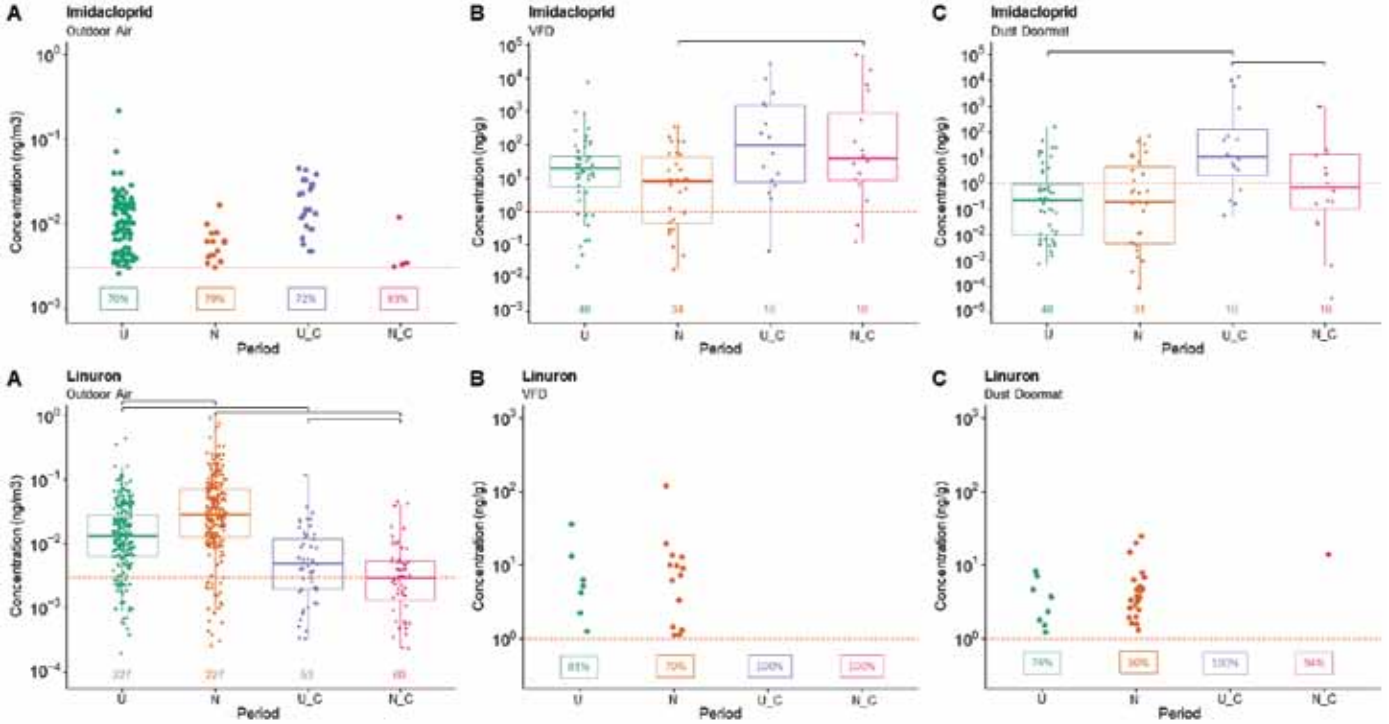

Figure 4.6: Measured concentrations of pesticides not applied during the measuring week or secondary products at location homes and control homes in the use and non-use periods.

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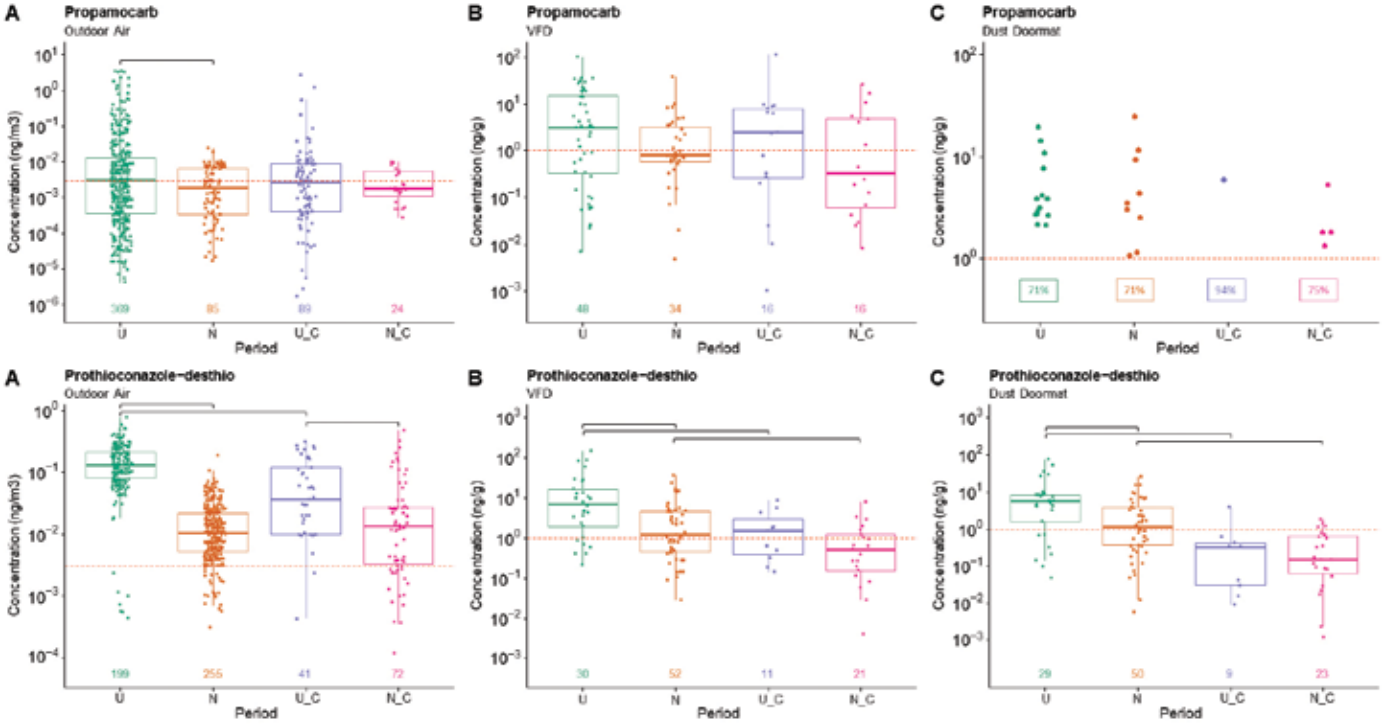

Figure 4.6: Measured concentrations of pesticides not applied during the measuring week or secondary products at location homes and control homes in the use and non-use periods.

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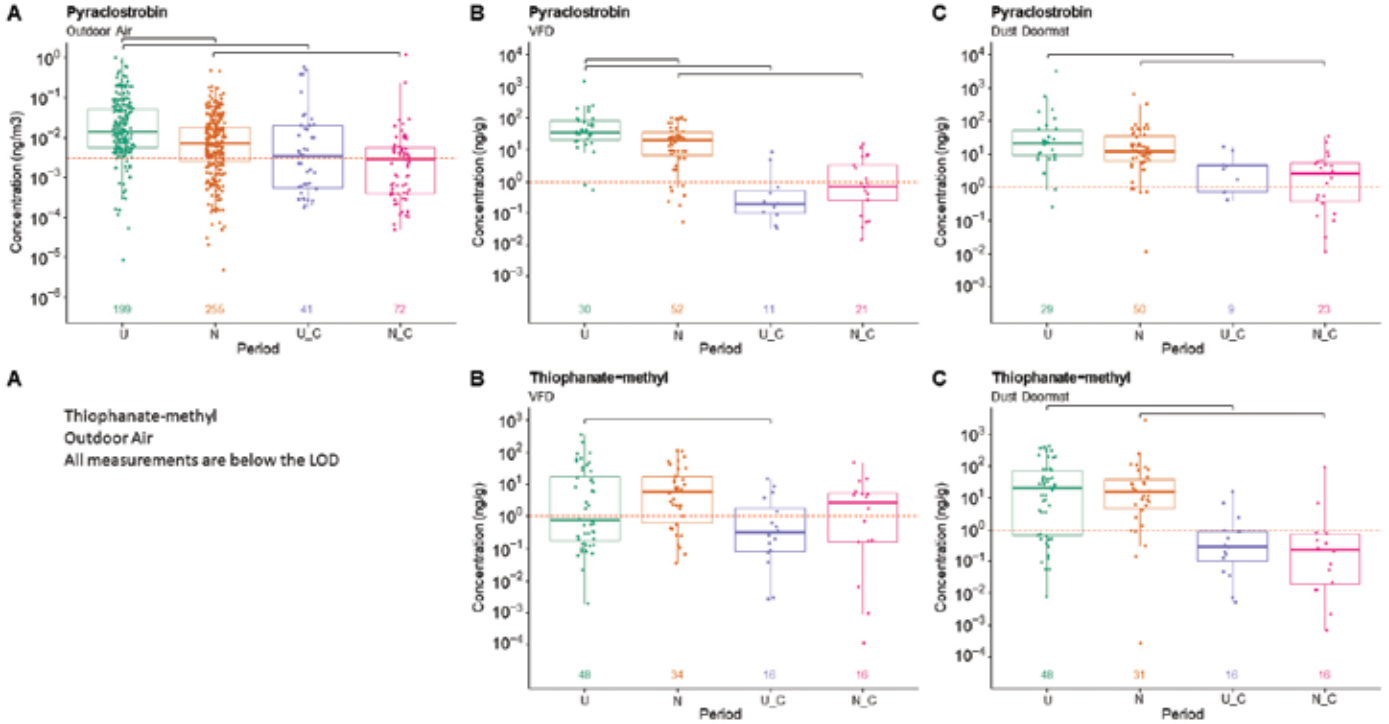

Figure 4.6: Measured concentrations of pesticides not applied during the measuring week or secondary products at location homes and control homes in the use and non-use periods.

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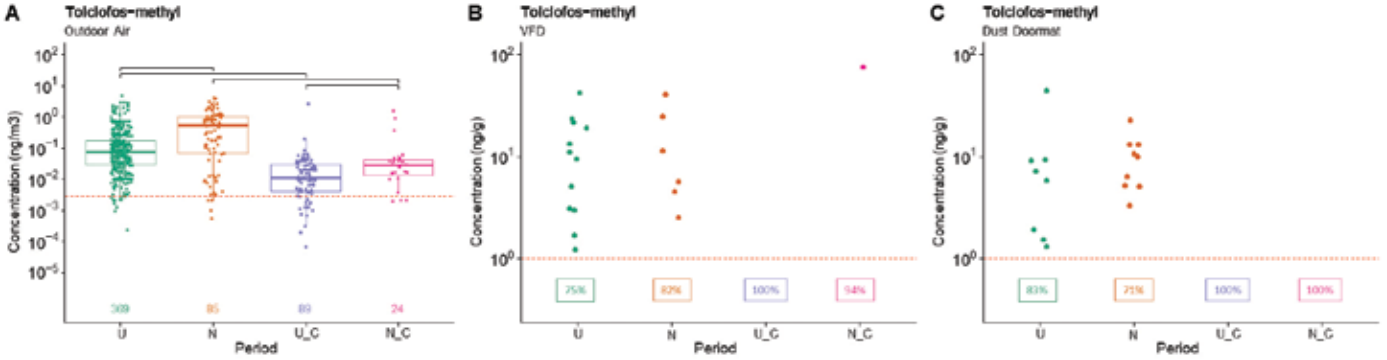

Figure 4.6: Measured concentrations of pesticides not applied during the measuring week or secondary products at location homes and control homes in the use and non-use periods.

On the x-axis is the period. U: location homes, use period; N: location homes, non-use period; U_C: Controls in use period; N_C: controls in the non-use period. In the box plot Figures the number of observations is shown. The red line represents the LOD. If imputation was not possible, the box below the LOD contains the percentage of samples below the LOD. (A) Results for outdoor air; (B) results for vacuumed floor dust (VFD); (c) results from dust from the door mat. The black line(s) above the boxplots inform on statistically significant difference between group means (t-test: $\alpha < 0.05$). The exact p-values are shown in table 4.6.

Overall, it appears that levels of pesticides in outdoor air from location homes are the highest, mainly in the use period. At control locations concentrations during the use period were elevated, comparable to the non-use period at location homes or sometimes higher. In the non-use period concentrations were lower for both location and control homes.

4.4.3 Effect of period and location on dust

VFD was collected from the living room floor and represents both settled airborne dust and materials dragged in while the doormat mainly represents drag-in of dust, sand or dirt from outside the home. Percentages of samples with pesticide levels above the LOD for both the VFD and the DDM are in Table 4.5. Many VFD samples had levels above the LOD. Differences in the percentages detected were observed between location homes and control homes and between periods. Also, in the non-use period, pesticides were frequently found in the dust from homes. As the doormat was a new doormat that was placed inside the home at the beginning of a measurement campaign and collected afterwards, and residents reported to vacuum their floors regularly, the findings in both types of dust indicate that indoor exposure continues outside the spraying period.

Graphs were made when a pesticide was detected in at least 40% of the samples for one medium (either outdoor air, VFD or DDM). Figure 4.4, panel B shows results from VFD for pesticides applied on target fields, and panel C shows results for DDM. P-values are in Table 4.6, panel “Applied in target fields”. For all pesticides (with imputed results) except for prochloraz, the differences between samples from location homes in the use and non-use period are statistically significant for VFD. For DDM, only pendimethalin, prothioconazole-desthio and tebuconazole are statistically significant. Differences between location homes and control homes in the use period were statistically significant for all pesticides except for tebuconazole for VFD and all pesticides except tebuconazole for DDM.

In Figure 4.5. panel B and C show the results for VFD and DDM for pesticides that were reported being applied on additional fields during our campaigns. Figure 4.6, panel B and C show secondary products or pesticides not reported to be applied during our campaigns. Corresponding p-values are presented in Table 4.6. Although differences are not as pronounced as for outdoor air samples, significant differences between locations and between periods can be seen.

Table 4.6: p-values for the differences between location homes and control homes and between periods shown in figure 4.4 – 4.6.

	Outdoor Air				VFD				DDM			
Active Ingredients	U vs N	U vs U_C	N vs N_C	U_C vs N_C	U vs N	U vs U_C	N vs N_C	U_C vs N_C	U vs N	U vs U_C	N vs N_C	U_C vs N_C
Applied in target fields												
chlorpropham	<0.001	<0.001	<0.001	<0.001								
flonicamid	<0.001	0.092	0.090	0.003	0.034	<0.001	0.130	0.225				
fluopyram	<0.001	0.002	0.450	0.016	0.045	0.001	0.175	0.555	0.164	0.002	<0.001	0.082
fluopyram-benzamide	<0.001	<0.001	0.691	0.218								
metamitron	<0.001	<0.001	0.206	0.139								
pendimethalin	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.078	0.600	<0.001	0.006	<0.001	0.230
prochloraz	0.094	<0.001	<0.001	0.812	0.747	<0.001	0.043	0.003	0.641	<0.001	0.006	0.679
prothioconazole-desthio	<0.001	<0.001	0.529	<0.001	<0.001	0.004	0.009	0.081	0.005	<0.001	<0.001	0.965
tebuconazole	<0.001	<0.001	0.408	0.001	0.014	0.062	0.172	0.335	0.006	0.451	0.165	0.009
Applied in additional fields												
boscalid	<0.001	0.130	0.100	<0.001	0.104	<0.001	0.008	0.946	0.024	4.31E-04	0.004	0.123
dimethenamid-P	<0.001	<0.001	<0.001	<0.001								
kresoxim-methyl	<0.001	<0.001	0.139	0.212								
S-metolachlor	<0.001	<0.001	<0.001	<0.001					0.188	0.020	3.74E-06	0.884
Not applied during measurement												
azoxystrobin					0.417	0.765	0.071	0.081	0.734	0.118	<0.001	0.551
fludioxonil					0.785	0.062	0.399	0.218				
imidacloprid					0.069	0.061	0.015	0.855	0.867	<0.001	0.296	0.030
linuron	<0.001	<0.001	<0.001	0.045								
propamocarb	0.002	0.334	0.087	0.890	0.170	0.452	0.413	0.547				
pyraclostrobin	<0.001	<0.001	<0.001	0.105	0.002	<0.001	<0.001	0.202	0.108	0.001	<0.001	0.262
thiophanate-methyl					0.173	0.032	0.072	0.603	0.854	<0.001	<0.001	0.480
*carbendazim**	0.387	<0.001	<0.001	0.965	0.329	<0.001	<0.001	0.921	0.752	0.620	0.001	0.007
toclofos-methyl	<0.001	<0.001	<0.001	0.018								

Legend	
	< 0.001
	< 0.01
	< 0.05
	> 0.05

Pesticides outline to right and italic: secondary products of the pesticide above.

* Carbendazim is a secondary product of thiophanate-methyl as well as a pesticide.

U: Location homes, Use period; N: Location homes, Non-use period; U_C: Control homes, Use period; N_C: Control homes, Non-use period.

4.4.4 Effect of distance to the applying field

The relation between the distance from a field to the home and the concentrations of pesticides in outdoor air, VFD and DDM was studied. To this purpose, log-linear trends were calculated and assessed for location homes. Separate calculations were carried out including the concentrations measured at the control homes.

Outdoor air

For outdoor air, pesticide concentrations of all measurement days during a measurement campaign are shown separately for location homes. For seven pesticides applied on target fields or additional fields, the percentage above LOD is shown in Table 4.7 and the relation between grouped distances and measured levels are shown in Figure 4.7 (Panel A). The p-values for the log-linear trends between categories of distance and air concentrations are in Table 4.8. As can be seen, there is a significant trend between air concentrations and distance to the field for all pesticides. Including control homes in the statistical tests provided similar results.

Dust

Table 4.7 shows for pesticides applied on target fields the percentage of collected dust samples with values above the LOD. Results from linear trend analysis for VFD and DDM are provided in Figure 4.7, panels B and C. Although the number of samples are lower compared to outdoor air, statistically significant linear trends between pesticide concentration and distance can be seen (Table 4.8). However, in contrast to outdoor air these trends are mostly dominated by the large difference between concentrations in dust at control homes and not due to differences between the concentration in location homes at different distances.

Table 4.7: Percentage of samples above the LOD for all tested pesticides, grouped by distance.

	Outdoor air					VFD				
	<50	50-150	150-250	250	Controls	<50	50-150	150-250	250	Controls
	Applied on target fields									
chlorpropham	100	100	100	100	100	56	NA	67	29	18
flonicamid	100	93	86	65	69	100	100	100	61	15
fluopyram	100	95	97	66	68	38	100	100	47	25
metamitron	98	76	76	66	36	83	50	42	37	0
pendimethalin	100	100	100	100	100	88	NA	100	73	27
prochloraz	100	96	NA	88	49	100	50	0	83	15
tebuconazole	95	96	98	92	69	100	86	100	83	69

	Dust Doormat				
	<50	50-150	150-250	250	Controls
chlorpropham	78	NA	100	38	29
flonicamid	50	67	0	18	0
fluopyram	88	50	50	50	14
metamitron	60	50	42	5	0
pendimethalin	100	NA	100	95	43
prochloraz	100	100	100	89	18
tebuconazole	80	86	50	96	91

Percentage of homes with pesticide levels above the LOD is indicated in grey bars.

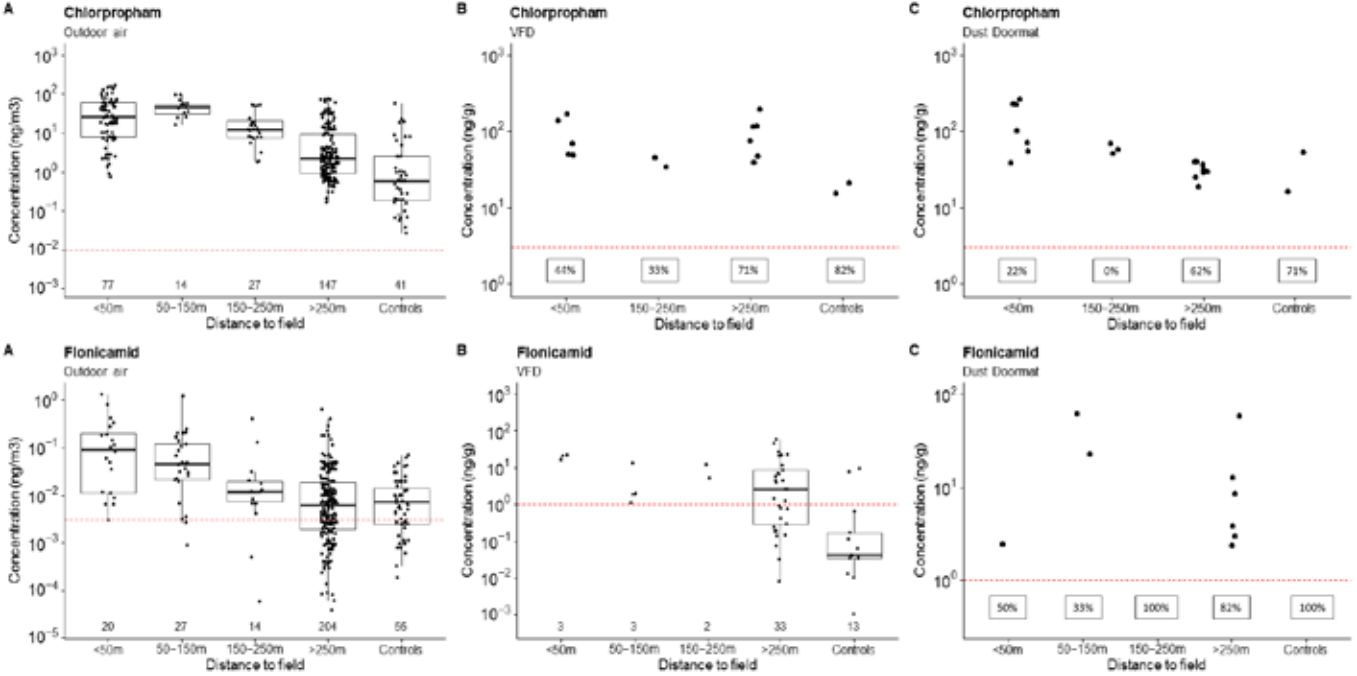

Figure 4.7: Distance to the applying field and concentration of pesticides applied on the target fields.
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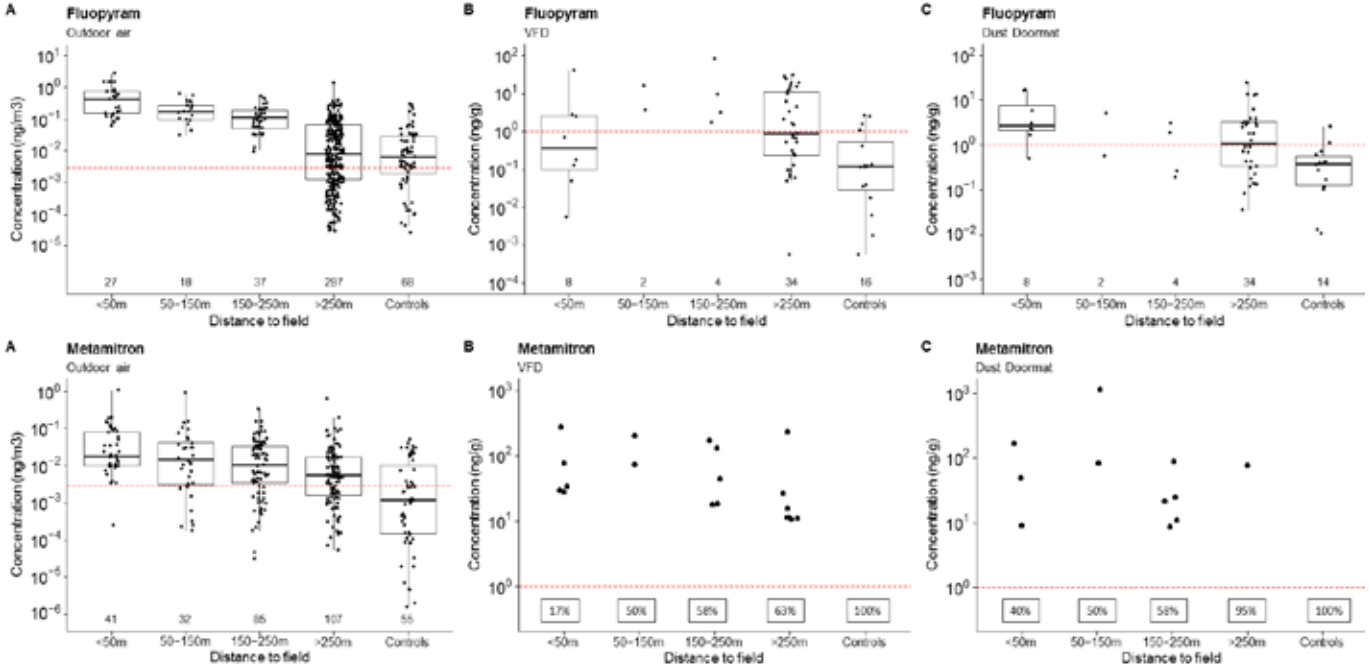

Figure 4.7: Distance to the applying field and concentration of pesticides applied on the target fields.
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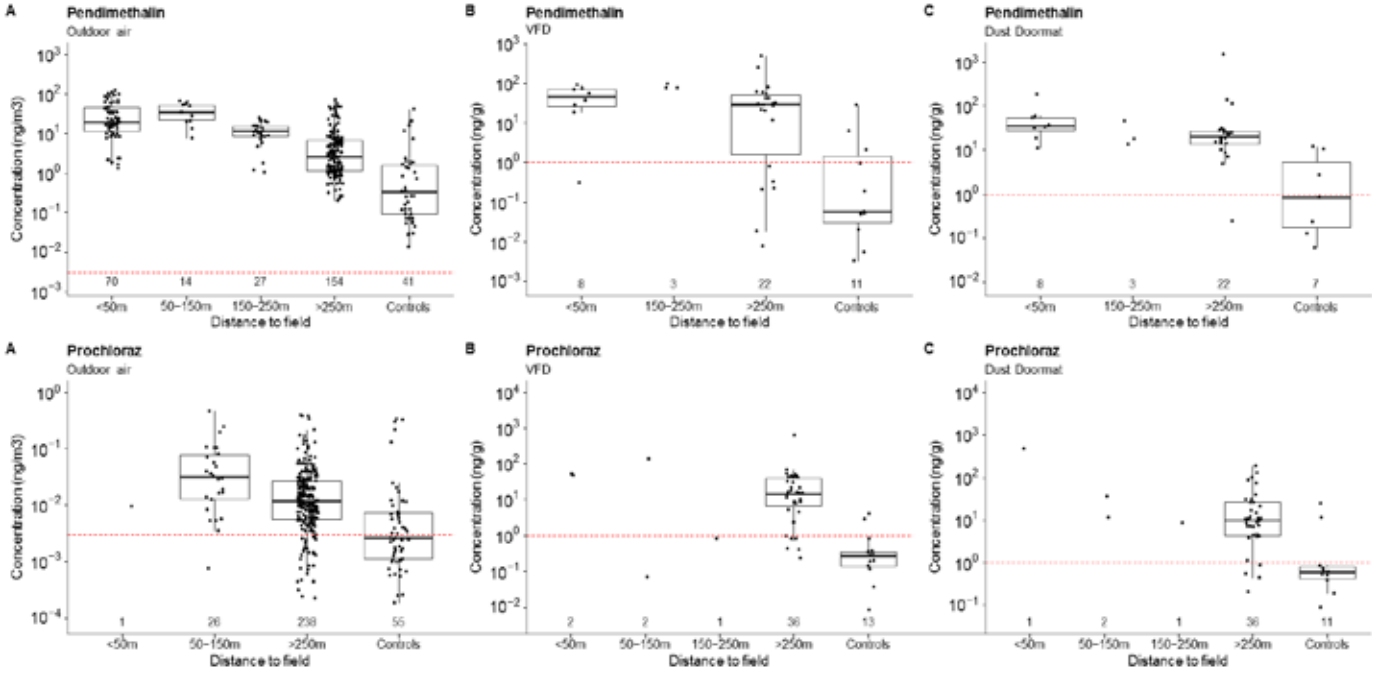

Figure 4.7: Distance to the applying field and concentration of pesticides applied on the target fields.
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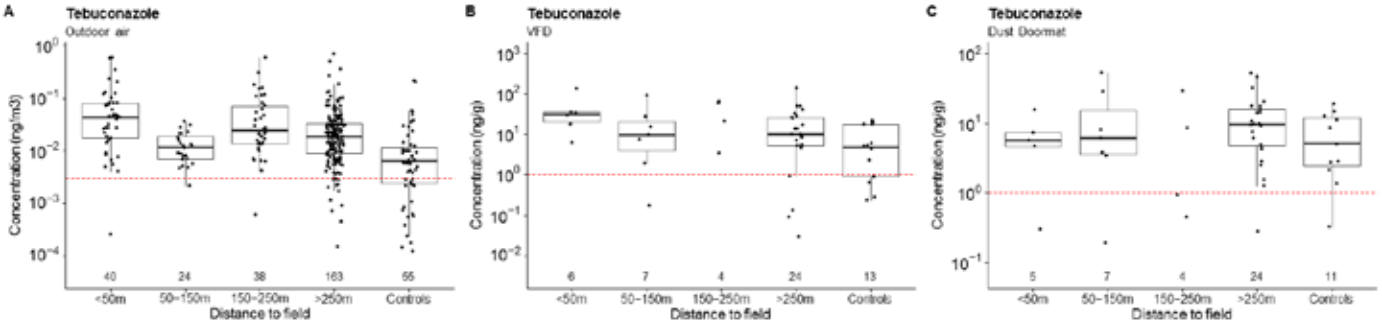

Figure 4.7: Distance to the applying field and concentration of pesticides applied on the target fields.
Boxplots for outdoor air samples (A), VFD (B) and dust from doormats (C) for the distance between the applying field and location homes and control homes. The red line represents the LOD for the specified pesticide. If imputation of the results was possible and N>4, boxplots are shown. If imputation was not possible we show the percentage of samples below the LOD in the graph. Data on log-linear relations are in Table 4.8.

Table 4.8: p-values for log-linear trends across distance categories.

	Location homes			Location and control homes		
Active Ingredient	Outdoor Air	VFD	DDM	Outdoor Air	VFD	DDM
Applied in target fields						
Chloorpropham	<0.001	NA	NA	<0.001	NA	NA
Flonicamid	<0.001	0.234	NA	<0.001	<0.001	NA
Fluopyram	<0.001	0.185	0.256	<0.001	0.003	0.004
Metamitron	<0.001	NA	NA	<0.001	NA	NA
Pendimethalin	<0.001	0.313	0.532	<0.001	<0.001	<0.001
Prochloraz	0.001	0.258	0.106	<0.001	<0.001	<0.001
Tebuconazole	0.018	0.323	0.569	<0.001	0.148	0.619

Legend	
	< 0.001
	< 0.01
	< 0.05
	> 0.05
NA	Not applicable

4.4.5 Correlations between different sample types

In the previous paragraphs, concentrations found in outdoor air, VFD and DDM for all participating homes were presented. This paragraph evaluates the correlation between the different sample types.

Dust

VFD and DDM were collected indoors. DDM may contain larger and heavier particles compared to VFD as the doormat is used for wiping shoes while the VFD is presumably more influenced by settling dust from the air. The number and percentage of paired observations and the corresponding Pearson correlation coefficients are shown in Table 4.9. Overall, moderate to good correlations between pesticide levels in the two different types of dust were observed.

Outdoor air and DDM

The median concentration of outdoor air samples of each measurement campaign was used for this comparison, given that only one dust sample was collected after each campaign. The number and percentage of paired observations, Pearson correlation coefficients and p-values between outdoor air and DDM are given in Table 4.10. Correlations between outdoor air and DDM were less strong compared to the two types of dust but still often moderate to good.

Outdoor air and VFD

Correlations between outdoor air and VFD are weaker compared to outdoor air and DDM concentrations, but in general still indicate a moderate association between outdoor air concentrations and the concentration of pesticides found in dust (Table 4.11).

Overall, the samples collected in and around the home were good to moderately correlated, indicating that higher outdoor exposure may lead to higher indoor exposure as well. Outdoor air entering the home and carry-in of dirt and dust by residents or their pets could represent the responsible transport routes.

Table 4.9: Correlations between VFD levels and DDM levels.

VFD vs DDM					
Active Ingredient	N-paired	%	Pearson Corr	Conf.Int	P-value
Applied in target field (s)					
acetamiprid	10	8	0.716	[0.156 , 0.927]	0.020
asulam	18	14.4	0.708	[0.361 , 0.883]	0.001
chlorpropham	15	12	0.176	[-0.36 , 0.631]	0.531
flonicamid	26	20.8	0.306	[-0.09 , 0.620]	0.128
fluopyram	125	100	0.408	[0.250 , 0.544]	<0.001
metamitron	15	12	0.223	[-0.32 , 0.660]	0.424
metamitron-desamino	12	9.6	0.138	[-0.47 , 0.659]	0.669
pendimethalin	125	100	0.443	[0.289 , 0.573]	<0.001
prochloraz	125	100	0.625	[0.504 , 0.721]	<0.001
prothioconazole-desthio	125	100	0.568	[0.435 , 0.676]	<0.001
tebuconazole	125	100	0.397	[0.238 , 0.535]	<0.001
Applied in additional field (s)					
boscalid	125	100	0.468	[0.318 , 0.594]	<0.001
chloridazon	16	12.8	0.573	[0.108 , 0.832]	0.020
S-metolachlor	38	30.4	0.458	[0.162 , 0.678]	0.004
Non-applied during measuring week					
azoxystrobin	125	100	0.315	[0.147 , 0.464]	<0.001
fludioxonil	27	21.6	0.007	[-0.37 , 0.386]	0.971
flutolanil	23	18.4	0.785	[0.551 , 0.904]	<0.001
imidacloprid	125	100	0.269	[0.098 , 0.424]	0.002
linuron	17	13.6	0.041	[-0.44 , 0.511]	0.877
propamocarb	39	31.2	0.340	[0.027 , 0.591]	0.034
pyraclostrobin	125	100	0.672	[0.562 , 0.758]	<0.001
thiophanate-methyl	125	100	0.524	[0.384 , 0.640]	<0.001
carbendazim	125	100	0.419	[0.262 , 0.553]	<0.001
toclofos-methyl	17	13.6	0.579	[0.136 , 0.828]	0.015

	Pearson Correlation	
Small	[0.1 , 0.3)	[-0.1 , -0.3)
Medium	[0.3 , 0.5)	[-0.3 , -0.5)
Large	≥ 0.5	≤ - 0.5

P-value
< 0.05
< 0.01
< 0.001

Table 4.10: Correlations between outdoor air levels and DDM levels.

	Outdoor air vs DDM		Outdoor air (median) vs DDM		
Active Ingredient	N-paired	%	Pearson Corr	Conf.Int	P-value
Applied in target field (s)					
chlorpropham	27	31	0.54	[0.201 , 0.763]	0.004
flonicamid	11	13	0.340	[-0.32 , 0.780]	0.306
fluopyram	87	100	0.445	[0.258 , 0.599]	<0.001
metamitron	11	13	0.131	[-0.50 , 0.677]	0.701
pendimethalin	87	100	0.569	[0.407 , 0.696]	<0.001
prochloraz	87	100	0.556	[0.391 , 0.686]	<0.001
prothioconazole-desthio	87	100	0.446	[0.260 , 0.600]	<0.001
tebuconazole	87	100	0.492	[0.314 , 0.636]	<0.001
Applied in additional field (s)					
boscalid	87	100	0.430	[0.241 , 0.587]	<0.001
S-metolachlor	87	100	0.479	[0.298 , 0.626]	<0.001
Non-applied during measuring week					
azoxystrobin	53	61	0.140	[-0.13 , 0.395]	0.318
carbendazim	87	100	0.203	[-0.00 , 0.396]	0.059
cyprodinil	10	11	0.135	[-0.54 , 0.704]	0.709
flutolanil	16	18	0.315	[-0.21 , 0.701]	0.235
imidacloprid	47	54	-0.001	[-0.28 , 0.286]	0.995
linuron	25	29	0.225	[-0.18 , 0.569]	0.279
propamocarb	23	26	0.380	[-0.03 , 0.684]	0.074
pyraclostrobin	87	100	0.560	[0.396 , 0.689]	<0.001
toclofos-methyl	14	16	0.440	[-0.11 , 0.786]	0.116

	Pearson Correlation	
Small	[0.1 , 0.3)	[-0.1 , -0.3)
Medium	[0.3 , 0.5)	[-0.3 , -0.5)
Large	≥ 0.5	≤ - 0.5

P-value
< 0.05
< 0.01
< 0.001

Table 4.11: Correlations between outdoor air levels and VFD levels.

	Outdoor air vs VFD		Outdoor air (median) vs VFD		
Active Ingredient	N-paired	%	Pearson Corr	Conf.Int	P-value
Applied in target field (s)					
chlorpropham	18	20	-0.012	[-0.47 , 0.457]	0.963
flonicamid	89	100	0.133	[-0.07 , 0.332]	0.214
fluopyram	89	100	0.256	[0.049 , 0.440]	0.016
metamitron	21	24	0.424	[-0.00 , 0.723]	0.055
metamitron-desamino	15	17	0.406	[-0.13 , 0.759]	0.134
pendimethalin	89	100	0.511	[0.339 , 0.650]	<0.001
prochloraz	89	100	0.436	[0.250 , 0.590]	<0.001
prothioconazole-desthio	89	100	0.399	[0.208 , 0.560]	<0.001
tebuconazole	89	100	0.385	[0.192 , 0.549]	<0.001
Applied in additional field (s)					
boscalid	89	100	0.262	[0.056 , 0.445]	0.013
kresoximmethyl	11	12	-0.016	[-0.60 , 0.589]	0.964
metolachlorS	22	25	0.160	[-0.28 , 0.544]	0.478
Non-applied during measuring week					
azoxystrobin	53	60	0.012	[-0.25 , 0.280]	0.934
carbendazim	89	100	0.300	[0.097 , 0.478]	0.004
difenoconazole	12	13	-0.115	[-0.64 , 0.491]	0.722
fludioxonil	15	17	0.262	[-0.28 , 0.682]	0.346
flutolanil	12	13	-0.088	[-0.62 , 0.511]	0.786
imidacloprid	48	54	0.228	[-0.06 , 0.480]	0.120
linuron	19	21	0.272	[-0.20 , 0.646]	0.261
propamocarb	89	100	0.163	[-0.04 , 0.358]	0.128
pyraclostrobin	89	100	0.341	[0.143 , 0.513]	0.001
toclofos-methyl	15	17	0.228	[-0.32 , 0.662]	0.415

	Pearson Correlation	
Small	[0.1 , 0.3)	[-0.1 , -0.3)
Medium	[0.3 , 0.5)	[-0.3 , -0.5)
Large	≥ 0.5	≤ - 0.5

P-value
< 0.05
< 0.01
< 0.001

4.4.6 Soil samples

The soil samples were intended to be top soil collected from a fixed surface area of the garden of the homes using a frame, with the same soil layer depth. The total amount of soil sample was weighed upon receipt. It appeared that sample collection was not always possible as intended (i.e. no consistent area/depth). The weight of the samples varied from 190 to 1938 gram (average 1094, RSD 28%, N=193). Before analysis, the soil sample was homogenized by manual mixing and a subsample was taken for extraction. No moisture content was determined, i.e. analysis results are based on soil as received.

Table 4.12 shows for the 124 collected samples the LOD in soil for each pesticide and the percentage of samples with levels above the LOD for soil collected from locations homes and from control homes. Results are shown for the use period and the non-use period. Only for 7 pesticides (boscalid, carbendazim, fluopyram, imidacloprid, pendimethalin, prochloraz and pyraclostrobin) enough samples had levels above the LOD for imputation of values below the LOD. Results from these pesticides are shown in Figure 4.8. Levels show no differences over the periods. For 3 pesticides (pendimethalin, prochloraz and pyraclostrobin), soil from location homes have significantly higher levels compared to control homes. P-values for the results from soil are presented in Table 4.13. It can be concluded that soil samples from location homes show higher pesticide levels (statistically significant for 38%) than control homes but no clear effect of period is seen.

4.5 Environmental samples: indoor air samples

In addition to outdoor air sampling, indoor air samples were taken in location homes participating in protocol B during the first 24 h after a spray event. In total, 24 indoor air samples were collected and analyzed. Indoor air samples were statistically analyzed on period, with respect to the correlation between indoor air and outdoor air and between indoor air and indoor collected dust. Since only homes within 50 m of a target field were included, the effect of distance on concentrations cannot be evaluated. Finally, as no samples were taken at control homes, we cannot compare indoor levels at locations to controls.

4.5.1 Effect of use period

Table 4.14 shows how many indoor air samples had pesticide levels above the LOD. As for other environmental samples, if > 40% of all the air samples (including outdoor, see also chapter 3) had levels above the LOD for a certain pesticide, imputation of values below the LOD was performed. For all pesticides with imputed results, the medians and ranges for concentrations in the use and non-use period are shown. The difference was evaluated using t-tests and p-values are also shown in Table 4.14. Concentrations during the use period are overall higher compared to the non-use period, being statistically significant for 3 pesticides: chlorpropham, pendimethalin and tebuconazole.

Table 4.12: Percentage of soil samples with pesticide levels above the LOD.

	Soil	Soil (% > LOD)			
Active Ingredient	LODs (ug/kg)	U	N	U_C	N_C
Applied in the target field(s)					
acetamiprid	1	0	0	0	0
asulam	1	0	0	0	0
chlorpropham	3	22	6	0	0
cyhalotrin-lambda	3	5	15	0	17
flonicamid	1	0	0	0	0
fluopyram	1	55	56	33	33
floupyram-benzamide	1	0	0	0	0
mepanipyrim	1	0	0	0	0
metamitron	1	22	0	0	0
metamitron-desamino	1	1	0	0	0
pendimethalin	1	81	71	33	14
prochloraz	1	50	71	8	22
prothioconazole	-	0	0	0	0
prothioconazole-desthio	1	10	8	0	0
pymetrozine	1	0	0	0	0
tebuconazole	1	10	2	33	0
thiacloprid	1	0	0	0	0
trifloxystrobin	1	0	0	0	0
trifloxystrobin-acid	1	0	0	0	0
Applied in the additional fields					
boscalid	1	95	88	75	67
chloridazon	1	7	0	8	0
dimethenamidP	1	3	2	0	0
kresoxim-methyl	3	0	0	0	0
S-metolachlor	1	28	6	0	0
spirotetramat	1	0	0	0	0
spirotetramat-enol	1	0	0	0	0
Not applied during measuring week					
azoxystrobin	1	12	14	11	19
cyprodinil	1	6	9	13	7
deltamethrin	10	9	5	0	5
difenoconazole	1	2	6	7	0
dimethomorph	1	2	3	7	7
fludioxonil	1	13	18	33	13
fluopicolide	1	0	0	0	0
flutolanil	1	17	12	7	7
fosthiazate	1	0	0	0	0
imidacloprid	1	36	44	67	53
linuron	1	0	2	0	0
oxamyl	1	0	0	0	0
primicarb	1	2	6	13	0
propamocarb	1	0	0	0	0
pyraclostrobin	1	67	55	10	15
sulcotrione	1	0	0	0	0
terbuthylazine	1	0	0	0	0
thiophanate-methyl	1	2	6	0	7
carbendazim	1	79	68	53	53
toclofos-methyl	1	0	0	0	0

U: Location homes, Use period; N: Location homes, Non-use period; U_C: Control homes, Use period; N_C: Control homes, Non-use period

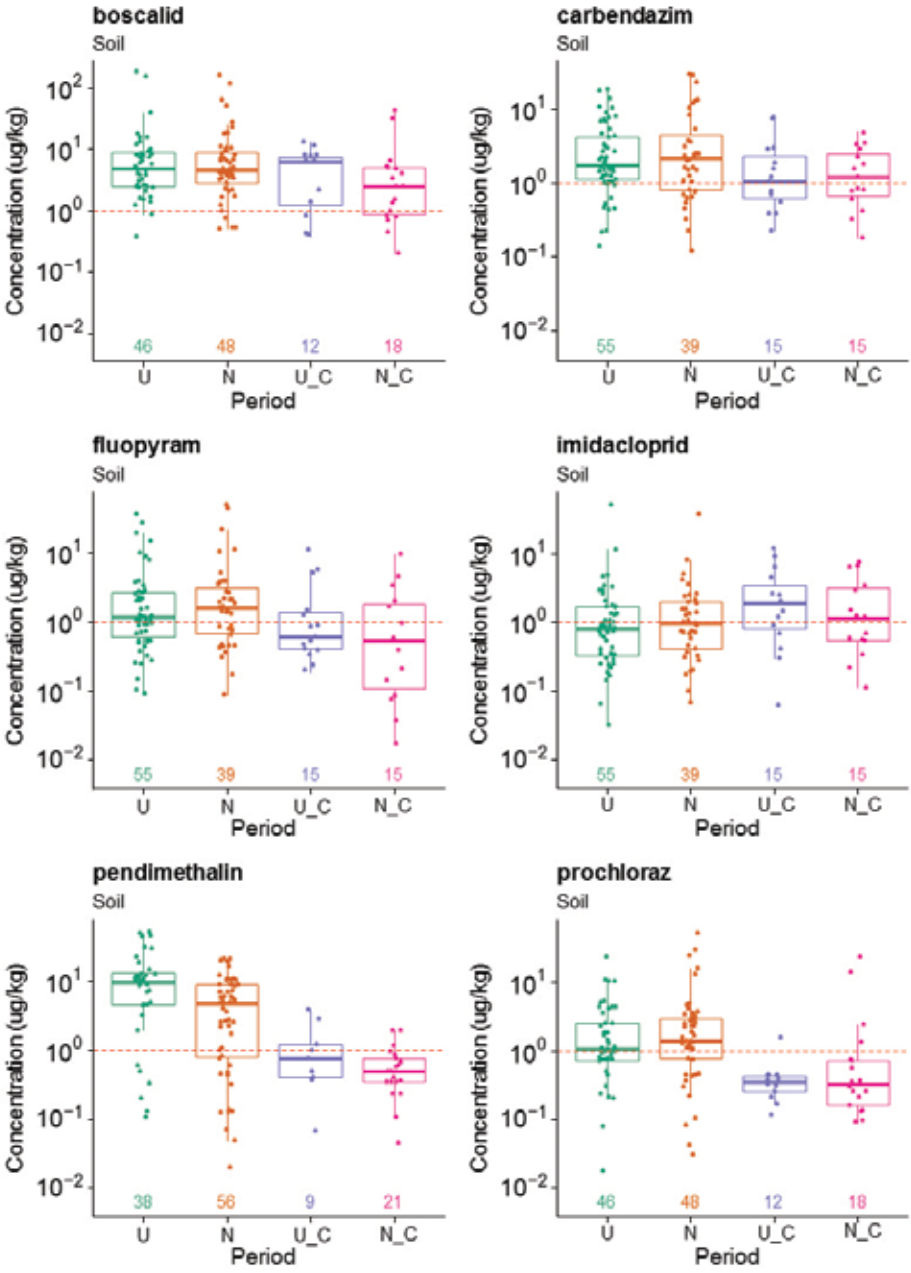

Figure 4.8: Pesticide levels in soil.
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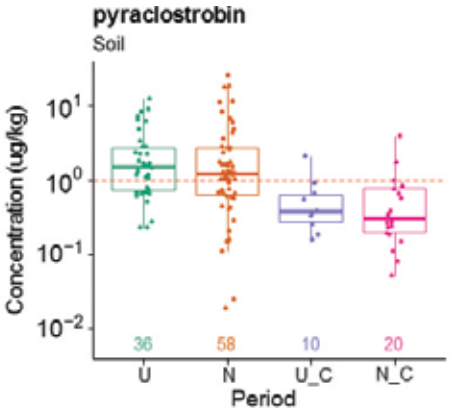

Figure 4.8: Pesticide levels in soil.
For seven pesticides with imputed levels, results from soil are shown for location homes in the use period (U), in the non-use period (N), for control homes in the use period (U_C) and the non-use period (N_C). The red line is the LOD for the specific pesticide. Number of samples per group are shown above the x-axis.

Table 4.13: p-values for soil samples in location homes and control homes.

	Soil - Pvalue table				
Active Ingredients	U vs N	U vs U_C	N vs N_C	N vs U_C	U_C vs N_C
boscalid	0.738	0.448	0.180	0.572	0.587
carbendazim	0.747	0.424	0.282	0.345	0.946
fluopyram	0.743	0.231	0.033	0.173	0.255
imidacloprid	0.707	0.086	0.468	0.160	0.522
pendimethalin	0.045	0.001	1.5E-06	0.024	0.350
prochloraz	0.639	3.1E-04	0.081	1.7E-04	0.368
pyraclostrobin	0.247	0.002	0.005	0.021	0.716

Legend	
	< 0.001
	< 0.01
	< 0.05
	> 0.05

U: Location homes, Use period; N: Location homes, Non-use period;
U_C: Control homes, Use period; N_C: Control homes, Non-use period

4.5.2 Correlation between indoor and outdoor air levels

Comparing paired indoor and outdoor levels, several pesticides display higher indoor levels compared to outdoor levels. Ratios (outdoor/indoor levels) are shown in Figure 4.9, with pesticides ordered by vapor pressure. Only pesticides are shown with at least five paired observations above the LOD. Imputed levels below the LOD were not used as the partly random characteristic of the imputation may unduly influence the ratio. For all paired observations with a ratio below 1, indoor levels of the specific pesticide are higher compared to outdoor levels. Based on the respective medians, this is the case for 14 out of 23 pesticides. Vapor pressure will affect the quantity of pesticide that will be in the gas-phase in both the outdoor and indoor environment, therefore influencing the ratio. Pearson correlation coefficients between indoor and outdoor air levels are shown in Table 4.15. We checked if Pearson correlation coefficients differed

Table 4.14: Indoor air samples: %>LOD and levels in the use and non-use period.

Active Ingredient	% > LOD		Use period (ng/m3)		Non-use period (ng/m3)		P-Value
	U	N	Median	Range	Median	Range	
Applied in target field(s)							
acetamiprid	18	0	< LOD	[< LOD , 0.012]	< LOD	NA	NA
asulam	25	0	< LOD	[< LOD , 0.149]	< LOD	NA	NA
chlorpropham	100	100	1.909	[0.526 , 25.00]	0.643	[0.039 , 11.41]	**0.009**
cyhalotrin-lambda	67	79	< LOD	[< LOD , 0.160]	< LOD	[< LOD , 0.230]	NA
flonicamid	100	100	0.029	[0.0003 , 0.187]	0.018	[0.0003 , 0.080]	0.584
fluopyram	100	100	0.004	[0.0005 , 0.764]	0.006	[0.0002 , 0.031]	0.397
floupyram-benzamide	100	100	0.019	[0.002 , 0.143]	0.019	[0.001 , 0.042]	0.498
mepanipyrim	67	37	< LOD	[< LOD , 0.076]	< LOD	[< LOD , 0.013]	NA
metamitron	100	100	0.013	[0.0005 , 0.484]	0.011	[0.0001 , 0.039]	0.073
metamitrondesamino	25	53	< LOD	[< LOD , 0.008]	< LOD	[< LOD , 0.023]	NA
pendimethalin	100	100	0.622	[0.101 , 3.000]	0.188	[0.007 , 3.955]	**0.006**
prochloraz	100	100	0.010	[0.001 , 0.029]	0.006	[0.001 , 0.081]	0.819
prothioconazole	0	0	< LOD	NA	< LOD	NA	NA
prothioconazoledesthio	100	100	0.017	[0.003 , 0.083]	0.014	[0.002 , 0.060]	0.242
pymetrozine	42	16	< LOD	[< LOD , 0.017]	< LOD	[< LOD , 0.01]	NA
tebuconazole	100	100	0.013	[0.001 , 0.447]	0.005	[0.001 , 0.011]	**0.012**
thiacloprid	25	5	< LOD	[< LOD , 0.009]	< LOD	[< LOD , 0.004]	NA
trifloxystrobin	33	32	< LOD	[< LOD , 0.017]	< LOD	[< LOD , 0.041]	NA
trifloxystrobin-acid	67	74	< LOD	[< LOD , 0.229]	< LOD	[< LOD , 0.057]	NA
Applied additional field(s)							
boscalid	100	100	0.008	[0.002 , 0.047]	0.004	[0.000 , 0.020]	0.051
chloridazon	43	29	< LOD	[< LOD , 0.058]	< LOD	[< LOD , 0.218]	NA
dimethenamid-P	100	100	0.046	[0.009 , 0.141]	0.016	[0.004 , 0.382]	NA
kresoxim-methyl	100	100	0.005	[0.0004 , 0.116]	0.005	[0.0001 , 0.032]	0.293
S-metolachlor	100	100	0.088	[0.009 , 1.061]	0.042	[0.001 , 0.322]	0.072
spirotetramat	40	0	< LOD	[< LOD , 0.047]	< LOD	NA	NA
spirotetramat-enol	20	5	< LOD	[< LOD , 0.008]	< LOD	[< LOD , 0.003]	NA
Non-applied during measuring week							
azoxystrobin	43	82	< LOD	[< LOD , 0.020]	< LOD	[< LOD , 0.467]	NA
cyprodinil	44	40	< LOD	[< LOD , 0.043]	< LOD	[< LOD , 0.010]	NA
deltamethrin	100	52	0.009	[0.003 , 0.026]	< LOD	[< LOD , 0.026]	NA
difenoconazole	63	73	< LOD	[< LOD , 0.090]	< LOD	[< LOD , 0.147]	0.141
dimethomorph	10	7	< LOD	[< LOD , 0.005]	< LOD	[< LOD , 0.008]	NA
fludioxonil	19	13	< LOD	[< LOD , 0.040]	< LOD	[< LOD , 0.016]	NA
fluopicolide	31	7	< LOD	[< LOD , 0.006]	< LOD	[< LOD , 0.007]	NA
flutolanil	19	13	< LOD	[< LOD , 0.021]	< LOD	[< LOD , 0.012]	NA
fosthiazate	63	7	< LOD	[< LOD , 0.009]	< LOD	[< LOD , 0.003]	NA
imidacloprid	44	47	< LOD	[< LOD , 0.01]	< LOD	[< LOD , 0.011]	NA
linuron	100	100	0.006	[0.0004 , 0.020]	0.009	[0.001 , 0.076]	0.091
oxamyl	10	10	< LOD	[< LOD , 0.012]	< LOD	[< LOD , 0.010]	NA
primicarb	38	40	< LOD	[< LOD , 0.011]	< LOD	[< LOD , 0.005]	NA
propamocarb	100	100	0.009	[0.0001 , 0.795]	0.006	[0.0004 , 0.022]	0.827
pyraclostrobin	100	100	0.014	[0.003 , 0.107]	0.020	[0.0001 , 0.075]	0.351
sulcotrione	0	0	< LOD	NA	< LOD	NA	NA
terbuthylazine	31	60	< LOD	[< LOD , 0.023]	< LOD	[< LOD , 0.006]	NA
thiophanate-methyl	0	0	< LOD	NA	< LOD	NA	NA
carbendazim	100	100	0.078	[0.009 , 0.304]	0.043	[0.001 , 0.256]	0.060
toclofos-methyl	100	100	0.072	[0.001 , 1.706]	0.038	[0.004 , 0.415]	0.969

p-values in **Bold/gray** are <0.05; U: Use period; N: Non-use period
Pesticides outline to right and italic: secondary products of the product above

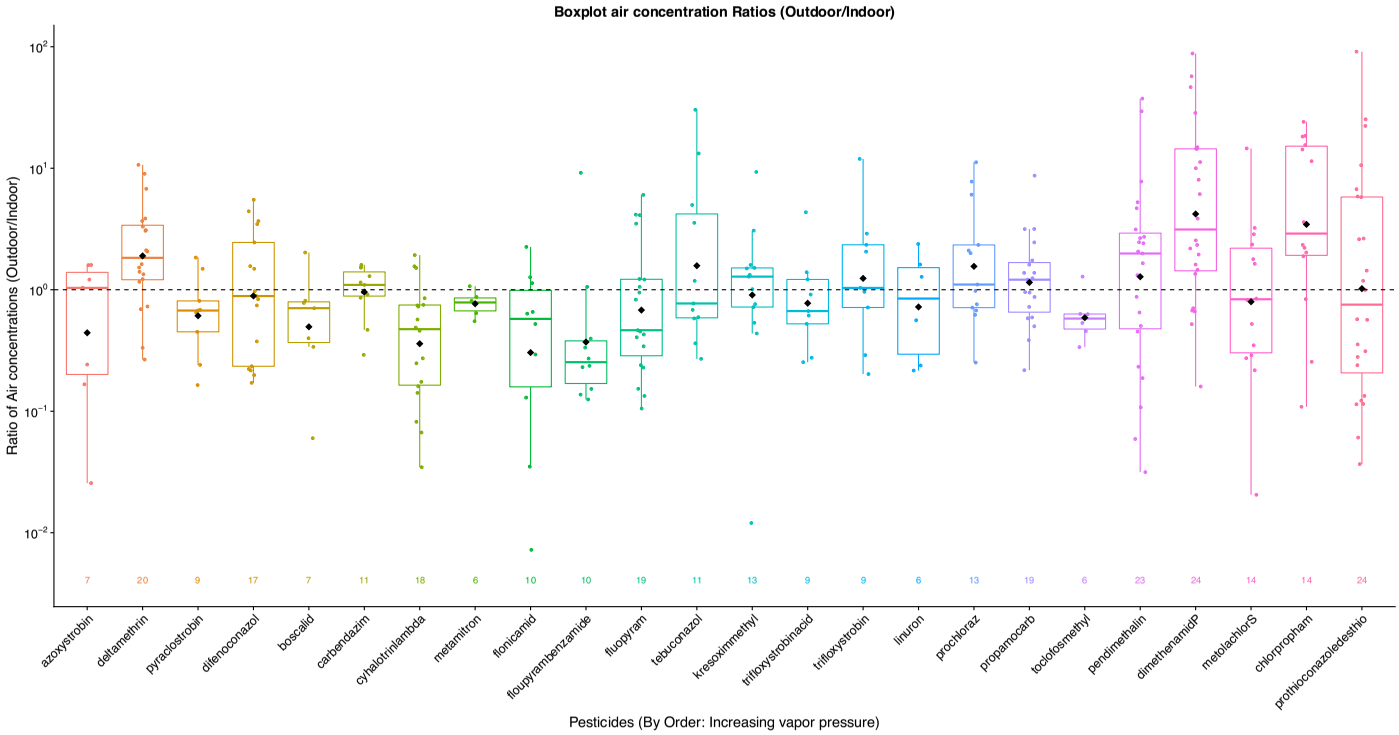

Figure 4.9: Ratios of outdoor to indoor air levels.
The ratio is expressed per pesticide with N>4 paired observations above the LOD. The number of paired observations is shown above the x-axis. The dotted line represents a ratio of 1. For an explanation of boxplots, see box xx on page x. Lines are medians, the mean is shown with a black diamond. Pesticides are ordered by vapor pressure (low to high).

Table 4.15: Pearson correlation coefficient for outdoor vs. indoor air levels for specified pesticides.

Active Ingredient	N-paired	Pearson Corr Coef.	95% CI	P-value
cyhalotrin-lambda	6	0.872	[0.205 , 0.985]	0.024
trifloxystrobin-acid	9	0.751	[0.172 , 0.944]	0.020
dimethenamid-P	24	0.667	[0.360 , 0.843]	4E-04
metolachlor-S	24	0.652	[0.337 , 0.835]	6E-04
fluopyram	24	0.597	[0.254 , 0.806]	0.002
kresoxim-methyl	24	0.533	[0.164 , 0.770]	0.007
pendimethalin	24	0.498	[0.118 , 0.750]	0.013
prochloraz	24	0.487	[0.104 , 0.744]	0.016
linuron	24	0.486	[0.102 , 0.743]	0.016
tebuconazole	24	0.480	[0.095 , 0.740]	0.018
toclofos-methyl	24	0.473	[0.085 , 0.735]	0.020
chlorpropham	24	0.472	[0.084 , 0.735]	0.020
deltamethrin	9	0.468	[-0.284 , 0.863]	0.203
propamocarb	24	0.460	[0.070 , 0.728]	0.024
boscalid	24	0.428	[0.029 , 0.708]	0.037
prothioconazole-desthio	24	0.426	[0.027 , 0.707]	0.038
carbendazim	24	0.333	[-0.081 , 0.648]	0.112
floupyram-benzamide	24	0.323	[-0.092 , 0.642]	0.124
pyraclostrobin	24	0.321	[-0.094 , 0.641]	0.126
metamitron	24	0.304	[-0.113 , 0.630]	0.148
flonicamid	24	0.239	[-0.181 , 0.585]	0.261
difenoconazole	7	0.169	[-0.669 , 0.817]	0.717
azoxystrobin	7	0.059	[-0.726 , 0.777]	0.899
trifloxystrobin	6	0.023	[-0.803 , 0.819]	0.965

	Pearson Correlation
Small	[0.1 , 0.3)
Medium	[0.3 , 0.5)
Large	≥ 0.5

P-value
< 0.05
< 0.01
< 0.001

Pesticides outline to right and italic: secondary products.

depending on the respective vapor pressure of the analyzed pesticide. This is shown in Figure 4.10. We can conclude that there is a moderate positive correlation between vapor pressure and the outdoor to indoor correlation of concentration in air.

4.5.3 Correlation between indoor air and dust

As shown in Figure 4.9 the indoor air levels of several pesticides were higher compared to outdoor levels. There are several potential explanations including for example an indoor source or resuspension of dust. In chapter 6 these will be addressed in more detail.

Table 4.16 shows the correlation between indoor air levels and levels in DDM for all pesticides with more than four paired observations above the LOD. We observe moderate correlations although none are statistically significant. Results for VFD correlations (Table 4.17) are similar to DDM, with only one pesticide showing a statistically significant correlation: fluopyram. Results are consistent with the results for outdoor air with the exception that statistical power in these analyses is much lower. In chapter 6 correlations, models and possible other predictors will be explored.

4.6 Personal samples: morning urines

Residents and controls (shown in Table 4.3) completed questionnaires at the start of the study, collected morning urines during measurement campaigns and filled out a diary

regarding diet, the activities they performed and locations they visited. Participants in the <50m protocol also collected first day urines and hand wipes.

Analysis of urine samples

As described in chapters 2 and 3, five (biomarkers of) pesticides were selected for measurements in urine samples: asulam, chlorpropham, prochloraz, tebuconazole and thiophanate-methyl/carbendazim. For each of these pesticides one specific biomarker was measured in the urine samples. The specific names of the selected biomarkers can be found in chapter 2, here they are referred to as biomarkers of the specific pesticide. Levels of biomarkers of pesticides in urine samples below the LOD were imputed when more than 40% of the results were above the LOD. All urine and diaper results were corrected for creatinine levels. Unadjusted results can be found in Appendix 12.

4.6.1 Selection

Selection of samples for analysis

As for environmental samples, due to budgetary constraints only selected urine samples were analyzed. Selection of urine samples for analysis is described in chapter 3.4.7. In short, morning urine samples from day 1, 2, 4 and 7 of all children and 1 adult living

Table 4.16: Correlations between indoor air levels and DDM levels.

	Indoor Air vs DDM				
Active Ingredient	N-Paired	%	Pearson Corr	Conf.Interval	p-value
fluopyram	22	100	0.264	[-0.17 , 0.617]	0.235
pendimethalin	22	100	0.370	[-0.06 , 0.684]	0.090
prochloraz	22	100	0.400	[-0.02 , 0.703]	0.065
prothioconazole-desthio	22	100	-0.082	[-0.48 , 0.352]	0.718
tebuconazole	22	100	0.256	[-0.18 , 0.611]	0.250
boscalid	22	100	0.294	[-0.14 , 0.636]	0.184
metolachlorS	22	100	0.295	[-0.14 , 0.637]	0.183
carbendazim	22	100	0.040	[-0.38 , 0.453]	0.861
pyraclostrobin	22	100	0.182	[-0.25 , 0.560]	0.417

	Pearson Correlation	
Small	[0.1 , 0.3)	[-0.1 , -0.3)
Medium	[0.3 , 0.5)	[-0.3 , -0.5)
Large	≥ 0.5	≤ - 0.5

P-value
< 0.05
< 0.01
< 0.001

Pesticides outline to right and italic: secondary products.

Table 4.17: Correlations between indoor air levels and VFD levels.

	Indoor Air vs VFD				
Active Ingredient	N-Paired	%	Pearson Corr	Conf.Interval	p-value
flonicamid	24	100	0.249	[-0.17 , 0.592]	0.241
fluopyram	24	100	0.470	[0.082 , 0.734]	0.020
pendimethalin	24	100	-0.026	[-0.42 , 0.381]	0.905
prochloraz	24	100	-0.045	[-0.44 , 0.364]	0.833
prothioconazole-desthio	24	100	0.222	[-0.19 , 0.574]	0.296
tebuconazole	24	100	0.342	[-0.07 , 0.654]	0.102
boscalid	24	100	-0.094	[-0.47 , 0.321]	0.663
azoxystrobin	17	71	-0.215	[-0.63 , 0.296]	0.408
carbendazim	24	100	0.160	[-0.26 , 0.528]	0.457
imidacloprid	10	42	0.116	[-0.55 , 0.695]	0.749
propamocarb	24	100	-0.264	[-0.60 , 0.155]	0.212
pyraclostrobin	24	100	0.138	[-0.28 , 0.512]	0.521

	Pearson Correlation	
Small	[0.1 , 0.3)	[-0.1 , -0.3)
Medium	[0.3 , 0.5)	[-0.3 , -0.5)
Large	≥ 0.5	≤ - 0.5

P-value
< 0.05
< 0.01
< 0.001

Pesticides outline to right and italic: secondary products.

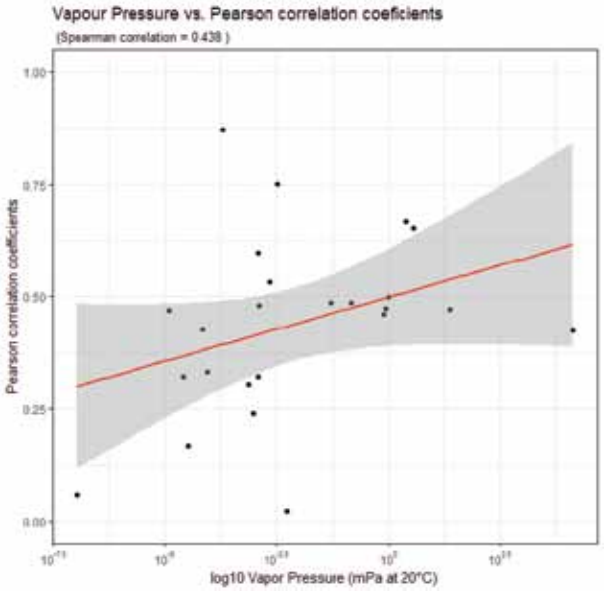

Figure 4.10: Relation between Pearson correlation coefficients of indoor and outdoor samples per pesticide and the vapor pressure.
Each dot represents a Pearson correlation coefficient for indoor and outdoor air samples for a pesticide, expressed against the vapor pressure of that pesticide. In red is a linear regression fit between the two variables, the 95% confidence interval is in gray. The overall correlation between the expressed results is rho = 0.438, p=0.032 (p-value computed using algorithm AS 89 (Best & Roberts 1975)).

in a selected location home or a control home were selected, which corresponded to analyzing samples of 66% of participants (Table 4.3). Results are shown separately for adults and children. For biomarkers of asulam, chlorpropham, prochloraz and tebuconazole, urine samples were selected when the pesticide was used on the target field during the measurement campaign at that location. For thiophanate-methyl/carbendazim, a pesticide not used on the fields but for bulb disinfection, the selection was based on the observed concentrations of carbendazim in dust (both VFD and DDM). Results are separately shown for children and adults.

Growers' families

The levels of biomarkers in morning urines of residents of farm homes (adults and children) can be found in Appendix 13.

4.6.2 Biomarkers in morning urine: adults

Levels

The number of analyzed morning urines of adult residents and controls and the percentage of samples above the LOD are shown per biomarker in Table 4.16. For 3 out of 5 biomarkers, imputation was not possible: asulam, thiophanate-methyl/carbendazim and prochloraz. For asulam, the highest percentage above the LOD was

Table 4.18: Levels of biomarkers in morning urine of residents (adults).

	Residents (adults)		Controls (adults)	
	U	N	U	N
Biomarker of asulam				
N	71	25	64	36
% > LOD	3	0	16	14
N > LOD	2	0	10	5
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD
max	0.18	NA	0.60	0.39
Biomarker of carbendazim				
N	118	60	64	36
% > LOD	21	18	11	11
N > LOD	25	11	7	4
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD
max	2.30	3.53	4.58	0.89
Biomarker of chlorpropham				
N	76	39	58	34
% > LOD	97	100	67	50
N > LOD	Imputation			
mean	7.95	3.29	1.87	0.47
median	0.74	0.52	0.34	0.11
min	4E-04	1E-01	7E-03	5E-03
max	177.87	47.76	22.12	4.08
Biomarker of prochloraz				
N	30	22	64	34
% > LOD	0	9	0	0
N > LOD	0	2	0	0
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD
max	NA	0.06	NA	NA
Biomarker of tebuconazole				
N	99	45	64	34
% > LOD	61	23	43	24
N > LOD	Imputation			
median	0.19	0.10	0.11	0.19
mean	0.56	0.22	0.38	0.92
min	2E-03	1E-03	2E-03	6E-03
max	7.38	1.94	3.41	6.16

Values are in µg/g creatinine.
N: number of samples; LOD: limit of detection; min: minimum value; max: maximal value; Imputation: levels below LOD are imputed: results pertain to the full sample. NA: not applicable.
U: Use period; N: Non-use period .

found for controls, both in the use and the non-use period. For prochloraz almost all samples had values below the LOD while for thiophanate-methyl/carbendazim, the percentage of samples above LOD was slightly but not statistically significantly higher in residents compared to controls and in the use period compared to the non-use period.

For the biomarkers of chlorpropham and tebuconazole, imputation of values below the LOD was possible. The mean, median and range of the results after imputation are provided in Table 4.18 and Figure 4.11. Differences were tested using t-tests, indicating differences between residents and controls and between periods (Table 4.19).

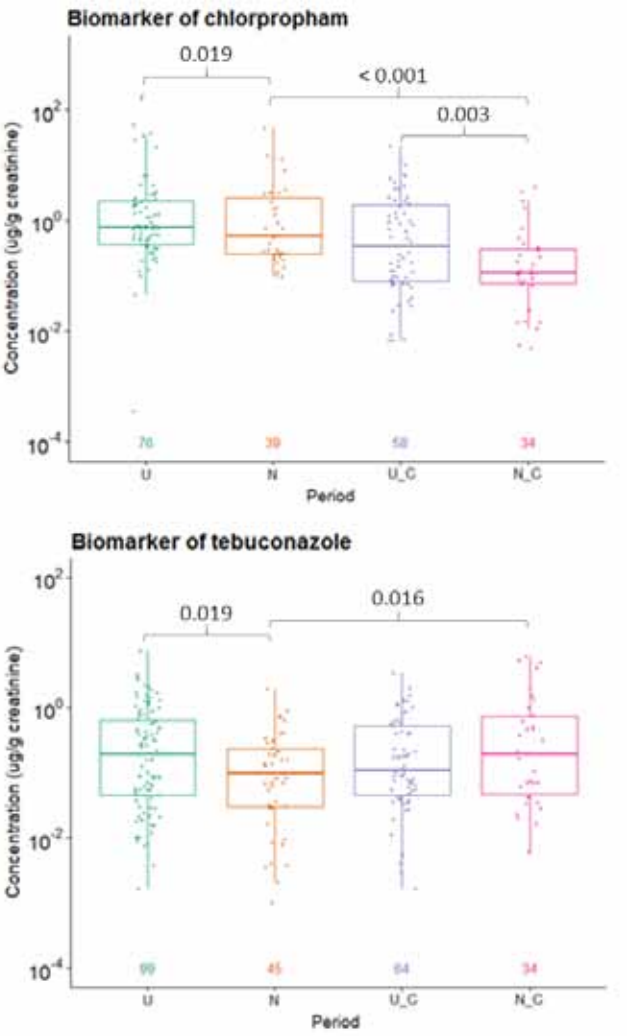

Figure 4.11: Biomarkers of chlorpropham and tebuconazole in urine (adults).
Levels of biomarkers of 2 pesticides, chlorpropham and tebuconazole, are shown for residents and controls, in the use and non-use period. Results are corrected for creatinine levels in urine. U: residents in use period; N: residents in non-use period; U_C: controls in use period; N_C: controls in non-use period. The number of samples is shown above the x-axis.

Table 4.19: P-values for t-tests between biomarkers levels in urines of residents and controls, in the use and non-use period.

	T-test P-values			
	U vs N	U vs U_C	N vs N_C	U_C vs N_C
Biomarker of chlorpropham	0.478	0.019	<0.001	0.003
Biomarker of tebuconazole	0.019	0.332	0.016	0.166

Legend	
	< 0.001
	< 0.01
	< 0.05
	> 0.05

U: residents during pesticides usage period; N: residents outside pesticides usage period; U_C: controls during pesticides usage period; N_C: controls outside pesticides usage period.

4.6.3 Biomarkers in morning urine: children

Age groups

Children were considered separately from adults, as we expected that children behave differently and therefore can have different exposure patterns. Ideally results from children would be analyzed per 5-years of age, however there was a lack of statistical power due to low numbers. For example, morning urines (not diapers) from only two children below the age of 4 were analyzed. In order to increase statistical power, children with urine samples (not diapers) were grouped in 2 age groups: 2 – 12 years and 13 – 17 years. The group ages are roughly linked to ages of children going to primary and secondary education respectively. Results of the concentrations of pesticides biomarkers for urines of children, corrected for creatinine, are in Table 4.20. Uncorrected values can be found in Appendix 12.

Three children, all from a target location (aged 2 – 4 years) wore diapers and urine extracted from these diapers was also tested. As the technique of urine collection and extraction is different from the other urines, these results are reported separately in Table 4.20 and values uncorrected for creatinine are in Appendix 12.

Results from urine samples and diapers for the biomarker of asulam show that only one diaper and one urine sample have values above the LOD. Similar results were found for the biomarker of prochloraz while for the biomarker of thiophanate-methyl/ carbendazim approximately 30% of the samples of residential children aged 2 – 12 years were above the LOD. Almost no samples above the LOD were found in the control group of children or children in the higher age group. Imputation was only possible for biomarkers of chlorpropham and tebuconazole. The number of children in the control group was too low to test for statistical differences with children from target locations.

For interpretation of the results from diapers it should be born in mind that the collection method differed (diapers versus free catch). Due to difference in the analytical procedures, this may have influenced results. As there were no children in the control population that used diapers, no diapers could be collected from children at control locations.

Table 4.20: Levels of biomarkers of pesticides in urines of children.

	Diapers (age: 2-4 yrs)		Age 2 to 12				Age 13 to 17			
	U	N	U	N	U_C	N_C	U	N	U_C	N_C
Biomarker of asulam										
N	7	1	11	5	3	2	9	4	3	2
N > LOD	1	0	0	0	0	0	0	0	0	1
% > LOD	14	0	0	0	0	0	0	0	0	50
mean	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
max	0.54	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	0.09
Biomarker of carbendazim										
N	7	1	27	17	3	2	9	5	3	2
N > LOD	0	0	9	5	0	0	1	1	1	0
% > LOD	0	0	33	29	0	0	11	20	33	0
mean	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
max	< LOD	< LOD	4.51	0.88	< LOD	< LOD	0.09	0.27	1.33	< LOD
Biomarker of chlorpropham										
N	7	1	4	2	3	2	16	7	3	2
mean	12.77	2.33	0.44	0.16	0.09	2.63	4.28	1.48	3.74	2.47
median	2.96	2.33	0.29	0.16	0.05	2.63	1.33	0.20	0.24	2.47
min	0.73	2.33	0.28	0.13	0.02	0.31	0.21	0.05	0.24	0.74
max	74.88	2.33	0.90	0.18	0.19	4.96	46.76	7.54	10.73	4.19
Biomarker of prochloraz										
N	12	1	4	2	3	2	-	3	3	1
N > LOD	0	1	0	0	0	0	NA	2	0	0
% > LOD	0	100	0	0	0	0	NA	67	0	0
mean	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	< LOD	< LOD	< LOD
max	< LOD	0.18	< LOD	< LOD	< LOD	< LOD	NA	0.01	< LOD	< LOD
Biomarker of tebuconazole										
N	12	4	30	15	3	2	17	9	3	1
mean	1.19	0.95	0.21	0.09	0.16	0.04	0.20	0.12	0.12	0.11
median	0.89	0.53	0.09	0.06	0.12	0.04	0.09	0.10	0.06	0.11
min	0.32	0.02	3E-03	4E-03	0.04	0.01	0.03	0.01	0.01	0.11
max	2.50	2.71	1.61	0.38	0.31	0.06	0.79	0.29	0.28	0.11

Values are in µg/g creatinine.
N: number of samples; min: minimum value; max: maximal value.
U: residents during pesticides usage period; N: residents outside pesticides usage period; U_C: controls. during pesticides usage period; N_C: controls outside pesticides usage period.

The results of biomarkers from urines of children show that for three out of the five analyzed pesticides the majority of samples are below the limit of detection. For chlorpropham and tebuconazole the highest value for a child was found in a diaper. There is however no clear pattern in de median urinary pesticide concentrations for location or period of pesticide use in any of the age groups. When comparing the results of chlorpropham and tebuconazole between children and adults, we see that the results of children are within the same range as the results of adults.

Season and location

For biomarkers of chlorpropham and tebuconazole the number of samples of control children per age group were too low to evaluate effects of location. Therefore the effects of location were assessed for all children combined (2 – 17 yrs). No statistically significant differences were found between concentrations observed in the different periods or locations.

4.6.4 Effect of days and distance

Days

As with environmental exposures, the effect of exposure following the spray event per measurement campaign was assessed. This was done for urine samples of all selected residents, independently of age (Appendix 13). Comparing the results of the biomarkers of tebuconazole and chlorpropham over the 7 days and per measurement campaign, no clear pattern emerged.

Distance

For chlorpropham and tebuconazole, the effect of distance to the target field on the levels of the biomarkers in urine was evaluated. Per person, all analyzed urine samples were included. During the measurement campaigns for both chlorpropham and tebuconazole, no additional field indicated spraying with these pesticides. Distance was therefore calculated with respect to the target field only. The effect of distance on biomarker levels of adults and children combined is shown in Figure 4.12. No significant log-linear trend was observed with distance.

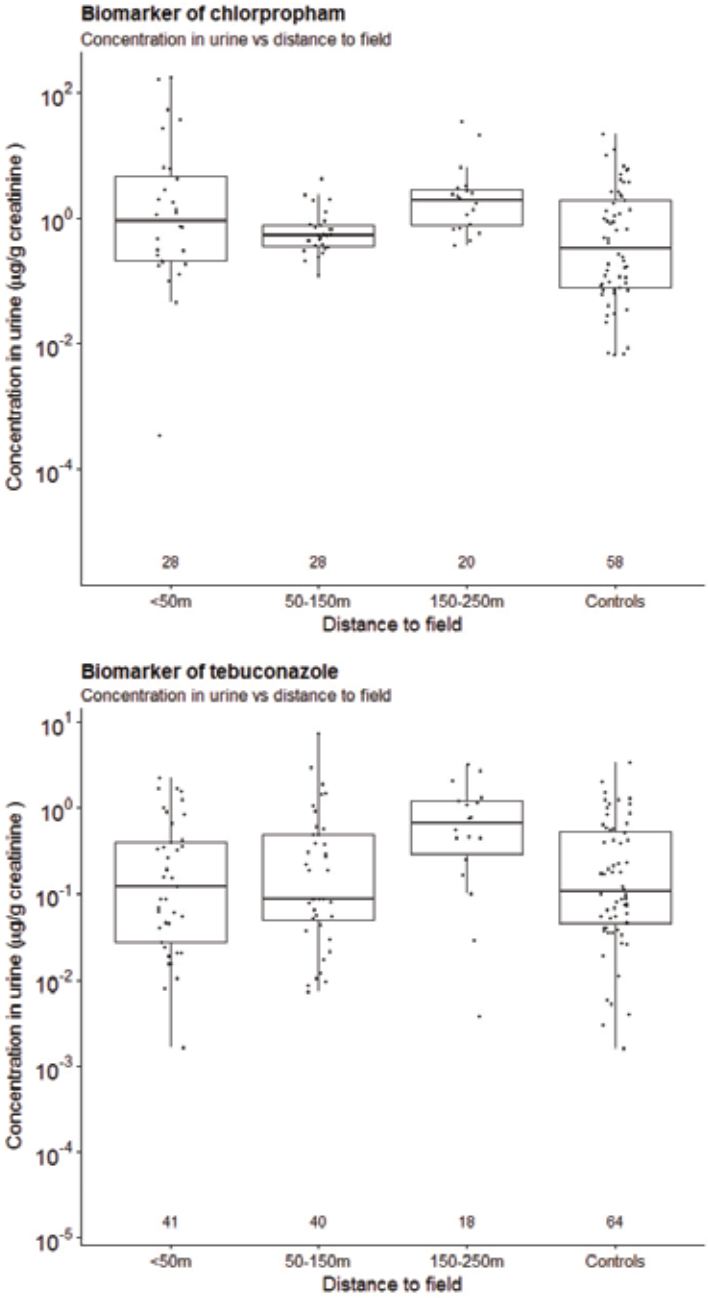

Figure 4.12: Distance to the target field and biomarker levels in urines.
For chlorpropham and tebuconazole, levels of biomarkers in urine are shown against the distance category to the applying target field. The number of urines is indicated above the x-axis.

4.6.5 Urine vs air and dust concentrations

To study the statistical relationship between urine and different environmental samples, concentrations of biomarkers of three different pesticides in urine were correlated: chlorpropham, tebuconazole and carbendazim with the concentration in outdoor and indoor air, VFD and DDM. The selected pesticides were based on the number of available urine samples above the LOD. Controls were not included in this approach.

For air, this was done pairing measured outdoor air concentrations of measurement day 1, day 2, day 4 and day 7 with measured concentrations in urine for each subsequent day. Since urine are point measurements and air samples are daily means, median and mean outdoor air concentrations over the same time period were also paired with median and mean concentrations in urine. For indoor air, since measured values were only available for the first day of spraying (day 1), day 1 concentrations in indoor air were paired with measured concentrations in urine of the following day. For VFD, the measured values (one measurement representing one week) were paired with mean and median concentrations in urine. The same comparison was done for DDM. Table 4.21 summarizes the results of these comparisons.

For chlorpropham, a stronger correlation between concentrations in urine and in air was observed and no correlation with VFD or DDM. For tebuconazole, correlations between concentrations in urine and air or dust levels are generally weak. Carbendazim concentrations in urine indicate a weak to moderate correlation with both air and dust levels. Indoor air concentrations of chlorpropham and carbendazim showed a strong correlation with their respective biomarker concentrations in urine.

4.6.6 Additional findings in morning urine

The methods for analyzing the morning urines were developed for biomarkers of the 5 selected pesticides, but also gave results for 18 other pesticides. The number of samples that have detectable levels of these additional biomarkers in morning urines is low and shown in Table 4.22. For several of these biomarkers larger fractions of concentrations above the LOD were seen for residents compared to controls. For some the opposite is found. Overall, we see no clear differences between periods.

Table 4.21: Pearson correlations – Urine vs other environmental samples.

Chlorpropham - Concentration in Urine* VS Other mediums				
Comparison	Paired by	Pearson	p-value	95% Conf.int
Urine - Outdoor Air	Days (1,2,4,7)	0.297	8E-07	[0.183 , 0.403]
	Median	0.383	0.011	[0.093 , 0.613]
	Mean	0.433	0.004	[0.153 , 0.649]
	Day 1	0.229	0.038	[0.013 , 0.425]
Urine - Indoor air	Day 1	0.674	1E-04	[0.395 , 0.838]
Urine - VFD	Median	-0.051	0.850	[-0.534 , 0.456]
	Mean	-0.108	0.691	[-0.573 , 0.409]
Urine - DDM	Median	0.094	0.761	[-0.482 , 0.613]
	Mean	0.197	0.519	[-0.397 , 0.675]
Tebuconazole - Concentration in Urine* VS Other mediums				
Comparison	Paired by	Pearson	p-value	95% Conf.int
Urine - Outdoor Air	Days (1,2,4,7)	0.125	0.034	[0.009 , 0.237]
	Median	0.128	0.379	[-0.158 , 0.395]
	Mean	0.107	0.465	[-0.179 , 0.376]
	Day 1	0.097	0.123	[-0.026 , 0.218]
Urine - Indoor air	Day 1	0.112	0.282	[-0.093 , 0.308]
Urine - VFD	Median	0.068	0.623	[-0.203 , 0.330]
	Mean	0.161	0.245	[-0.111 , 0.411]
Urine - DDM	Median	-0.018	0.899	[-0.284 , 0.251]
	Mean	-0.009	0.948	[-0.276 , 0.259]
Carbendazim - Concentration in Urine* VS Other mediums				
Comparison	Paired by	Pearson	p-value	95% Conf.int
Urine - Outdoor Air	Days (1,2,4,7)	0.395	0.001	[0.175 , 0.578]
	Median	0.461	0.006	[0.145 , 0.691]
	Mean	0.454	0.007	[0.137 , 0.687]
	Day 1	0.264	0.324	[-0.267 , 0.672]
Urine - Indoor air	Day 1	0.631	0.012	[0.175 , 0.864]
Urine - VFD	Median	0.316	0.044	[0.009 , 0.568]
	Mean	0.317	0.043	[0.011 , 0.569]
Urine - DDM	Median	0.466	0.003	[0.177 , 0.682]
	Mean	0.470	0.003	[0.182 , 0.684]

	Pearson Correlation	
Small	[0.1 , 0.3)	[-0.1 , -0.3)
Medium	[0.3 , 0.5)	[-0.3 , -0.5)
Large	≥ 0.5	≤ - 0.5

P-value
< 0.05
< 0.01
< 0.001

* Urine adjusted for creatinine values was used for this comparison.

Table 4.22: Additional biomarkers of pesticides in morning urine.

	Residents				Controls			
	Use		Non-use		Use		Non-use	
Biomarkers	N	%>LOD	N	%>LOD	N	%>LOD	N	%>LOD
6-chloronicotinic acid	101	2	49	0	70	0	40	0
acetamiprid	163	0	85	0	70	1	40	0
Boscalid-OH	280	61	126	56	70	87	40	83
flonicamid	302	3	131	3	70	1	40	3
fluopyrambenzamide	163	6	85	7	70	9	40	0
Imidacloprid	302	1	131	0	70	11	40	13
Metamitron	302	4	131	1	70	0	40	0
Metamitron-desamino	302	1	131	0	70	0	40	0
Metolachlor Mercapturate	280	9	127	9	70	0	40	0
propamocarb	163	5	85	2	70	0	40	0
prothioconazole-desthio	163	0	85	0	70	0	40	0
Spirotetramat-enol	315	1	127	6	70	0	40	0
thiacloprid	163	0	85	1	70	1	40	0
trifloxystrobin acid	403	3	151	1	70	9	40	23

Use: During pesticides usage period; Non-use: Outside pesticides usage period.

4.7 Personal samples: first day urines

Only residents participating in protocol B collected all urines following the spray event until the next morning. Biomarker concentrations of chlorpropham and tebuconazole were determined in these first day urines. As thiophanate-methyl/carbendazim was not sprayed and the percentages of samples with concentrations above the LOD for biomarkers of asulam and prochloraz were generally low in morning urines, these were excluded from analyses of first day urines. Results of analyses are shown in Appendix 12. For tebuconazole, results indicated higher concentrations shortly after application. This pattern was not observed for chlorpropham. Ultimately, these results indicate that the applied methods in OBO flower bulbs were not capable to identify through urine samples possible high exposure events.

4.8 Personal samples: hand wipes

Hands of residents participating in protocol B were wiped before dinner on the evening after a spray event with a wet wipe. Extracts from the wipe were tested for the presence of the five selected pesticides. In this case, the pesticide (the parent compound) was measured, not the biomarker. As before, residents from farm homes were excluded from the main analysis, their stratified results can be found in Appendix 9. For residents and children (<18 yrs.) results are shown in Table 4.23. Imputation was performed on results of hand wipes for tebuconazole and thiophanate-methyl/carbendazim and only percentages of samples above the LOD are shown for asulam, chlorpropham and prochloraz. Maximal found levels were high, until 0.14 gram per wipe for thiophanate-methyl/carbendazim, which was about 10% of what was applied in the volunteer experiment (which was close to the ADI, chapter 2). For the percentages above the LOD for asulam, chlorpropham and prochloraz pesticides, no significant differences were

Table 4.23: Hand wipe results or residents and residential children.

		Residents		Residential children	
		Use	Non-use	Use	Non-use
Number of Handwipes		34	20	15	10
Asulam	LOD	0.5 ng/wipe			
	% > LOD	9	5	13	0
	median	< LOD	< LOD	< LOD	NA
	mean	NA	NA	< LOD	NA
	min	< LOD	< LOD	< LOD	NA
	max	5.2	887.7	1.9	NA
Carbendazim	LOD	0.5 ng/wipe			
	% > LOD	82	95	100	80
	median	42.4	11.5	76.8	5.7
	mean	4155.9	71.3	122.8	13.7
	min	0.08	0.20	14.6	0.07
	max	136147	892	448.1	48.0
Chlorpropham	LOD	2.5 ng/wipe			
	% > LOD	26	35	0	30
	median	< LOD	< LOD	NA	< LOD
	mean	NA	NA	NA	3.2
	min	< LOD	< LOD	NA	< LOD
	max	1723.9	149.1	NA	3.9
Prochloraz	LOD	1 ng/wipe			
	% > LOD	15	25	27	10
	median	< LOD	< LOD	< LOD	< LOD
	mean	NA	NA	6.9	0.6
	min	< LOD	< LOD	< LOD	< LOD
	max	761.2	48.1	11.1	0.6
Tebuconazole	LOD	0.25 ng/wipe			
	% > LOD	44	30	53	20
	median	< LOD	< LOD	0.6	< LOD
	mean	0.9	0.8	1.1	1.7
	min	0.0006	0.0002	0.002	0.001
	max	7.9	7.5	6.1	14.6

Use: During pesticides usage period; Non-use: Outside pesticides usage period; Results are in ng/hand wipe.

observed between adults and children nor between periods. For thiophanate-methyl/ carbendazim in hand wipes of children significantly higher levels were observed in the use period versus the non-use period (p=0.011).

4.9 Add-on's

During the OBO flower bulb fieldwork, three additional pilot studies were conducted within the OBO flower bulb study to explore new methods to measure exposure levels. For each of these Add-on's, a study protocol was written and permission for each Add-on was obtained from the OBO Stuurgroep, RIVM and the Ethical Review Board (METC). Results from these Add-ons are presented in separate appendices of this report. Appendix 27 describes personal sampling performed with silicon wrist bands, Appendix 28 presents results regarding indoor and outdoor passive sampling with polyurethane foam disks and Appendix 29 reports on biomonitoring using hair samples.

4.10 Summary and discussion

4.10.1 Summary of the residential field study

In the residential field study of OBO flower bulbs, pesticide concentrations in outdoor air, indoor air and dust samples were measured in homes located within 250 m of agricultural fields cultivating flower bulbs. Measurements were conducted at 9 locations, with a target field and surrounding homes per location. In total, 80 homes within 250 m of a target field were included in the study. Also 16 control homes were included in the study. These control homes were more than 500 m away from any agricultural field but in a similar rural area of the country, within 20 km of a target location.
During the spraying season, measurement campaigns started with the application of a specified pesticide on a target field (spray event). Outdoor air samples (24 h samples) were collected from both location homes and control homes during 7 consecutive days and vacuumed floor dust and doormat dust were collected after these 7 days. In homes within 50 m of the field indoor air samples were collected during the first 24 h. In total, 14 spray events were included in the study. Outside the spraying period, air and dust samples were collected for 2 consecutive days. In all environmental samples, the concentration of 46 different pesticides was determined.

During the measurement campaigns, morning urine samples were collected by residents from the location (target) homes and the control homes. All participants collected morning urine during the 2 or 7 days of the measurement campaign. Additionally, residents living within 50 m of the target field collected all urine during the first day (24 h) after the spray event and sampled their hands using a hand wipe.

4.10.2 Environmental samples

Summary of the results

On the 9 target fields, 14 spray events with 28 pesticides were followed. After a spray event, concentrations of the sprayed pesticide were detected in the majority of the outdoor air samples. In total, 46 different pesticides were measured in the air samples. Of these 46, 43 were detected at least once in an outdoor air sample. For the pesticides sprayed on target fields the measured concentrations were higher on the day of the spray event compared to the following six days. Concentrations were overall higher in air samples taken from location homes than in samples from control homes and the concentration decreased with the distance to the target field. Additionally, concentrations in outdoor air were found to be higher during the use period compared to the non-use period.

In homes, pesticide levels in two types of dust were determined: in purposely installed clean DDM and in VFD. Pesticide levels in both types of dust were often below the LOD. Patterns with location, distance and pesticide use period were also detected for both types of dust but less pronounced than in air. In general, vacuumed floor dust levels

and levels from dust in the doormat were moderately correlated with outdoor and indoor air concentrations.

Pesticides applied on the target fields were detected in most of the indoor air samples, collected in homes within 50 m of a target field. Also, measurable concentrations of other pesticides were found. The correlation with outdoor air levels was moderate to high and most evident for the pesticides applied on the target or other fields. Indoor air concentrations and levels in dust were less correlated.

Discussion for environmental samples

Not all homes were selected for analyses of their samples. As described in chapter 3, homes with expected higher and at least one home with expected lower concentrations were selected for analyses. This selection may have influenced the results as the presented pesticide concentrations are not necessarily representative for the population living within 250 m of agricultural fields: Homes with expected higher concentrations are overrepresented in our field study, which may have resulted in higher average concentrations.

The methods for pesticide detection were very sensitive and the list of pesticides that was investigated is rather large, including 46 pesticides. The list of selected pesticides was built upon the aim to maximize the ability to detect what could be used in the area. Not all analyzed pesticides were used in the area during our measurement campaigns. Whether pesticides can be found in the environmental samples depends on many factors such as the LOD and the usage of the pesticide in the area in the period of sampling.

Of the contacted growers of possible target fields, 17% participated in the study. Of the residents at these locations 4.5% were willing to participate. The low participation rates among both growers and residents may have had implications for the generalizability of the results. Growers could contribute to the resident field study, with either their field being a target field or an additional field. This provided much information on pesticide application on the target field and in the area, not only during our measurement campaign but throughout the 2 years of the study. As much information as possible was collected. However, not all spray registration from all fields could be collected. If possible, schemes of pesticide application for fields without spray registration were used. These schemes introduced uncertainty as they were based on applications reported by other growers with the same type of flower bulbs or crops. Several pesticides are available to a grower to use for a specific application. In some cases, a grower that did not share his registration could have used pesticides that were not on our schemes. Also the day of application of a specific pesticide in the schemes can be uncertainty.

Since 2016, a new assessment methodology is used by the Ctgb to include exposure of residents in the authorization procedures (EFSA, 2014). For all compounds with low volatility (vapor pressure < 0.005 Pa), exposures are calculated assuming a default concentration of the pesticide in the air of 1 µg/m^3. For all moderately volatile compounds (vapor pressure ≥ 0.005 Pa and < 0.01 Pa), exposures are calculated assuming a default concentration in the air of 15 µg/m^3. Concentrations found in the residents' field study of OBO flower bulbs were all below these default concentrations.

4.10.3 Personal samples

Summary of the results

From residents in location and control homes we collected morning urines. Biomarkers from 5 different pesticides were determined in the urine samples from 4 pesticides that were applied on the target fields (tebuconazole, asulam, chlorpropham and prochloraz) and from 1 pesticide that was frequently detected in environmental samples (thiophanate-methyl/carbendazim). Biomarkers from asulam, prochloraz and thiophanate-methyl/carbendazim were detected in almost no urine samples. Biomarkers from tebuconazole and chlorpropham were detected in most morning urine samples. For adults we found slightly different patterns between locations and control locations and between periods of use and non-use. For children such patterns were less obvious, possibly due to a low sample size. Urine samples collected during the first day in residents participating in protocol B showed no specific elevation of excretion of biomarkers during the first day following the pesticide application.

Hand wipes were collected in residents living within 50 m of a target field. Extracts from the hand wipe were tested for the 5 pesticides (not their biomarkers). Asulam, chlorpropham and prochloraz were detected in less than half of the wipes. Tebuconazole and thiophanate-methyl/carbendazim were found in the majority of hand wipes. Only for carbendazim in children's wipes, concentrations during pesticides non-use period were found to be lower to compared to wipes during pesticides use period.

Discussion for personal samples

In the residents' field study we were able to measure (biomarkers of) five different pesticides in personal samples. However, it emphasized that analyses were performed for 5 pesticides only, therefore no conclusions can be drawn for different pesticides. In chapter 6 a comparison between calculations with the results of resident's urine samples and the ADI is given.

In the residents' field study, 192 residents were included (locations and controls) from 96 homes in the study, with an average of two persons per home. The aim was to include one adult and one child per home. However, only 43 children under the age of 18 were included. The children in the study were divided in two age groups: 2 - 12 years and 13 – 17 years. It can be argued that the age groups are too wide for the

objectives of the study. It would have been interesting to look at toddlers under the age of 4 years separately, however the number of children in this age group was not sufficient. Nevertheless, we were able to detect biomarker levels in urine samples of toddlers.

Results from Farm homes and growers' families were analyzed separately from the other results. Higher pesticide concentrations were found in farm homes and in urines of growers' families. This may be due to occupational exposure to pesticides of growers and transfer of pesticides from work to the home, as reported before (Coronado 2006; Thompson et al, 2003; Thompson et al, 2014). In addition, farm homes were on average situated closer to agricultural fields then the location homes. This may also have influenced the measured concentrations in air, dust and/or urine but we cannot distinguish between these two effects.

4.10.4 Predictors of exposure

In this chapter the effect of several predictors of exposure, like distance, period of application, location and age was investigated. Home and personal characteristics as well as information on food intake and behavior was also collected in the study. Analyses of these predictors and modelling of exposure can be found in chapter 6.

5. Studies on spray drift and volatilization

In the OBO study, the potential exposure of residents is quantified based on outdoor and indoor air sampling and deposition of pesticides. The outdoor environmental measurements include outdoor air sampling, as well as soil and vegetable samples where this could be obtained. Important exposure routes include spray drift during application and vapor from the treated fields after application. Experiments and measurements to quantify these routes are described in this chapter for spray drift (Chapter 5.1) and volatilization (Chapter 5.2).

5.1 Spray drift

In the OBO study the potential exposure of residents is quantified based on outdoor and indoor air sampling and deposition of pesticides. The outdoor environmental measurements include outdoor air sampling, as well as soil and, when possible to obtain, vegetable samples from the home garden. Important exposure routes include spray drift during application and vapor from the treated fields after application. Experiments and measurements to quantify these routes are described in this chapter for spray drift. Spray drift is defined as "the quantity of pesticides that is carried out of the sprayed (treated) area by the action of air currents during the application process" (ISO22866, 2015).

5.1.1 Aims of spray drift experiments

In OBO, spray drift measurements were performed to:

1. quantify spray drift in the real-life situation in practical circumstances;
2. generate knowledge on airborne and ground deposition spray drift data up to 50 m distance;
3. underpin and validate a spray drift model with the experimentally obtained data.

Two types of spray drift experiments are performed in OBO.
Part 1 deals with spray drift in residential situations/practical locations, with buildings, fences etc. near the field. In Protocol C, three measurements on spray drift at the locations of the residents' field study were planned. In section 5.1.3 results are presented of spray drift field measurements from a sprayed flower bulb field (C-protocol; field A; Zande et al., 2016) using spray techniques as used in practice and under real-life conditions (field and weather). For practical reasons, measurements were performed using a fluorescent tracer instead of a pesticide. In spring 2017 it became clear that it was no longer possible to perform spray drift field experiments on locations of the residents' field study. Experiments were therefore relocated to WageningenUR – on fields of the experimental farm "Unifarm". In 2017, spray drift field measurements were performed spraying a bare soil surface alongside different types of 'garden' and

a home (C protocol; experiments 2017; Zande et al., 2018a). These results are in 5.1.3 Results - Research field experiments.
Part 2 deals with additional field measurements (C protocol; Spray drift exposure within 50 m of the field edge; Zande et al., 2018b) done in 2015 and 2016, in order to get experimental data on ground deposition and airborne spray drift up to 50 m from the treated field. These experiments were designed to also underpin the spray drift model IDEFICS with the obtained data (Holterman et al., 1997). These results can be found in 5.1.3 Results - Spray drift exposure within 50 m of field edge.

5.1.2 Methods of spray drift experiments

Spray drift measurements were performed spraying a bare soil surface or a cropped area using a specified spray technique. Spray drift was measured downwind of the treated area either as spray deposition on the ground or as airborne spray drift at different heights and distances from the treated area. Spray drift measurements were repeated in time to include different weather conditions and crop development stages. The crop was described in height, plant density and crop growth development stage using the BBCH scale (BBCH, 2001).

Position of last nozzle

When spraying a crop, the position of the last downwind nozzle relative to the last crop row is determined. From this last nozzle position the distances for the ground collectors and the position of the airborne spray drift poles were determined. For flower bulbs the last nozzle position was straight above the edge of the last flower bulb bed.

5.1.2.1 Ground deposition of spray drift

Downwind of the treated area (bare soil, crop) spray drift deposition was measured at a bare soil area, which extended for at least 5 m further than the last collector position. In this strip of land, a double line of ground collectors was positioned at 2 m spacing between the lines (Figure 5.2, 5.5, 5.7). Spray drift collectors (Technofil TF 290; 10x50 cm and Technofil TF 100 10x100 cm) were placed perpendicular to the crop rows and travel direction of the sprayer to quantify spray drift deposits at ground level at in general the following positions:

- At 0.5-10 m in a continuous line of collectors of 0.50 m length;
- At 15-16 m, 20-21m, 25-26 m, 30-31 m, 35-36 m, 40-41 m, 45-46 m and 49-50 m at collectors of 1 m length.

To check the applied spray volume, several collectors (Technofil TF 290; 10x100 cm) were positioned in the sprayed area at leaf canopy height on both sides of the sprayer underneath the spray boom. These collector sets were positioned below the center of each boom half 10 m before and 10 m after the spray drift collector lines.

5.1.2.2 Airborne spray drift

Airborne spray drift was measured with passive collectors and collectors in an active air suction device.

Vertical poles with passive collectors (Siebauer Abdriftkollektoren art. nr. 00131; Figure 5.1 left) were placed at different distances (e.g. between 5 m and 50 m) from the last nozzle in double lines with collectors at 0.50 m spacing up to 10 m height (Zande et al., 2016, 2018a, 2018b). The collectors were attached to a nylon wire of 5 mm diameter.

The active sampling of airborne spray drift involved a technique developed at WPR (Stallinga et al., 2008). Masts can be positioned at different distances e.g. 5 m, 15 m and 50 m downwind with a double row of suction heads (Figure 5.1 right; diameter 32 mm 3 m s^{-1} air suction speed) from 0.37 m to 6 m height. Filters used in the suction heads were Schleicher & Schuell nr. 2282 (48 mm diam.; thickness 1.45 mm). The inside diameter of the suction head is 34 mm and the effective suction head surface diameter (and of the filter paper) is 32 mm.

The air speed through the filters in the suction heads was intended to be adjusted to approximately 3 m s^{-1}. The air speed through the suction heads was measured using a mini vane anemometer and turned out to deviate from the intended equal air speed. Recorded air speed of the suction heads is presented in Table 5.1. Recorded differences of air speeds through the filters between the masts can be dealt with in future data analysis; e.g. to present the data normalized for equal air speeds. This is not done in this report. On average, air speed through the filters in the suction heads was 3.19 m s^{-1} for the mast at 5m, 3.60 m s^{-1} for the mast at 15 m and 3.55 m s^{-1} for the mast at 50 m.

Table 5.1: Air speed (m s-1) through the filters in the suction heads at different heights and average per pipe and per mast of the three masts used for measuring airborne spray drift with active samplers.

position	pipe	0.37	0.75	1	2	3	4	5	6	Avg pipe	Avg mast
5m	Left	3.27	3.19	3.45	3.22	3.26	3.08	3.23	3.23	3.24	
	Right	3.47	3.10	3.20	3.06	2.97	3.11	3.04	3.11	3.13	3.19
15m	Left	3.91	3.69	3.59	3.26	3.59	3.39	3.62	3.35	3.55	
	Right	3.86	3.57	3.62	3.47	3.58	3.53	3.63	3.57	3.60	3.60
50m	Left	3.74	3.73	3.63	3.46	3.55	3.64	3.57	3.68	3.63	
	Right	3.75	3.67	3.53	3.65	3.56	3.42	3.48	3.34	3.55	3.55

Figure 5.1: Passive collector (left) and active collector in suction head (right) for measuring airborne spray drift.

5.1.2.3 Analyses

The spray liquid was water with added fluorescent dye (Brilliant Sulfo Flavine; BSF, Chroma 1F 561, CI 56205, 3-5 g L^{-1}) and a non-ionic surfactant (Agral Gold; 0.075 mL L^{-1}). After spraying, collectors were placed in plastic bags, labelled and transported to the lab for further analysis of the deposited amount of BSF using fuorimetry (Zande et al., 2016, 2018a, 2018b). Every measurement day samples were taken of the tank concentration of the sprayed tank mix by taking a sample from below a spraying nozzle. In the analysis the background fluorescent signal of the collectors, the recovery of the collectors for the used BSF batch, as well as the
degradation in sunlight of the BSF batch (Stallinga et al., 2012) when deposited on the collectors was determined. As collection time of the collectors in the field was on average within 10-15 minutes; correction for sunlight degradation was not performed.

5.1.2.4 Calculations

Percentage spray drift

From the measured concentration of BSF from the washed collectors the amount of spray volume per unit area was calculated. The percentage of spray drift was calculated by expressing the spray drift deposition per unit area as a percentage of the applied spray volume in the field per unit area (Zande et al., 2016, 2018a, 2018b).

Threshold value

To determine the background fluorescence, several blank collectors were analyzed separately. These measurements gave an average background fluorescence of the blank collectors and its standard deviation. In the calculation of the spray drift deposition the average value of the background fluorescence was used. In the performed experiments, very low spray drift deposits were measured with values close to and even below the average background fluorescence of the blank collectors. Calculated spray drift deposition can therefore be below 0%. The threshold value (LOD) used in this report is defined by the average fluorescence value of the blanks plus two times its standard deviation. This threshold value is expressed as % spray drift deposition. The threshold value is dependent of the measured spray technique (applied spray volume), used extraction volume, collection surface area of the collector and the tank concentration and can therefore differ for each spray drift measurement.
In (Zande et al., 2016, 2018a, 2018b) the calculated spray drift deposition values are given also when they are below the threshold value. Values below the threshold value are presented in italics and by the phrase '< threshold value' e.g. '<0.006'.

5.1.2.5 Weather conditions

During the spray drift experiments the weather conditions were recorded. Air temperature was measured at 0.5 and 4 m height (Pt100 device), the relative air

humidity at 1.5 m height (% RH, Rhotronic), the wind direction (00 = perpendicular to the crop rows) at 10 m height and the wind speed (using cup anemometers) at 0.5 m, 2 m, 3 m, 4 m and 10 m height. These weather conditions were recorded at a time interval of 5 s. The weather station was positioned at 50 m downwind of the last nozzle. Every time the sprayer passed the collector lines the time at the data logger display was recorded. Afterwards, from the collected weather data the data of 15 s before to 15 s after the time of passage were averaged (Annex 1). Next to the weather station also an ultrasonic anemometer (Metpak) was positioned at 2 m height. During the measurements with the bare soil surface an additional Metpak was positioned at 2 m height, 50 m upwind from the last nozzle and in line with the spray drift collector arrays.

5.1.3 Spray drift measurements

5.1.3.1 Field experiment on practical location

The first spray drift measurements within the OBO project to quantify potential spray drift exposure of residents downwind of sprayed flower bulb fields were performed under real-life conditions at 25 May 2016 (following ISO22866, 2005; CIW, 2003; Zande, 2016). At the target field of location A the downwind swath and the second swath were sprayed with the flower bulb grower's sprayer applying a tracer (three repetitions). At the edge of the field was a 2 m high wooden fence at 5 m distance from the edge of the last planted bed in the field (Figure 5.3). The sprayer used was a 24 m working width Beyne mounted sprayer equipped with Agrotop Airmix 11003 flat fan nozzles (2 bar spray pressure; DRN75, TCT, 2018). Measured flow rate of the nozzles was 1.0 L/min. Nozzle spacing at the spray boom was 50 cm and average recorded forward speed was 5.5-6.2 km/h thereby applying on average a spray volume of 207 L/ha.
The flower bulb crop sprayed were 7 beds (12.6 m) of muscari at the edge of the field and the rest of the field planted with hyacinths. Crop height was 10-20 cm and beds were fully covered with crop leaf canopy. Width of the flower bulb beds was 1.80 m.

To quantify the spray drift deposition downwind collectors were placed on the ground in the area between the last sprayed flower bulb bed and the edge of the field (Figure 5.2). The fluorescent tracer was sprayed and the non-ionic surfactant was added to the spray liquid, water was taken from the ditch in front of the grower's farm. To verify added quantity of tracer to the spray liquid tank mixture samples were taken from a spraying nozzle at start, in between spray drift measurements and after spraying. Average tank concentration of the tracer was 2.85 g/L.

As there was limited space between the edge of the field and the wooden fence at the field edge, no drift measurements could be done up to larger distances (behind the fence in the residents garden). It was therefore decided to perform the spray drift measurements spraying the outside swath (24m) and the second swath (24 m) separately as well as the outside swath and second swath jointly (48 m) to gather more

information about swath contribution and analyzing planned number of collectors. By doing so it was possible to discriminate between the contribution to spray drift exposure from edge of field applications and further away applied spray liquid. About

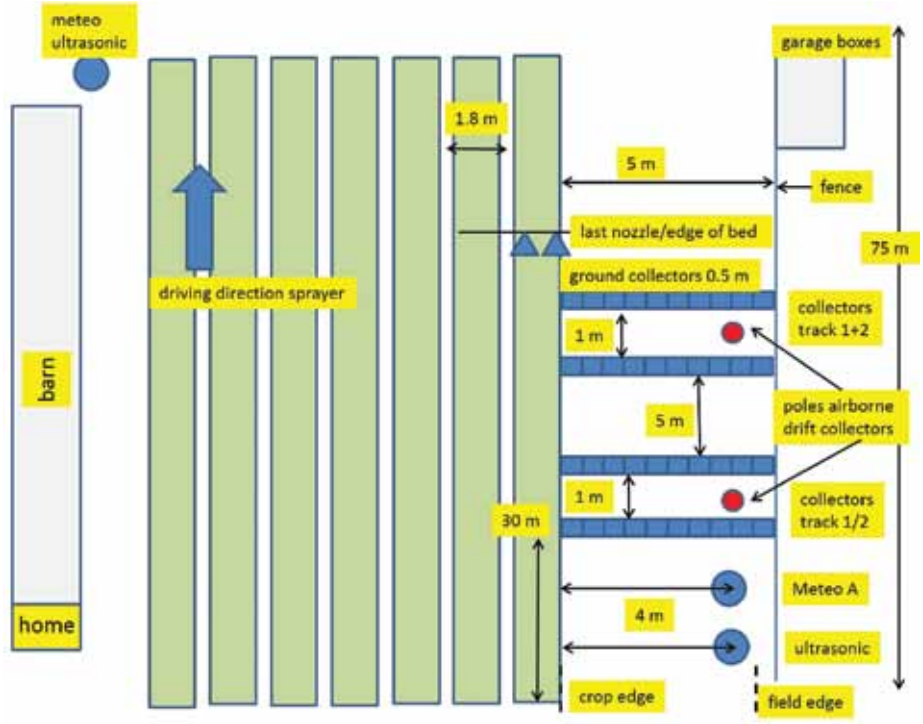

Figure 5.2: Schematic layout of the spray drift ground collectors, airborne spray drift measuring poles and weather stations at the edge of the target field at practical location in between edge of last flower bulb bed and residents garden fence.

Figure 5.3: Overview of field layout of the spray drift measuring setup for the exposure of residents of flower bulb target field at a practical location (25 May 2016).

75 m length of flower bulb crop was sprayed at both spray swathes.
Spray drift measuring setup was placed at 30 m and 36 m from the start of the flower beds in the field. Ground collectors (Technofil TF-290; 0.10 m × 0.50 m) were placed from last nozzle position, the edge of the last flower bulb bed, to the fence which was over 5 m in distance. Ground collectors were placed in a double array at 1 m spacing. At 4 m distance from the last nozzle a 3 m pole was installed with two lines with airborne spray drift collectors (Siebauer Abdriftkollektoren art. nr. 00131) separated at 0.50 m height interval over 0-3 m height.
The collectors at sampling position one were collected in between the outside swath spraying (track 1) and the second swath spraying (track 2). At sampling position one, fresh collectors were placed before spraying the second swath. At sample position two, the collectors were kept in place for the outside and the second swath spraying (track 1+2).
Downwind at 4 m from the last crop row and 1 m in front of the fence also a pole was positioned with cup anemometers at 0.5 m, 2 m, 3 m, 4 m height and at 4 m height a wind vane. Temperature was also measured at 0.5 m and at 2 m height using Pt 100 sensors (PT1, PT2) and a RhoTronic sensor, (RhoT). On average wind speed during the spray drift measurements was 2.3 m/s (at 2 m height), temperature was 13°C and Relative Humidity (RhoT) was 75%. Weather conditions during the measurements of the individual swathes are presented in Table 5.3 showing that average wind speed (at 2 m height) of repetition 1 was 1.5 m/s, of repetition 2 was 2.5-3.2 m/s and of repetition 3 was 2.4-2.8 m/s. Wind directions were respectively 47-57, 61-58 and 75-58 degrees to rectangular to the driving direction. Negative values for wind direction indicate that the wind is coming from behind the sprayer and is in the driving direction.

Recorded wind directions during the spray drift experiments show that the situation was not worst-case as this occurs with wind directions perpendicular (+/- 30°) to the driving direction of the sprayer.

Table 5.2: Weather data (at 2 m height) of the ultrasonic measuring (Metpak) device downwind of the sprayed field at 25 May 2016.

					Wind direction (°)	
rep	track	wind speed [m/s]	RH[%]	Temp[°C]	25s*)	1 min.
1	1	1.3	78	12.8	-122	-94
	2	0.8	79	12.9	-77	-40
2	1	1.6	75	13.5	-116	-87
	2	1.3	78	12.9	-29	-70
3	1	2.0	78	12.6	-115	-114
	2	1.9	75	13.5	-14	-16
	avg	1.5	77	13.0	-79	-70

*) wind direction deviation from perpendicular to the driving direction (average over 25 sec. of pass and 1 min. of pass of measuring setup).

Table 5.3: Weather data (Meteo A) during the spray drift experiments of target field A at 25 May 2016.

		Temperature (°C)									
		PT1	PT2	RhoT	RH (%)	wind speed (m/s)				wind direction (°)	
rep	track	0.5 m	2 m	2 m	2 m	1 m	2 m	3 m	4 m	25 s*)	1 min.
1	1	13.5	12.3	14.7	74	1.0	1.5	1.6	1.9	-57	-60
	2	13.7	12.8	15.0	74	1.2	1.5	1.6	1.9	-47	-52
2	1	14.0	12.7	15.6	69	2.0	2.5	2.5	2.2	-61	-59
	2	13.1	12.3	14.3	75	2.6	3.2	3.4	2.0	-58	-66
3	1	13.5	12.5	14.7	73	2.1	2.4	2.5	2.2	-75	-53
	2	14.5	13.0	15.6	70	2.3	2.8	2.8	2.5	-58	-53
	avg	13.7	12.6	15.0	73	1.9	2.3	2.4	2.1	-59	-57

*) wind direction deviation from perpendicular to the driving direction (average over 25 sec. of pass and 1 min. of pass of measuring setup).

5.1.3.2 Research field experiments

In a field experiment at 23 and 25 October 2017 spray drift of a trailed conventional boom sprayer (John Deere) was measured with and without the occurrence of shields at the edge of the field (Fig. 2.1). Sprayer working width was 27 m. Spray applications were done with a spray boom height of 0.50 m using standard flat fan nozzles (TeeJet XR 11004, 3 bar spray pressure). Spray applications (three repetitions) were performed at a bare soil surface field of the WageningenUR experimental farm (Zande et al., 2018a). At 15 m downwind distance from the last nozzle was a greenhouse tunnel with a length of 69m and a height of 3.90 m. The plastic greenhouse tunnel was a surrogate for the residents' homes. The flat vertical wall (2.5 m height) of the greenhouse tunnel was than the surrogate for the wall of the residents' home. Spray drift was assessed for the following four objects:

A Open area – bare soil surface and flat covered surface area next to tunnel;
B Open garden in front of tunnel;
C Half open garden in front of tunnel – vegetation; permeable shield at field edge;
D Closed garden in front of tunnel – screen; closed shield at edge of field.

The half open garden (object C) was simulated by using a screen with a 30% wind-closed windbreak shield (Mevolon 622 WG, mesh size 1x3 mm, wind reduction 45% at 30 m/s and 33% at 9 m/s). The closed garden (object D) was simulated using a screen with a 0% wind-open anti-root growth cloth (110 g/m^2). The screens were positioned at 5 m distance from the last nozzle. The screens were at 10 m in front of the greenhouse tunnel (schematic overview experimental layout, Figure 5.4; overview measurement setup, Figure 5.5 and individual objects, Figure 5.6). Spray drift was assessed in front of

the screens and behind the screens in the gardens, as well as spray drift deposition at ground surface as airborne spray drift. In addition, spray drift deposit at the wall of the greenhouse was also measured (Zande et al., 2018a).

Average weather conditions during the spray drift experiments are presented in Table 5.4.

During the spray drift measurements average temperature at 2 m height was 14.9 ^{0}C, average wind angle (absolute) perpendicular to the driving direction was 19^o and average wind speed at 2 m height was 4.5 m/s.

Table 5.4: Average weather conditions during the 2017 spray drift experiments.

repetition	date	temperature [^{0}C] at heights		% RH	wind angle perpendicular to driving direction (abs) *)	wind speed at heights (m) (m/s)			
		0.5 m	2 m		perp=0^0	0.5	2	3	4
1	23-10-2017	15.3	14.7	60	20	3.7	4.7	4.9	5.1
2	25-10-2017	15.0	15.2	80	24	3.7	4.7	5.1	5.5
3	25-10-2017	15.0	14.9	86	13	3.3	4.2	4.3	4.5
avg		15.1	14.9	75	19	3.6	4.5	4.7	5.0

*) wind direction deviation from perpendicular to the driving direction.

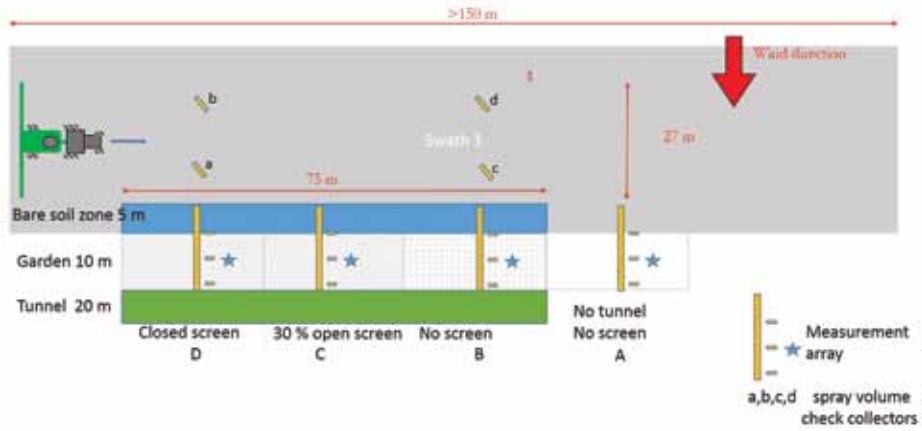

Figure 5.4: Schematic presentation of the position of the greenhouse tunnel, spray swath and measuring area.

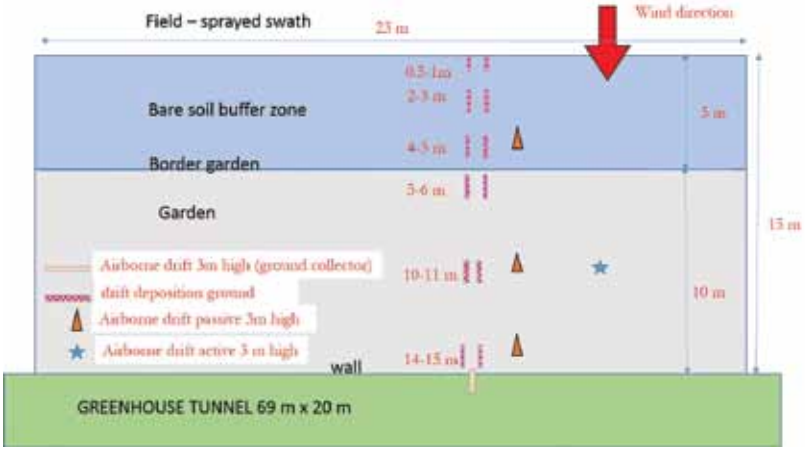

Figure 5.5: Schematic overview of the collector positions in different collector arrays, garden border and (green) house wall per measuring object.

Figure 5.6: Overview of the measuring setup with a closed screen (D; black), permeable screen (C; light green) the open garden (B) and the full open space (A) in front of the tunnel with collectors in front and behind the screens.

5.1.3.3 Spray drift exposure within 50 m of field edge

Spray drift experiments spraying a bare soil surface were done at 4 and 5 November 2015 and at 20 and 21 April 2016. The spray drift measurements with an onion crop were done at 17 and 18 August and 20 and 23 September 2016. The treated bare soil and onion crop fields were at the WageningenUR experimental farm (Unifarm) in Wageningen. A total of 10 measurements (6 with XR11004 and 4 with XLTD11004 nozzle types) were done at the bare soil and 16 measurements (both XR11004 and XLTD11004 nozzle types 8 measurements) in the developed onion crop (Zande et al., 2018b).

Description of crop

To mimic a flower bulb crop an onion crop was used as both crop types are grown on beds, are more easy to grow, are cheaper in plant material and have a similar growth pattern and leaf structure. The onion crop was planted on beds of 1.50 m with a net bed width of 1.20 m. On the net bed surface 5 rows of onions were sown (row spacing 20 cm). Below the center of the sprayer was one planted bed and the track was positioned in 2 times a half bed of bare soil (so 3 m under the sprayer with on both sides 8 beds under the spray boom; in total 1+16 beds under a working width of 27 m). During the experiments, the onion crop was a standing crop (with crop height 50 cm).

For the experiments on the bare soil surface the treated area was a large bare experimental field in which an area of two swaths (total width 54 m) and 150 m long was laid perpendicular to the expected wind direction for the day of the measurements (Figure 5.7). The setup of the collectors to measure downwind spray drift is presented in Figure 5.7.

Weather conditions

During some of the measurements the temperature sensor and the relative humidity sensor were not properly functioning. Instead the recorded temperature and relative humidity values of the Metpak ultrasonic anemometers are presented. During the spray drift experiments with the bare soil surface the average temperature was 15^{0}C, the average wind direction perpendicular to the driving direction was 29^o and the average wind speed at 2 m height was 2.3 m/s. During the spray drift experiments with the onion crop, the average temperature was 20^{0}C, the average wind direction perpendicular to the driving direction was 21^o and the average wind speed at 2 m height was 2.5 m/s.

Table 5.5: Average weather conditions for the different spray techniques during the spray drift experiments.

Nozzle	Crop situation	n-rep	temperature [^{0}C]	% RH	Wind angle to rectangular to driving direction abs	Wind speed [m s-1] at height [m]				
					rect=00	0.5	2	3	4	10
XR11004	bare soil	5	15	59	31	1.9	2.2	2.5	2.6	4.7
	onion	8	20	53	21	2.3	2.5	2.7	3.1	4.0
XLTD11004	bare soil	4	15	68	26	2.0	2.4	2.7	2.8	3.2
	onion	8	21	51	21	2.5	2.6	2.8	3.6	4.7
average	bare soil		15	63	29	2.0	2.3	2.6	2.7	4.0
	onion		20	52	21	2.4	2.5	2.7	3.3	4.4

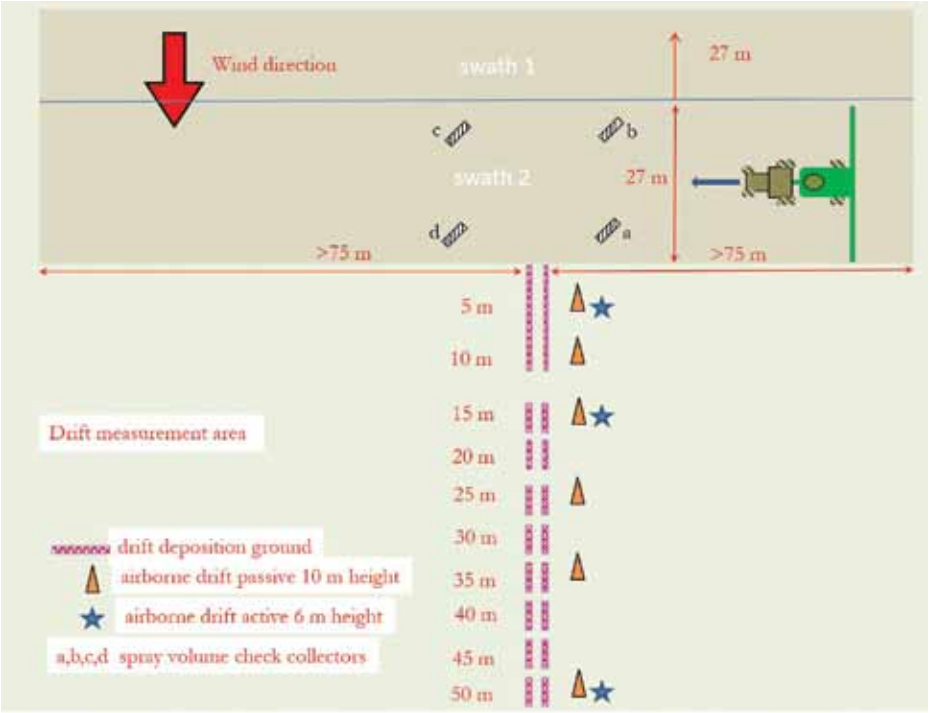

Figure 5.7: Schematic presentation of the spray drift collector setup in the downwind drift measurement area and the treated area (swath 1 + swath 2 and on top of crop canopy (a, b, c, d) to check applied spray volume) at the experimental field.

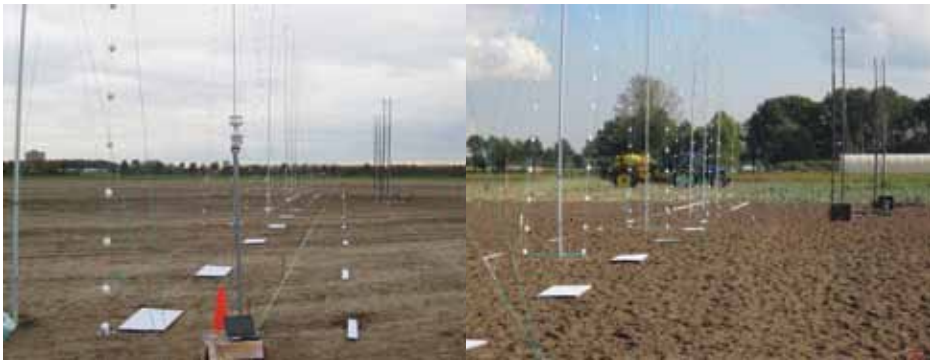

Figure 5.8: Spray drift measurement setup during experiments on the bare soil surface (left) and with the onion crop (right).

5.1.4 Results

5.1.4.1 Field experiment on practical location

Results of the spray drift measurements are separated in spray drift deposition at ground surface and in airborne spray drift (Zande et al., 2016).

Spray drift deposition at ground surface

Spray drift deposition of the outside swath spraying (track 1; 24 m working width) at 0-5 m from the edge of the crop, is presented for the two rows of collectors of the three repetitions in Figure 5.9.

A steep decline in spray drift deposition outside the field is seen in the area 0-1 m from the edge of the bed and last nozzle position. In the area to the fence; 1-5 m from the edge of the bed, spray drift deposition is slowly declining and is around 0.1% of applied spray volume.
The contribution of the second swath spraying (track 2; 24 m working width) to the outside field spray drift deposition is very limited and only around 0.01% of the applied spray volume. Many of the samples are lower than the detection level, which was 0.005%.

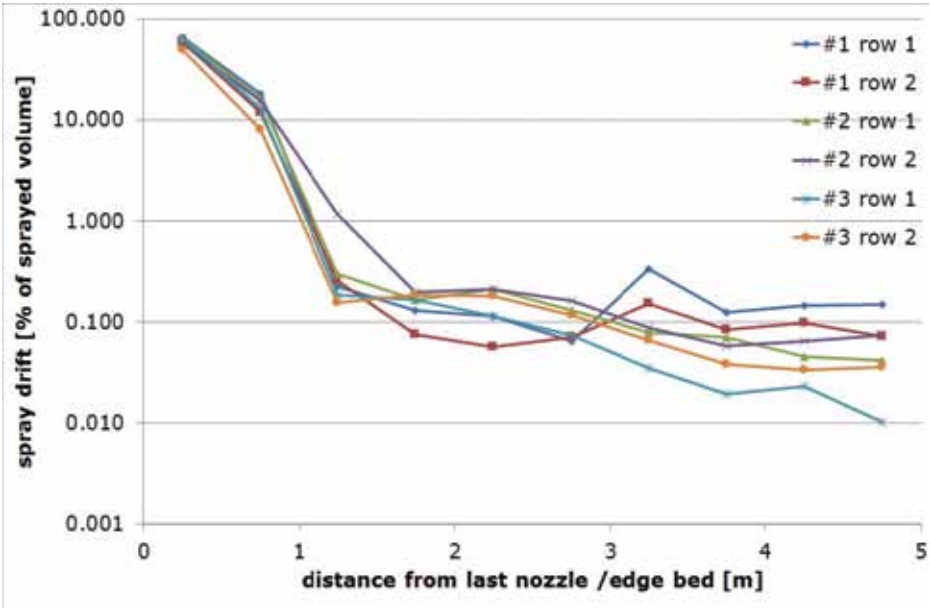

Figure 5.9: Spray drift deposition (% of sprayed volume) at ground level downwind of the sprayed outside swath (24 m) of a practical flower bulb field.

Spray drift deposition of the outside and the second swath spraying jointly (track 1+2; 2*24 m working width) at 0-48 m from the edge of the crop is similar to that of the outside swath spraying (Figure 5.9) as there is little contribution of the second swath spraying. For the two swaths sprayings a large variation is measured between the two rows of collectors for repetitions two and three whereas for repetition one spray drift deposition of the both rows of collectors are similar.
Average spray drift deposition (3 repetitions) for the sprayer pass at the downwind edge of the field, the second more upwind sprayer pass, a working width away from the edge of the field and for both the sprayer passes sampled together show that spray drift deposition of the outside sprayer pass and the joined outside and second working width together are similar. Spray drift deposition of the second sprayer pass spraying is very low. The small difference in spray drift deposition between the outside working width spraying and the joined outside and second working width spraying can also occur because of the 5 m difference in collector position along the edge of the field and the small variations in wind speed and wind direction during application.

Airborne spray drift (passive and active collectors)

Airborne spray drift at 4 m distance from the edge of the last sprayed bed (last nozzle position) of the outside swath spraying is presented in Figure 5.10 for the two rows of collectors of the three repetitions. Airborne spray drift of the first repetition (0.02%-0.13%) is much lower than for repetition three (0.17%-0.84%) and two, which is the highest (0.08%-0.41%). This is mainly because of the differences in wind speed and wind direction between the repetitions; resp. 1.5 m/s for repetition one and 2.5 m/s for repetitions two and three. Variation in airborne spray drift is also large between the individual rows of collectors, especially for repetition two.

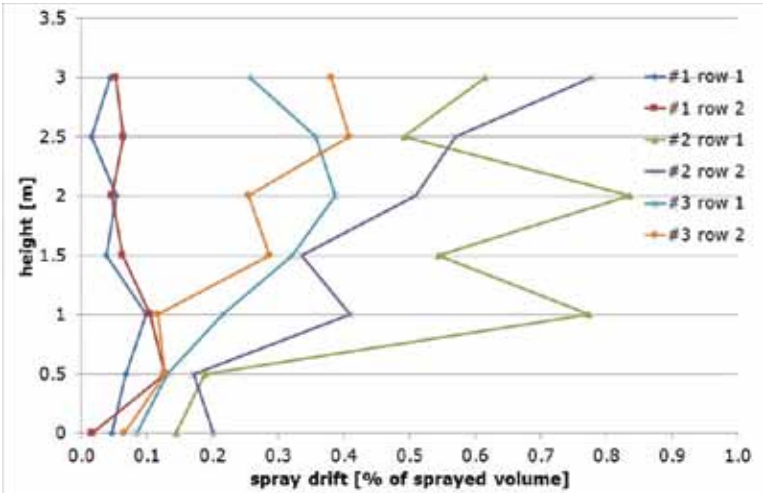

Figure 5.10: Airborne spray drift (% of sprayed volume) at different heights at 4 m distance downwind of a sprayed flower bulb field spraying the outside swath (24 m; track 1).

Airborne spray drift at 4 m distance from the edge of the last sprayed bed (crop edge) is for the second swath spraying at 24-48 m from the crop edge very low (0-0.05% of applied spray volume) and for some values even negative and lower than detection level. Variation between airborne drift at collectors of row 1 and row 2 of e.g. repetition two is at 1 m height more than fivefold different (Zande et al., 2016).
The pattern of airborne spray drift at 4 m distance from the edge of the last sprayed bed is for the outside and the second swaths spraying (Track 1+2) at 0-48 m from the crop edge similar to that of the outside swath spraying (Figure 5.10) applying at 0-24 m from the crop edge. There is little additional contribution from the second swath spraying applying at 24-48 m from the crop edge. Highest measured airborne spray drift is at 1 m height from repetition 2 at collector line 1 (0.6% of applied volume; Zande et al., 2016).
Similar as with ground deposition, airborne spray drift of the outside swath and the joined outside and second swath are very similar, and of the second swath spraying is very low. The difference in airborne spray drift between the outside swath spraying and the joined outside and second swath spraying is possibly introduced by the 5 m difference in airborne collector pole position along the edge of the field and the small variations in wind speed and direction during applications.
Especially for the outside swath spraying it is obvious that highest airborne spray drift is at 2-3 m height, above the fence height, and is on average about 0.35% of applied spray volume (Zande et al., 2016). This is about 5 times higher as spray drift ground deposition at the same distance.

Results indicate that with the spray technique used, a 75% drift reducing technique, the downwind spray drift originates mainly from the outside 24 m swath. Very little is added by a second 24 m swath spraying applied at 24-48 m from the crop edge. This holds as well for the spray drift deposition at the ground level as for the airborne spray drift up to 3m height. These results are similar to what has been previously reported by e.g. Stallinga et al. (2007), Wolters et al. (2008) and Zande et al. (2010). Because of a 2 m high fence situated at 5 m distance from the edge of the last treated flower bulb bed (crop edge) it was not possible to measure at larger distances and to evaluate at what distance spray drift was no longer measurable.
At 4 m distance just 1 m in front of the 2 m high fence the airborne spray drift was highest at 2-3 m height, just above the fence height. At this height airborne spray drift was about 3-5 times higher than ground spray drift deposition at the same distance 4-5 m from the edge of the treated field (crop edge). As this amount is passing over the fence towards the gardens and residents' homes, it is unknown how this amount of spray drift diffuses or where it deposits.
Based on the high amounts and increasing airborne spray drift with height at the edge of the field it would be interesting to measure also at higher heights and at greater distances from the field, preferably also in the resident's gardens.

5.1.4.2 Research field experiments

Following the results and recommendations from the 2016 experiment the initial plan for 2017 was to measure spray drift deposit in resident's gardens with and without artificial or natural barriers at the field edge to quantify the exposure of persons in the garden and on the wall of the house. Because the measurements could not be made in a realistic flower bulb situation, measurements were performed using shields to mimic fences and hedges and a plastic greenhouse tunnel as resident's home (Zande et al., 2018a). The effect of a field edge barrier on airborne spray drift and spray drift ground deposit in front and behind the barrier was measured; spraying a bare soil surface using a conventional boom sprayer operating at 0.50 m spray boom height, and standard flat fan nozzles (XR11004). Screens covered with 30% wind-closed windbreak shield was used to model a hedgerow and screens covered with anti-root growth cloth as a closed fence. Spray drift experiments were performed under practical circumstances, representative for pesticide applications in a flower crop.

The results of the spray drift deposition at ground surface downwind of the sprayed area are for the different 'garden' objects (A,B,C,D) and airborne spray drift presented for the passive collectors and for the filters of the active sampling technique.

Spray drift deposition at ground surface

Average spray drift deposition at ground surface downwind of the sprayer spraying a bare soil surface swath alongside the different types of enclosed 'gardens' is presented in Figure 5.11. Spray drift deposition at the Open Area (A) is highest. Spray drift deposition at the Open Garden (B) is close to the sprayed swath (1-5 m) somewhat lower than at

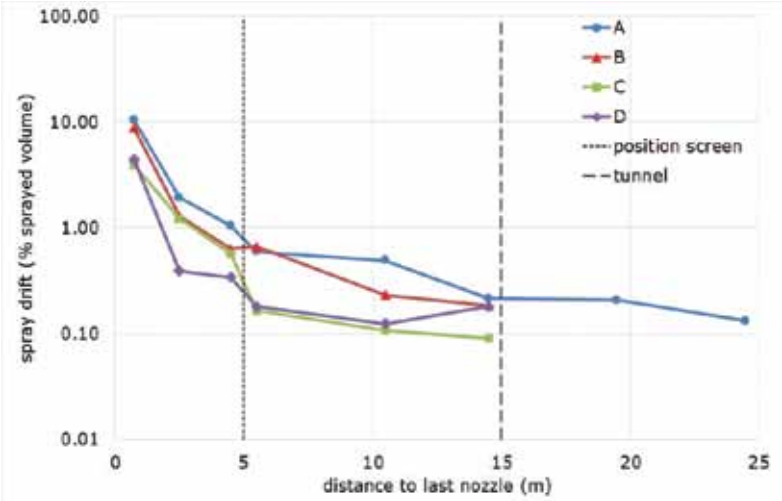

Figure 5.11: Mean spray drift deposition at different distances.

Mean spray drift deposition (% of applied spray volume per unit area) at different distances from the last nozzle when spraying one swath (27 m) of a bare soil surface using a conventional boom sprayer equipped with a standard nozzle (XR11004) and 50 cm spray boom height per object (A=Open area; B=Open garden; C=Half Open garden; D=Closed garden).

the Open Area (A) whereas at 14-15 m distance, in front of the greenhouse tunnel, drift deposition is similar to that in the Open Area (A). Drift deposition in front of the screens of the Half Open (C) and the Closed (D) garden is lower than of both the Open Area (A) and the Open Garden (B). Just behind the screens (5-6 m) spray drift deposition in the Half Open garden and the Closed garden is lower (70%) than at the same distance in the Open Area. Clearly drift deposition just behind the screens (5-6 m) is lower than just in front (4-5 m) of the screens. In the garden area of the Half Open garden and the Closed garden (5- 6 m behind the screens at 10-11 m from the last nozzle) drift deposit is also lower. Just in front of the greenhouse tunnel drift deposition in the Half Open garden is still lower than at the same distance in the Open Area. In the Closed garden drift deposition just in front of the greenhouse is of the same level as in the Open Area. In the center of the garden (10-11 m) spray drift deposition in the Half Open (C) and the Closed (D) garden is clearly lower (50%) than compared to at the same distance in the Open Area and the Open Garden.

Airborne spray drift (passive and active collectors)

Passive collectors

Average airborne spray drift measured with passive collectors when spraying a bare soil surface area alongside different gardens using a boom sprayer are presented for different objects and distances in Figure 5.12.

Airborne spray drift measured with passive collectors spraying alongside the Open Area is higher for all heights above ground level compared to spraying alongside the other gardens (Figure 5.12). At 4 m, 10 m and 14 m distance from the last nozzle airborne spray drift was resp. 3.2%, 2.2% and 1.9%. The average airborne spray drift is for the Open garden resp. 2.0%, 1.5% and 0.87% and clearly lower than in the Open Area. Airborne drift in the Half Open garden is with resp. 1.2%, 0.7% and 0.79% again lower as in the Open garden. At 4 m and 14 m distance airborne spray drift in the Closed Garden is lowest with resp. 1.2% and 0.68%, whereas at 10 m distance airborne spray drift is 0.37% being almost 50% lower as in the Half Open garden.

At 4 m distance of the last nozzle (in front of the screens) airborne spray drift decreases with height. At 10 m distance (behind the screens) airborne spray drift decreases with height in the Open Area and the Open Garden whereas in the Half Open garden and the Closed garden airborne drift increases with height. Airborne spray drift at 1-2 m height is in the Half Open garden and the Closed garden resp. 0.30% and 0.63% and at 2-3 m resp. 0.55% and 0.74%. It looks like the screens of the Half Open and the Closed gardens lead to another wind profile behind the screens in the center of the garden (10 m) and therefore airborne spray drift is higher and found at higher heights. Especially in the Closed garden this is the case.

In all situations at 14 m distance and 3 m height, airborne spray drift values higher than 0.70% are found. This means that in fact to catch the complete plume of spray drift passing the highest collector (3 m) was not high enough. Three meter height coincides more or less with the ground floor of a home. It can therefore be expected that at the second floor of a home (> 3 m) still spray drift deposit can occur.

Active sampling technique

Average airborne spray drift in the center of the garden at 10 m distance from the last nozzle measured with active suction head collectors spraying a bare soil surface alongside different gardens is presented in Figure 5.13.

Average airborne spray drift over 3 m height measured with the active suction head collectors at 10 m distance from the last nozzle (center of the garden); is highest in the Closed Garden (2.9%). Airborne spray drift is a little lower in the Open Area (2.6%) and again lower in the Half Open garden 2.1%. Lowest airborne spray drift is measured in the Open garden (1.8%). Airborne spray drift at 1-3 m height is in the Open Area lower than at 0.37-1 m height. In the Open Garden airborne drift at these heights is similar. Whereas in the Closed Garden airborne drift at 1-3 m height is higher than at 0.37-1 m height. Because of the screens at the garden edge, the wind profiles change (to higher heights), causing in the center of the garden behind the screen a higher airborne spray drift at higher heights.

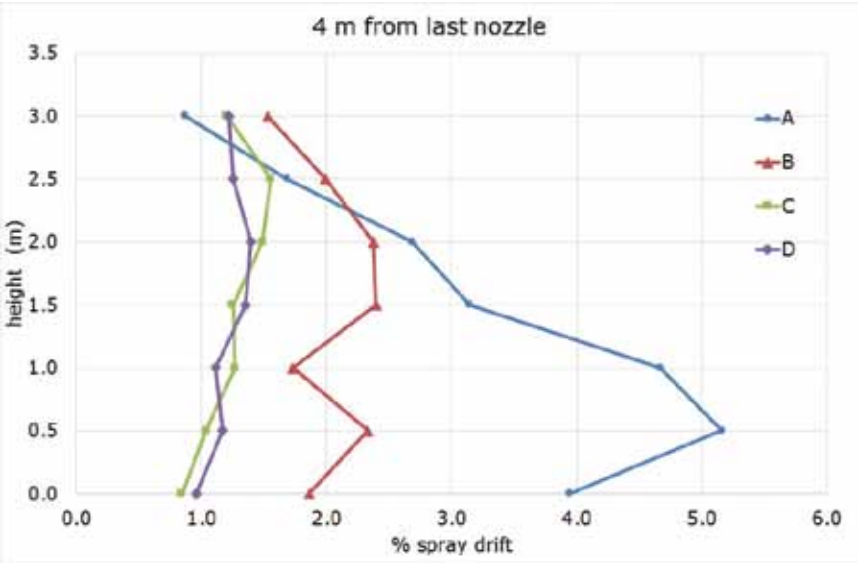

Figure 5.12: Mean airborne spray drift measured with passive collectors at different heights.
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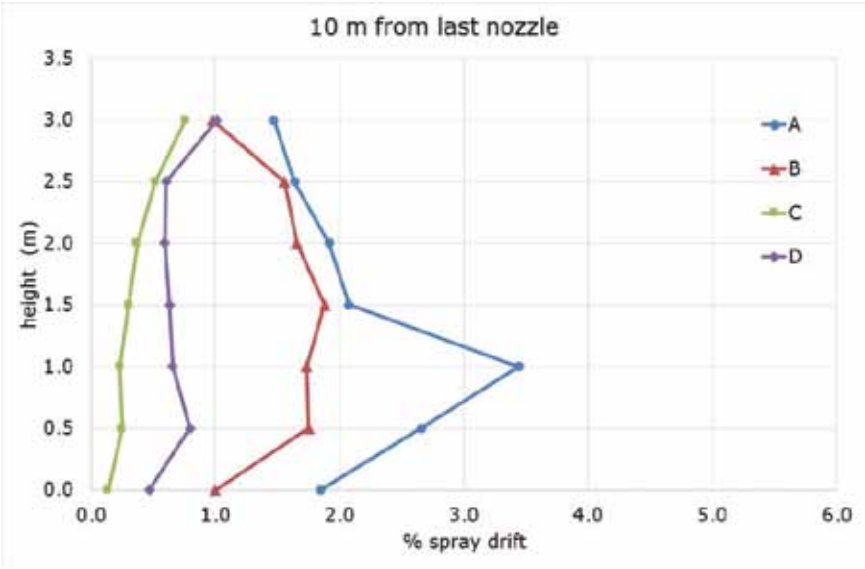


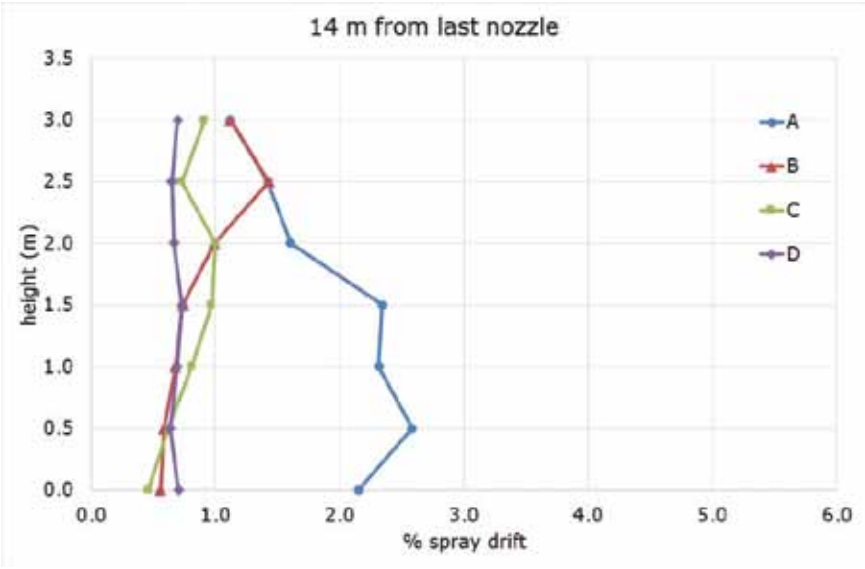


Figure 5.12: Mean airborne spray drift measured with passive collectors at different heights.
Mean airborne spray drift (% of applied spray volume per unit area) measured with passive collectors at different heights at 4 m, 10 m and 14 m from the last nozzle spraying the outside swath (27 m) of a bare soil surface area using a boom sprayer equipped with a standard nozzle (XR11004) at 50 cm spray boom height passing different gardens (A= Open Area, B = Open Garden, C= Half Open garden, D= Closed Garden).

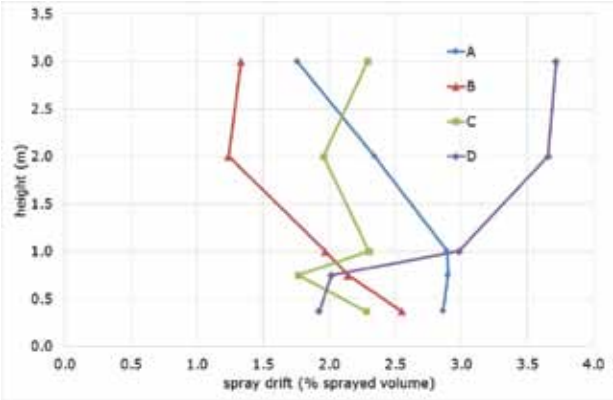


Figure 5.13: Mean airborne spray drift measured with suction head collectors at different heights.
Mean airborne spray drift (% of applied spray volume per unit area) measured with suction head collectors at different heights at 10 from the last nozzle spraying the outside swath (27 m) of a bare soil surface area using a boom sprayer equipped with a standard nozzle (XR11004) at 50 cm spray boom height passing different gardens (A= Open Area, B = Open Garden, C= Half Open garden, D= Closed Garden).

Spray deposition at "wall"

Average spray drift deposition at the wall of the greenhouse at 14 m distance from the last nozzle spraying a bare soil surface alongside different gardens is presented in Figure 5.14.

At all heights, spray drift deposition on the wall of the greenhouse is lowest in the Open garden (B; 0.11%). Average over height (0-3 m) there is no difference in spray drift deposition between the Open Garden (B) and the Closed Garden (D). However differences do occur depending on the height considered. At 0-1 m height spray drift deposition against the wall of the greenhouse is in the Open Garden with 0.42% higher than of the 0.34% in the Closed Garden. At 2-3 m height however, the spray drift deposition against the wall is in the Closed Garden higher (0.15%) compared to the Open Garden (0.09%).

The use of screens at the field edge reduces spray drift ground deposit as well as airborne spray drift behind the screens. At 4-5 m behind a 30% wind-closed windbreak screen spray drift reduction was 78% when spraying a bare soil surface using standard flat fan nozzles (XR11004) at 0.50 m boom height. Using a closed screen, spray drift reduction at this distance was 73%.

Airborne spray drift at 5 m distance behind the screens over 0-3 m height was for the 30% wind-closed windbreak screen 83% when measured with passive collectors. Airborne spray drift reduction for the closed screen was for this situation 68%.

Airborne spray drift measured with active sampling techniques over 0-3 m height, was almost not reduced (17%) because of the usage of 30% wind-closed windbreak screens at the field edge. Using the closed screen at the field edge resulted in an increase in airborne spray drift measured with active sampling techniques of 12%.

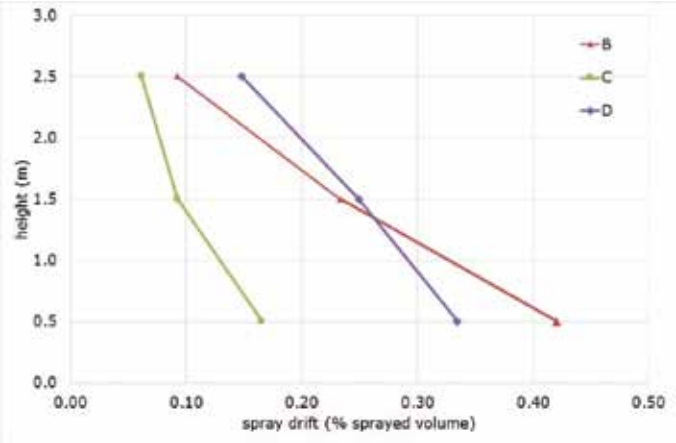


Figure 5.14: Mean spray drift deposition at the wall of green house at different heights.
Mean spray drift deposition (% of applied spray volume per unit area) at the wall of the greenhouse at different heights at 14 m from the last nozzle spraying the outside swath (27 m) of a bare soil surface area using a boom sprayer equipped with a standard nozzle (XR11004) at 50 cm spray boom height passing different gardens (B = Open Garden, C= Half Open garden, D= Closed Garden).

Spray drift deposition at 0-3 m height collectors positioned at the wall of the (green) house at 15 m distance from the last nozzle was on average 0.25%. When screens are positioned at 5 m distance from the last nozzle; spray deposit at the wall 10 m behind the screens was similar for the closed screen and 57% lower using a 30% wind-closed windbreak screen.

5.1.4.3 Spray drift exposure within 50 m of field edge

In 2015 and 2016 additional spray drift measurements were performed to quantify the real situation up to 50 m from the field edge. Results of these measurements can also be used to validate the spray drift model IDEFICS (Holterman et al., 1997).
In this section the exposure route spray drift is quantified for a spray treatment on a bare soil surface and the full growth situation of an onion crop (mimicking a flower bulb crop). The spray techniques used were a standard boom sprayer equipped with standard flat fan nozzles and with venturi 90% drift reducing flat fan nozzles and were operated under practical spray conditions (field and weather) applying 300 L ha^{-1}. Spray drift was measured up to 50 m from the treated field both as ground deposit and as airborne spray drift using active air sampling collectors and passive collectors up to 10 m height. For practical reasons the measurements are performed using a fluorescent tracer.

Spray drift deposition at ground surface

The measured average spray drift deposition at ground surface downwind of the sprayed bare soil surface and onion field are presented in Figure 5.15. In Table 5.6 average spray drift deposition at the ground is calculated for the zones 1-5 m, 5-10 m, 10-15 m, 1-15 m, 15-25 m and 25-50 m from the last nozzle.

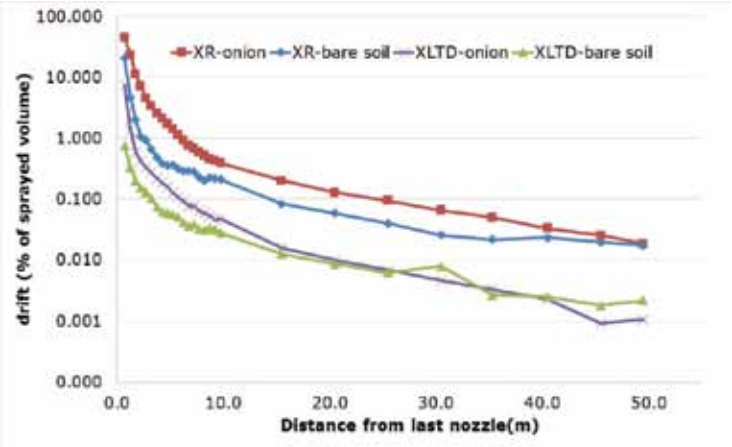


Figure 5.15: Mean spray drift deposition at different distances from the last nozzle.
Mean spray drift deposition (% of applied spray volume per unit area) at different distances from the last nozzle when spraying two swaths (2x27 m) of a bare soil surface and an onion crop using a conventional boom sprayer equipped with a standard nozzle (XR11004) and a 90% drift reducing nozzle type (XLTD11004; DRN90) and 50 cm spray boom height.

For both nozzle types Figure 5.15 indicates that spray drift deposition on the ground downwind of the treated area is higher for the sprayed onion crop than for the sprayed bare soil surface area. Spray drift deposition of the standard flat fan nozzle (XR11004) is always higher than that of the drift reducing venturi flat fan nozzle (XLTD11004; DRN90). Threshold value for the measurements spraying a bare soil surface is 0.005%. Figure 5.15 shows that at 50 m distance from the last nozzle spray drift deposition for the standard nozzle is still above
the threshold value. For the DRN90 nozzle spray drift deposition at 30 m and beyond is below the threshold value of 0.005%. For the spray drift measurements spraying an onion crop the threshold value is around 0.01%. At 50 m distance from the last nozzle spray drift deposition for the standard nozzle is still above the threshold value of 0.01% spraying an onion crop. For the DRN90 nozzle spray drift deposition from 20 m onward is below the threshold value of 0.01% spraying an onion crop.
When spraying an onion crop, spray drift deposition at different distance zones from the last nozzle is always higher than when spraying a bare soil surface (Table 5.6). The values in Table 5.6 show that spray drift deposition at the 1-5 m zone is about 3 to 5 times higher when spraying an onion crop compared to spraying a bare soil surface area. This holds for both the standard and the DRN90 nozzle type.

Table 5.6: Mean spray drift deposition (% of sprayed volume per unit area) at different zones from the last nozzle spraying.

Mean spray drift deposition (% of sprayed volume per unit area) at different zones from the last nozzle spraying the outside two swaths (2x27 m) of a bare soil surface area and an onion crop using a boom sprayer equipped with a standard nozzle (XR11004) and a 90% drift reducing nozzle (XLTD11004; DRN90) at 50 cm spray boom height

distance to nozzle (m)	XR11004		XLTD11004	
	bare soil	onion	bare soil	onion
1-5	1.3	7.0	0.14	0.44
5-10	0.26	0.73	0.038	0.075
10-15	0.15	0.30	0.020	0.032
1-15	0.70	3.3	0.080	0.23
15-25	0.061	0.14	0.009	0.011
25-50	0.025	0.048	<0.005	<0.010

Spraying a bare soil surface area using a standard nozzle on a boom sprayer results in spray drift deposition values at the zones 1-15 m, 15-25 m and 25-50 m from the last nozzle of resp. 0,70%, 0,061% and 0,025%. Using a DRN90 nozzle type instead results in spray deposition values at 1-15 m and 15-25 m from the last nozzle of resp. 0.080% and 0.009% whereas at the zone 25-50 m spray drift deposition is lower than 0.005%. Note that the average values at 25-50 m for the DRN90 experiments are below the corresponding thresholds.

Spraying an onion crop using a standard nozzle on a boom sprayer results in spray drift deposition values at the zones 1-15 m, 15-25 m and 25-50 m from the last nozzle of resp. 3.336%, 0.141% and 0.048%. Using a DRN90 nozzle type instead spraying an onion crop results in spray deposition values at 1-15 m and 15-25 m from the last nozzle of resp. 0.226% and 0.011% whereas at the zone 25-50 m spray drift deposition is lower than 0.010%.

In some cases spray drift deposits on single collectors were observed that were below the threshold value determined for the blank collectors. Consequently, the calculated spray drift deposition values would be below 0%. In order to know the occurrence of these low values of spray drift depositions the percentage of collectors above the threshold value is presented at different distances in Table 5.7.

Table 5.7: Percentage of measurements above the threshold value at different distances from the last nozzle spraying.

Percentage of measurements above the threshold value at different distances from the last nozzle spraying the outside two swaths (2x27 m) of a bare soil surface area and an onion crop using a boom sprayer equipped with a standard nozzle (XR11004) and a 90% drift reducing nozzle (XLTD11004; DRN90) at 50 cm spray boom height.

distance to nozzle (m)	XR11004		XLTD11004	
	bare soil	onion	bare soil	onion
49-50	60	85	37	4
45-46	67	83	32	0
40-41	63	77	42	19
35-36	77	90	37	15
30-31	87	100	58	21
25-26	100	100	53	31

When spraying a bare soil surface area using a boom sprayer equipped with standard nozzles spray drift deposition at 25-26 m from the last nozzle is for all measurements (100%) above the determined threshold value of the blank collectors (Table 5.7). However, using DRN90 nozzles instead 53% of measurements are above the threshold value at that distance. Further downwind, at 49-50 m from the last nozzle 60% of the measurements for the standard nozzle and 37% of the measurements of the DRN90 nozzle are above the threshold value.
Similarly, when spraying an onion crop, at 25-26 m from the last nozzle all measurements are above the threshold for the standard nozzle while this is 31% for the DRN90 nozzle. At 49-50 m distance from the last nozzle 85% of the spray drift deposition measurements of the standard nozzle are above the threshold whereas this is only 4% for the DRN90 nozzle.

Airborne spray drift (passive and active collectors)

Passive measurements with spherical collectors

Average airborne spray drift measured with passive collectors when spraying a bare soil surface area and an onion crop using a boom sprayer equipped with standard nozzles (XR11004) and DRN90 nozzles (XLTD11004) are for different distances presented in Figure 5.15. In Figure 5.16 airborne spray drift at 25 m (top) and 50 m (bottom) from the last nozzle are presented. The results of the airborne spray drift measured at different height layers is presented in Table 5.8.
Airborne spray drift at heights 0-1 m, 0-2 m and 3-6 m can be seen as representative for resp. children, adults and the first floor of a resident's home.
Spraying a bare soil surface using a boom sprayer equipped with standard (XR11004) nozzles results in an airborne spray drift measured with passive collectors at 25 m distance from the last nozzle at the height layers of 0-1 m, 0-2 m and 0-3 m of resp. 0.52%, 0.54% and 0.51%. At 50 m distance these values are resp. 0.23%, 0.29% and 0.29%. When the boom sprayer is equipped with DRN90 nozzles than the airborne spray drift at the height layers 0-1 m, 0-2 m and 0-3 m are resp. 0.079%, 0.075% and 0.068% at 25 m distance from the last nozzle and 0.046% for all three height layers at 50 m distance.

Spraying an onion crop using a boom sprayer equipped with XR11004 nozzles results in an airborne spray drift measured with passive collectors at 25 m distance from the last nozzle at the height layers of 0-1 m, 0-2 m and 0-3 m of resp. 1.55%, 1.63% and 1.62%. At 50 m distance these values are resp. 0.58%, 0.58% and 0.60%. When the boom sprayer is equipped with DRN90 nozzles than the airborne spray drift at these height layers are resp. 0.19%, 0.19% and 0.18% at 25 m distance and 0.11% for the three heights at 50 m distance from the last nozzle.

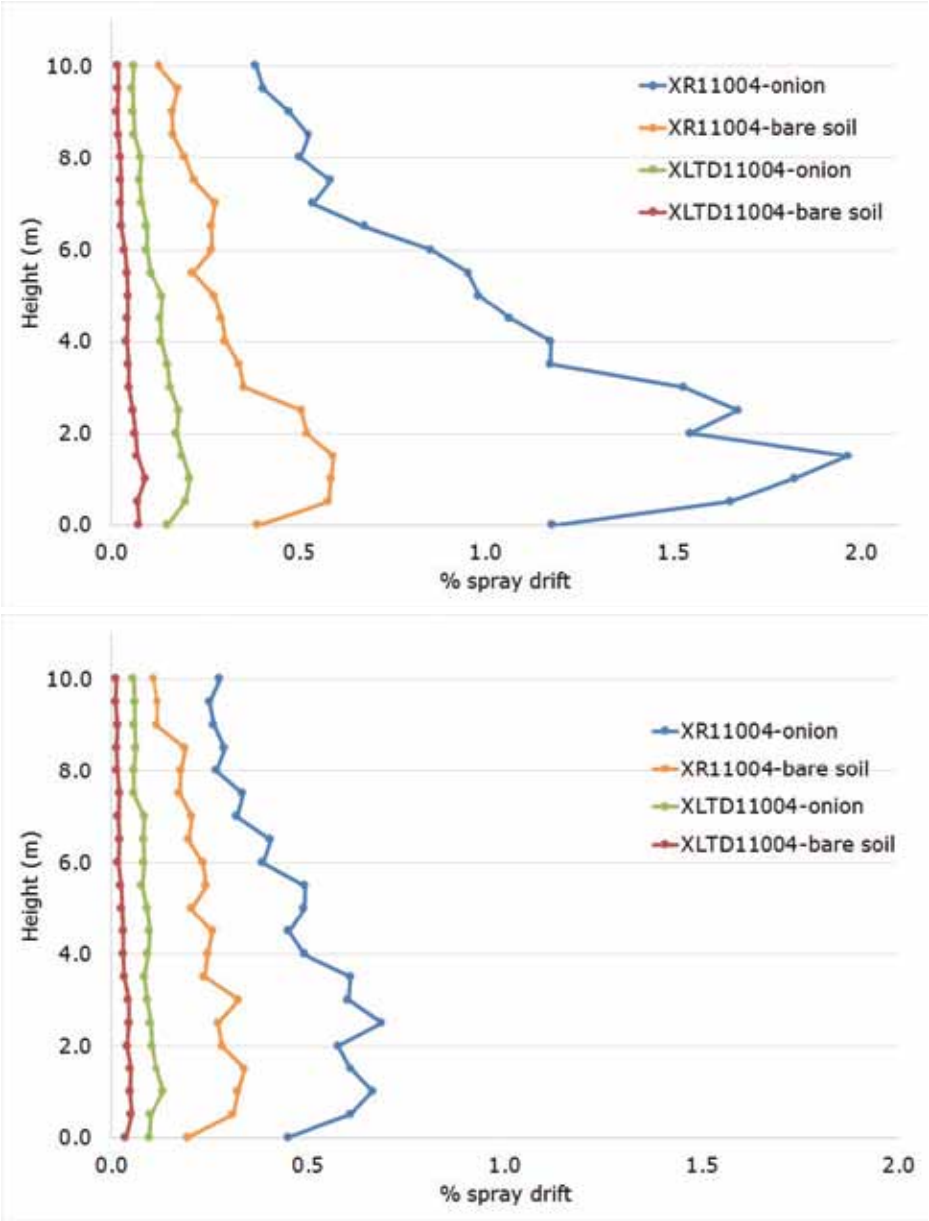


Figure 5.16: Mean airborne spray drift (% of applied spray volume per unit area) measured with passive collectors at different heights.

Mean airborne spray drift (% of applied spray volume per unit area) measured with passive collectors at different heights at 25 m (top) and 50 m (bottom) from the last nozzle spraying the outside two swaths (2x27 m) of a bare soil surface area and an onion crop using a boom sprayer equipped with a standard nozzle (XR11004) and a 90% drift reducing nozzle (XLTD11004; DRN90) at 50 cm spray boom height.

Table 5.8: Mean airborne spray drift measured with ball shaped collectors at different height layers and distances from the last nozzle spraying.

Mean airborne spray drift (% of applied spray volume per unit area) measured with ball shaped collectors at different height layers and distances from the last nozzle spraying the outside two swaths (2x27 m) of a bare soil surface area and an onion crop using a boom sprayer equipped with a standard nozzle (XR11004) and a 90% drift reducing nozzle (XLTD11004; DRN90) at 50 cm spray boom height.

		bare soil						onion					
nozzle	height layer	5 m	10 m	15 m	25 m	35 m	50 m	5 m	10 m	15 m	25 m	35 m	50 m
XR11004	0-1 m	1.642	1.172	0.792	0.521	0.341	0.277	4.634	2.426	1.912	1.551	1.016	0.575
	0-2 m	1.441	1.123	0.789	0.536	0.333	0.291	3.953	2.276	1.879	1.633	1.063	0.583
	0-3 m	1.241	1.011	0.734	0.506	0.318	0.293	3.486	2.097	1.834	1.624	1.074	0.601
	3-6 m	0.431	0.442	0.389	0.295	0.236	0.251	1.384	1.181	1.285	1.104	0.884	0.504
	0-10 m	0.586	0.517	0.407	0.327	0.221	0.228	1.644	1.154	1.135	1.032	0.798	0.454
XLTD11004	0-1 m	0.214	0.142	0.134	0.079	0.069	0.046	1.093	0.330	0.228	0.188	0.157	0.111
	0-2 m	0.180	0.129	0.118	0.075	0.065	0.046	0.957	0.323	0.248	0.186	0.161	0.110
	0-3 m	0.156	0.119	0.105	0.068	0.062	0.046	0.843	0.308	0.246	0.182	0.154	0.107
	3-6 m	0.053	0.058	0.044	0.044	0.042	0.031	0.365	0.156	0.164	0.132	0.134	0.089
	0-10 m	0.073	0.062	0.054	0.044	0.041	0.030	0.423	0.165	0.151	0.124	0.120	0.086

Active measurements with suction heads

Average airborne spray drift measured with the suction head collectors spraying a bare soil surface area and an onion crop using a boom sprayer equipped with standard nozzles (XR11004) and 90% drift reducing nozzles (XLTD11004; DRN90) are presented for different distances in Figure 5.17. The results of the airborne spray drift measured at different height layers are presented in Table 5.9.

Measured airborne spray drift with the suction head collectors (Figure 5.17; Table 5.9) shows for both nozzle types (XR11004 and DRN90) a higher airborne spray drift when spraying a crop than when spraying a bare soil surface area. In all cases airborne spray drift of the boom sprayer equipped with standard nozzles was always higher than when the sprayer was equipped with 90% drift reducing nozzles. Airborne spray drift measured with the suction heads is for the standard nozzle spraying an onion crop highest at 0.37 m height and at 5 m distance 33.7% and reducing to 7.8% at 50 m distance. For the DRN90 nozzle at 5 m distance and 0.37-0.65 m height airborne spray drift is 3.4% and this percentage was attenuated to 0.9% at 50 m distance. Threshold values of the blank filter collectors used in the suction heads is for the spray drift measurements spraying a bare soil surface 0.004-0.006%. For the spray drift measurements in the onion crop the threshold value of the blank filters was 0.005-0.010%. For all spray drift experiments spraying a bare soil surface and an onion crop for both nozzles types (standard, DRN90) at all heights and distances the spray drift deposition values measured with the suction heads are above the threshold value of the blank filter collectors.

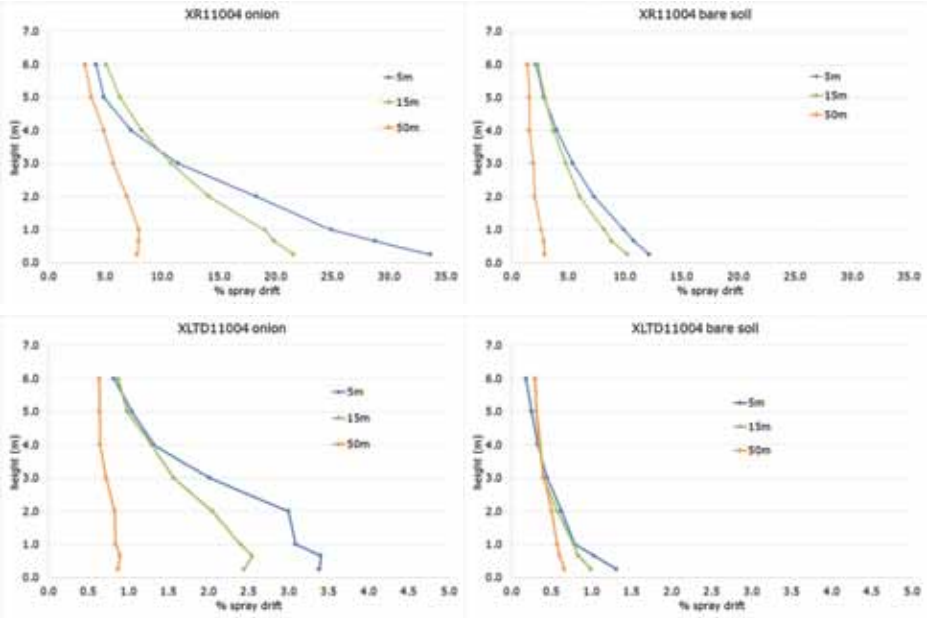


Figure 5.17: Average airborne spray drift measured with suction head collectors at different heights. Average airborne spray drift (% of applied spray volume per unit area) measured with suction head collectors at different heights at 5 m, 15 m and 50 m from the last nozzle spraying the outside two swaths (2x27 m) of a bare soil surface area and an onion crop using a boom sprayer equipped with a standard nozzle (XR11004) and a 90% drift reducing nozzle (XLTD11004; DRN90) at 50 cm spray boom height.

At 50 m distance from the last nozzle spraying a bare soil surface using a boom sprayer equipped with a standard nozzle results in an airborne spray drift value at 0-1 m, 0-2 m and 0-3 m height layers of resp. 2.8%, 2.6% and 2.5% when measured with suction heads (Table 3.12). When the boom sprayer is equipped with DRN90 nozzles than airborne spray drift values at these height layers are resp. 0.615%, 0.589% and 0.554%. When spraying an onion crop using a boom sprayer equipped with standard nozzles, airborne spray drift at 50 m distance from the last nozzle is at the height layers 0-1 m, 0-2 m and 0-3 m resp. 7.9%, 7.7 % and 7.3% when measured using suction heads. When the boom sprayer is equipped with DRN90 nozzles instead than the airborne spray drift at the different height layers are resp. 0.869%, 0.860% and 0.832%.

Table 5.9: Mean airborne spray drift (% of applied spray volume per unit area) measured with suction head collectors.

Mean airborne spray drift (% of applied spray volume per unit area) measured with suction head collectors at different height layers at 5 m, 15 m and 50 m distance from the last nozzle spraying the outside two swaths (2x27 m) of a bare soil surface area and an onion crop using a boom sprayer equipped with a standard nozzle (XR11004) and a 90% drift reducing nozzle (XLTD11004; DRN90) at 50 cm spray boom height.

		bare soil			onion		
nozzle	height	5 m	15 m	50 m	5 m	15 m	50 m
XR11004	0-1	10.9	9.1	2.8	29.1	20.2	7.9
	0-2	10.0	8.3	2.6	26.5	18.7	7.7
	0-3	9.1	7.6	2.5	23.4	17.1	7.3
	3-6	3.6	3.5	1.6	7.0	7.6	4.4
	0-6	6.8	5.9	2.1	16.7	13.2	6.1
XLTD11004	0-1	1.0	0.87	0.61	3.3	2.5	0.87
	0-2	0.94	0.80	0.59	3.22	2.36	0.86
	0-3	0.84	0.72	0.55	2.98	2.20	0.83
	3-6	0.30	0.34	0.34	1.30	1.18	0.66
	0-6	0.62	0.57	0.46	2.26	1.77	0.76

5.1.5 Discussion

In order to compare the collected spray drift deposition and the airborne spray drift collected with the passive collectors the average values of airborne spray drift over 0–1 m, 0–2 m and 0–3 m height are presented over distance spraying a bare soil surface area (Figure 5.17) and an onion crop (Figure 5.19). Sampled airborne spray drift over the different height layers is much higher than collected spray drift deposits at the ground collectors at the same distance. This is both the case for the standard flat fan nozzle as for the drift 90% reducing venturi flat fan nozzle.

Bare soil surface spraying

For the standard nozzle airborne spray drift (0–2 m height) is 1.44% at 5 m distance (Table 5.8) whereas ground deposition is 0.37% and respectively 0.18% and 0.05% for the DRN90 nozzle spraying a bare soil surface. At 50 m distance airborne spray drift (0–2 m height) is 0.31% and 0.046% for the standard and DRN90 nozzles and ground deposition is respectively 0.02% and 0.002% for both nozzle types (and below threshold value of resp. 0.005% for the DRN90). This shows that airborne spray drift (0–2 m height) is about 4 times higher at 5 m distance (Table 5.10) and that this ratio increases with distance.

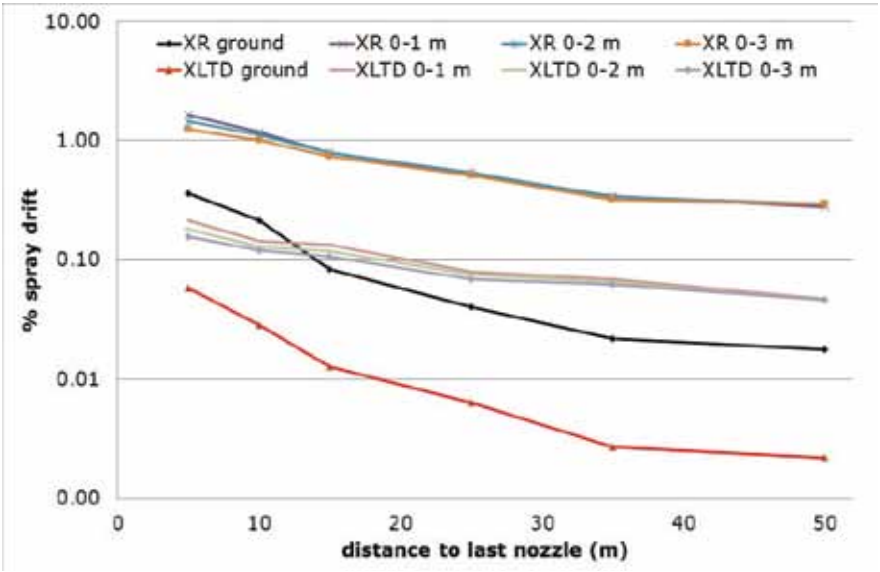


Figure 5.18: Airborne spray drift (% of sprayed volume) measured with passive collectors at different height layers above ground and spray drift deposition at ground collectors.
Airborne spray drift (% of sprayed volume) measured with passive collectors at different height layers above ground and spray drift deposition at ground collectors downwind of a 54 m wide bare soil surface area sprayed swath using a 27 m working width conventional boom sprayer at 50 cm boom height and two nozzle types (XR11004, standard flat fan nozzle; XLTD11004 drift reducing venturi nozzle type) applying 300 L ha-1 at up to 50 m distance from the last nozzle.

Table 5.10: Ratios in spray drift deposition between spray drift deposition at ground level, passive collectors over 0–2 m height and active air sampling over 0–2 m height.
Ratios in spray drift deposition between spray drift deposition at ground level, passive collectors over 0–2 m height and active air sampling over 0–2 m height for a 54 m sprayed bare soil surface swath with a conventional boom sprayer at 50 cm boom height and equipped with XR11004 standard flat fan nozzles and XLTD11004 drift reducing venturi flat fan nozzles at 5 m, 15 m and 50 m distance from the sprayed swath (last nozzle position).

		5 m	15 m	50 m
Passive 0–2m/ground	XR	4	9	17
Passive 0–2m/ground	XLTD	3	9	21
Active/passive 0–2 m	XR	7	11	9
Active/passive 0–2 m	XLTD	5	7	13
Active 0–2 m/ground	XR	28	91	142
Active 0–2 m/ground	XLTD	16	63	>150

When spraying a bare soil surface area the airborne spray drift in the 0–2 m height layer is four times higher than ground deposits at 5 m distance and increases to 17 times higher at 35–50 m distance from the last nozzle for the standard nozzle. For the DRN90 nozzle this ratio increases from 3 at 5 m distance up to 21 at 35–50 m. Bystanders and residents (of 2 m height) standing around the field can therefore expect up to a 20

times higher exposure based on these passive airborne spray drift data than of the ground deposition data at the same distance. In a similar way the passively and actively collected airborne spray drift differ. Whereas the passive method collects mainly the 'wet' particles (airborne droplets) in the air the active sampling method takes up also the already dried particles from the passing air. The active samplers collect about 5–7 times more drift at 5 m distance up to 9–13 times more drift at 50 m distance (Table 5.10). Comparing the collected airborne spray drift with the active air sampling collectors and the spray deposition at ground level at the same distance, data show a 16–28 times higher airborne spray drift collected at 5 m distance up to 142 times higher airborne spray drift over 0–2 m height at 50 m distance from the treated bare soil surface field.

Crop spraying

When spraying an onion crop using the standard nozzle airborne spray drift (0–2 m height) is 3.95% at 5 m distance (Table 5.8) whereas ground deposition is 1.43% and respectively 0.96% and 0.13% for the DRN90 nozzle. At 50 m distance airborne spray drift (0–2 m height) is 0.58% and 0.11% for the Standard and DRN90 nozzles and ground deposition is respectively 0.02% and 0.001% for both nozzle types (and below threshold value of 0.010% for the DRN90). This shows that airborne spray drift (0–2 m height) is about 3 to 7 times higher at 5 m distance (Table 5.11) and that this ratio increases with distance.

When spraying a cropped area the airborne spray drift in the 0–2 m height layer increases from 3 times higher than ground deposits at 5 m distance up to 31 times higher at 50 m distance from the last nozzle for the standard nozzle. For the DRN90 nozzle this ratio ranges from 7 at 5 m distance up to more than 100 at 50 m, which is caused by the very low spray drift deposition values at 50 m distance of the DRN90 nozzle (below threshold value). Bystanders and residents (of 2 m height) standing around the field can therefore expect up to a 3-100 times higher exposure based on these passive airborne spray drift data than of the ground deposition data at the same distance. In a similar way the passively and actively collected airborne spray drift differ. The active samplers collect about 3–7 times more drift at 5 m distance up to 8–13 times more drift at 50 m distance (Table 5.11).

Comparing the collected airborne spray drift with the active air sampling collectors and the spray deposition at ground level at the same distance, data show a 17–22 times higher airborne spray drift collected at 5 m distance up to more than 150 times higher airborne spray drift over 0–2 m height at 50 m distance from the treated field crop.

From earlier spray drift experiments performed in the Netherlands and the UK, it was known that airborne spray drift was higher than ground deposit at the same distance (Zande et al., 2017; Butler Ellis & Miller, 2010). Butler Ellis & Miller (2010) reported airborne spray drift over 0-2 m height at 2 m distance from the field edge to be 1-4 times higher than ground deposit at 2 m distance. Zande et al. (2017) found at 5 m distance from the treated field, airborne spray drift (0-3 m height) to be 1-4 times

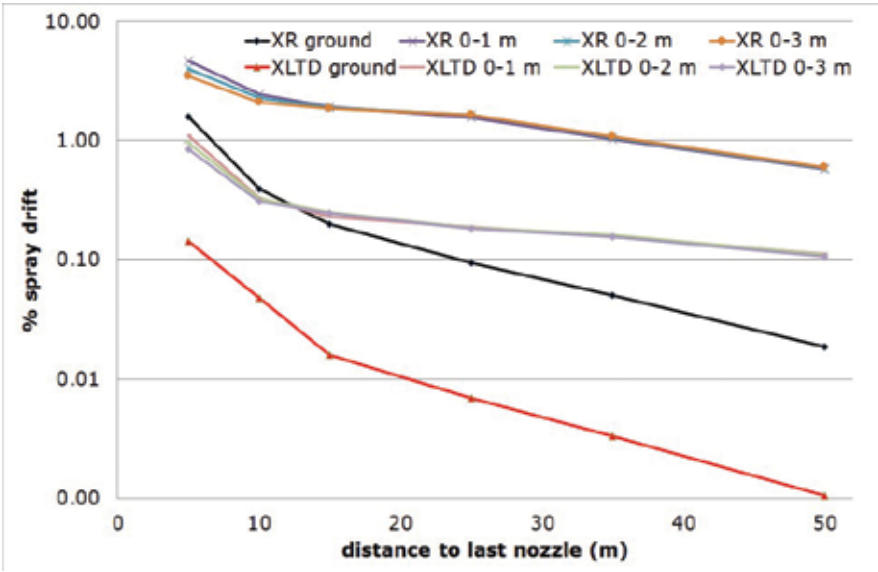


Figure 5.19: Airborne spray drift (% of sprayed volume) measured with passive collectors at different height layers above ground and spray drift deposition at ground collectors.
Airborne spray drift (% of sprayed volume) measured with passive collectors at different height layers above ground and spray drift deposition at ground collectors downwind of a 54 m wide onion crop sprayed swath using a 27 m working width conventional boom sprayer at 50 cm boom height and two nozzle types (XR11004, standard flat fan nozzle; XLTD11004 drift reducing venturi nozzle type) applying 300 L ha-1 at up to 50 m distance from the last nozzle.

higher than spray drift deposition at ground level. At larger distances the ratio airborne to ground deposition of spray drift could be as high as 140 which was dependent on the used spray technique (standard and DRT) and distance. However, Zande et al. (2017) presented results based on estimates of airborne spray drift at larger distances as airborne spray drift in the past was mainly measured only at 5 m distance and only in a few cases at other distances further away from the treated area. In this study, airborne spray drift measurements are performed up to 50 m from the treated area and show that airborne spray drift is much higher at distances further away from the treated area. Therefore, the airborne/ground spray drift deposition ratio measured in this study is much higher than estimated earlier (Zande et al., 2017). In this study, airborne spray drift (measured with passive collectors) is measured at higher levels (above threshold value 0.05%) at larger distances (up to 50 m) from the treated area than estimated by Zande et al. (2017), also with the 90% drift reducing nozzle type. Ground spray drift deposition of the 90% drift reducing nozzle type is below threshold level (0.010%) already at 25 m distance from the treated area.

Table 5.11: Ratios in spray drift deposition between spray drift deposition at ground level, passive collectors over 0–2 m height and active air sampling over 0–2 m height.
Ratios in spray drift deposition between spray drift deposition at ground level, passive collectors over 0–2 m height and active air sampling over 0–2 m height for a 54 m sprayed swath onion crop with a conventional boom sprayer at 50 cm boom height and equipped with XR11004 standard flat fan nozzles and XLTD11004 drift reducing venturi flat fan nozzles at 5 m, 15 m and 50 m distance from the sprayed swath (last nozzle position).

		5 m	15 m	50 m
Passive 0–2m/ground	XR	3	9	31
Passive 0–2m/ground	XLTD	7	16	105
Active/passive 0–2 m	XR	7	10	13
Active/passive 0–2 m	XLTD	3	10	8
Active 0–2 m/ground	XR	17	85	>150
Active 0–2 m/ground	XLTD	22	149	>150

5.1.6 Conclusions and recommendations

Results of the presented spray drift measurements show that when spraying a bare soil surface and an onion crop with a standard flat fan nozzle and a 90% drift reducing venturi flat fan nozzle, airborne spray drift is higher than drift deposits on ground collectors at the same distance from the treated field. Spray drift ground deposits as well as airborne spray drift is higher when spraying a developed crop (0.50 m crop height) than when spraying a bare soil surface. With a conventional boom sprayer equipped with standard flat fan nozzles operating at a spray boom height of 0.50 m above ground, both spray drift deposits at the ground and airborne spray drift are above the detection limit, up to 50 m distance and 10 m height. For the 90% drift reducing venturi flat fan nozzle the ground deposits of spray drift are lower than the detection limit at 25 m downwind and beyond, whereas the airborne spray drift at 50 m still is above the detection limit for the passive airborne collectors. Airborne spray drift for the active sampling devices is about 3 to 13 times higher than that of the passive airborne drift collectors. At 5 m from the treated field, the airborne spray drift averaged over 0–2 m height measured using passive sampling is up to 7 times higher than drift deposits at ground collectors. At 50 m distance passive airborne drift is up to 100 times higher than that on ground collectors. The ratio of airborne drift to ground deposits for active airborne samplers is even higher: averaged over 0–2 m height at 5 m distance this ratio is up to 28, while at 50 m distance from the treated field the ratio is more than 150.

In this study, airborne spray drift measurements are performed up to 50 m from the treated area and the results show that airborne spray drift is much higher than ground deposits at distances further downwind from the treated area. Therefore the airborne/ground spray drift deposition ratio measured in this study is also much higher than determined in earlier studies.

Spray drift measurements are most of the time focused on deposition at ground level to quantify the exposure of surface water and non-target zones for plants and

arthropods. From the spray drift measurements performed in these studies it becomes clear that more attention is to be paid to airborne spray drift. As a potential route of exposure, airborne spray drift can be relevant for dermal exposure (passive collectors), inhalation exposure (active suction collectors) of residents standing outside and the exposure of resident's homes. Future spray drift experiments are advised to take up also airborne spray drift at multiple distances as part of the protocol.
From the 50 m distance spray drift measurements in 2015 and 2016 it was concluded that at 50 m distance airborne spray drift was measured both with passive collectors as with active suction collectors. This was even so for the 90% drift reducing nozzle used. It is therefore recommended to do more 'long distance' spray drift experiments to quantify the effect of spray drift reducing techniques (DRT) at higher levels to quantify if 'no drift' situations can occur with the highest DRT classes, being a 95%, 97,5% and 99% drift reducing technique.

As we were unable to measure in practice the spray drift deposition around garden fences, in gardens and at the wall of resident's homes it is advised to do these quantifications more in future.

Preliminary results of spray drift studies mimicking fences and vegetative barriers show that decreases in exposure behind the barrier can occur but also that higher deposits are the case depending on the openness of the barrier to wind. This is to be assessed more in depth with the use of different drift reducing techniques, weather conditions and types of fences and vegetative barriers as well as for downward directed spray techniques used in arable crops as for sideways and upward directed spray techniques as used in fruit crops.

5.2 Volatilization

In the OBO study measurements were done to determine exposure of residents to pesticides due to the application of these substances in flower bulb crops. One part concerns measuring volatilization of the pesticide immediately after spraying (source strength measurement).

The volatilization of pesticides from soil and from crop can be quantified using micro-meteorological methods. These are based on the relation between the vertical concentration gradient in the air and the source strength (also called flux). Such methods have commonly been used to determine the source strength of volatilization from soil and crop surfaces (e.g. Majewski et al., 1990, Leistra et al., 2006).

For a source strength measurement apart from measurements of concentrations of substances in the air detailed measurements of the meteorological conditions at the time of the air sampling are required. Furthermore, the residue of the substance on the leaves is determined as well to relate the strength of volatilization to the remaining

mass of the substance on the leaves. This also helps to determine to which extent and for how long the volatilization could continue.

In this study, measurements of volatilization rate from the plants are based on the aerodynamic (or gradient) method. This method relies on the so-called flux-profile relationships in the layer close to the Earth's surface, the atmospheric surface layer (ASL; Stull, 1988). The ASL has a typical height of a few tens to one hundred meters, depending on the meteorological conditions. In this layer, the fluxes are assumed to be constant with height and are driven by the vertical gradient of the quantity that is being considered.

According to surface layer theory (Garratt, 1992; Stull, 1988):

$$c(z) = c_0 + \frac{c_*}{\kappa}\left[\ln\left(\frac{z}{z_c}\right) - \Psi\left(\frac{z}{L}\right)\right] \quad (1)$$

where c [g m^{-3}] is the concentration, z [m] is height, c_0 [g m^{-3}] is the concentration at the roughness length for scalars z_c [m]. Concentration c_0 is obtained by extrapolation of concentration profile $c(z)$ to the surface. Furthermore, in (1) c^* [g m^{-3}] is the characteristic concentration scale or friction concentration that can be negative (upward flux like volatilization) or positive (downward flux, like deposition), κ = 0.4 [-] is the Von Kármán constant, L [m] is the Monin-Obukhov length scale and $\Psi(z/L)$ [-] is the integral of the stability function for scalars, used to account for stability effects on the flux-profile relationship.

Here, Equation (1) is fitted to the observed concentration profile to obtain c* and hence the volatilization rate J_{vol} [g m^{-2} s^{-1}]:

$$J_{vol} = -u_* c_* \quad (2)$$

where u_* [m s-1] is the friction velocity which is directly determined from the wind velocity fluctuations measured by means of the sonic anemometer.

The fit is most easily obtained by plotting the concentrations versus ln(z), from which a linear fit can be determined with slope c*/κ. The slope and c* are expected to be negative in the case of volatilization. The slope is neither sensitive to c_0, nor to z_c, but it may be somewhat sensitive to the stability correction. However, for our experiments the observed concentration profile, obtained between a height of 1.0 and 2.5 m was found to be hardly affected by the stability term and therefore, it was decided to ignore this effect.

Concentration gradients of the applied active substance in the air above the sprayed crop were measured in the field. At each sampling time the concentration in the air on the windward side of the field was measured too. The lowest measuring height depends on the displacement height and roughness length. These parameters can be estimated from the crop height (Van den Berg et al., 2016). Further details on the concentration measurements are given in Section 5.2.1.2 and Appendices 17 and 18.

5.2.1 Materials and methods

5.2.1.1 Meteorological observations

Meteorological observations were done in support of the volatilization measurements. The main goals of these observations during the volatilization experiment were:

1 Quantification of the turbulent exchange, which is required to compute the volatilization from the measured vertical concentration profiles in air of the pesticide;
2 Collection of data for interpretation of the measured volatilization and for testing and improving the volatilization model.

The instruments were mounted in two masts, depending on the type of measurement. One mast was equipped with sensors for "slow" meteorological observations: the radiation components, air temperature and humidity. Precipitation, air pressure, leaf wetness and leaf temperature were logged via the same mast. The data from these instruments were logged each 10 seconds. These data were then converted to 10-minute averages or sums (precipitation) and leaf wetness period.

The other mast was equipped with a sonic anemometer for turbulence measurements. This instrument measures wind speed fluctuations in three directions, from which temperature fluctuations can be determined as well. The frequency of these measurements was 10 Hz (10 per second). The turbulence measurements were processed and quality checked following internationally accepted guidelines (Aubinet et al., 2012). Half-hourly averages were computed from the 10 Hz samples, including half-hourly averaged wind speed, wind direction and turbulent fluxes. More information on the equipment is presented in Appendix 16.

5.2.1.2 Measurement of concentration in the air

Two sampling units were used; one for sampling the pesticide concentration in air upwind from the field and the other for measuring the vertical pesticide concentration gradient above the crop. Both systems consist of a vacuum pump with buffer vessel and pressure valve. Electricity was provided by 220 V generators. The units were covered with a plastic foil during spraying. Each sampling unit with XAD-2 adsorbent was connected with the central buffer vessel via a manifold. A flow meter with restriction (Brooks Instruments type 8-1307-V, maximum flow rate 5 m^3/h) and a gas meter

(Schlumberger, type G 4-250, maximum flow rate 6 m^3/h) were coupled to a plastic tube (inner diameter 12 mm). The air flow from each sampling unit with adsorbent was set to a flow rate of approximately 3 m^3/h. The upwind samples were taken using a flow rate of approximately 4 m^3/h to enable lower detection levels. The exact air volume sampled in a sampling period was read from the gas meter.

Concentrations in air were determined using the polystyrene adsorbent XAD-2 (SERDOLIT, Serva, research grade). The sampling units are made of glass tubes (inner diameter 35 mm) with screw thread on both ends.

5.2.1.3 Measurement of volatilization on location A

Description of the field and the application

The field is located on a representative bulb-growing farm on the Western side of OBO location A (Province of North-Holland). The surface area of the field is 1.865 ha; the length of the field is mostly 350 m and for a smaller section (27 m out of the total width of 61 m) the length is 250 m. The orientation of the field is overall SSW-NNE. In Figure 5.20 an overview of the location of the field is given.

North of the field there is an embankment with a ditch running parallel. Between the ditch and the northern edge of the bulb-growing field there is a path to accommodate the passing of tractors. To the East of the field there were dwellings. On the 20 m wide section between the gardens and the field there were 7 beds planted with grape hyacinth (Muscari) and 2 beds with bare soil. On the Southern edge of the field first there is a ditch, then there is a road and a row of farm buildings. Close to the SW corner of the field there is the house and the other buildings of the bulb-growing farm. To the West there are other bulb-growing fields. On the field adjacent to the selected field, bulbs had been planted, but the plants had not yet emerged at the time of the volatilization measurements.

The bulbs on the field of study were planted on 32 beds of 1.50 m wide with paths 0.40 m in between. Bulbs of 5 hyacinth varieties with were planted: White Pearl, Purple Star, White Ideal, Blue Star, Pink Pearl. For each variety, bulbs of different size classes had been planted. The size classes, based on the circumference of the bulbs in cm, were 0-6, 3-6, 6-9, 9 and 9-11. In each plant bed bulbs of up to three varieties were planted. The size class and variety combination determined the plant density, the plant height, the soil cover and the Leaf Area Index (LAI). The plant density varied from 140 to 800 bulbs per running m of bed (data of bulb-growing farmer).

On 26 May 2016 a field with hyacinths was sprayed with a solution of the two active ingredients tebuconazole and thiacloprid using a Beyne field sprayer with a working width of 24 m and 48 spray nozzles at about 0.5 m boom height. The Agrotop Airmix 11003 flat fan nozzle type was used and the spray pressure was set at 2 atmosphere. A volume of 1220 L was added to the tank with spraying solution.

To determine the average concentration in the spraying solution samples of the spraying solution in the mixing tank were taken prior to the spraying, about half-way the spraying of the field and at the end of the spraying. The spraying started at 13:40 h and it ended at 13:57 h.

The areic application rate of tebuconazole (including the paths) was 75.2 g/ha. This application rate is about 50% of the recommended application rate, i.e. 1.5 - 2 L/ha, which is equivalent to 150 – 200 g active ingredient per ha). The amount of thiacloprid applied is calculated to be 238 g, which results in an application rate of 128 g/ha. This application rate corresponds fairly well to the recommended rate of application, i.e. 120 g/ha. More detailed information on the measurement of these compounds in the spraying solution and the procedure to calculate the application rates is presented in Appendix 17.

The vapor pressures of thiacloprid and tebuconazole are $3 \cdot 10^{-7}$ (25°C) and $1.3 \cdot 10^{-3}$ mPa (25°C), respectively. For thiacloprid and tebuconazole no data on the effect of the formulation were available. Furthermore, no pilot measurements were done on the volatilization of these protocol B compounds under field or laboratory conditions, so it was not certain that the concentrations in air could be quantified.

On 9 June 2016 the crop height with reference to the level of the flower-bulb beds was measured to be 37 ±3 cm, the minimum value being 31 cm and the maximum 42 cm. Based on visual observations on 28 May 2016 the soil cover at 5 m from the edge of the bed (64 observations) was 70 ±20% with a minimum of 30% and a maximum of 100%.

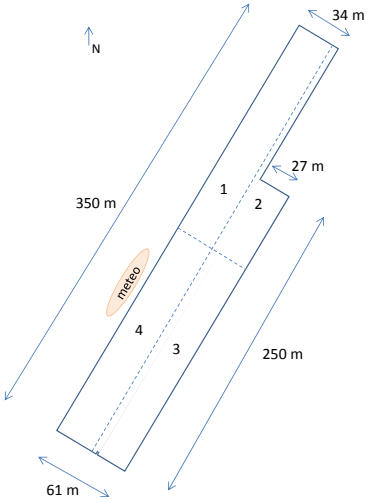


Figure 5.20: Size of the field.
The partitioning of the field into 4 sections (for sampling plant leaves) and the numbers of these sections are shown in this figure.

Figure 5.21: Meteorological equipment applied during the OBO volatilization experiment in May 2016.

The LAI was determined based on the leaf surface of 5 plants from 5 different beds (beds 3, 4, 6, 7, 10), each bed containing different variety – bulb size combinations.

Meteorological measurements

An overview of the installation of the meteorological equipment is shown in Figure 5.21. The equipment was set up close to the Eastern border of the field at about a distance of 40 m from the nearest farm building. East and South of the location with the meteorological equipment there are homes.

Measurement of concentrations in air

Air samples were taken on the day of application and on three days during the first week after application. The last samples were taken on the fourth day after the day of application.

The concentration gradient of the active ingredient in the air above the treated crop was measured at the downwind side of the treated field. The height of the lowest possible sampling point depends on the displacement height and the roughness length. The crop height was measured to be about 0.3 m. The upwind fetch was estimated to range from 60 to 350 m. in case of a fetch of 60 m the sampling heights need to be in the range between 0.75 and 1.5 m above the soil surface. During each sampling period an air sample was taken at several tens of meters from the upwind side of the treated field.

During the experimental period, the air sampling equipment was moved twice due to a change in the wind direction. The first relocation took place on the day of application shortly after the end of the first sampling period. The second time occurred on the fourth day after the day of application, prior to the last sampling series. The location of the sampling equipment is indicated by “A” on the maps shown in Figure 5.22. Because of the change of the wind direction the site for the upwind sampling had to change too. This site is indicated by “B” on the maps shown in Figure 5.22.

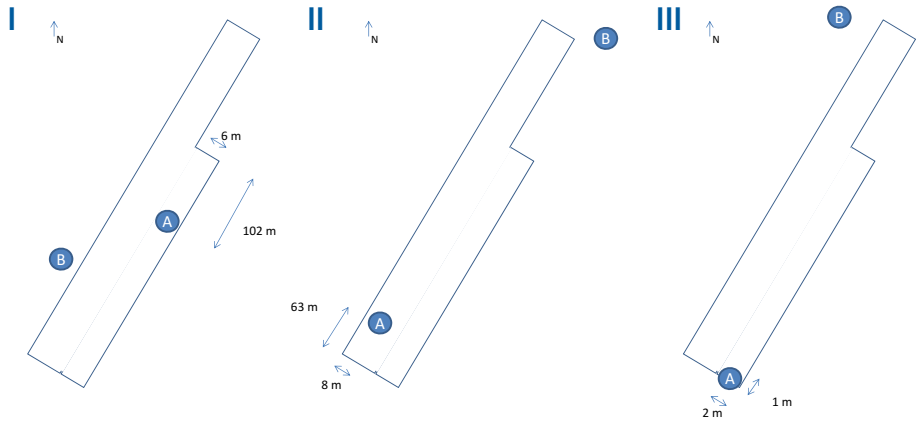


Figure 5.22: Position of sampling units.
Position of downwind (A) and upwind (B) air sampling units on day of application for first sampling series (I), from second sampling series on day of application as well as for the sampling on the first two days after the day of application (II) and for air sampling on the fourth day after the day of application (III).

Measurement of decrease of pesticide mass from leaves

The areic mass of the active ingredient on the plant leaves was measured at four times. The plant leaves were collected from the same flower-bulb beds at each sampling time. The plant leaves were sampled on one hour, one day and four days after the application.

5.2.1.4 Measurement of volatilization on field research site

Description of the field and the application

Because no suitable fields with a flower bulb crop were available, a field with an onion crop was selected. Onion plant and crop structure are similar to flower bulb plant and crop structure, and are therefore expected to be good alternative.

The field is located on the farm of Applied Arable and Vegetable Research of Wageningen University & Research in the province of Flevoland (see Figure 5.23). On 1 August 2017, a field consisting of plot numbers G103-2, G103-3 and partly G103-4 was sprayed. The orientation of this rectangular field is North-South and the total area is 14.94 ha (673 x 300 m). Figure 5.23 shows the layout of the treated field.

North of the field the farm is located, surrounded by paved and unpaved areas. The fields west of the field were bare soil, peas had been grown there previously. The remaining part of G103-4 (5.25 ha), South of the treated field, was sprayed on the same day with the same products and with the same intended application rate. Because the fetch for sampling in A (see Figure 5.24) is large enough, the application on this remaining part of plot G103-4 did not affect the measurements of the concentrations

Figure 5.23: View on the onion field (photo taken from west-side of the field).

at sampling site A. South of plot G103-4 a strip was located with trees and bushes of approximately 10 m wide. The fields east of the onion field were grown with winter cereals. The cereals were harvested during the period of the measurements, but not at times that the measurements were done.

The field was planted with onions (variety Crimson) except for tractor paths at the eastern and western inner border of the field. The onions were planted in beds oriented east-west. On the beds of 175 cm wide eight rows of onions were grown (25 cm between rows). The paths between the beds were 53 cm wide. Four units of 250 000 onion seeds each were sown per hectare. On the basis of an expectation of 90% of the planted onions surfacing the estimated density is 900 000 plants per hectare. The area of the field with onion beds, hence without headlands, is 13.8 ha.

The height of the crop above the bed surface was measured in each quadrant in five different beds on 2 August 2017. The average of the 20 measurements was 47±9 cm. More detailed information on these measurements is presented in Appendix 18.

The average soil cover for the beds in the field was 60%. The LAI was measured to be 3.253 m^2/m^2 for onions on the beds.

The substance measured is the substance chlorothalonil, a substance that has been measured in a source strength measurement before by van den Berg et al. (1995). At the same time also prochloraz was sprayed, for which was expected that concentrations in the air could be sufficiently high to be measurable. Therefore, both these substances were analyzed in tank, air and crop samples.

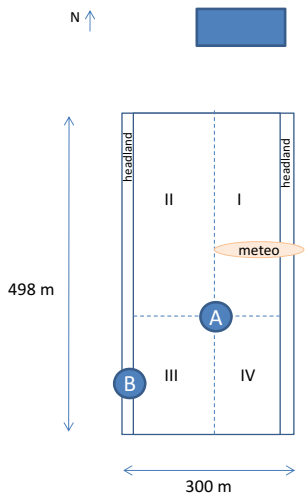


Figure 5.24: Dimensions of the field.
The field is divided into four quadrants for sampling of leafs and characterization of the crop. The quadrant numbering is indicated in the figure by Roman numbers I – IV. A = position of the air sampling unit for sampling in the field, B = position of the sampling unit for upwind sampling, and meteo = position of meteorological equipment. The headlands on both sides of the field were without onions.

On 1 August 2017 the spray tank was filled with a solution of the active ingredients chlorothalonil and prochloraz. Also the active ingredient mancozeb and a wetting agent, alcoxylated alcohol were added to the spray solution.

The field with onions was sprayed (see Figure 5.25) with the described solution. The spraying machine (Agrifac A3400) with spray booms of 24 m long (working width 48 m), with 48 nozzles (Airmix 110-03 Agrotop 90% drift reduction) set at 250 L/ha.

The dosage applied was measured to be 399 g/ha. The recommended dosage is 1.25 L Allure per ha, which results in a dosage of 416 g/ha; hence the applied dosage was 13% lower than the recommended dosage.

The dosage of prochloraz applied was measured to be 113 g/ha. The recommended dosage is 1.25 L Allure per ha, which corresponds to 131 g/ha; hence the applied was 21% lower than the recommended dosage. The difference in the percentage of the recommended dosage may be due a different ratio of these compounds in the spraying solution as compared to the ratio in the original product. Furthermore, it should be noted that the duplicate measurements for the samples taken of the spraying solution just before spraying showed a substantial variability (up to 20%).

Figure 5.25: Spraying of the onion field on 1 August 2017.

On 4 August 2017 at 2 p.m. the onions were sprayed with MH Royal (11599N, active ingredient maleïnehydrazide, 3.75 kg/ha) and 0.4 kg/ha WETCIT wetting agent (14036N) for sprout inhibition of the onion. The application was after sampling time t = 7 (4 August, 12:46 to 13:46 h).

Meteorological measurements

The location of the meteorological measurements is indicated in Figure 5.24. The installation of this equipment is shown in Appendix 16. Meteorological observations as described in section 5.2.1.1 in support of the volatilization measurements were carried out between 6 July and 9 August 2017.

The crop height was estimated at 0.5 m. The lowest measuring height is estimated to be equal to the sum of the displacement height and 15 times the roughness length. When the samples are taken in the middle of the field, the windward fetch is minimally 140 m (east or west). For a crop height of 0.5 m the sampling heights for a minimum fetch can then be between roughly 1.0 and 2.8 m. The sampling heights were set at 1.00, 1.50, 2.00 and 2.50 m. The sampling position is indicated by position A indicated in Figure 5.24. The samples taken upwind were taken at position B indicated in Figure 5.24. At the times of the measurements the direction of the wind was between South-east and east. Hence it was not necessary to move the upwind sampling point B.

The required turbulence measurements to determine u* were performed using the equipment described in Section 5.2.1.1 Unfortunately, the logging of the turbulence measurements stopped unexpectedly on 5 August, 00:00 MEWT, for an unknown reason. This means that u* for the last experiment had to be estimated using an

internationally recognized gap filling technique. To do this, a "lookup table" gap-filling technique as described in Aubinet et al. (2012) was used. Missing values are then taken to be the average of valid measurements of the missing variable occurring under similar meteorological conditions. To complete the turbulence data set of the field experiment, the weather observations at the Lelystad weather station, operated by the Royal Netherlands Meteorological Institute (KNMI), were compared with the turbulence data at the field research site as obtained from measurements before 5 August, considering wind speed and direction, solar radiation, and temperature to define similar weather conditions (see Appendix 16). Upon application of the rules of this gap filling technique, suitable data could be found to fill the missing records.

Measurement of concentrations in air

Air samples were taken on the day of the application and on the first, third and sixth days after the day of application. The air samples were taken at four heights above the crop (from the bottom of the bed); at 1.0, 1.5, 2.0 and 2.5 m height. The upwind air sample was taken at a height of 2 m. The air samples were taken at 8 times; two times on the day of application, three times on the first day after spraying (Day 1), two times on Day 4 and one on Day 7. The duration of sampling was 1 hour, except for the last measurement, on Day 7, which was 3 hours, because then the concentrations in the air were expected to be lower. The air samples were stored in a refrigerator at the farm and were transported to WENR and stored at -18°C, thereafter transported in a cooling box to TNO on 9 August 2017.

Because possible influence of weather condition on the breakthrough in the field, in each sample series one control on breakthrough was taken along at the lowest measurement at 1.0 m, because the highest concentrations are to be expected closest above the crop.

Measurement of decrease of pesticide mass from onion leaves

Areic mass of active substances chlorothalonil and prochloraz on the onion leaves was measured at three times. In each of the four quadrants (see Figure 5.24) 10 leaves were cut from the onion plants. The samples were taken at one hour, one day and four days after the application of the pesticides.

5.2.2 Results

5.2.2.1 Volatilization on location A

Meteorological conditions

An overview of the meteorological conditions during the period of 26 – 30 May 2016 is presented in Figure 5.26. In this figure 10-min averages are presented of the incoming global radiation, the air temperature and air humidity as well as 30-min average values of the wind speed and wind direction. Further, the air temperature is compared to the

leaf temperature and the air humidity is compared to the length of the leaf-wetness period. The leaf temperature is the average of the measurements of two sensors. The leaf wetness period is the maximum of the measurements of 2 sensors and this entity is expressed in minutes per 10 minutes. A value of 10 minutes implies that the plant leaf has been wet throughout the whole 10 minute averaging interval. In the period of 26 to 30 May, 9.4 mm of rainfall was recorded of which 8. 4 mm of rain fell on 30 May between 20:30 and 22:30 h, which was well after the end of the volatilization experiment.

On 26 May the wind direction turned sharply from South (180 degrees) via West (270 degrees) to Northwest (315 degrees) and from the afternoon onwards the wind direction was around Northeast (45 degrees). Throughout the whole experimental period the wind direction did not change very much, it varied between North and Northeast (0 and 45 degrees). On 30 May the wind turned gradually to North – Northwest (around 360 degrees). This change of the wind direction was favorable for the volatilization measurements, since after this change the direction of the wind was roughly parallel to the direction of the long edge of the field. Under these conditions there was a great fetch for the measurement of the concentration gradient at the downwind side of the field.

The wind speed showed an upward trend in the course of time of the volatilization experiment, from a daily maximum of 3 m/s to 8 m/s on 30 May. During the night (intensity of the global radiation around 0 W/m^2) the wind speed was overall substantially lower than during the day. This lower wind speed at night-time concurs with a lower air temperature and a higher air humidity. As expected, these variables react very clearly to the radiation intensity. In the beginning of the experimental period the global radiation increased to a level of around 1000 W/m^2. Later on, the radiation levels decreased because of more cloudy weather conditions. The changes in air temperature and air humidity are also correlated to changes in global radiation. The variations in these variables are much more pronounced on days with clear skies than on days with overcast weather conditions.

Incoming radiation warms up the leaf surface directly. At night heat loss from the surface occurs by long-wave radiation. Consequently, the leaf temperature during the day is much higher than the temperature of the surrounding air, and differences of up 10 °C are not uncommon. During the night the differences are less pronounced, but they can be as high as 2°C. The differences are greater under clear skies. At the same time, the relative humidity increases during the night and decreases during the day. So at lower temperatures during the night condensation of water may occur at the leaf surface resulting in a wet condition of the leaves, even if there has been no rain during the night. After sunrise, however, the plant leaves can dry up fairly quickly.

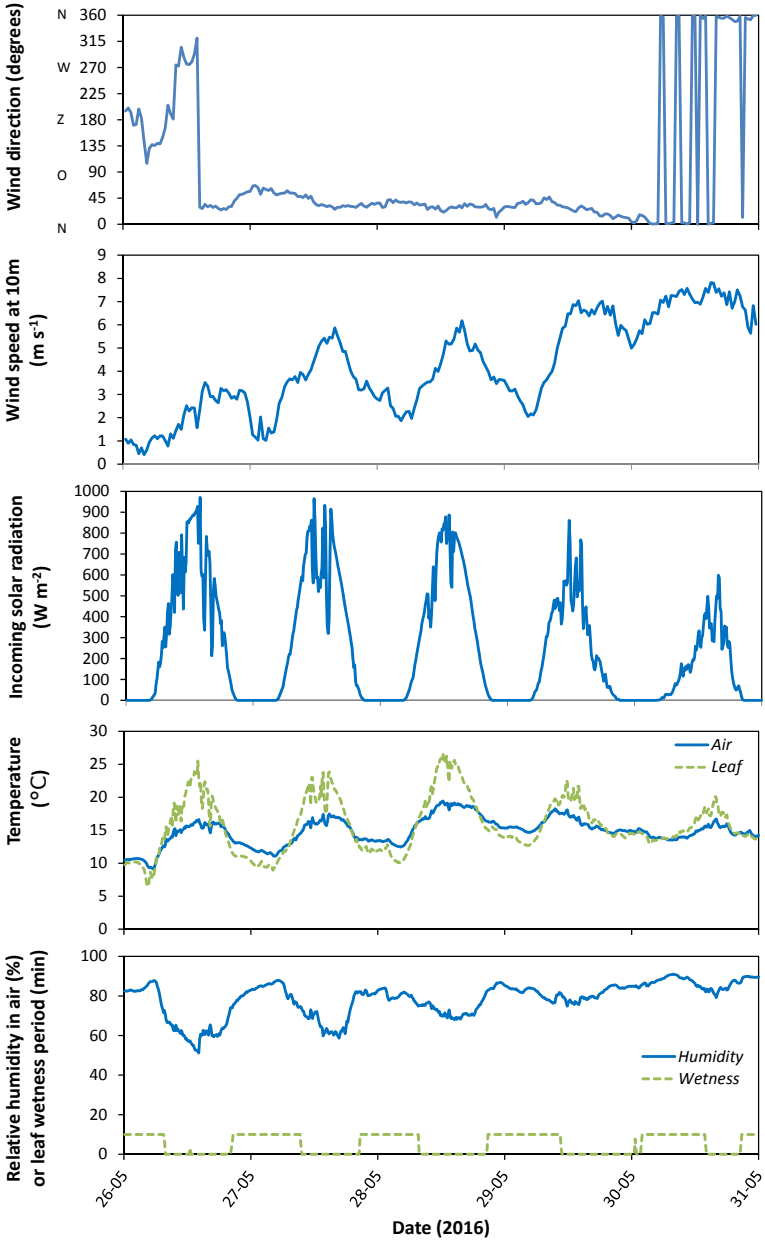


Figure 5.26: Weather conditions.

Weather conditions during the volatilization experiment at OBO location "A", 26-30 May 2016. from top to bottom: wind speed, wind direction, short-wave radiation, air – and leaf temperature, relative humidity and leaf-wetness period. Labels next to Y-axis for wind direction indicate North, West, South and East.

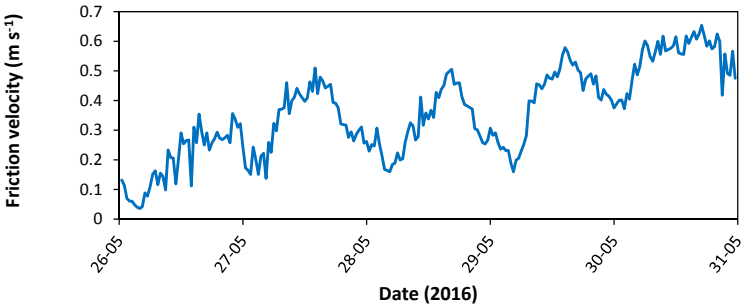


Figure 5.27: Friction velocity measured in the period 26-30 May 2016.

In Figure 5.27 the course of the friction velocity with time is shown. This property is the most important factor affecting the transport coefficient, which value is needed to calculate the volatilization rate from the concentration gradient. The transport coefficient is also influenced by the height and the stability of the air layer between the earth's surface and this height. The friction velocity is calculated from data on the turbulence and this is a measure for the production of turbulence by vertical differences in wind speed close to the surface. Above a rough surface more turbulence is generated. More turbulence is generated also at higher wind speeds and more turbulence also increases the friction velocity. The temporal pattern of the measured friction velocity resembles therefore that for the wind speed measured, but the latter shows a higher variation, which is typical for a turbulence-dependent property.

For calculations on dispersion of substances in air data on the dispersion coefficients are needed. These coefficients affect the extension of the plume containing contaminants due to atmospheric turbulence which results in a dilution of the contamination. The dilution in the horizontal and vertical direction perpendicular to the wind direction is affected by turbulence in the atmospheric boundary layer. This turbulence can be described using data on fast lateral and vertical fluctuations in the wind speed. This turbulence is affected by the presence of obstacles in the vicinity of the measurement site and the extent of this effect is described in more detail in Appendix 14.

Volatilization rate

The concentrations of tebuconazole and thiacloprid in air measured were below the limit of quantification (LOQ) in most cases. The LOQ on the adsorbent is 1 ng for both substances. Based on a volume of 3 m^3 air sampled in one hour the limit of detection (LOD) is about 0.3 ng m^{-3}.

Decrease of pesticide mass on leaves

The decrease of the mass of tebuconazole and thiacloprid on the plant leaves was calculated using the average values as measured in the field at three times, i.e. at 1.5 h and at 0.9 and 3.9 d after application. The mass measured on the day of application

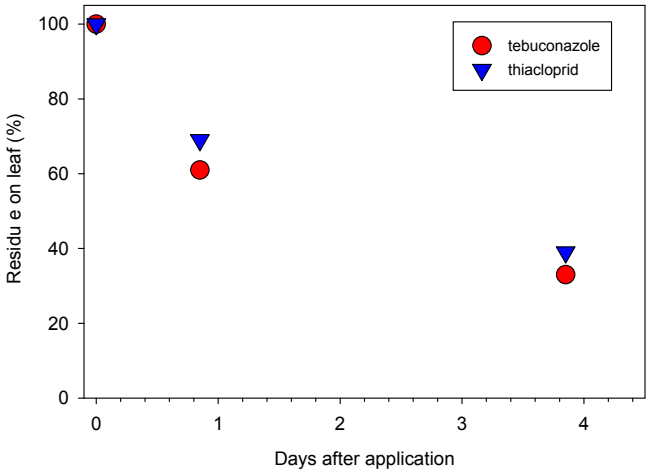


Figure 5.28: Residue of tebuconazole and thiacloprid on leaves after application.
Residue measured at 0.06 d after application set to 100%.

was set to 100 %. Figure 5.28 shows the decrease of the residue of both compounds on the plant leaves. For tebuconazole about 33% was calculated to remain at 3.9 d after application, whereas for thiacloprid it was 39% of the mass measured at 0.9 h after application.

For both substances the residue on the leaves decrease with time. The decrease is strongest during the first day after application. The extent of the decrease is similar for both compounds, although tebuconazole is more volatile than thiacloprid, the saturated vapor pressures at 25 °C being $1.3 \cdot 10^{-3}$ and $3 \cdot 10^{-7}$ mPa. As the formulated product has been applied, the effective vapor pressure of tebuconazole in this product could have been lower than that of the pure compound.

5.2.2.2 Volatilization on field research site

Meteorological conditions

Figure 5.29 summarizes the observed meteorological conditions during the volatilization measurements (1 - 7 August 2017). For incoming solar radiation, air temperature and humidity, leaf temperature and leaf wetness period 10-minute averages observed at the OBO field research site are displayed. The leaf wetness is given in minutes per 10-minute interval. A value of 10 minutes therefore means that the leaf may be considered wet during the entire averaging interval.

It can be seen that the wind was mainly from directions between South (180°) and West (270°). This was also the case during the actual volatilization measurements on 1, 2, 4 and 7 August. The wind speed at a height of 10 m was generally between

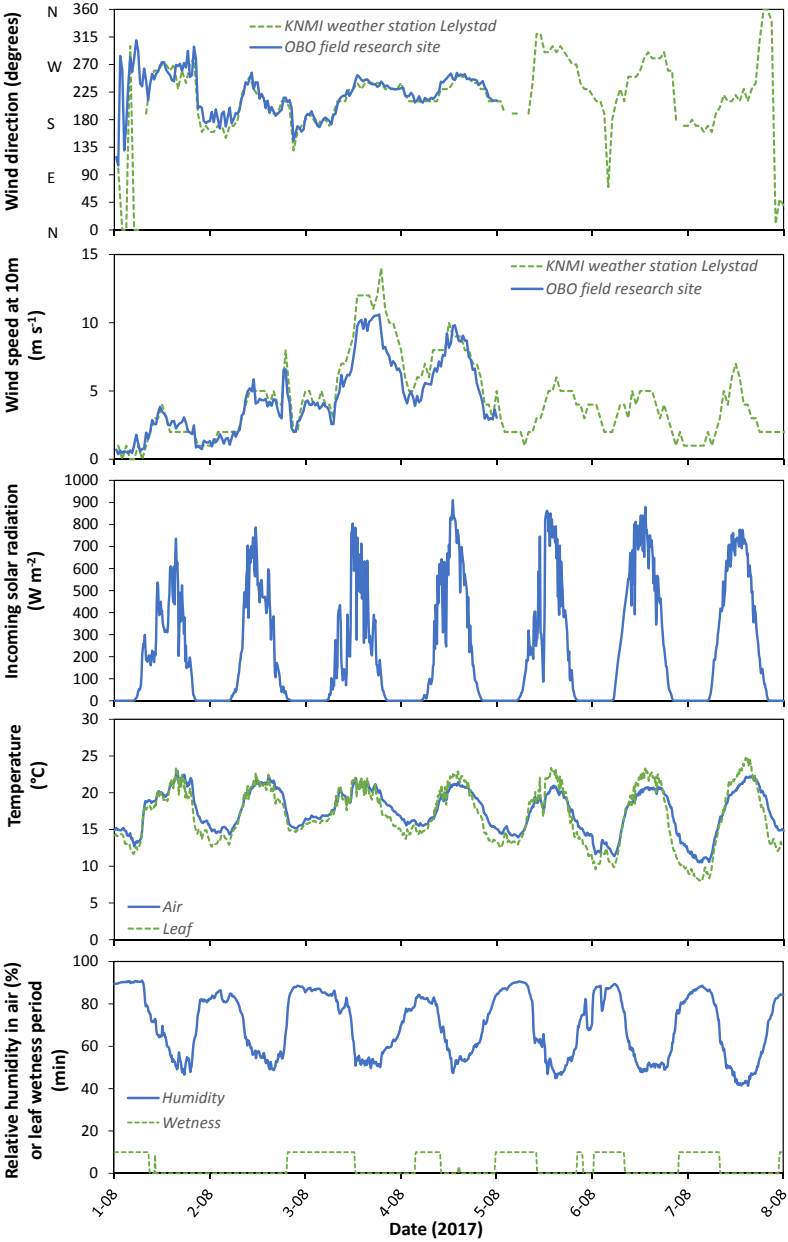


Figure 5.29: Meteorological conditions during the OBO volatilization measurements, 1-7 August 2017. From top to bottom: wind direction, wind speed, incoming solar radiation, air temperature and leaf temperature, relative humidity and leaf wetness period. Labels alongside the y-axis of wind direction: North (N), West (N), South (S) and East (E).

1.6 and 5.5 m s^{-1} (2-3 Beaufort), although afternoon wind speeds on 3 and 4 August reached 8-10 m s^{-1} (5 Beaufort) during some hours. The observed wind speed tends to be higher in the late afternoon and early evening than during the night and morning. This is important, since lower wind speeds promote stable conditions during the night without incoming solar radiation, and unstable conditions during daytime with strong incoming solar radiation. On the other hand, stronger winds tend to promote more neutral conditions.

The observed solar radiation shows strong variations and maximum levels between 700 and 900 W m^{-2}. Such a behavior is typical for early-August conditions with scattered clouds. This assessment is confirmed in the temperature record, which also shows much short-term variation and only moderate differences between daily maximum and minimum temperatures. In addition, differences between the leaf (surface) temperature and the air temperature are limited, which is also typical of (partly) cloudy conditions. Only towards the end of the period, on 6 and 7 August, the amplitude of the air temperature tends to increase somewhat, with smaller relatively fast variations and larger differences between the air and surface temperature. This is typical of weather with extended clear spells. In total, only 6.2 mm of precipitation was observed, of which 4.2 mm was received on 6 August between 3 and 4 MEWT. Yet, like in the previous experiment in 2016 leaves could be considered as “wet” during large parts of most nights of the experimental period. The wet leaf conditions correspond to a relative humidity in the air of over 90% during the night, with minimum temperatures between 10 and 15 °C. Maximum temperatures vary between 20 and 25 °C and correspond to the lower relative humidity of about 50%. During daytime and in the absence of rain the leaves can therefore be considered “dry” in general.

Figure 5.30 shows the measured friction velocity u_* during the observational period until 5 August 2017, when the system to measure turbulence unexpectedly stopped logging data. Values of this quantity are required to compute the volatilization rate (see Equation 2). It can be seen that observed values vary between about 0.05 and 0.8 m s^{-1} and that the overall trend of u_* follows the one of the wind speed (see Figure 5.29).

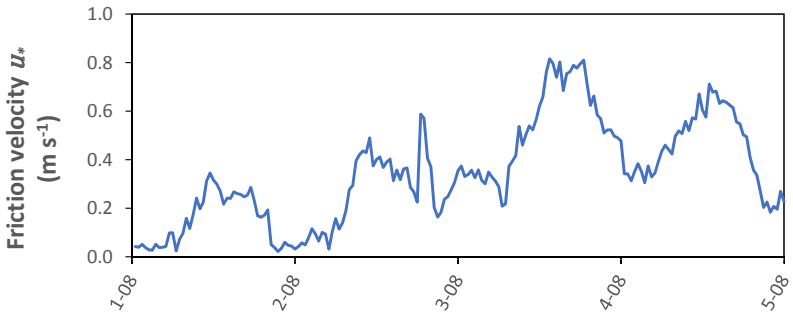


Figure 5.30: Observed friction velocity u_* in the period 1-5 August 2017.

Application of the flux-gradient relationships underlying (1)-(2) requires the flux and gradient to be in equilibrium. This is the case if the so-called fetch or source area is large enough. Footprint calculations (Schuepp et al., 1990) based on the turbulence measurements indicate that the footprint for measurements at a height of 2.5 m was well below 300 m during most volatilization measurements. More detailed information on the footprint calculations for the volatilization measurements at the field research site is given in Appendix 15.

Since the turbulence system stopped logging on 5 August no turbulence data are available for sampling time 8. Therefore, values for relevant parameters, notably u_* and footprint distance, were estimate using a technique similar to a gap filling technique that is quite commonly applied when micrometeorological estimations fail, but time series of weather conditions are available (Aubinet et al., 2012). This technique and the results for the meteorological conditions for the field research site are described in Appendix 16.

Volatilization rate chlorothalonil and prochloraz

In Table 5.12 the computed volatilization rate for all sampling times is presented. These rates are obtained using the fitting procedure described in Section 5.2. The calculated volatilization rates range from 5.1 to 34.7 µg m^{-2} h^{-1}. The highest volatilization rate was determined from the concentrations measured on the day of application four hours after the application. Lowest volatilization rates were determined from the concentrations measured at t = 1, t = 3 and t = 8.

Table 5.12: Volatilization rates computed from the concentration gradient and friction velocity measured.
The columns contain the computed volatilization rate per sampling time (details are given in Appendix 18). n.d. = not determined; at least three out of four concentrations measured were below LOQ.

Sampling time	Volatilization rate
	µg m-2 h-1
1	5.10
2	34.70
3	6.47
4	n.d.
5	10.86
6	n.d
7	n.d
8	6.06

Masses of prochloraz in the samples were all below the limit of quantification (LOQ) of 25 ng on the adsorbent. Hence the concentration in air in the first measurement after the application closest above the crop (at 1 m height) was < 5.8 ng/m^3 (volume of air pumped was 4.321 m^3).

Decrease of chlorothalonil and prochloraz on leaves

The theoretical mass of chlorothalonil on the leaves is calculated by dividing the dosage calculated from the concentration in the spray solution of 39.9 mg/m^2 (399 g/ha) by twice (deposition on both sides of leaves) the LAI of 3.253 m^2/m^2 results 6.13 mg/m^2 leaf area, or 0.613 µg/cm^2. Hence the mass measured on leaves six days after the application is roughly 1/3 of the mass calculated from the application rate.

Results for chlorothalonil could not be used to determine decrease because chlorothalonil transformed in the extract with plant leaves. The mass measured at day 7 application is roughly 1/3 of the mass calculated from the application rate. As the sample taken at this day
was comparatively little affected to degradation, it gives an indication of how much mass was present on the leaves on that day.

The decrease of mass of prochloraz on the leaves was calculated with the average values calculated for the three sampling times. The mass on the leaves at one hour after the application as taken as 100%. The decline in the mass on the leaves over time is shown in Figure 5.31.

The theoretical mass of prochloraz on the leaves resulting from the application is calculated by dividing the dosage calculated from the concentration in the spray solution of 11.3 mg/m^2 (113 g/ha) by twice (deposition on both sides of leaves) the LAI of 3.253 m^2/m^2 results 1.74 mg/m^2 leaf area, or 0.174 µg/cm^2. Hence the mass measured on leaves 1 hour after the application is 61% of the mass calculated from the application rate.

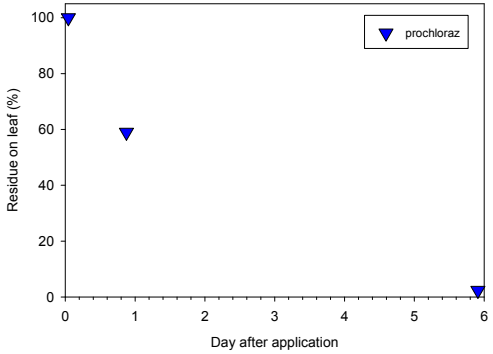


Figure 5.31: Residue of prochloraz on leaves after application.
Mass residue of first sampling time was set to 100%.

5.2.3 Discussion

5.2.3.1 Volatilization on location A

The concentrations of tebuconazole and thiacloprid in air were at or below the level of quantification, i.e. 0.3 ng m^{-3} for both substances. As the vertical concentration gradients at the downwind side of the treated field could not be quantified, it was not possible to calculate the rate of volatilization from the plant surfaces. However, concentrations in air above the crop below a level of 0.3 ng m^{-3} indicate that the rate of volatilization from the plant leaves is low.

The selection of compounds for protocol B has been based on a number of criteria. The most important criterion was whether there was a suitable metabolite of the active compound that could be measured in urine samples. Most of the compounds selected (see Chapter 2) had low vapor pressures. But even a comparatively high vapor pressure does not necessarily result in a high volatilization, because the volatilization potential of an active ingredient may be strongly reduced due to the presence of adjuvants in the formulation.

The mass of tebuconazole and that of thiacloprid remaining on the plant leaves was measured about 1.5 h after application and at about 0.9 and 3.9 days after application. The decrease in the mass of both substances was fast during the first 24 h after application. The residue of tebuconazole and thiacloprid on the plant leaves decreased to 61% and 69% of that measured shortly after application. In the subsequent three days the decrease in the residue was more gradual. For tebuconazole it decreased further to 33% and for thiacloprid it decreased to 39% of the residue measured shortly after application. Although tebuconazole is more volatile than thiacloprid, the rate of decline in the mass remaining on the plant leaves was similar for both compounds. Possible, other compounds present in the formulated product affected their behavior on the plant leaves. This may have resulted in a lower effective vapor pressure of tebuconazole in the formulated product than that of the pure compound. In addition, other substances in the formulated product may have affected the penetration of the substance into the plant leaves, and that would result in a decrease of the mass available for volatilization on the leaf surface.

5.2.3.2 Volatilization on field research site

The measured concentrations of prochloraz in air were below LOQ of approximately 6 ng/m3 (calculated for sample t = 0 at 1 m height). Therefore volatilization fluxes could not be calculated for this substance.

The results of the chlorothalonil measurements were compared with the measurements of Van den Berg et al. (1995). They measured the fate of chlorothalonil after application of 1940 g chlorothalonil per ha on a potato crop in Biddinghuizen

(province of Flevoland) in the first week after application in August. They measured volatilization rates ranging from 10 to 182 µg m^{-2} h^{-1}, measured with two methods; Bowen ratio (BR) and Aerodynamic (AD). In the first days after the application the rates were roughly 150 µg m^{-2} h^{-1} (BR) and 80 µg m-2 h-1 (AD). In four out of five of our measurements the volatilization rate was 5 to 11 µg m^{-2} h^{-1}. Correcting these values for the five times lower application rate used in this experiment gives 25 to 55 µg m^{-2} h^{-1}. These are lower than the rates determined by Van den Berg et al. (1995). However, our highest volatilization rate corrected for the application rate is 185 µg m^{-2} h^{-1}. Hence at the same level as the highest rate of 182 µg m^{-2} h^{-1} of Van den Berg et al. (1995). Lower volatilization rates can be due to the formulation of the products that were sprayed (see Houbraken et al., 2015). The formulation may affect attachment of chlorothalonil to leaves and consequently the rate of volatilization. The formulations of Daconil sprayed in Biddinghuizen and Allure sprayed in the current study differ. Furthermore in the current study other formulated products were added to the tank; Milcozeb and Certain. Van den Berg et al. (1995) observed that in the week after the application the fraction of the dosage remaining on the leaves hardly decreased. In our study the fraction remaining on the leaves was at least 1/3, but may have been higher because chlorothalonil was transformed in the extraction solution.

The LOQ for chlorothalonil and prochloraz measured in the current experiment was approximately 8 ng/m^3 air. In the 2016 experiment the LOQ of tebuconazole and thiacloprid measured was approximately 0.3 ng/m^3 air. Hence, the concentrations levels that could be measured in the current experiment are not as low as in 2016. The higher LOQ's of the current study are due to the more complicated extraction procedure needed to extract chlorothalonil from the adsorbent. Therefore, the analytical method need to be improved in order to properly quantify the concentrations in the air under field conditions.

The vapor pressure of chlorothalonil is 0.076 mPa at 25 °C and that for prochloraz is 0.15 mPa at 25 °C, so based on the vapor pressure a higher rate of volatilization of prochloraz would be expected. However, the source strength of prochloraz measured is lower than that measured for chlorothalonil. The effect of the higher vapor pressure of prochloraz may have been counteracted by competing processes occurring on the plant leaves, such as penetration into the plant tissue and photo-transformation.

The footprint distance, defined as the distance over which 80% of the flux originates varied between 100 m and 264 m during sampling times. An exception was the sampling time around dawn at 5 a.m. of 2 August when stable conditions occurred. Under these stable conditions the computed footprint was much longer and varied between 634 m and 5408 m, so this would imply that the actual volatilization rate was underestimated for that sampling period.

5.2.4 Conclusions and recommendations

The rates of volatilization of tebuconazole and thiacloprid in the 2016 experiment were too low to be quantified. Although the vapor pressure of tebuconazole is more than three orders of magnitude higher than that of thiacloprid, this did not result in concentrations in the air above the crop that could be quantified. Presumably, processes competing with volatilization, such as penetration into the plant leaves, have a significant impact on the behavior of this compound. Further, other substances in the formulation may also affect the volatilization behavior of the compound. Therefore, competing processes as well as effects of the formulation need to be taken into account when assessing the volatilization of pesticides from crops.

The volatilization rates of chlorothalonil from the onion crop as measured in the 2017 experiment on the field research site ranged from 5.1 to 34.7 µg m^{-2} h^{-1}. The highest volatilization rate was determined from the concentrations measured on the day of application four hours after the application. One week after the application the volatilization rate determined was 6 µg m^{-2} h^{-1}. At six days after the application the remaining mass measured on leaves is roughly 1/3 of the mass calculated from the application rate. Therefore, volatilization can be expected to continue for a longer period.

Volatilization of prochloraz could not be quantified. Although the vapor pressure of prochloraz is about two times higher than that of chlorothalonil, concentrations of prochloraz in air above the crop were all below the limit of quantification. This indicates that other processes need to be taken into account to describe the behavior of this compound on the plant leaves. This is confirmed by the rate of decline of the residue on the plant leaves: 40% of the applied dosage during the first day after application. So the vapor pressure is not the sole factor to be considered when assessing the volatilization potential of a pesticide.

The results of the measurements on the turbulence in the atmospheric boundary layer at the OBO “A” field location of the 2016 experiment suggest that in particular the horizontal and lateral dilution of the contaminant plume originating from the application to OBO location “A” could be higher than would be expected using the approach described in the literature using measurements obtained for homogeneous surfaces under neutral conditions. The large variation observed at OBO location “A” could be due to the presence of obstacles (building, hedgerows etc.) in the vicinity of the measurement site. Further, the atmospheric stability may also have affected the differences observed.

Further study is required in order to obtain a better insight in the importance of obstacles and atmospheric stability on the dispersion in the air resulting from agricultural use of pesticides. A greater dilution in the plume does not automatically mean that concentrations will decrease in the whole area. Quasi-stationary eddies,

so-called lee eddies, could result in locally higher concentrations in air then would be expected using the standard dispersion coefficients used in atmospheric models.

The data for volatilization of chlorothalonil collected in the 2017 experiment are used to test the module for volatilization from plants in the PEARL model. The results of this test is described in Section 6.4.2.

The results of the meteorological measurements in both experiments, in particular the dispersion measurements, could be explored further to improve the concepts to describe the resistances to the transport of the substance from the leaf surface into the atmospheric boundary layer. Furthermore, the data on leaf wetness could help to understand the volatilization under different weather conditions and could also guide further improvement of the concepts for volatilization as implemented in the PEARL model.

6. Modelling - Integrative analysis of the exposure routes

6.1 Introduction

6.1.1 Aim of the modelling

The aim of the modelling effort in OBO is to estimate exposure to pesticides of residents living near fields (< 250 meters) where pesticides are applied. For this, an integrated modelling framework was developed.

The modelling framework of the OBO flower bulbs project follows closely the exposure routes described in the report of the Health Council of the Netherlands (see Chapter 1) that details how pesticides may migrate from the site of application to homes and eventually could lead to exposure of residents (Health Council of The Netherlands, 2014).

Ultimately, the aim of a modelling strategy is to be able to generalize results of limited number of experiments to several agricultural fields, other pesticides and larger population groups.

6.1.2 Structure

A model framework was developed, consisting of different deterministic models, to calculate the exposure of residents to pesticides and subsequently compare the modelled data with the measured data in air and dust, for verification purposes.

For each simulation individual exposure of the participating residents was calculated based on information on the application only. Additionally, the residents' exposure from measured air and dust samples were calculated. These modelled values were later compared with the measured values in urine.

Finally, possible predictors of exposure to pesticides were studied by means of statistical modelling, namely regression analysis, where the measured biomarkers in urine were the outcomes and other variables, such as environmental samples and data gathered from diaries and questionnaires, were explored as possible predictors.

6.1.3 Processes and Models

The purpose of this section is to explain how a resident can be exposed to an applied pesticide and how the selection of a set of models, representing the aforementioned processes, was done.

Processes involved on residents' exposure to pesticides

The processes leading to residents' exposure to pesticides are shown in chapter 1, Figure 1.1. Below a brief overview of involved processes, described as a causal chain, is presented.

1) Application on a target field occurs during a short period of time (e.g. half-hour per field), where the sprayer moves at a given speed and sprays the pesticide(s), from a tank using a wide spray boom. In the tank pesticides are mixed with water and possibly adjuvants.
2) During application, droplets can evaporate, drift and remain airborne (depending largely on droplet size) and deposit. Deposition can take place in or outside the field.
3) A fraction of the deposited ingredient can volatilize from both the target and off-target areas (i.e. areas surrounding the crop). The volatilization rate depends strongly on the vapor pressure of the substance (i.e. potential to volatilize), as well as weather conditions. However, other factors like solubility in water or organic materials and susceptibility to degradation play a role too. The volatilized ingredient is transported downwind. Depending on its vapor pressure it may adhere to existing particles.
4) A fraction of the substance that is applied can bind to soil particles and due to erosion be transported in particle-phase form.
5) Once airborne, the pesticide can be transported through the air and infiltrate homes via open doors, windows, cracks, chimneys and other openings. In the indoor environment, circulation of air and deposition as well as resuspension of particles play an important role governing indoor concentration levels.
6) Besides these processes, dragging of pesticides into homes by humans and pets is also a possible route of exposure in homes. However, to our knowledge, no model exists to describe this. Therefore, it was not taken into account in the selection of the models.
7) Finally, the extent to which an individual resident is exposed will depend, not only on the processes described above, but also on personal routines and individual characteristics (e.g. weight, height, age). This exposure can occur via several routes: inhalation, dermal uptake, dust ingestion and food intake.

Selection of Models

A screening of existing deterministic models describing pesticide concentrations related to spraying events using a boom sprayer, including articles published until January 2017, was carried out. Models that included at least one of the processes mentioned above were considered.

Subsequently, the best suitable combination of models to assess residents' exposure to pesticides was assessed. These models were selected based on how well they were described in literature, including evaluation/validation status, whether they could be used on different spatial scales, the possibility to link with other models and if they

were open source or otherwise accessible. Experience with certain models within the consortium was also considered during selection.

The selected models appeared to cover all major processes needed to describe residents' exposure to pesticides (except for drag-in of dust) and were combined to create a deterministic modelling framework. The selected models are explained individually in the next sub-chapter. The list of screened models can be found in Appendix 19.

Some processes were not included in the framework because they did not reflect exposure via boom sprayer applications (e.g. dietary exposure) or they reflected a negligible contribution to total exposure of residents in the this study (for example, erosion of soil and the coupled emission of particle bound pesticides).
Dietary exposure was explored in the statistical modelling (subchapter 6.6.3). Some notes regarding dragging-in of pesticides and erosion of soil can be found in Appendix 20.

6.2 Deterministic modelling framework

6.2.1 Individual models

In this subchapter, the selected models are briefly described. The data required to run each model can be found in the respective references.

IDEFICS: Model for Drift

The model chosen to study drift is IDEFICS, since it was considered to be a useful tool to investigate spray drift under varying conditions. It is a physical model for spray applications with boom sprayers that describe the trajectories of droplets by combining deterministic models for the movement of droplets combined with statistical variations of air turbulence (Holterman et al. 1997).
The outcomes of the IDEFICS model are the amount of pesticides (deposits) on the crop, deposits on the ground downwind to the crop and the vertical distribution of airborne spray and vapor at downwind locations.

PEARL-OPS: Model for Volatilization & Dispersion

PEARL - Model for Volatilization

The model chosen for pesticides volatilization was PEARL (Pesticide Emission Assessment at Regional and Local Scales). PEARL is a deterministic model of pesticide behavior in the soil-plant system which has been developed by two Dutch institutes (Alterra and RIVM) in close co-operation.
Using this model, volatilization from soil and plants can be estimated using the physico-chemical properties of the pesticide and the prevailing meteorological conditions as input. PEARL calculates the emission rate from soil and plants for a given pesticide (Van den Berg et al. 2016).

OPS-St - Model for Dispersion

The model chosen to calculate dispersion of airborne pesticides was OPS-St (Short term Operational Priority Substances). OPS is an atmospheric dispersion model developed by RIVM in the Netherlands. It is an *advanced* Gaussian plume model designed to simulate the sequence of dispersion, transport, chemical conversion and finally deposition of various pollutants in the air (Van Jaarsveld, 2004). In this study the short term (OPS-St) version was used to assess dispersion at short distances from pollutant sources. The physical principles underlying this special version are the same as the ones for the long-term (standard) version of OPS. However OPS St computes hourly concentrations, based on local hourly meteorological observations instead of summary statistics of meteorological conditions. Furthermore, OPS-St can deal with hourly source strength variations that are typical for the volatilization of pesticides. The source can be an area source, at a height nearby the land surface, typical of a source level within crops (i.e. one to several decimeters) (Van Pul et al. 2008).
The output of the model is the concentration of a given pollutant, computed at specific receptor points or given in grid form.

Coupling (PEARL and OPS-St)

For the OBO study PEARL and OPS-St have been coupled to allow seamless simulations of pesticide volatilization and resulting 3D concentration patterns of pesticides at short distance around treated fields. See Van Den Berg et al. (2016) and the references cited there for further details on both models and their coupling. The model combination has recently been included in the BROWSE (Bystanders, Residents, Operators and Workers Exposure models for plant protection products) tool, a set of models to assess various routes of exposure of residents, operators, workers, bystanders and residents to pesticides (Van den Berg et al. 2016; Butler-Ellis et al. 2017).

gComis: Outdoor to Indoor

To address outdoor and indoor mass exchange, the zone model gComis (Feustel & Smith 1997) was used. It is a model that, taking building characteristics into account, uses air flow to estimate indoor air concentrations of any given compound based on outdoor air concentrations and meteorological conditions, such as temperature, humidity, barometric pressure, wind speed and wind direction.
This model calculates concentration gradients between outdoor and indoor environments and is used in the framework to calculate hourly or daily mean indoor concentrations.
To model each home individually, cadastral data and home characteristics collected during home visits and from questionnaires were used. A summary of home characteristics used by the gComis model is provided in Appendix 21.

Dustpred: Concentration of pesticide in dust

The selected model to estimate concentration of pesticides in settled indoor dust was based on an empirical equation described by Weschler & Nazaroff et al. 2010.

This model, named here Dustpred, assumes equilibrium between the gas-phase concentrations and concentrations of pesticides on settled dust indoors.

Exposure to environmental concentrations

To calculate exposure to pesticides concentrations in the environment, models were combined using MATLAB R2016a. The models consist of a set of equations and are described below for each exposure route. Some residents' characteristics were also used to estimate exposure, such as age, height, weight and time spent indoors in their home. A summary table of these can be found in Appendix 22.

Dermal

Dermal exposure to airborne pesticides (both dermal exposure caused by direct gas-to-skin contact and by particle deposition) is calculated using the mathematical formulations presented in Shi & Zhao (2014).

In addition to this model, we also used equations developed by Schlich et al. (2010) to calculate skin surface area. We used Shanshan Shi & Bin Zhao (2013) formulations for seasonal variation effects on deposition velocity onto human body surfaces. In these calculations no clothing barrier was assumed, since Morrison et al. (2016) showed that wearing clothing that had absorbed pollutants could increase dermal uptake by substantial amounts relative to bare skin.

Dermal contact

Dermal contact to particle-phase pesticides was calculated using the formula presented in Zheng et al. (2017). This route refers to direct contact between skin and a surface that might contain pesticides bound to particles.

Inhalation

Inhalation exposure to airborne pesticides was calculated using the mathematical formulations presented in Shi & Zhao (2014) using inhalation rates used by the US-EPA (EFH CH6) (US-*EPA*, 2011).

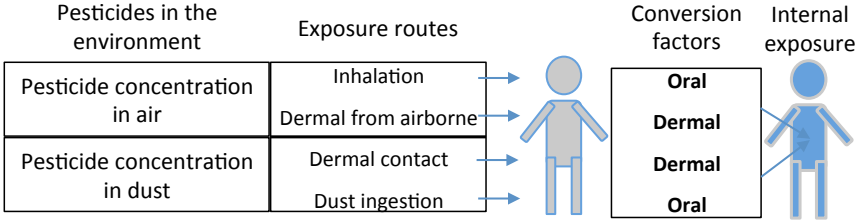
Incidental dust ingestion

Dust ingestion to particle-phase pesticides was calculated using an equation published by Zheng et al. (2017). This route refers to the incidental (i.e. there is a chance) oral ingestion of dust containing pesticides. An example is hand-to-mouth transfer of dust, which can contain pesticides. Dust ingestion rates used for this model are the ones presented in Wilson et al. (2016) (e.g. DustEx RIVM, version 1.0).

Internal exposure

Internal exposure refers to that fraction of the initial pesticide dose that is absorbed and distributed through the body via systemic circulation. To calculate internal exposure, conversion factors derived from the methodological sub-studies (chapter 2, Table 2.5)

Box 6.1: From concentrations in the environment to internal exposure using conversion factors.



The color blue refers to the pesticide. Firstly, it comes in contact with the body via exposure routes and then a fraction enters into the body (internal exposure). Conversion factors are used to calculate this fraction (uptake).

were used. These conversion factors are given separately for oral and dermal exposure and allow to go from uptake to biomarker concentration in urine (the result of internal uptake). Box 6.1 describes how the calculation was done.

6.2.2 Connection between models

In this subchapter it is explained how the different models were connected into a framework. This connection is shown in Figure 6.1. All models function independently (except for PEARL-OPS).

The first step is the application on the target field, where the model IDEFICS simulates the spray application (that occurs in the first hour). Airborne drift is then calculated at 5 meters away from the field, as shown in Figure 6.2. The output of IDEFICS is a vertical column with concentrations at different heights at 5 m away from the field, which serves as input for the OPS-St model.

PEARL uses the amount of deposited material and calculates volatilization from the plant canopy. The resulting source strength due to volatilization is assigned to the entire field, divided into a 10x10 m grid of which the grid elements represent individual sources (centroids in Figure 6.2). The computed volatilization strength for each of the grid cells serves as input for the OPS-St model.

Using the output form IDEFICS (Holterman & van de Zande, 2018) and PEARL, OPS-St then simulates dispersion and transport of small droplets and aerosols (input from IDEFICS) and gaseous pesticides (input from PEARL) downwind from the target area. Dispersion is calculated for the distance between the target area boundary (5 meters from the field) and a resident's home. The output of OPS is a vertical profile of pesticide concentrations in air at two different heights (1.5 and 6 meters) outside each home.

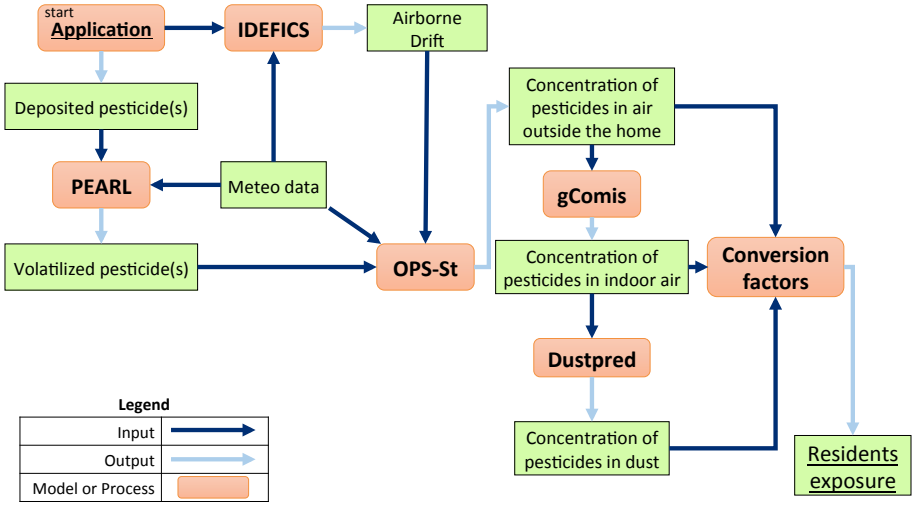


Figure 6.1: Modelling framework.
Connections between models.

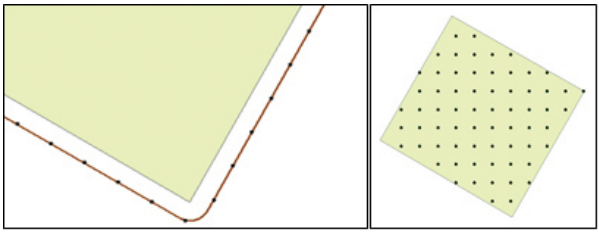


Figure 6.2: IDEFICS and Pearl – connections to OPS-St.
Left: the points at 5-meter downwind airborne concentration calculated from IDEFICS, subsequently used as input for OPS-St. Right: the source raster cell centroids that are calculated from PEARL and that serve as input to OPS-St.

gComis uses the output of OPS-St to estimate hourly mass transfer between the outdoor and indoor environment.

After calculating the median one-week indoor concentration of pesticides in air using gComis output, Dustpred calculates concentration of pesticides in indoor settled dust.

Taking the personal characteristics of each resident (collected during the OBO residents' field study) into account, exposure is then calculated using as input the concentrations of pesticides in air, both outdoor and indoor and the concentrations in dust. These inputs are provided as daily means.

Using the conversion factors from volunteer studies, internal exposure is then derived from the exposure to environmental concentrations.

6.3 Modelling setup

6.3.1 Fields and Applications

Fields

The simulations comprised 9 target fields. For five of these fields two separate applications were simulated. All target fields included in our simulations are described in Table 4.1 (Chapter 4). For modelling purposes, additional neighboring fields were also included in the simulations if at least one pesticide that was also used in the target field was (most probably) applied in those fields during the application day. A total of 26 additional fields were simulated.

Table 6.1: Sprayer settings; nozzle type (pressure, drift reduction, applied dose), the use of air assistance and the drift reducing technology (DRT) class of the used spray technique as a whole used in the simulations for the different fields.

Case	Nozzle type	Liquid pressure [kPa]	DRN [1] reduction [%]	Applied dose [L/ha]	Forward speed [m/s] [6]	Air assistance reduction [%]	DRT [2] reduction [%]
1	AM11003	200	75	200	1.62		75
2	AM11003	200	75	200	1.62		75
3	ID11004	300	90	200	1.62		90
4	AM11003	200	75	200	1.62		75
5	ID11004	300	90	200	1.62		90
	ID11004	300	90	400 [5]	1.32	50	95
6	AVI11003	300	50	200 [5]	1.62		50
7	AM11003	400	50	200 [5]	1.62	50	90
8	AM11003	400	50	400 [5]	1.32	50	90
	TKSS10/35	300	75	400	1.32		75
9	AM11003	300	50	200	1.98	50	90
10	AM11003	300	50	200	2.28	50	90
11	DG8003	300	[3]	200	2.28	50	95 [4]
12	DG8003	300	[3]	250	0.99 [7]	50	95 [4]
13	DG8003	300	[3]	220	1.80	50	95 [4]
14	AIXR11003	200	75	220	1.80		75

1 DRN = Drift reducing nozzle in classes 50%, 75%, 90%, 95% following NL certification; DRD list: https://www.helpdeskwater.nl/onderwerpen/emissiebeheer/agrarisch/open-teelt/driftreducerende/

2 DRT = Drift Reducing Technology in classes 50%, 75%, 90%, 95%, 97.5%, 99%, following NL certification: https://www.helpdeskwater.nl/onderwerpen/emissiebeheer/agrarisch/open-teelt/driftreducerende/

3 nozzle-pressure combination not certified separately.

4 Spray technique combination: the combination 30 cm boom height, nozzle spacing 25 cm, nozzle type ID90015 (300 kPa) with air assistance is certified as DRT97.5; it is assumed that spray quality of the DG8003 at 300 kPa is comparable to that of the ID90015 and can be classified accordingly; to account for the uncertainty in this assumption the current combination is classified one class lower (DRT95).

5 dose rate used in simulation differs from CLM survey (incomplete survey data at time of simulation).

6 driving speed computed from nozzle flow rate, nozzle distance and applied dose in the field.

7 a forward speed of only 0.99 m/s is rather low; yet is results from specified nozzles and pressure and applied dose in the CLM survey.

Applications

Self-reported applied dosage was used in our simulations (Table 4.1 - Chapter 4). Additional information regarding pesticide mixtures in the tank, field size, type of boom sprayer and nozzle, amount of liquid sprayed, speed of the boom and percentage of field sprayed was collected during field visits (Table 6.1). Used spray techniques were all drift reducing and in the range of 75% to 95% (Holterman & van de Zande, 2018).

A total of 14 one-week simulations, were performed. In total 14 different pesticides were included in the modelling exercise. For each simulation the daily exposure of each participating resident to the pesticide or mixture of pesticides was calculated.

The month of application for each campaign as well as meteorological conditions can be found in subchapter 6.3.2.

6.3.2 Meteorological conditions

Meteorological data of the two weather stations, De Kooy and Schiphol, were used in our simulations. The data were collected from the KNMI database and the stations selected were the closest to the target fields.
In all simulations, wind speeds were recorded at 10 meters height ranged from 2m/s to 7m/s during spraying time. Wind conditions are shown in chapter 4, Figure 4.2. Table 6.2 gives a summary of meteorological conditions for each measurement campaign.

Table 6.2: Meteorological conditions – Summary Table.

Location	Measurement campaign	Month	Mean (Min,Max) - Day 1			Mean (Min,Max) - Days 2 to 7		
			Temperature (˚C)	Humidity (%)	Wind Speed (m/s)	Temperature (˚C)	Humidity (%)	Wind Speed (m/s)
A	1	May	**13** (10,16)	**80** (61,95)	**3** (1,5)	**16** (12,20)	**84** (71,99)	**5** (2,8)
B	2	July	**23** (17,32)	**72** (37,96)	**6** (2,8)	**19** (14,23)	**87** (62,98)	**3** (0,7)
C	3	February	**5** (3,6)	**87** (79,95)	**6** (2,12)	**6** (3,9)	**92** (72,98)	**8** (2,14)
	4	May	**9** (7,11)	**68** (60,79)	**3** (1,5)	**14** (7,21)	**72** (36,98)	**5** (2,9)
D	5	January	**4** (4,5)	**88** (83,98)	**3** (2,6)	**5** (1,11)	**86** (79,98)	**4** (0,7)
	6	June	**19** (16,25)	**70** (51,83)	**5** (3,10)	**19** (12,27)	**77** (48,99)	**4** (1,9)
E	7	May	**9** (7,12)	**68** (60,79)	**3** (1,5)	**14** (7,22)	**73** (36,98)	**5** (2,9)
	8	May	**17** (12,24)	**73** (38,97)	**4** (1,8)	**17** (9,31)	**79** (32,98)	**4** (1,8)
F	9	March	**16** (12,22)	**62** (46,74)	**5** (3,7)	**10** (5,21)	**78** (50,98)	**4** (1,10)
	10	June	**24** (18,30)	**65** (44,93)	**2** (1,6)	**20** (14,28)	**70** (43,98)	**6** (2,10)
G	11	August	**18** (15,20)	**75** (64,89)	**5** (3,7)	**18** (12,21)	**79** (48,96)	**7** (0,14)
	12	August	**20** (17,23)	**76** (54,91)	**3** (2,5)	**17** (10,22)	**84** (64,99)	**5** (0,9)
H	13	May	**22** (17,26)	**57** (46,74)	**5** (4,7)	**19** (9,30)	**63** (35,95)	**4** (0,9)
I	14	April	**9** (4,13)	**76** (48,94)	**5** (2,8)	**7** (0,12)	**76** (39,95)	**5** (0,10)

Wind speed recorded at 10 meters height.

6.3.3 Model assumptions

The following assumptions were made regarding the model simulations:

1) Based on photos taken during site visits from fields in different growing periods, it was assumed that two thirds (2/3) of each field had vegetative cover in the periods of April to August. In January-March a ratio 1/3 was assumed instead, independent of crop type.

2) Since there was no information available about the exact hour of spraying on additional fields, these fields were assumed to be sprayed at the same time as the target field (because this point in time represented favorable spraying conditions).

3) Rainfall was taken into account in the PEARL model, but no competing processes (e.g. sorption to soil, wash off, degradation in the soil) were taken into account in the simulation of volatilization.

6.4 Modelling - Output

6.4.1 Drift

Verification

The verification of the drift model was done using an experimental setup (Zande et al., 2018b) and it is described in detail in chapter 5. The experiment concluded that the model accurately calculates airborne concentration at different heights for different distances from the field.

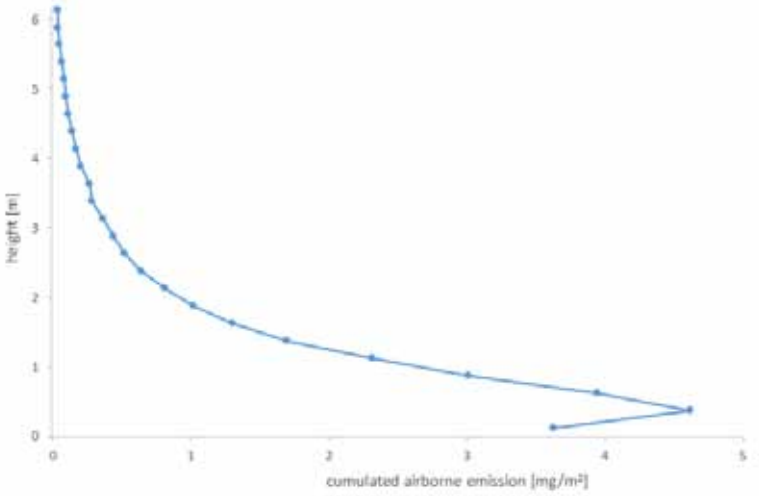


Figure 6.3: Example output of IDEFICS showing airborne emission with height, at 5 m downwind from the sprayed field, at the SW edge of location I (campaign 14).

Results

One of the results of the IDEFICS model is the vertical distribution of airborne emission. This is the amount of pesticide passing through an imaginary vertical window at 5 m downwind from the treated field during the spray application (Holterman & van de Zande, 2018). Figure 6.3 gives the IDEFICS output for campaign 14 as an example. Typically, emission is highest near the ground (or at about 0.5 m above the ground) and it decreases rapidly with increasing height.

As drifting spray drops lose their water content by volatilization, they become smaller until they are completely dry and solid particles remain. At 5 m downwind from the sprayed field, the airborne emission mainly consists of dried particles, although some drops may still be present. This is illustrated in Figure 6.4, where the size distributions for campaign 3 (left) and campaign 4 (right) are shown. The blue bars represent the computed actual size distribution (dried particles including drops); the orange bars represent the size distribution assuming all drops would have dried completely. With campaign 3, the wind speed was relatively high, while temperature was low and RH relatively high. Consequently, volatilization of the solvent was slow, and many drops were still present in the airborne emission. In campaign 4, wind speed was lower, temperature higher, and RH lower. In these conditions, most drops were dry before reaching the 5 m downwind evaluation point: the orange and blue bars are almost equal. Still, in both campaigns the diameter of most particles is much smaller than 50 µm. This implies that the particles in the drifting cloud behave like aerosols, which is an essential assumption in the next step, where the drift results are used in the OPS dispersion model.

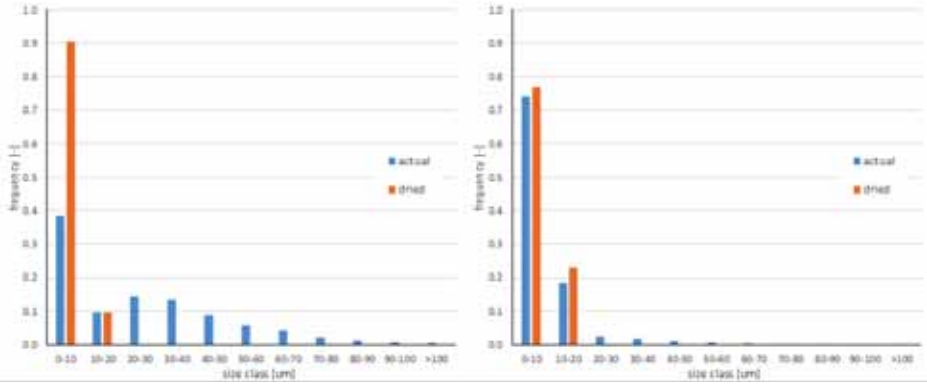


Figure 6.4: Particle size distribution of airborne emission, 5 m downwind from the treated field.
Left: campaign 3; right: campaign 4. Blue bars: computed actual particle size distribution; orange bars: size distribution when all particles would have dried.

6.4.2 Volatilization and dispersion

Volatilization – PEARL-OPS

The performance of the model combination PEARL-OPS was evaluated using observations of a pesticide volatilization experiment performed on a field of the farm of Applied Arable and Vegetable Research of Wageningen University & Research (see Chapter 5), in the province of Flevoland, near Lelystad. The field was planted with onions (variety Crimson) except for tractor paths at the eastern and western inner border of the field. On 1 August 2017 the onion crop was treated with 399 g chlorothalonil per hectare. At the time of application, the soil cover was estimated to be 0.6 m2m-2 and the average crop height was about 0.47m. See Chapter 5 for more details.

The volatilization experiment was conducted between 1 and 7 August 2017. Volatilization was determined using the so-called gradient method, as described in Chapter 5. Here, we compare the emission strength from PEARL-OPS simulations with the observed volatilization rate from the experiment. Since the observations rely on observed concentration gradients over the treated field, the concentrations from PEARL-OPS can also be evaluated to some extent, since OPS is able to provide within-field concentration estimates as well. During the experiment concentration measurements were performed at four heights: 100 cm, 150cm, 200cm and 250 cm above the ground. The observations at 150cm and 200cm were available on most of the experimental days. Therefore, the concentrations at these levels were used for the present evaluation (see Chapter 5).

PEARL-OPS simulations were performed using observations from the meteorological station “Lelystad”, a nearby site run by the Royal Netherlands Meteorological Institute (KNMI).

Application with chlorothalonil was assumed to occur between 9:00 and 10:00 UTC. Since PEARL simulates volatilization from plants only, the amount of chlorothalonil intercepted by the plants must be estimated. In this case the estimated amount was 240 g ha^{-1}, which was obtained by multiplying the application rate of 399 g ha^{-1} with the average plant cover of 0.6. A field with dimensions of 300m x 300m was used to define the source, with receptors in the center of the field at a height of 1.5m and 2.0m, respectively. The chosen field size implies that simulated measurements were taken with a uniform fetch of 150m - 210m, which corresponds well with the average footprint length of 169m derived from the meteorological observations. For the present purpose, the effective source height was assumed to be 32cm, approximately corresponding to the displacement height (approximated as 2/3 of the crop height) plus the roughness length for scalars (approximated as 1% of the crop height). Simulations were performed without and with competing processes such as degradation in the plant or soil. The simulation without competing processes likely results in an overestimation of the volatilization and can be regarded as a worst-case scenario simulation. For the simulation that took competing processes into account,

a plant penetration half-life of 5 days and a photo degradation half-life of 3 days for chlorothalonil was assumed (Leistra and Van den Berg, 2007).

Figure 6.5 shows the volatilization rate computed by PEARL (upper panel) and mid-field concentrations (lower panel) from OPS along with their observed values, for the case without competing processes. The simulated concentrations are of the same order of magnitude as observed concentrations. Given the uncertainties in the observations as well as in the simulations, this is considered a quite reasonable result. Near the end of the period some overestimation of volatilization rate and hence concentration was expected because the competing processes were ignored. This can be clearly seen in the runs which take into account photo degradation and plant penetration (Figure 6.6), in particular on day 6 since the start of the measurements. On this day, a slight underestimation can be seen instead of the overestimation that is obtained in the run without competing processes.

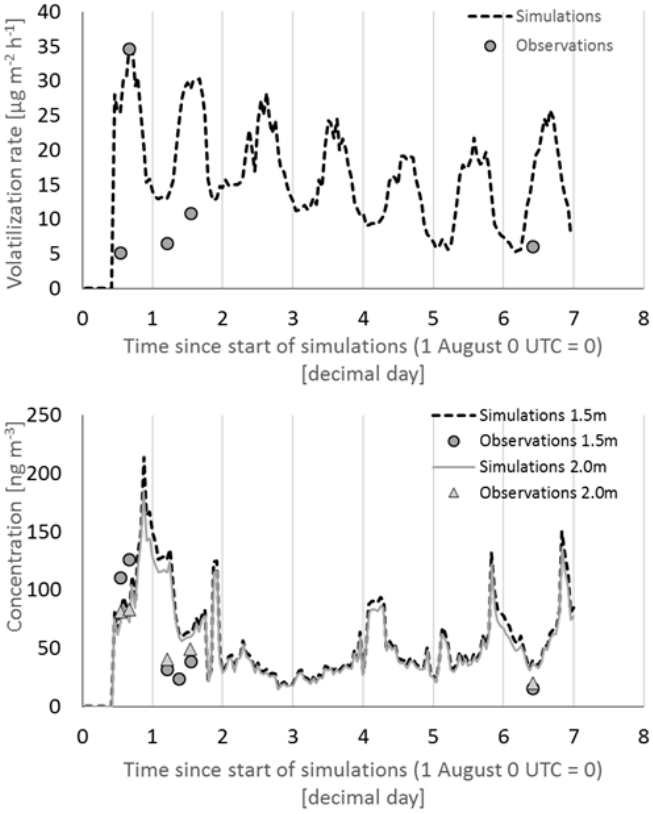


Figure 6.5: Simulated and observed volatilization rates and concentrations at two levels without taking into account competing processes.
Volatilization rates (upper panel) and concentrations at two levels (lower panel).

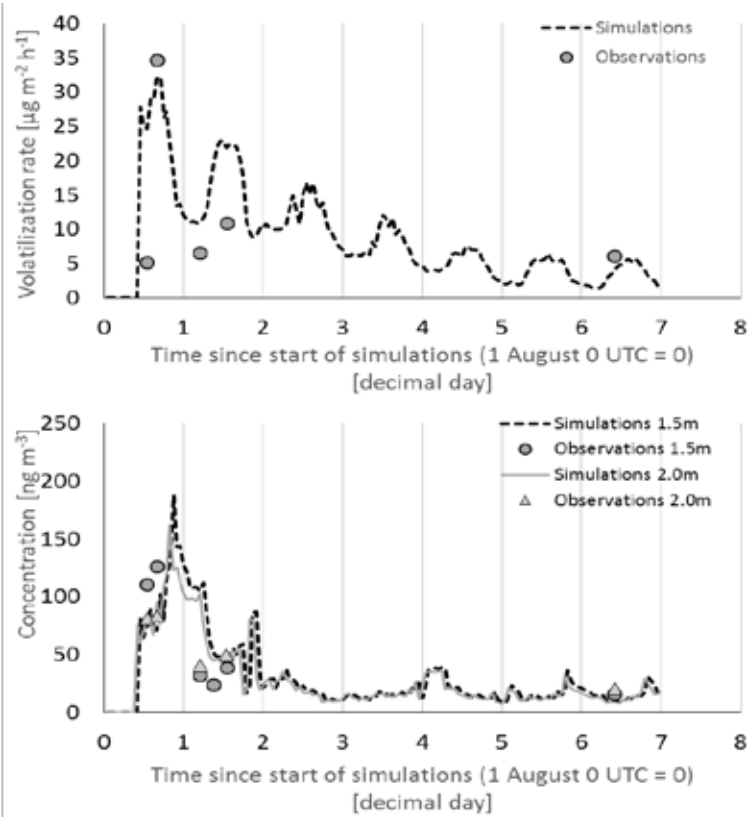


Figure 6.6: Simulated and observed volatilization rates and concentrations at two levels taking into account photo degradation and plant penetration of chlorothalonil.
Volatilization rates (upper panel) and concentrations at two levels (lower panel).

Verification – Volatilization and Dispersion

The output of the volatilization (PEARL) and dispersion (OPS-St) models is the volatilized amount of an applied pesticide from the field and the modelled concentration of pesticides in air outside each home, respectively. The results of the modelled values where compared to the measured values for each home where measured data was available. A comparison was done per pesticide and per time-period. Measured values for day 1 were compared to modelled values for day 1 and measured values for 1-week periods were compared to modelled values for the same period (Table 6.3).

The comparison was made two-fold. Firstly, the modelled data from the target field was used. Due to possible simultaneous applications in additional fields, such model was expected to underpredict the volatilized amount and concentration of pesticides. Therefore, secondly, modelled data from target field and the additional fields was used. By adding the additional fields, the model was expected to yield values closer to

the mean measured concentrations albeit information on the additional field(s) had more uncertainties in timing of spray events.

In Table 6.3, different metrics to measure goodness of fit are shown, as well as mean and standard deviation of both measured and modelled data. These are described below:

- Pearson correlation – Measure of strength of a linear correlation between measured and modelled data. It is non-dimensional and can have values between +1, a perfect positive linear correlation and -1, a perfect negative linear correlation. The closer to +1 the better the agreement between measured and modelled data is.
- Root Mean Square Error (RMSE) – Measure of difference between modelled values and measured values. It is a metric used to estimate model accuracy (i.e. proximity to measured values).
- Precision – Measure of statistical variability, describes the nearness between the measured data and modelled data.

An example, a model has high accuracy (measured by RMSE) but low precision if, generally, the measured values for a given pesticide are close to the mean measured value, but the modelled values are far from each other even if the mean modelled value is equal to the mean measured value.

- Bias – Measure of systematic difference between modelled values and measured values (over- or under predicting). A negative bias indicates under prediction and a positive bias over prediction, so the closer to zero the better.

The results of this comparison show that model performance is mainly affected by the input parameters of each simulation.

For example, the model performs well for pymetrozine (Table 6.3), which was only applied on the target field. Conversely, when looking at chlorpropham, a pesticide with high background concentrations, the model predicts less well the concentrations. Additionally, chlorpropham was always applied in multiple fields on the same day as the target field. Since the time of spraying was not known for several fields it was more difficult to predict the outdoor air concentrations outside each home.

It can be concluded, by looking at the Pearson correlation (median=0.4), that there is a good agreement between modelled and measured outdoor concentrations for several pesticides

Overall, looking at the Pearson correlation, the model shows higher positive correlation with measured data on day 1 than on subsequent days, indicating that the application and resulting volatilization are well captured during the day of application. This could be caused by other applications on the following days. This influences the 7 days comparison, since those applications would have larger emissions.

Table 6.3: Modelled Outdoor concentration vs Measured Outdoor concentration.

			Just target field (Model Vs. Measured)						**Target + additional fields** (Model Vs. Measured)					
Active Ingredient	Time-frame	Data	Mean	Std.Dev	Pearson	RMSE	Precision	Bias	Mean	Std.Dev	Pearson	RMSE	Precision	Bias
Tebuconazole	1st day	Mod	0.36	0.71	**0.43**	0.67	0.22	0.24	0.38	0.72	**0.46**	0.67	0.22	0.26
		Meas	0.12	0.23					0.12	0.23				
	7 days	Mod	0.10	0.29	0.39	0.27	0.03	0.02	0.11	0.30	**0.40**	0.27	0.03	0.03
		Meas	0.08	0.12					0.08	0.12				
Flonicamid	1st day	Mod	0.21	0.38	**0.74**	0.30	0.32	-0.17	0.12	0.29	**0.75**	0.25	0.16	-0.16
		Meas	0.38	0.40					0.29	0.29				
	7 days	Mod	0.04	0.15	**0.63**	0.22	0.05	-0.16	0.04	0.11	**0.51**	0.21	0.03	-0.14
		Meas	0.20	0.20					0.17	0.18				
Trifloxistrobin	1st day	Mod	0.09	0.14	**0.79**	0.11	0.06	-0.03	0.11	0.14	**0.71**	0.12	0.06	-0.01
		Meas	0.12	0.17					0.12	0.17				
	7 days	Mod	0.09	0.17	**0.66**	0.13	0.02	0.02	0.11	0.06	**0.68**	0.14	0.02	0.04
		Meas	0.06	0.10					0.18	0.10				
Pendimethalin	1st day	Mod	0	0	-	18.15	2.32	-17.06	182.66	127.31	0.08	204.32	45.07	165.60
		Meas	17.06	6.57					17.06	6.57				
	7 days	Mod	10.93	10.52	**0.69**	51.19	4.35	-43.90	86.43	81.72	-0.39	103.39	11.17	31.60
		Meas	54.84	32.63					54.84	32.63				
Prochloraz	1st day	Mod	7E-04	6E-04	-0.55	0.11	0.03	-0.10	0.42	0.10	-1.00	0.53	0.34	0.31
		Meas	0.10	0.04					0.48	0.04				
	7 days	Mod	9E-04	2E-03	0.37	0.09	0.01	-0.08	0.08	0.08	-0.09	0.24	0.06	-5E-04
		Meas	0.08	0.05					0.23	0.05				
Mepanipyrim	1st day	Mod	0.45	0.67	**0.57**	0.70	0.47	0.44	2.90	1.11	-0.77	3.03	0.79	2.89
		Meas	3E-03	2E-04					3E-03	2E-04				
	7 days	Mod	0.67	0.67	0.05	0.86	0.16	0.54	1.74	1.27	**0.55**	1.98	0.29	1.61
		Meas	0.13	0.18					0.13	0.18				
Fluopyram	1st day	Mod	0.33	0.51	**0.40**	0.49	0.20	0.18	0.42	0.50	**0.54**	0.52	0.19	0.28
		Meas	0.15	0.06					0.15	0.06				
	7 days	Mod	0.38	0.58	0.07	0.63	0.08	0.22	0.48	0.61	0.28	0.66	0.09	0.32
		Meas	0.16	0.18					0.16	0.18				
Pymetrozine	1st day	Mod	0.10	0.14	**0.83**	0.08	0.10	0.02	*For the additional fields where information was available, none applied Pymetrozine*					
		Meas	0.08	0.09										
	7 days	Mod	0.09	0.12	0.32	0.13	0.03	0.06						
		Meas	0.03	0.05										
Acetamiprid	1st day	Mod	10	20.26	-	21.02	9.06	10	69.82	20.04	-	71.71	14.17	69.82
		Meas	1E-03	0					1E-03	0				
	7 days	Mod	3.82	9.52	0.01	10.17	1.39	3.82	21.56	27.09	0.23	34.12	6.06	21.56
		Meas	2E-03	3E-03					2E-03	2E-03				
Thiacloprid	1st day	Mod	*Modelled values equal to 0 ng/m3 and all measured values below LOD*											
		Meas												
	7 days	Mod	9E-05	7E-05	0.06	0.01	0.002	-7E-03	2E-04	8E-05	0.17	0.01	2E-03	-0.01
		Meas	7E-03	4E-03					7E-03	4E-03				
Chloorpropham	1st day	Mod	46.22	106.59	-0.16	-0.25	110.70	0.14	962.01	1255	0.07	0.15	1526.50	919.76
		Meas	42.25	27					42.25	27				
	7 days	Mod	15.57	44.02	0.13	0.53	65.16	-31	179.81	577.47	0.03	0.58	591.01	134.07
		Meas	45.74	44.12					45.75	44.12				

Mod = Modelled; Meas = Measured / All units are in ng/m^3 except for Pearson correlation (no units).

Predicting outdoor air concentration outside each home seems more difficult when volatilization after the first day of application is the source. As exemplified by the situation when chlorpropham was used, this is probably mainly due to the fact that other fields might have applied the same pesticide during those days.

It can also be concluded, by comparing the RMSE with the mean values, that quite often the absolute differences between the modelled values and the measured values are low, indicating good model accuracy. This is true for both day 1 comparison and week comparison. By looking at the bias, it can be concluded that sometimes there is over prediction of the concentrations (e.g. Tebuconazole and Fluopyram) and other times under prediction (e.g. Flonicamid and Prochloraz). It seems that more often concentrations are over predicted when including all fields (target + additional).

Finally, when looking at the precision (i.e. prediction of variability), the model performs generally less well, thus showing that it is more difficult to predict differences in concentrations between residents' homes at short timescales.

Results

Due to the extensive output of all simulations, only selected results from calculations with the dispersion model are presented.

For all locations, exposure due to spraying and volatilization from both the target field and additional fields were simulated. The simulations showed that in some periods the emissions had contributions from the additional fields but not from the target field. This is illustrated in the figures below: some periods have no contribution from the target field because of wind direction (gaps in first plot Figure 6.7). Combining the information from the target field and the additional fields show significant contributions from the additional fields leading to a more continuous exposure profile (second plot Figure 6.7).

This shows that additional fields are important for variability in concentrations and that it is impossible to relate observations to atmospheric contributions from one specific field alone. This is further illustrated in Figure 6.8, where the results are presented for tebuconazole simulation in campaign 4. Owing to its low volatilization rate, the peak concentration due to spray drift in the first hour (during spraying) stands out, however, there are also subsequent peaks during the one-week simulation, due to volatilization (see Figure 6.9).

In contrast, an example for a more volatile compound, chlorpropham, is given in Figure 6.10. Model results indicate a constant decrease in outdoor concentration near the homes located downwind of spraying (Figure 6.11). After the third day (72 hours) the contribution due to volatilization is close to zero, due to change of wind direction and less material being volatilized. It is also clear that only home 7 (H7) was downwind during spraying (1st hour).

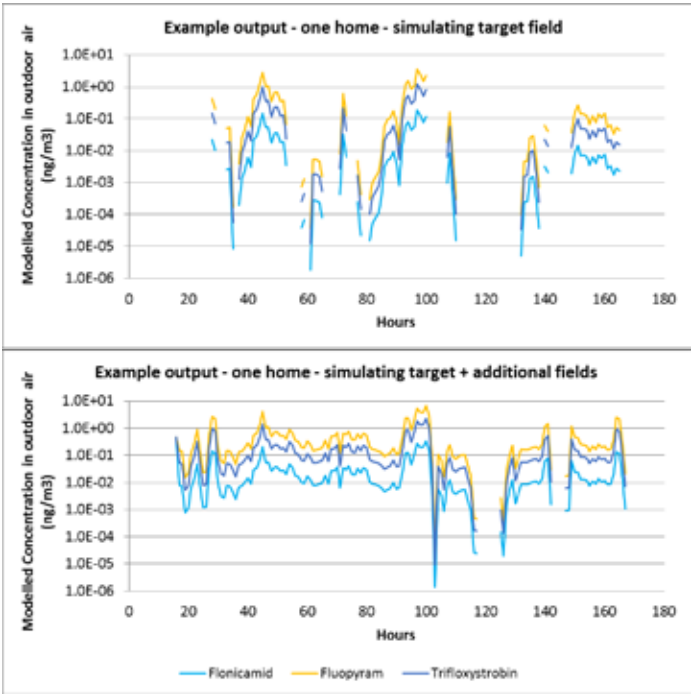


Figure 6.7: Example output of dispersion model for one home – simulation just including target field and then including also additional fields - Campaign 2.

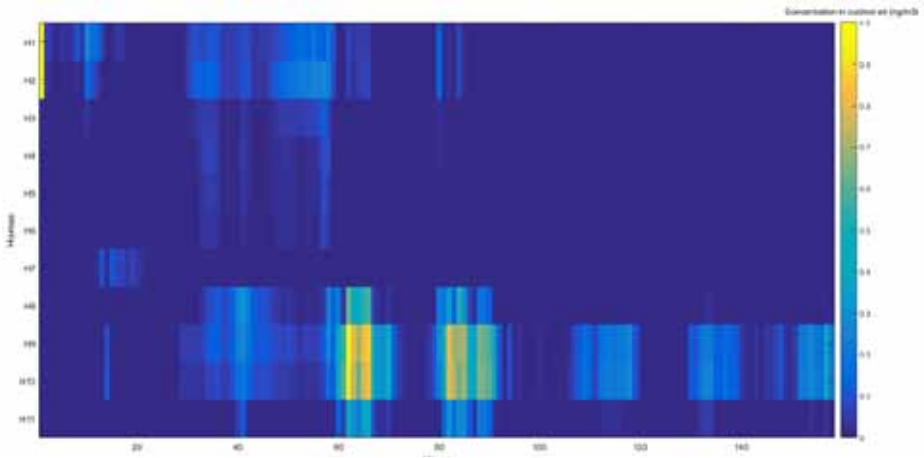


Figure 6.8: Tebuconazole - Output of dispersion model for all homes – simulation including both target field and additional fields - Campaign 4.

On the x axis, each block of 24 hours represents a simulated day. On the y axis, each row represents a home. Colors indicate the concentration in outdoor air in (µg/m³).

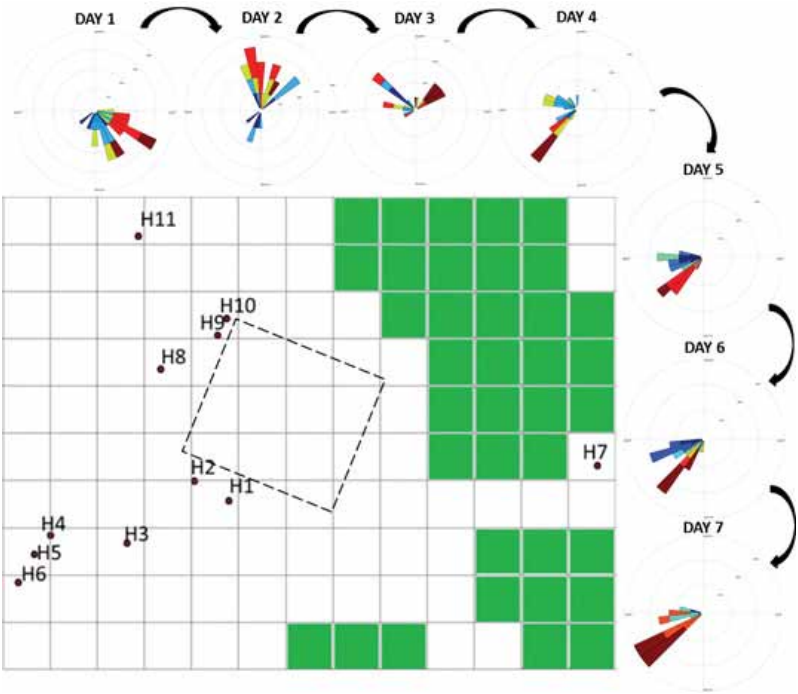


Figure 6.9: Wind-roses for each day during Campaign 4, location C and position of homes with measurements.
Target field of location C is represented with a black dashed line, underlying grey grid cells have a size of 50x50meters. The wind roses, depicted per day, show the frequency of winds originating from different directions, darker color represents higher wind speeds.

Additional simulations – 1 month volatilization

Simulations for the period of one week suggested that the contribution of volatilization can go on and lead to exposure for a much longer period of time. Therefore, additional simulations of volatilization strength were carried out for a period of one month as to understand how much pesticide would have volatilized during the first week period.

Figure 6.12 shows that for many pesticides after one week typically around 80% of the material has been lost by volatilization. It should be noted that the volatilization rate is not proportional to the amount of pesticides remaining on the surface. Volatilization may continue at nearly the same rate but it stops when all material is evaporated.
The results indicate that the source strength (i.e. the quantity of pesticide that goes away from the field) due to volatilization is expected to have been reduced to near-zero within one to two weeks. Furthermore, it should be noted that in these one-month simulations the half-life of the different pesticides was taken into account using data on half-life's obtained by Fantke et al. 2014.

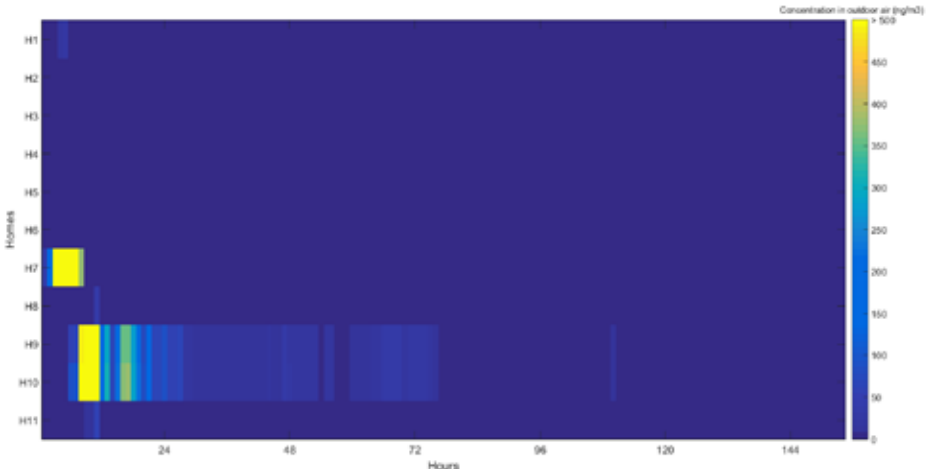


Figure 6.10: Chlorpropham - Output of dispersion model for all homes – simulation including both target field and additional fields - Campaign 3.
On the x axis, each block of 24 hours represents a simulated day. On the y axis, each row represents a home.

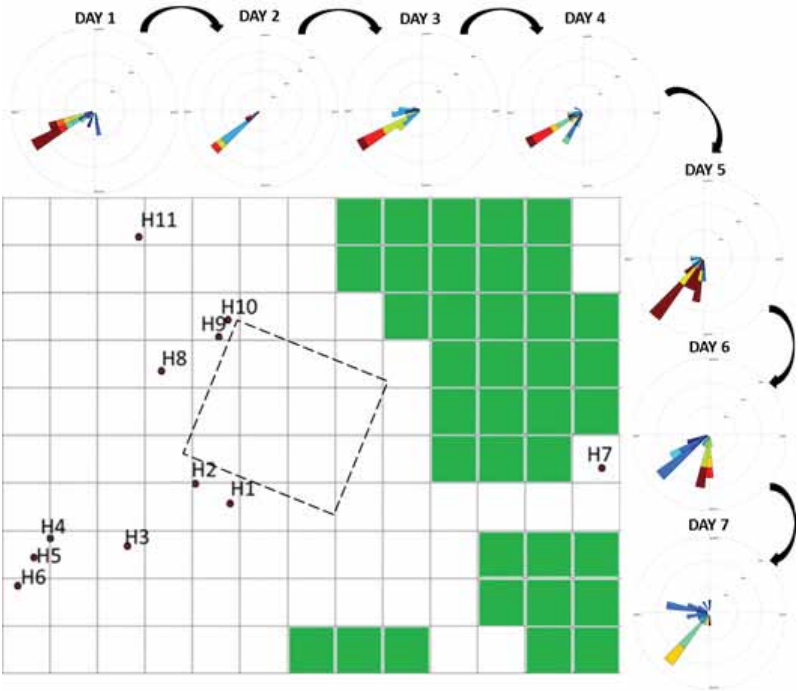


Figure 6.11: Wind-roses for each day during Campaign 3, location C and homes position.
Target field of location C is represented with a black dashed line, underlying grey grid cells have a size of 50x50meters. The wind roses, depicted per day, show the frequency of winds originating from different directions, darker color represents higher wind speeds.

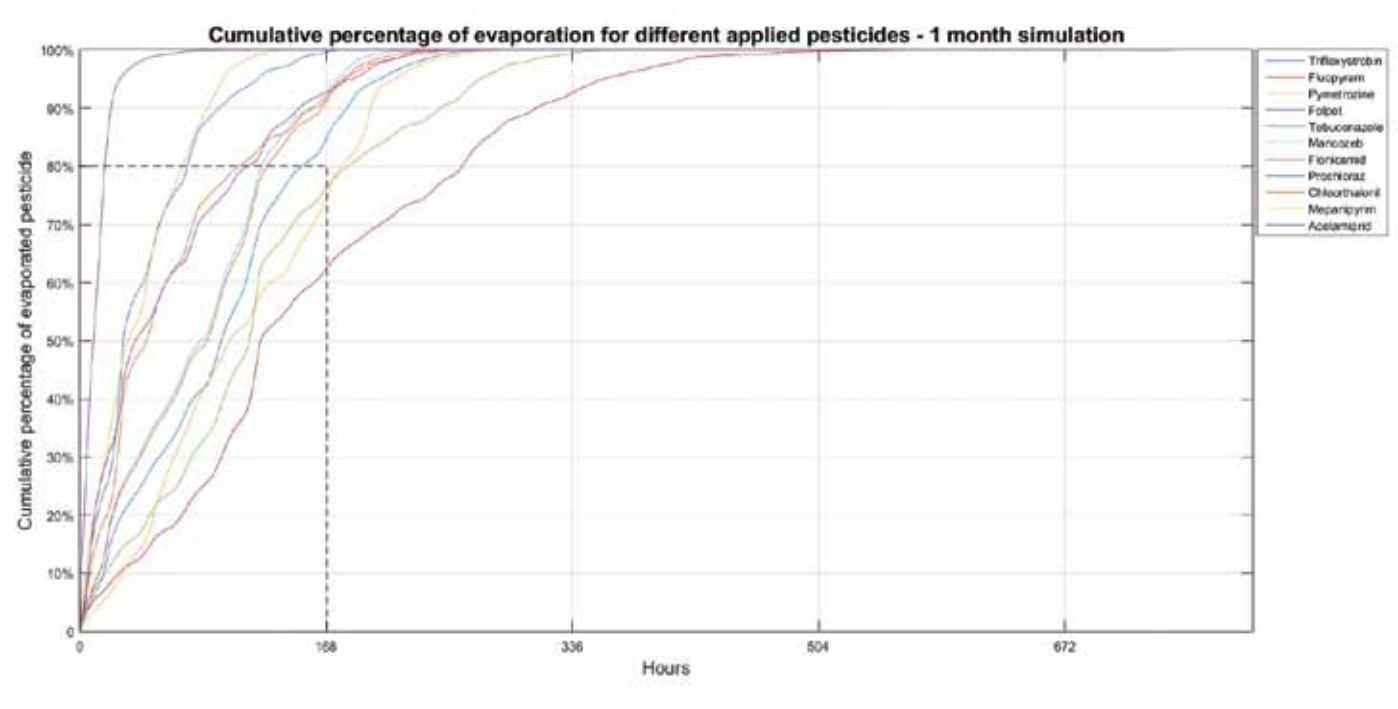


Figure 6.12: Output of OPS-St– 1 month simulation done in different target fields for different pesticides.

6.4.3 Unfavorable conditions – Drift and volatilization

During the OBO study all target fields applied pesticides during periods when wind was not towards most homes, meaning that applications during unfavorable weather conditions could provoke higher concentrations than the ones observed in the measurement campaign. To understand how much concentrations can increase when spraying application occurs during unfavorable, but still realistic, conditions, simulations were performed for both drift and volatilization.

Drift

The simulation of unfavorable conditions for drift was performed by changing the application parameters and weather conditions for campaign 4. The original situation is identified as case A. Assuming the wind speed would have been 8 m/s at 10 m height, and its direction perpendicular to the field edge, the situation for drift would be worse. In this case (identified as case B) many more drops would drift downwind and airborne emission would increase. An even worse situation (case C) would occur when in case B the evaporation would be enhanced, with an air temperature of 20°C and a RH of 25%. In such a situation small airborne drops would lose their water content very fast. Medium sized drops that might have deposited onto the ground under normal conditions, may in case C contribute to airborne emission. Figure 6.13 shows the airborne emission profiles with height at 5 m downwind from the SW field edge. A field width of 60 m is assumed. Case A (blue curve) represents the original situation of campaign 4. A cross wind of 8 m/s (at 10 m height) leads to an increase in airborne

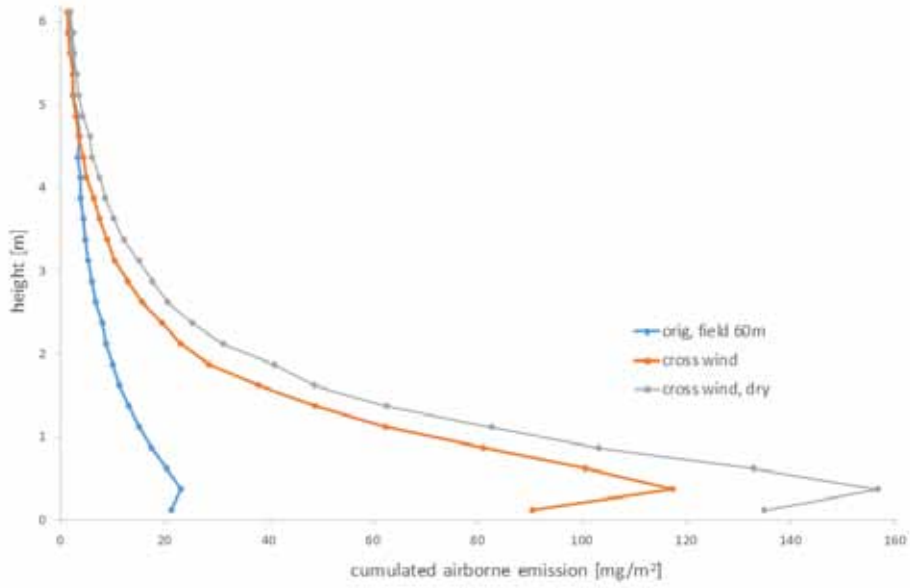


Figure 6.13: Comparison of airborne emission profiles with height in cases A, B and C.

emission, particularly at low heights (orange curve, case B). A further increase (grey curve, case C) is obtained under highly evaporative conditions.

It can be concluded, when observing Figure 6.13 (comparing case A with B and C), that application with unfavorable conditions can lead to an increase in airborne concentrations due to drift by a factor between 5 and 10.

Besides airborne emissions, downwind ground deposits are affected as well. In Figure 6.14 ground deposits are shown for the three cases. The lowest deposits occur in the original situation. With increased wind speed (and perpendicular direction), ground deposits increase significantly. Again, at higher evaporation rate the deposits increase further, as drops that would deposit nearer to the field edge may now deposit further downwind as their size is reduced by evaporation. Note that at 5 m downwind the deposits in case C are about 10 times higher than in the original situation.
In sum, ground deposit concentrations can also increase by a factor between 5 to 10 due to unfavorable weather conditions during pesticides spraying.

Volatilization

For volatilization, a simulation using the pesticide chlorothalonil was performed. This pesticide was selected since it is a widely applied fungicide and has a reasonably high vapor pressure (7.6E-2 mPa at 25 °C). It is therefore suitable to better understand the effect of weather conditions on concentrations outside the homes.

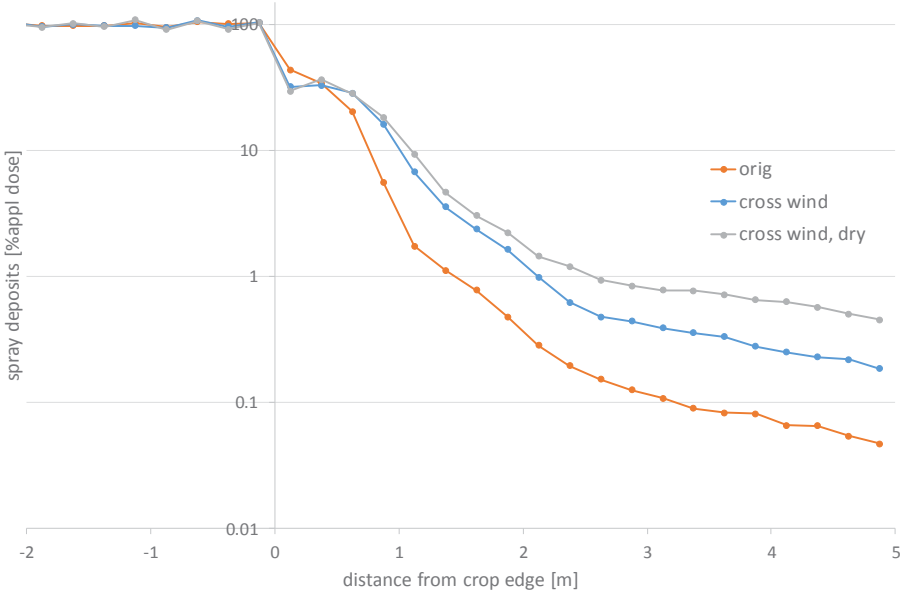


Figure 6.14: Downwind ground deposits for cases A, B and C. An increased wind speed and evaporation rate leads to increased downwind deposits.

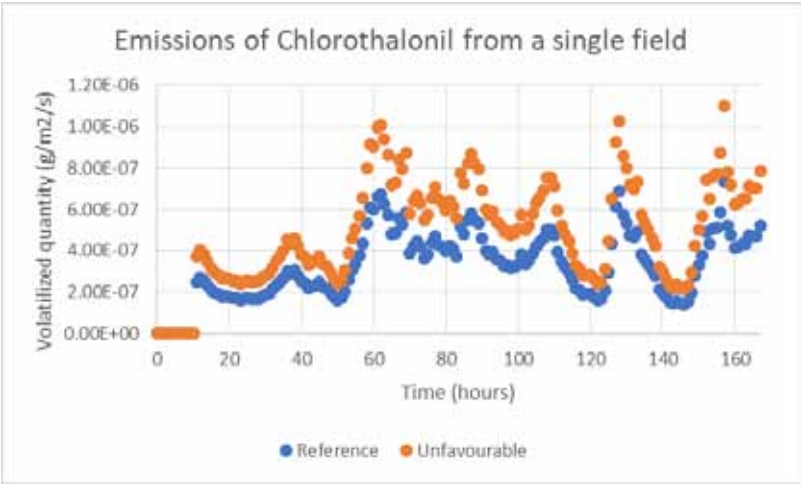


Figure 6.15: Emission strength of Chlorothalonil from a single field – Reference and unfavorable simulations.

Firstly, a simulation was performed using the same weather conditions as in campaign 3 but with the application of chlorothalonil. This is identified as the reference simulation. Secondly, the same simulation was performed but with changes in both weather and field conditions that would allow for higher emission of chlorothalonil due to volatilization as well as more homes downwind of application. The changes in conditions include constant low wind speeds (2 m/s), wind at a fixed direction towards the homes, full plant coverage and no competing processes. The last two contributing to higher concentrations of chlorothalonil that can be lost to air via volatilization.
The simulation does not combine effects of spray drift and volatilization. It represents solely the possible increase in concentration due to volatilization. Results for emission of chlorothalonil from volatilization are shown in Figure 6.15.

It can be concluded that for the simulated case, during unfavorable conditions, emissions of chlorothalonil would increase by a factor of 1.5 due to volatilization (Figure 6.15). Concentrations in downwind homes would also increase, with a general increase proportional to the increase in emission of chlorothalonil from the field.

6.4.4 Outdoor to indoor pesticide concentrations

Verification

The verification step for the gComis model was done as follows: For each home with at least 10 paired observations (i.e. measured concentrations inside and outside the home) the ratio between the concentration outside and inside was calculated. The minimum number of paired observations was set to 10.

This resulted in a dataset of 16 homes. Indoor air measurements were only available for the day of application, and since the model was used for the periods where spraying application occurs, off-season measurements were not used in this process. For this step, only values above the LOD were used, since the distribution of measured values below the LOD is unknown, leading to estimated ratios that would be relatively uncertain.

For verification purposes measured outdoor air concentrations were used as model input to calculate indoor concentrations, and in a second step, the measured indoor concentrations were compared with the modelled indoor concentrations. The results for each individual home are provided in Appendix 23. Two representative examples are shown below (Figures 6.16 and 6.17).

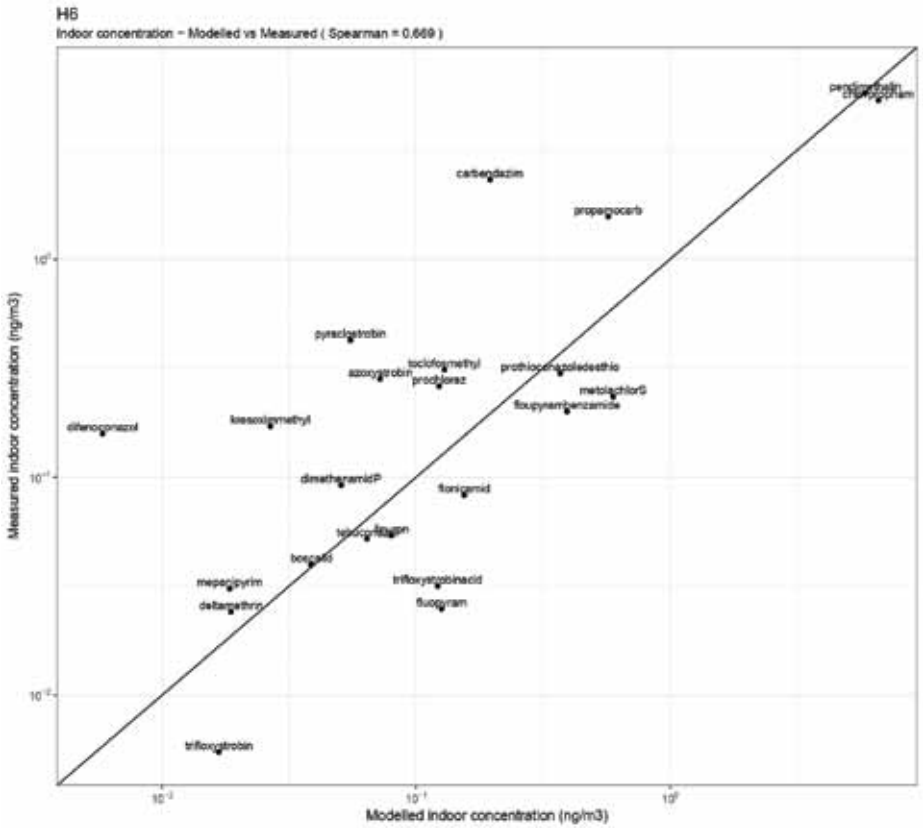


Figure 6.16: gComis verification –Example for one home (H6).
The black line represents the 1:1 line (y=x). Each dot represents a different pesticide. On the x axis the modelled indoor concentration, on the y axis the measured indoor concentration is depicted.

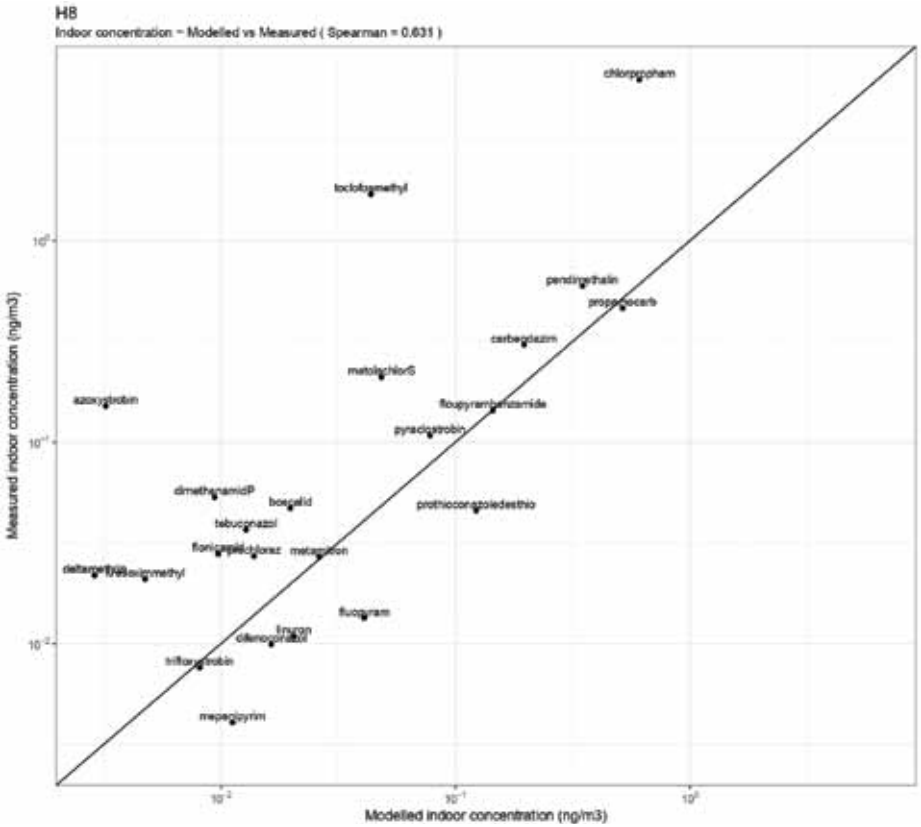


Figure 6.17: gComis verification –Example for one home (H8).
The black line represents the 1:1 line (y=x). Each dot represents a different pesticide. On the x axis the modelled indoor concentration, on the y axis the measured indoor concentration is depicted.

The verification step shows that overall the modelled values are close to the measured values (nearness to the 1:1 line), with a difference between modelled and measured data of less than one order of magnitude. This represents good agreement between modelled and measured indoor concentrations.
It is acknowledged that there might be other factors, such as indoor sources and/or sinks that were not accounted for in the model and that the indoor concentration on previous days, for which there was no information available, may have influenced indoor concentrations.

One of the sources that was not accounted for in the model was resuspension. Resuspension is mentioned in the scientific literature (e.g. Qian et al. 2014) as an important factor for indoor exposure to particle-bound compounds. In a sensitivity analysis this was included in the model as a source. Assuming reasonable resuspension rates no significant influence from resuspension was found on the indoor air

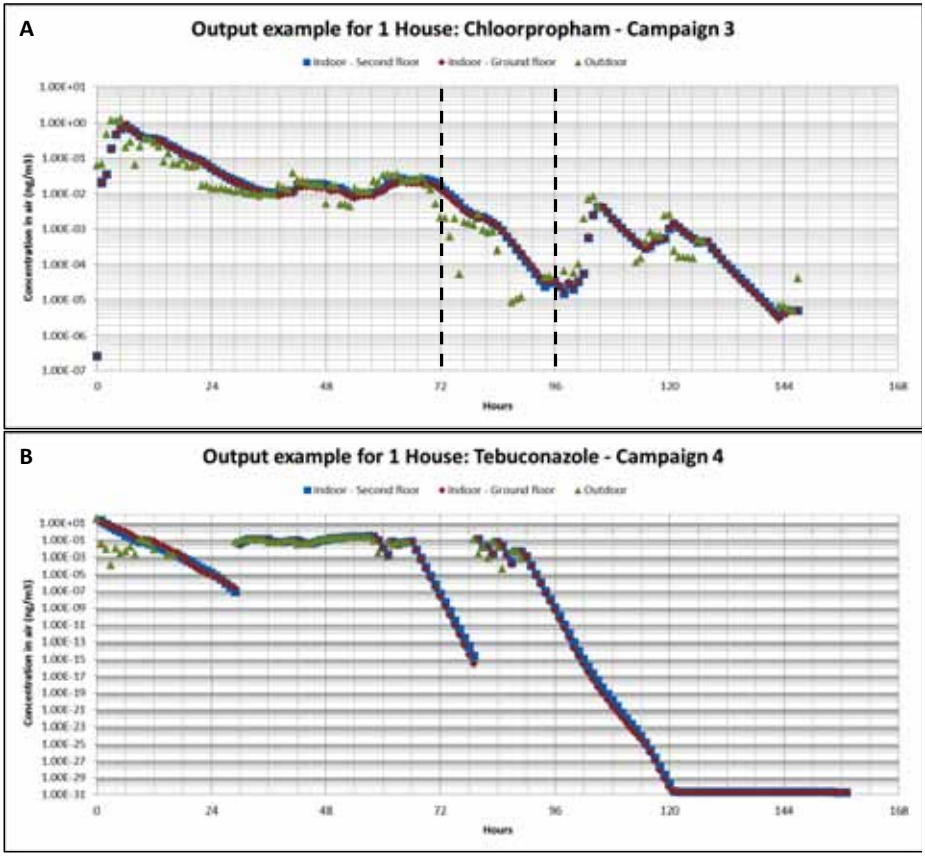


Figure 6.18: gComis output – hourly picture.
The green triangles represent modelled outdoor concentrations. The red diamonds show modelled indoor concentrations on the ground floor and the blue squares the modelled indoor concentration on the second floor.

concentrations (Appendix 24). Consequently, it was not included in further indoor air concentration modelling.

Results

In the previous section modelled indoor concentrations, using measured data, were compared with measured indoor concentrations.

The following section provides an overview of the gComis results, showing modelled indoor concentrations using modelled outdoor concentrations and results of PEARL-OPS. In total, concentrations in 103 homes were modelled.

Figure 6.18, shows the modelled hourly concentrations inside the home on the ground

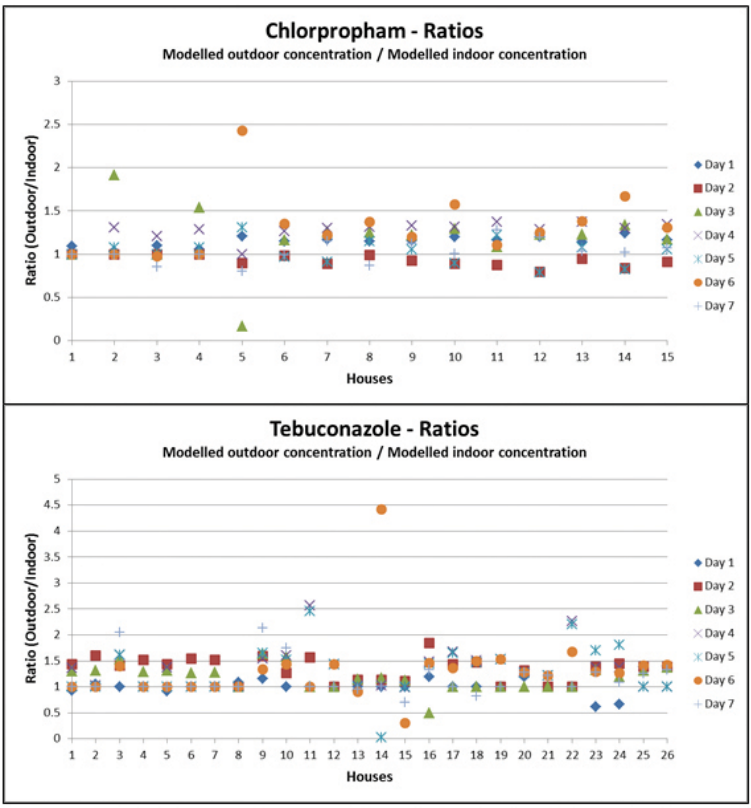


Figure 6.19: gComis output – Ratios – Outdoor/Indoor for different homes.
Each day is represented by a different geometrical shape. On the x axis each number represents a different home. On the y axis, the ratio of the modelled outdoor concentration by the modelled indoor concentration is displayed. The dotted black line indicates ratio=1, meaning outdoor levels equal indoor levels.

and second floor, as well as modelled outdoor concentrations at the same time. Indoor air concentrations appear to have a slight lag in time compared to outdoor air concentrations.

For example, a decrease in outdoor concentration of a given pesticide, due to e.g. a change in wind direction, leads to a decrease in indoor concentrations that lag a few hours behind the decrease in outdoor concentrations. This can be observed just after the 72-hour time frame shown on panel A of Figure 6.18, where at that specific time point, there is a slow decrease of the concentration in air indoor compared to air concentrations outdoor. For an increase in outdoor air concentrations the opposite is observed in the first hour of modelling where outdoor air concentrations are higher than indoor air concentrations. This means that observed differences in indoor and outdoor air concentrations may in fact be due to the time it takes to establish

equilibrium. Correspondingly, daily ratios between modelled outdoor and indoor concentrations tend to be close to one (Figure 6.19).

Additionally, it can be concluded that equilibrium of concentrations inside the home is established quite rapidly, since the absolute difference between the concentrations at different floors tends to be zero. Therefore, we can assume that daily average concentration in indoor air is the same for any home compartment.

In conclusion, the results of the gComis model show that it is important to assume that outdoor concentration is different from indoor concentration on an hourly scale, but when considering daily averages, the assumption that outdoor concentrations are equal to indoor concentrations seems reasonable.

6.4.5 Concentration of pesticides in dust

Verification and Results

Modelled concentrations of indoor dust were compared to measured concentrations in VFD. VFD represents general indoor dust potentially better than the concentration measured in doormats as doormats contain probably a strong contribution from materials dragged into the home.

In chapter 4, Tables 4.12 and 4.16 show a better agreement between VFD and median outdoor air concentrations than between VFD and the 1st day measured indoor concentration. Therefore, for verification purposes, median outdoor air concentrations were used to predict concentration in indoor dust, instead of using the 1st day measured indoor air concentration to predict concentration in indoor dust. This was done per pesticide, for the pesticides where enough measured VFD samples (N>5) where available for comparison with the modelled concentrations in indoor dust (24 different pesticides). The resulting comparison is shown in Figure 6.20.

For about 66% of the pesticides, when comparing modelled vs measured concentration of pesticides in dust, the model predicts the median concentration in dust (ng/g dust)

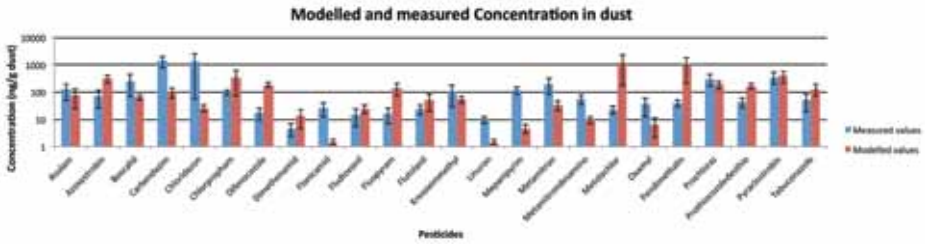


Figure 6.20: Median Concentration in dust – Modelled vs Measured.
The blue color represents the measured values in VFD (ng/g) and the red color represents the modelled values in indoor dust (ng/g). The error bars indicate standard errors. The number of homes differ per pesticide differ.

within a factor of 1 to 10 of the measured value. In some cases, for example carbendazim and chloridazon, the model under-predicts, and in other cases, for example, metolachlor and pendimethalin, the model over-predicts concentration in dust.

Hypothetically, under-prediction in the model can be explained by factors, such as dragging-in of particle-phase pesticides and lower removal rates from the indoor environment. Over-prediction of the model can happen when removal rates are higher, either because of high air exchange rates between indoor and outdoor environments or vacuum or wet cleaning, which will affect dust elimination rate in the indoor environment (Allot et al. 1993).

Concentrations of pesticides in dust are difficult to predict. Firstly, they are highly variable and can be a result of accumulation of dust over long periods of time. Secondly, besides sorption of gas-phase pesticides, settling of particle-phase pesticides and drag-in material also contribute to the indoor concentration in dust. Thirdly, information on removal rates of dust from the indoor environment, which is highly variable between homes, is also important to understand dust dynamics indoors.

Summarizing, the results of the calculations with the DustPred model yield variable results, showing that in some cases it is possible to predict mean concentrations in dust. However, in other cases it is quite difficult, most likely due to the processes mentioned above. As indicated previously, no model exists for estimating drag-in of dust particles into the home. Soil-contamination measurements presented in Chapter 4 have indicated that soil in the areas of intensive pesticide use have elevated levels and its drag-in in could thus be a source of indoor exposure to the residents.

6.4.6 Exposure

With the aim of understanding how much residents are exposed to pesticides applied in the bulb fields, exposure was calculated (1) using measured concentrations in air and dust and (2) using modelled concentrations in air and dust. Of the five pesticides measured in urine, conversion factors derived from the volunteer studies (chapter 2) were used to calculate internal exposure.

This chapter is divided into three parts:

1. The contribution of different routes to exposure by using both modelled and measured data is discussed. The results of the modelled internal exposure using the measured and the modelled data as inputs are compared.
2. The modelled internal exposure (concentrations) are compared to the measured urine concentrations
3. Additional exposure routes that influence concentrations in urine across different residents groups are discussed.

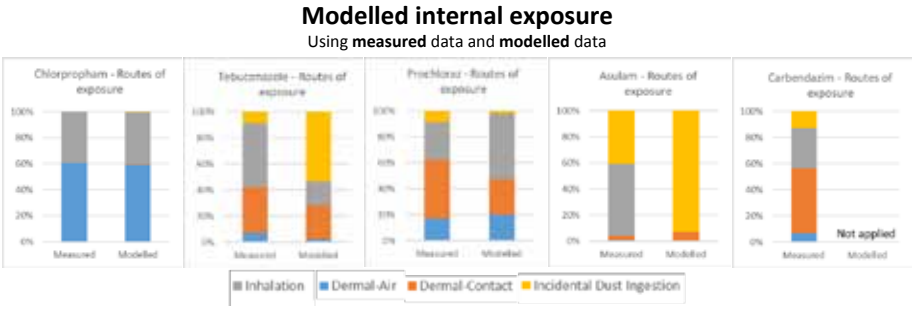


Figure 6.21: Contribution of different routes to residents' internal exposure to pesticides.
The upper panel of histograms refers to exposure modelled using solely *measured data* in air and dust. The lower panel of histograms refers to exposure modelled using solely *modelled data* in air and dust.

Results - Contribution from different routes

The contribution of each route to residents' exposure was calculated as described in section 6.2.1. The internal exposure calculation includes, firstly, the 4 routes that lead to environmental concentrations to enter the residents' body: Dermal contact, dermal uptake from airborne pesticides, inhalation and dust ingestion; and secondly, the conversion factors to understand how much will end up in urine.

We evaluated the contribution of the different routes to total exposure per pesticide, using both measured and modelled data as input to the exposure model.
This comparison was done to assess how well the modelled values predicted the percentage of each route contributing to total exposure. In Figure 6.21 it is possible to compare the contribution of different routes to internal exposure, as well as the differences in modelled contribution of each route when using measured or modelled data.

Similar patterns were observed when comparing modelled exposure using either measured or modelled values. In our study, when observing modelled internal exposures in Figure 6.21, it can be concluded a more equal contribution of the different routes to total internal exposure.

Verification – Modelled internal exposure vs Urine concentrations

The following section discusses the modelled internal exposure values for four of the pesticides measured in urine and their urinary concentrations. A comparison was done between modelled internal exposure using measured data and the concentrations found in urine measurements (Table 6.4). With this verification step, the accuracy of the model is assessed.

The results shown in Table 6.4 are stratified by residents in farm homes (Farm Homes), Residents and Controls. Note that the model only explains the contribution to internal exposure from concentrations in air and dust, whilst the measured values in urine account for all exposure sources, e.g. food intake.

Table 6.4: Modelled internal exposure and measured urine concentrations.

Modelled internal exposure and **measured** concentrations in urine (ug/kgbw/day)		**Farm Homes**		**Residents** (excluding Farm Homes)		**Controls**	
		Mean	95th	Mean	95th	Mean	95th
Chlorpropham	Internal exposure	3E-02	4E-02	4E-03	5E-03	9E-04	1E-03
	Measured in urine	3E-01	2E+00	1E-01	4E-01	4E-02	2E-01
Tebuconazole	Internal exposure	1E-04	3E-04	8E-06	1E-05	4E-05	5E-05
	Measured in urine	1E-02	4E-02	1E-02	4E-02	5E-03	2E-02
Carbendazim	Internal exposure	2E-03	3E-03	3E-05	5E-05	*Not applicable*	
	Measured in urine	2E-01	4E-01	1E-02	5E-02	1E-02	3E-02
Prochloraz	Internal exposure	2E-05	4E-05	2E-07	4E-07	3E-07	4E-07
	Measured in urine	< LOD	2E-01	< LOD	< LOD	< LOD	< LOD
Asulam	Internal exposure	2E-06	7E-06	2E-07	6E-07	*Not applicable*	
	Measured in urine	< LOD	2E-01	< LOD	2E-02	< LOD	< LOD

The following conclusions can be drawn from this comparison:

1. For all residents, measured concentrations in urine were higher than modelled concentrations of internal exposure. This may be due to the fact that dietary contributions were not considered in the integrated model. In line with this observation, similar ratios between modeled and measured concentrations were also observed among controls.
2. When looking at measured concentrations in urine, a clear pattern with [Farm Homes] > [Residents] > [Controls] is seen. The same pattern is seen when looking at modelled internal exposure.
3. For Prochloraz and Asulam, almost all values measured in urine were below LOD. The model also predicted very low concentrations (below LOD) for these two compounds.

Various input parameters to the exposure model, such as dust ingestion rates and frequency of contact with surfaces, are highly variable between residents and can easily shift the model results to over or under-predict concentrations in urine. Additionally, there is also uncertainty associated with the conversion factors, since this are based on 48 hours after exposure by the participant in the volunteer study, which differs from residents, whom have a different pattern of exposure.

When comparing which parameters are more sensitive, dust ingestion rates come as the most uncertain and the one that can shift the modelled results the most. The reason being that although there is uncertainty in frequency of contact with surfaces, the dermal conversion factors are much lower compared to oral, therefore the contribution from ingestion to internal exposure will be higher than contact with surfaces. Considering the ranges mention in literature (0-100 mg/day) for dust ingestion rates and the quantities of pesticide measured in dust from residents' homes, it can be concluded that this route can easily shift each individual's exposure.

Finally, the model does not take into account food intake, which, by comparing modelled results with concentrations measured in urine, most likely contributes to a big portion of the exposure.

6.5 Urine

6.5.1 Urine – Residents

Time of urine collection

In chapter 4 urine concentrations are plotted per resident, per day, across season, for both day urines and morning urines. The conclusion was that when comparing the daily urine concentration means there was no significant difference between the times of collection.

In this section, time of urine collection was explored as a predictor for urine concentration values. A linear mixed regression model was built to understand the effect of time of collection on the measured urine concentrations. The model takes urinary biomarkers' concentration as the outcome variable and both the time urine was collected and urinary creatinine concentration as predictors.

Models were built separately for chlorpropham, tebuconazole and carbendazim, for which enough measurements where above LOD. For all substances no statistically significant effect of time of collection was observed.

Effect of sex and age

Similarly to the approach taken in the previous section, age and sex were included in the mixed model. However no statistically significant effect was seen for both these predictors. These results are in agreement with the results from the volunteer experiments, where sex and age did not influence concentrations of the aforementioned pesticides biomarkers in urine in the controlled exposure experiments.

6.5.2 Comparison with ADI and ARfD

For comparison of urinary concentrations of the measured biomarkers in the residents with the acceptable daily intake (ADI) and the Acute Reference Dose (ARfD), the measured biomarkers were compared to the data obtained in the volunteer study as

the volunteers were exposed just below the level of the ADI. It is important to note that the ADI is derived for oral uptake, only, whereas for the residents we know that also inhalation and/or dermal uptake have contributed. Therefore the method used here to compare our results with the ADI and ARfD is only indicative.

Per pesticide the mean value (µg/g creatinine) was calculated from the six volunteers and was compared to the individual results (in µg/g creatinine) from the participants and expressed as a percentage compared to the mean volunteer levels.

For all the analyzed urines (n=1102), only 6 participants showed, for the biomarker of chlorpropham, to have a potential concentration in urine higher than the ADI, with 4 being control participants and 1 living in a farm home and 1 participant living close (<50 m) to a target field. Additionally, regarding the other four biomarkers, only 1 participant (living in a farm home) showed, for the biomarker of prochloraz, potential concentration in urine higher than the ADI. All residents' urines were below the ARfD for all biomarkers (median = 1% ARfD).

6.6 Statistical modelling

As an exploratory analysis, statistical models for assessing potential predictors that explain the variation of concentrations in urine were evaluated.

6.6.1 Regression analysis

As mentioned in chapter 4, biomarkers of five pesticides were analyzed in urine (tebuconazole, chlorpropham, carbendazim, prochloraz and asulam). The aim of this section is to explore, by means of regression analysis, the different possible predictors for pesticide levels in urine. Regression analysis helps understanding how variations in the observed concentrations in urine ("dependent variable") can be explained by the variation of predictors ("independent variables").

Table 6.5 summarizes how the outcome was defined in the statistical modelling, and how the three source predictors (Air, VFD and DDM concentrations) were defined in the model.

Table 6.5: Setup of the statistical modelling.

<table>
<tr><th colspan="2"></th><th>Tebuconazole</th><th>Chlorpropham</th><th>Carbendazim</th><th>Prochloraz</th><th>Asulam</th></tr>
<tr><td colspan="2">Outcome:</td><td colspan="2">Continuous</td><td colspan="3">Detected (Y/N)</td></tr>
<tr><td rowspan="3">Predictors</td><td>Air</td><td colspan="2">Continuous</td><td rowspan="3">Continuous</td><td rowspan="3">Detected (Y/N)</td></tr>
<tr><td>VFD</td><td rowspan="2">Continuous</td><td rowspan="2">Detected (Y/N)</td></tr>
<tr><td>DDM</td></tr>
</table>

The outcome variable was defined as a continuous measure if there were at least 40% observations above the LOD and the data was analyzed with a linear regression model. However, when less than 40% of observations were above the LOD, the outcome was modelled as detected vs not detected, that is > LOD vs < LOD, respectively, using a logistic regression model.

Predictors used in the statistical model selection are listed in Appendix 25.

6.6.2 Selection – statistical models

Due to the large number of possible predictors, a stepwise backward regression procedure was used. During model selection, creatinine was included as a default co-variate. Resident ID was used as a random effect to account for repeated measurements within individuals.
Urinary biomarkers' concentrations were log transformed (in the linear regression model). Therefore, the models are log-linear mixed models for tebuconazole and chlorpropham and mixed effects logistic regressions for carbendazim, prochloraz and asulam.

Finally, since it was suspected that drivers of exposure could vary by season, the model were stratified by season. All model results can be found in Appendix 26. In the following section the statistical models results are discussed.

6.6.3 Urine – Statistical model results

A detailed summary of all results for log-linear mixed models developed for tebuconazole and chlorpropham biomarkers in urine, as well as logistic mixed models developed for carbendazim biomarker in urine are shown in Appendix 26.

Log-linear mixed effects model

Models were developed for tebuconazole and chlorpropham with the aim of understanding what could explain the variation seen in urine concentrations between different residents.

In summary, different predictors were retained in the final model, some related to environmental sources (e.g. concentration in air or dust), others related to home characteristics (e.g. floor type or number of residents per home) and others related to food consumption (e.g. specific food items or eating food from own garden). This shows that the different routes could all be important for internal exposure to pesticides, which supports the deterministic modelling presented in this chapter. When stratifying the models by season predictors tended to change, indicating that depending on whether urine samples are collected during or outside the spraying season concentrations in urine will vary according to different predictors. The results of the models are consistent with the correlations found between urine and environmental concentrations in Sub-Chapter 4.6.5.

Logistic mixed effects model

Models were developed for carbendazim, prochloraz and asulam in an attempt to study the odds of finding a detectable level of these biomarkers in urine.

Firstly, due to the low number of detects it was not possible to find any statistically significant predictor for either asulam or prochloraz present in urine.

For carbendazim, the same conclusions can be drawn as for the log-linear models, the drivers being in general the same; with VFD (environmental predictor), number of people living in the home (home related characteristics) and creatinine values (personal) being related to the odds of detection of carbendazim in urine. The results of the model for carbendazim are consistent with the correlations found between urine and dust samples as presented in Sub-Chapter 4.6.5.

6.7 Uncertainty

There are inherent uncertainties in the modelling process that concern uncertainties in the input parameters, model choice and model specification. The main uncertainties during the modelling process were related to applications that might have occurred in additional fields at the same time as the application on the target field and for which no information was available. Similar uncertainties can be expected when additional applications occurred during the week simulation period.

There are also other uncertainties that, although not directly related with the modelling framework, will influence exposure to pesticides. The main source of such uncertainties in this study are the possible occupational and food intake exposures, which weight largely in the prediction of concentrations in urine.

6.7.1 Deterministic models

During the deterministic modelling different uncertainties were revealed, mainly regarding the modelling setup. These are listed below and discussed afterwards.

1 Other fields might have applied at the same time or later on the first day or even on days 2 to 7. Since the exact time of spraying is unknown, the relevant (variable) wind direction is unknown;
2 Adjuvants added.

First, regarding point 1, the application of other fields was taken into account when information was available or was possible to infer on what and when application occurred, thus reducing the error on our predictor that is related to the magnitude of modelled concentrations. Regardless of wind direction and speed, the more fields are involved the higher will be the concentration in air. Therefore, by trying to account for additional fields the model comes closer to the mean measured concentrations.

This can have an effect on understanding the variability between homes, since in most cases, homes were surrounded by multiple fields with spraying activity, but no exact time of application was known.

Second, regarding point 2, adjuvants are used to enhance effectiveness of pesticides, and were taken into account in the tank mixture by the IDEFICS model. If no information was provided regarding adjuvants it was assumed that no adjuvants were added. Added adjuvants in the tank mixture that were not reported creates uncertainty regarding the drift model, since, it is the total concentration of products that determines the size of airborne particles. Adjuvants may change the drop size distribution and at this time it is not known how adjuvants (or chemical products in general) may change drop size distributions of a spray. Additionally adjuvants can also affect volatilization, for example supressants can be addedd to decrease the vapor pressure of water, which will reduce the quantity of pesticide emitted over time.

6.7.2 Statistical models

The statistical modelling resulted in models that varied by exposures and seasons. This variation is likely in part caused by the fact that no robust models could be constructed due to low numbers of samples especially when stratifying results by factors such as season. In addition, we had a large set of potential explanatory factors some of which were correlated leading to problems in variable selection and statistical inference. These problems are compounded by the fact that variations in biomarker concentrations in urine between residents/days were small, limiting the ability to filter background/noise.

6.8 Conclusion

6.8.1 Environmental

During the different modelling steps within the framework it became clear that, depending on the pesticide, some routes of exposure (e.g. inhalation and dermal from airborne) had more influence in the uptake and consequently on the concentrations in urine. The modelling framework was capable of capturing both spatial and temporal differences and the modelled results were within the same order of magnitude as the measured data. The modelling framework seemed to be better for day 1 than for the simulation of the whole week, mainly due to the uncertainty regarding spray events occurring in additional fields during that week. The framework can be used to simulate exposure from boom sprayer application in different seasons but corrections need to be done regarding plant coverage for winter, since the model will over-predict volatilization in winter.

It can be concluded that some predictors of concentration of pesticides biomarkers in urine are related to environmental sources, some are related to food, others to home characteristics and some to the resident's personal characteristics.

6.8.2 Personal

This study/simulation highlighted the fact that, excluding food intake, incidental dust ingestion and inhalation are the routes that contribute the most to individual exposure to pesticides. This is mainly due to the higher uptake rates through these routes as compared to absorption of pesticides via the dermal route. The percentage each route contributes varies per pesticide and for the pesticides analyzed in urine. The conclusion is that exposure due to boom sprayer applications seems to account for a small percentage of the measured urine concentrations, whilst, food intake likely accounts for a greater portion.

7. OBO flower bulbs: discussion and conclusions

7.1 The OBO bulb flower study

Approximately 30% of all Dutch homes are situated within 250 m of any agricultural field. This goes down to 18% if grass land is not considered in this calculation. Concerns have been raised about the exposures to pesticides of these residents and possible associated health effects. Several international studies on exposure of residents to pesticides have been carried out but have shown variable findings. Some observed differences in exposure levels between urban and rural populations (Courture et al, 2009) whereas others did not (Kimata et al, 2009; Koureas et al 2009). Given these differences and the lack of information on exposure levels of the Dutch (rural) population in relation to pesticide use on agricultural fields, the OBO study was initiated. This research project addressed the recommendations from the Health Council of the Netherlands (Health Council of the Netherlands, 2014) and was commissioned by the Dutch Ministries of Infrastructure & Water Management and Economic Affairs & Climate Policy.

The OBO study aimed to assess the exposure to pesticides of residents living within 250 m from an agricultural field. To address this aim, a study design was applied that combined environmental sampling (outdoor and indoor air, dust from the doormat, vacuumed floor dust, and soil from the garden), personal sampling (urine and hand wipes), and exposure models. To limit costs however, OBO was split into phases. The ministries selected flower bulbs as the crop to be studied first. This is a crop that is typically grown with extensive use of pesticides. Flower bulb growing fields are always sprayed using downward spraying techniques. Cultivations treated with side- or upward spraying techniques, such as fruit orchards, are not covered in OBO flower bulbs. The main research questions of OBO flower bulbs are:

i) What are concentrations of pesticides in the environment of residents living near agricultural land with the cultivation of flower bulbs compared to residents living further away?
ii) What is the personal exposure to pesticides of residents living near agricultural land with the cultivation of flower bulbs compared to residents living further away?
iii) What are the exposure sources and routes contributing to personal and environmental exposure to pesticides in areas with the cultivation of flower bulbs?

The OBO flower bulb study was conducted from 2016 to 2018. It included experimental measurements on spray drift and volatilization and the residents' field study. Measurements in the residents' field study, carried out in 2016 and 2017, included environmental measurements (outdoor air, indoor vacuumed floor dust, dust from indoor doormats and soil from the garden) in homes of residents within 250 m of a

target field with cultivation of flower bulbs. Growers living within 250 m of the field were also invited to participate as residents. Samples taken from this group and their environment were treated separately in the analysis of the data. A control group was recruited from areas with less than 1500 addresses per km^2, with no agricultural fields within at least 500 m but within 20 km from the target field. Residents from both location homes and control homes participated in biomonitoring and therefore collected morning urines. A pesticide application on the target field started the week-long sampling protocol. Homes and residents within 50 m of the edge of the target field participated in an additional protocol, collecting indoor air samples, first day urines and a hand wipe in the first 24h after the application. Measurements outside the period of pesticide application were also conducted during two days in both location and control homes. Selected environmental samples were analyzed on 46 different pesticides while biomarkers of five different pesticides were assessed in selected urine samples. Spray registration was collected from all fields in the area. Of the approached growers, 17% participated offering a target field and 36% shared their spray registration. Of the approached residents at the locations, 4.5% participated. The effect of the response rate for the different groups on the results is unknown.

This chapter is organized to first provide an overall summary of the main results, followed by addressing the aforementioned research questions individually with study results and discussion.

7.2 Summary of main findings

Samples were taken on many locations and under variable conditions with respect to housing, distance to fields, meteorological conditions, spraying features etc. Moreover, pesticides are not a homogeneous group of chemical compounds but cover a wide range of compounds with a large range in chemical and physical properties such as the vapor pressure of the pesticide. As a consequence, the concentrations observed show a wide range covering sometimes orders of magnitude. The summary findings describe general patterns. Results for specific pesticides can be found in chapters 4 – 6 of the report.

For environmental samples, we found higher concentrations of several pesticides inside and outside the homes of people living close to bulb fields (residents) compared to homes further away (controls). Relationships between distance to the field and pesticide concentrations as well as between periods of pesticide use/non-use and pesticide concentrations were clear for both outdoor air and indoor dust measurements, with decreasing concentrations with increasing distance. In personal samples, we detected biomarkers of pesticides in the urine samples of residents and controls, including (young) children, both during and outside periods of pesticide use. Relationships with distance or period were less evident for pesticide concentrations found in the urine of residents. However, looking at individuals, urinary concentrations correlated with the concentrations of pesticides in air and/or house dust to which they were exposed.

Drift of aerosols towards homes during actual spraying was not observed during our field measurements since the wind direction during the applications was away from the homes. The dispersion of pesticides after volatilization from the field and contact with and ingestion of house dust (possibly dragged into the homes from outside) were identified as major routes of exposure in our study.

Concentrations of pesticides in the living environment of growers and their family members were generally higher than those of residents in the same area. However, levels in urine samples from growers and their family members are in the range of those of other residents. The concentrations of measured pesticides inside and outside the homes and in the urine samples of controls indicate an exposure that is not driven by applications nearby homes. These background levels were higher during the period of pesticide use than the non-use period. From our experimental studies we concluded that the drift of pesticides downwind from downward spraying leads to measurable concentrations at greater distances (>50 m) and height (10 m) in the air than known before. Therefore, drift could still be an important route of exposure if the wind is directed towards homes during application of pesticides even at these larger distances. Predicting the total exposure of all residents near bulb fields and other crops with downward spraying, via both air and house dust, for all pesticides, all locations in the Netherlands and all moments is not yet possible. The research conducted thus far offers the components to develop models for residential pesticide exposures and thus may represent a way to upscale pesticide exposure assessment for large scale population studies.

The main findings of OBO are summarized in Box 7.1:

Box 7.1: Main findings of OBO

1. Higher concentrations of several pesticides were found in environmental samples collected from inside and outside the homes of people (residents) living close to bulb fields compared to concentrations in homes further away from the fields (controls).

2. These higher concentrations of pesticides were observed in the homes of people living close to bulb fields, both in the use and non-use period.

3. Biomarkers of two out of the five analyzed pesticides were found in more than half of the urine samples from persons, including (young) children, in both residents and controls. This was observed inside as well as outside periods of pesticide use. Relationships between the concentrations of these two pesticides in urine and distance to sprayed fields or periods of pesticide use were not consistently observed. However, concentrations found in urine correlated with the concentrations of pesticides inside and outside the homes.

4. Concentrations of pesticides inside and outside the homes of growers were generally higher than those found for residents living near agricultural land.

5. Calculations showed that volatilization of pesticides from the field after spraying and pesticides in house dust are likely the most important routes for exposure to pesticides of residents living close to bulb fields in our study. Because wind during spraying was not directed towards the homes of residents, drift was not observed in the field study. From experimental studies within OBO flower bulbs we conclude that drift can reach higher altitudes and larger distances than thought before.

6. The research has generated tools for a time-resolved predictive model to estimate exposure of residents of bulb fields and other crops with downward spraying, via both air and house dust, for all pesticides, locations and moments. However, important knowledge and information gaps still remain precluding estimates on a national scale.

The OBO study looked at exposure to pesticides of residents living near agricultural land. The study did not assess possible health effects of such exposures.

Below, the results will be discussed according to the three aims that were set for OBO flower bulbs.

7.2.1 Environmental exposure

What are concentrations of pesticides in the environment of residents living near agricultural land with the cultivation of flower bulbs compared to residents living further away?

We found elevated concentrations of pesticides in soil, outdoor and indoor air, and both vacuumed floor dust and dust from doormats of residents' homes located within 250 m of agricultural fields compared to control homes. This observation is based on the comparison of the exposed locations (residents living within 250 m of treated fields) to control locations (residents living in a non-urban area with no agricultural cultivations, defined above) and when comparing at exposed locations the use and non-use periods of studied pesticides. Pesticide concentrations in outdoor air close to the homes of residents of exposed locations were generally a factor ten or more higher than outdoor concentrations at control locations. Pesticide concentrations in both vacuumed floor dust and dust from doormats in homes of residents of exposed locations were generally a factor five higher than concentrations observed in control homes in both the use and non-use period. For some pesticides, this difference reached up to a factor 100. As expected, outdoor air concentrations tended to decline with

increasing distance to the agricultural field. The highest concentrations were found within 50 m from the treated fields and lower concentrations between 150 to 250 m. Even at the latter distances, concentrations were generally higher than the ones found at the control locations.

Elevated concentrations of pesticides in soil, outdoor and indoor air, and both types of dust samples were also found for several pesticides not applied close to the residents' homes during the measurement period. These pesticides may have been used before the measurement period started and volatilized from soil or dragged into the home, or they may have been applied further away from the homes, or used for other purposes than field spray applications. For example, elevated concentrations were found for thiophanate-methyl (as its environmental degradation product carbendazim) and pyraclostrobin. Both compounds are used in bulb disinfection. This implies that outdoor and indoor exposure levels are not only related to pesticide applications on the field but may also be related to other sources such as emissions from bulb disinfection activities or storage facilities in the neighborhood. It should also be noted that in this region pesticides have been used for many years and more persistent ones (such as carbendazim) may remain in the environment for a longer period, leading to ongoing exposures for residents.

Homes of people working in the agricultural sector ("growers") were not considered in the main analyses and the results of measurements in the growers' homes ("farm homes") were interpreted separately. Concentrations in outdoor air and both types of indoor dust samples were clearly higher in the farm homes compared to those found in the residents' homes. Concentrations of pesticides were generally a factor of two higher in air and a factor of ten higher for house dust. The higher concentrations in air were partially explained by the shorter distances to sprayed fields as compared to the homes of residents. A possible additional explanation could be bulb disinfection activities or storage facilities near farm homes. The higher concentrations in dust in comparison to residents' homes close (< 50 m) to agricultural fields may be due to (unintended) carrying pesticides to home from work through, for example, contaminated work clothing and shoes.

What are the exposure sources and routes contributing to environmental exposure to pesticides in areas with cultivation of flower bulbs?

In figure 7.1, adapted from the Health Council of the Netherlands, the different exposure routes that eventually could lead to human exposure are depicted. In this section we discuss these different routes step by step in the context of our results.

1. Spray drift
   The first step in Figure 7.1 is spray drift. During the field study, there were no applications that resulted in drift of aerosols towards the residents' homes. It is a preferred practice of the growers to apply pesticides when the wind blows away from residents' homes. However, in certain situations (not encountered in this study) homes could be situated or be build at more than one side of the field, the wind direction can shift towards the homes during an application or an application is urgently performed due to an emerging pest while the wind speed and/or direction are unfavorable. In a sensitivity analysis simulating unfavorable conditions, we found that in such cases, spray drift exposure may be more than a factor of ten higher than exposure observed in this study, which was based on the growers using 75% - 95% drift reducing techniques. The experiments carried out in this study showed that drift can reach greater heights and larger distances than reported in previous studies. Airborne spray drift is a factor ten to 100 higher than ground deposition at the same distance. In contrast to general belief, drift found behind a wind barrier is not always lower but can also be higher. This is based on experimental results from this study and depends on the porosity of the wind barrier.

2. Volatilization
   Volatilization was the dominant contributor to air concentrations on the days after an application. While the cumulative amount emitted into the air during application was about 0.2% of the dosage, the cumulative amount emitted due to volatilization can range up to several tens of percent of the dosage even for less volatile compounds. For compounds with high vapor pressure the emission from volatilization is much larger. However, the rate and extent of volatilization can be strongly affected by other processes occurring on the plant leaves, such as penetration into the plant tissue, photo-transformation, wash-off and the presence of adjuvants in the formulated product.

3. Concentrations in soil
   Concentrations of some pesticides (i.e. pendimethalin, prochloraz and pyraclostrobin) measured in soil samples collected in gardens near the residents' homes were a factor of five to ten higher than those for control homes. Clear differences in pesticide concentrations were not observed between pesticide use and non-use periods. Explanations for this observation were not investigated but slow degradation of these compounds in soil could play a role. Possibly, contaminated soil contributes to elevated levels in house dust through drag-in. The importance of this route however is not fully understood and the evidence is too limited to support strong conclusions.

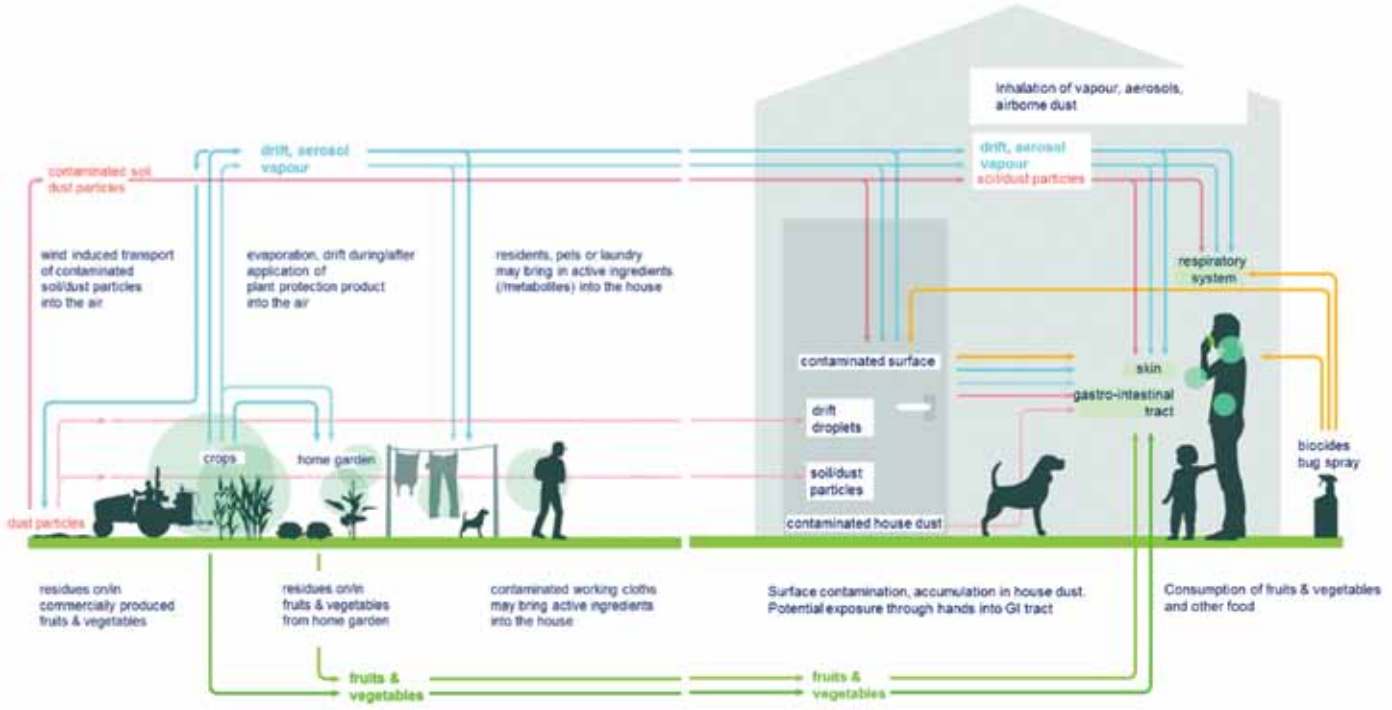


Figure 7.1: Exposure sources and exposure routes.

Different suggested sources and routes of exposure (left panel: outdoor; right panel: indoor). Colored arrows represent different type of routes: blue: direct exposure; red: indirect exposure via particles; green: indirect exposure via food; yellow: direct and indirect exposure from products used at home (Adapted from: Health Council of the Netherlands, 2014).

4. Residues on fruits and vegetables from home gardens
   A limited number of home grown fruit and vegetable samples were taken. Generally, no or only traces of pesticide residues (below 10 µg/kg, i.e., the default maximum residue limit (MRL) for pesticides not registered for use on vegetables or fruits) were observed. Overall, pesticide residues content exceeding 10 µg/kg were found in six samples (30% of tested samples). Two of these samples came from the garden of a farm home. A comparison with the situation for control residents could not be made because no fruits and vegetables samples were available from these locations.

5. Exposure related to working clothes
   The next step in figure 7.1 is exposure related to (working) clothes. This was not studied in OBO flower bulbs. Contaminated working clothes have been indicated to influence exposure of families of growers and pesticide applicators (Curwin et al, 2002). This could be related to direct contact, volatilization of pesticides from the clothes, or other routes. We did not collect information on individual habits regarding working clothes (e.g. changing of clothes outside the home, separate washing of work clothing). Therefore, the contribution of this exposure route cannot be assessed in this study.

6. Concentrations in house dust
   Elevated concentrations of pesticides were observed in house dust collected in homes of residents compared to those in control homes. The level of pesticides in house dust (i.e. vacuumed or collected from doormats) did not show a clear relationship with distance to the sprayed field. The occurrence of pesticides in house dust could be caused by several mechanisms. One is the absorption of gaseous pesticides to already present house dust. Another is the direct deposition of spray drift related particles in the house from previous applications in the vicinity of the home or from applications further away. Also, a relation with drag-in of contaminated particles is possible. Relationships between concentrations in dust and distance to fields were investigated but the results do not allow conclusions regarding the dominant mechanism and this aspect needs further research.

7. Concentrations on outdoor surfaces
   Another exposure pathway in Figure 7.1 is the contamination of surfaces. The deposition of drift, aerosols and vapor could lead to contaminated surfaces around the homes of residents. We did not measure the amount of pesticides on surfaces such as garden furniture and playground equipment. In principle, estimates could be made using the models tested in this study. We did not perform such analyses given the uncertainty regarding how this would relate to personal exposure as it would require detailed information on time-activity and use patterns. The contribution of this route therefore remains uncertain.

7.2.2 Personal exposure

What is the personal exposure to pesticides of residents living near agricultural land with cultivation of flower bulbs compared to residents living further away?

Personal exposure to pesticides in the OBO study was measured through monitoring of five biomarkers of pesticides in urine samples (asulam, thiophanate-methyl/carbendazim, chlorpropham, prochloraz, and tebuconazole). These pesticides were chosen based on their use, feasibility of analysis, as well as representativeness of different types of pesticides, and reflect different physical-chemical properties. All, except thiophanate-methyl/carbendazim, were applied on the target fields. Thiophanate-methyl is used as a bulb disinfectant, is degraded to carbendazim in the environment, and was found as carbendazim in many of the dust samples. In an experimental study within OBO flower bulbs (the volunteer study), where volunteers were exposed via dermal or oral routes to pesticide concentrations just below the level of the Acceptable Daily Intake (ADI), the suitability of specific urinary biomarkers of exposure for each of the five pesticides was confirmed. The identified biomarkers are also the major biomarkers found in animal studies. Furthermore, the volunteer study demonstrated that urinary biomarkers were rapidly excreted after oral exposure (50% of dose excreted between three to 25 hours). Excretion rates were much lower after dermal exposure compared to oral exposure. Uptake by the skin is a comparatively slow process resulting in a slow absorption into the blood circulation, and excretion continued for at least 48 h after exposure. Conversion factors were calculated based on molar fractions for each of the individual pesticides. These factors were used for the calculation of the biomarkers excreted through urine based on the amount of the pesticide taken up via oral and dermal routes.

In the residents' field study urinary biomarker concentrations of asulam, thiophanate-methyl/carbendazim and prochloraz were generally below the limit of detection. Urinary biomarkers of chlorpropham and tebuconazole were detected in 82% and 63% of urine samples respectively, including samples from diapers. Pesticides were detected in urine samples from young and older children at levels in the same order of magnitude as found in adults. Urinary concentrations of chlorpropham were a factor two higher among residents than controls. No difference in urinary concentrations of chlorpropham was found between pesticide use and non-use periods. For tebuconazole a slight difference of a factor two in urinary concentrations was found for the residents between pesticide use and non-use periods, but not between the residents and controls. In addition, urinary concentrations of chlorpropham and carbendazim correlated with the concentrations of the pesticides in air and house dust measured in the persons' living environment. These results suggest an environmental contribution to the measured urinary pesticide concentrations of the residents for some pesticides.

Hand wipes from the day of application were collected from residents living within 50 m of the field. The five pesticides from the biomonitoring could also be identified

on the hand wipes. However, as only residents living in close proximity of the field collected hand wipes, no comparison could be made to residents living further away or controls.

Urine levels in context of the ADI

A comparison of the urine levels found in this study with a measure like the Acceptable Daily Intake (ADI) may help to place the levels in a context. There is no direct way to calculate levels in urine back towards intake. However, results from the volunteer study provided indications on how to calculate back towards intake. The observed concentrations of biomarkers in the participants' and growers' urine were in general lower compared to those in the volunteers, who received a single oral or dermal dose just below the ADI. The ADI is a measure of the amount of a specific substance that can be ingested orally on a daily basis over a lifetime without an appreciable health risk. However, this dosage comparison with the results from the volunteer study has limitations. First, the results for the five included pesticides cannot be generalized or extrapolated to other pesticides or scenarios because the ADI is different for each pesticide. Furthermore, 'worst case' scenarios for pesticide exposure were not encountered in the study. In addition, exposure of the residents is a combination of contributions through the oral, dermal, and inhalation route. As the ADI only addresses the oral intake and possible associated health effects, the applicability of the ADI as a reference for total internal exposure is uncertain. For example, respiratory pesticide intake and associated health effects are not considered by the ADI. Moreover, residents are not exposed to a single pesticide but to more pesticides at the same time. It is suggested that there might be additive or synergistic effects of being exposed to different pesticides that share a similar (biological) mode of action. Lastly, the pesticides studied here were not selected for their potential toxicity and/or health effects. Therefore, these results do not provide information regarding the presence or absence of a health risk for the residents.

It should be noted that the ADI might not be applicable for unborn and young infants until the age of 16 weeks, a phase of very rapid development (EFSA, 2017b; EFSA, 2018). However, as the youngest participant in OBO was 2 years old, this is not applicable for the presented results.

What are the exposure sources and routes contributing to personal exposure to pesticides?

Based on the modeled and measured concentrations we estimated the potential contributions of the different exposure sources and routes to personal exposure. These results indicate that when accounting for dermal and oral/inhalation uptake rates, inhalation, dermal uptake, and incidental dust ingestion could all be important contributing routes for exposure. Relative contributions differ, depending on the concentrations of the pesticide in the different compartments and on the uptake rates through the different routes.

7.3 Modelling - Integrative analysis of the exposure routes

One of the aims of the OBO-study was to develop an integrated framework of models suitable to assess exposure of residents to pesticides from nearby treated fields. As OBO flower bulbs only covered crops sprayed with downward spray techniques, the current integrated model is only field tested for these conditions. Significant progress was made in developing an integrated model framework that currently consists of a chain of inter-dependent models that predicts exposure on an hourly basis. Model verification, both through experimental studies and field observations, indicated that the developed integrated model framework could be suitable for estimating residential pesticide exposure levels on a high spatial and temporal resolution. Most of the individual models in the integrated model framework produced estimates that were within the same order of magnitude as measured levels. An exception to this were pesticide concentrations in indoor dust. These could not be explained by the existing models of gas to particle conversion. This could be because current models do not account for other sources such as the contribution of active drag-in of pesticide containing dust from outdoors to indoors. No comparisons were made between the integrated framework to dynamically model the exposure of pesticides of residents with regulatory models.

7.4 Recommendations

Based on the results of the OBO flower bulb study several recommendations can be made.

1. Estimating potential health implications of the measured environmental concentrations was not an aim of the study. However, given that measurable concentrations of some pesticides were found in urine samples among participants and controls, including children, and that correlations were found between environmental and urinary concentrations of these pesticides the current results need to be explored in relation to possible health implications. Such an evaluation should take more features into account, like other pesticides, varying layouts of locations, different soil types, more weather conditions, more routes of exposure and susceptible subgroups (e.g. unborn and young children, individuals with co-morbidities). It should be noted that detection of pesticides in urine samples of young children may cause concerns because unborn and very young children are in a phase of rapid development. Disruption of the normal development could occur at levels that are not considered hazardous for adults (Berghuis et al., 2015, Council On Environmental Health, 2012).

2. The insights obtained in this study indicate that exposure gradients were relatively modest within 250 m of fields but more pronounced when compared to homes further away (> 500 m). The recently conducted exploratory Health Survey in the Netherlands (RIVM Rapport 2018-0068) focused on presumed exposure-response functions across very short distances (0 - 50, 50 – 100, 100 – 250 and 250 – 500 m) to fields. The results from the OBO flower bulb study necessitate a re-evaluation of the Health Survey that would more specifically focus on health effects within 0-250 m of fields as compared to further away and less on increasing risk estimates with decreasing distance to fields. Such re-evaluation of the Health Survey may lead to potential additional findings above the currently reported health associations.

3. Results from this research have indicated that the exposure gradients for house dust are less clear and that routes leading to pesticides in dust (e.g. drag-in) are not well understood. As pesticides in house dust could be an important source of exposure, especially for children (due to a potentially higher intake of dust), more information on the pesticide levels in house dust and its driving factors (drag-in, absorption of gaseous pesticides to house dust) needs to be collected. We therefore recommend to carry out measurements on pesticide levels in indoor dust among residents living close to agricultural fields and compare them to controls living further away. Such a survey would need to cover a variety of crops and farming systems to understand the distribution and concentration of pesticides in house dust and to improve predictive models.

4. The current study focused on flower bulb cultivations for which downward spraying techniques were used. As indicated at the onset of the project, this does not provide insight in the exposure of residents living near crops where sideways or upward spraying techniques are used (such as fruit trees). It is known that these techniques have higher emissions due to a higher drift potential, leading to possibly higher exposure of the residents. To study these techniques and associated exposures and to improve the integrated model framework to accommodate these application techniques, it is recommended to carry out a verification study on pesticide exposure in homes surrounding orchards. This would also allow further development of models addressing other transport pathways such as drift and volatilization (e.g. further insight in the effect of obstacles).

5. The data on the residents' exposure and how the different transport pathways contribute to this exposure could be used to develop exposure scenarios for the assessment of exposure in the framework of the European authorization procedures of pesticides. The modelling framework developed in this project could be used to calculate exposure under different scenarios and could be used to improve the recently developed regulatory models (e.g. OPEX, BREAM), which now have incorporated procedures to estimate residential exposures.

6. In order to apply the integrated model framework to estimate population level exposures, the model chain will need to be further developed and computing efficiency should be increased. One of the main sources of uncertainties, however, arises from the fact that input data on applications on specific fields are difficult to obtain. In our study we were able to obtain the information related to pesticide applications (e.g. type of pesticide applied, application time) as this was asked from the growers. The timing of other applications on the target fields or other fields in the vicinity were assigned based on knowledge of used application schedules. However, to derive valid hourly/daily estimates of population level residential exposures it will be important to improve the reporting of all pesticide use by all growers. Estimates on longer time scales (such as annual averages) for indoor and outdoor air concentrations could potentially be calculated using currently available methods as exact timing of applications would be less critical. Such results could be used to highlight potentially important areas, crops, and/or pesticides for residential environmental exposure.

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Appendices

Appendix 1: Gross list of plant protection products

Table 1 Active substances from commonly applied products in tulip and lily and their options for chemical analysis[1].

Substance	Product name(s)	Tulip	Lily	LC-MS	GC-MS	SRM
acetamiprid	Gazelle	Y	Y	1	0	
asulam	Asulox	Y	Y	1	0	
boscalid	Collis	Y	N	1	1	
chloridazon	Pyramin DF	Y	Y	1	(1)	
chlorothalonil[3]	Allure vloeibaar[5]	Y	Y	0	1	
chlorpropham	Certis Chloor IPC 40% Vloeibaar, Intruder	Y	Y	1	1	
deltamethrin	Decis EC	Y	Y	(1)	1	
dimethenamide-P	Wing P	Y	Y	1	1	
diquat[2]	Mission 200 SL	Y	Y	0	0	1
esfenvalerate[3]	Sumicidin Super	Y	Y	0	1	
flonicamid	Teppeki	Y	Y	1	0	
fluopyram	Luna Experience, Luna Sensation	Y	Y	1	1	
folpet[3]	Mirage plus 570 SC[5], Spirit[5]	Y	Y	0	1	
glyphosate[2]	Roundup Ultimate	Y	Y	0	0	1
iprodion[3]	Rovral Aquaflo	Y	Y	0	1	
kresoxim-methyl	Collis	Y	N	1	1	
lambda-cyhalothrin	Karate Zeon	Y	Y	(1)	1	
mancozeb[2,4]	Fythane DG, HF Mancozeb DG, Mastana SC, Penncozeb SC	Y	Y	0	0	1
metamitron	Goltix SC	Y	Y	1	(1)	
mineral oil, light and heavy[2]	11 E Olie, OVIREX VS, Sunspray 11-E	Y	Y	0	0	1
paraffin oil[2]	Olie H	Y	Y	0	0	1
pendimethalin	Stomp 400 SC, Wing P	Y	Y	1	1	
prochloraz	Allure vloeibaar, Mirage plus 570 SC	Y	Y	1	(1)	
prothioconazole	Rudis	Y	Y	1	(1)	
pymetrozine	Plenum 50 WG	N	Y	1	0	
S-metolachlor	Dual Gold 960 EC	Y	Y	1	1	
spirotetramat	Movento	Y	Y	1	1	
tebuconazole	Folicur, Folicur SC, Luna Experience, Spirit	Y	Y	1	1	
thiacloprid	Calypso	Y	Y	1	0	
trifloxystrobin	Flint, Luna Sensation	Y	Y	1	1	

[1] LC-MS: multi-residue method based on liquid chromatography with mass spectrometry. GC-MS: multi-residue method based on gas chromatography with mass spectrometry. SRM: Single Residue Method, dedicated method only measuring one substance. 1 = suited, (1) = moderately suited, 0 = not suited

[2] Excluded from scope because analysis requires a single residue method (substance not amenable to multi-residue methods)

[3] Excluded from scope because substance cannot be analysed sensitively by liquid chromatography-mass spectrometry (LC-MS)

[4] Products based on mancozeb are not authorised on sandy soils in flower bulb region 'Bollenstreek'

[5] Products containing a second active substance which is included in the scope

Table 2: Active substances which are suited for LC-MS, in products commonly used by tulip and lily growers. Arranged by product use. With the relevance to tulip and lily cultivation, dose rate and actual number of applications, saturated vapour pressure, estimated skin penetration, and remarks on analytical reference standard

substance name	product use	tulip	lily	dose rate (kg as ha^{-1})	frequency	vapour pressure (mPa)	skin penetration (µg cm^{-2} hr^{-1})	Aspects related to analysis of urine for biomonitoring Urinary excretion and metabolites	Anal. Ref. Std available?
asulam	H	Y	Y	4	2	5.0E-04	?	70-80% excretion as parent substance	Y (parent)
chloridazon	H	Y	Y	2.25	1	1.0E-06	2.3E-01	85-90% excretion as OH-metabolite + Glu/SO4 conjugates	N
chlorpropham	H	Y	Y	3	2	2.5E+01	2.9E+00	Mostly excreted through urine, mainly as OH metabolite / SO4 conjugate	Y (4-HSA, 4-OH-metabolite)
dimethenamide-P	H	Y	N	3.5	1	2.5E+00	1.5E+01	35-47% elimination via urine metabolism primarily via glutathione conjugation pathways	N
metamitron	H	Y	Y	3	1	7.4E-04	8.4E-01	50% urinary excretion. Desamino-metamitron + hydroxylation products	Y (desamino-metamitron)
pendimethalin	H	Y	Y	4	1	1.9E+00	6.5E-02	Extensive metabolisation	N
S-metolachlor	H	Y	Y	1.5	1	3.7E+00	3.1E+00	Metolachlor-mercapturate has been used as human biomarker	Y (metolachlor-mercapturate)
acetamiprid	I	Y	Y	0.23	4	1.7E-04	1.4E+00	60-70% through urine as 6-chloronicotinic acid, 2 other metabolites and low % of parent substance	Y (6-chloronicotinic acid, parent)
deltamethrin	I	Y	Y	0.4	2	1.2E-05	6.5E-05	3-PBA is known human biomarker, DBCA	Y (3-PBA, DBCA?)
flonicamid	I	Y	Y	0.14	3	9.4E-04	7.4E-01	50% as parent in urine	Y (parent)
lambda-cyhalothrin	I	Y	Y	0.05	11/20	2.0E-04	1.0E-03	3-PBA is known human biomarker, TFMCVA	Y (3-PBA, TFMCVA?)
pymetrozine	I	N	Y	0.2	3	4.2E-03	2.6E-02	70% through urine, parent + several OH-metabolites	Y (parent)
spirotetramat	I	Y	N	0.5	2	5.6E-06	2.2E-05	Mainly through urine; -enol is human metabolite	Y (-enol)
thiacloprid	I	Y	Y	0.25	2	3.0E-07	7.9E-02	50-60% through urine. 6-chloronicotinic acid, glycine derivative, other metabolites and 1-6% of parent substance	Y (6-chloronicotinic acid, parent)
boscalid	F	Y	N	0.7	3	7.2E-04	7.9E-03	20% through urine. M510F01, Gluc and SO4 conj. + minor others	Y (M510F01)
fluopyram	F	Y	Y	0.3	5	1.2E-03	2.1E-02	40% through urine. Extensive metabolism, most abundant: fluopyram benzamide, fluopyram pyridyl acetic acid, 7-OH-phenol, fluopyram, 7- or 8-OH fluopyram and fluopyram ethyl diol glucuronide accounting each for 6-28 %	Y (fluopyram benzamide, PAA, PCA)
kresoxim-methyl	F	Y	Y	0.7/0.4	3/6	2.3E-03	1.2E-02	20% through urine. Many metabolites	N
prochloraz	F	N	Y	1.75	6	1.5E-01	2.3E-01	15-44% through urine. 2,4,6-trichlorophenoxyacetic acid is a major urinary metabolite	Y (2,4,6-trichlorophenoxyacetic acid)
prothioconazole	F	N	Y	0.4	3	4.0E-04	3.2E+00	Mainly excreted as parent through faeces. % urine? Desthio + several others	Y (prothioconazole-desthio)
tebuconazole	F	Y	Y	1.5/1.75	4	1.3E-03	3.7E-01	15-35% through urine. OH-metabolite has been used as biomarker in human urine	N
trifloxystrobin	F	Y	Y	0.3	5	3.4E-03	5.0E-03	15-20% through urine, the acid is a major urinary metabolite	Y (Trifloxystrobin acid, CGA 321113)

Appendix 2: Determination of pesticide in air samples

Outdoor and indoor air samples analyzed for pesticide content using the same chemical analysis procedure For the determination of the pesticides the XAD[1]-2 and glass filter were transferred from the holder to the cells of the "accelerated solvent extraction" system (Thermo Fisher Scientific). A mix of Deuterium labelled pesticides was added to the samples to act as an internal standard. Analytical reference standards were purchased from the LGC, Sigma or Santa-cruz. The reference standards (solid or liquid) were dissolved in methanol or acetonitrile in a concentration of 1000 mg/L. From this, a mixture of 46 compounds (pesticides metabolites and isomers) was prepared in methanol at concentrations of 10 mg/L. The pesticide mixture was used for addition to blank XAD-2 as a quality control in the analysis. The pesticide mixture was diluted for assessment of linearity and response. The pesticide mixture was diluted in Ultra-pure water and methanol (50:50) in concentrations of 0, 1, 2, 5, 10, 20 50, 70, 100, 200 and 500 ng/ml corresponding to a concentrations in 100 m^3 air.

In each batch of samples, a reagent blank and a quality control sample were included. A dilution of the pesticide mixture, final concentration of 1 mg/L, was used for addition of 5 ng/pesticide to blank XAD-2 as a quality control in the analysis.
The "accelerated solvent extraction" system heated the cell with sample and a methanol acetonitrile (2/8) mixture to 75˚C for 20 minutes and this was repeated 3 times. De extracts were collected in a glass jars concentrated in a rotary evaporator system (45˚C , 117 mbar) to a low volume that was further concentrated under a nitrogen flow at room temperature to a fixed volume of 1 ml methanol. From this extract a 50 µl aliquot of the methanol extract was diluted with 50 µl ultra-pure water for instrumental analysis.

The instrumental analysis was performed on a Agilent technologies instrument, a 1260 series Liquid chromatography system coupled to a 6460 triple quadrupole mass spectrometer (LC-MS/MS) by injection of 5 µl onto a Kinetex 2.6 µm Biphenyl 100 Ă 100x2.1 mm column (Phenomenex), maintained at 60˚C. Gradient elution was performed at a flow rate of 0.5 ml/min., using a water/methanol gradient containing 5 mM ammonium formate and 20 µl/L formic acid. MS/MS measurement was performed using Electron Spray Ionisation (ESI) in positive mode (except fludioxonil, negative mode), acquiring at least two transitions for each pesticide/metabolite. A 6-point calibration curve was used for quantification of the concentration of pesticides. Extracts with responses exceeding the linear range of the corresponding pesticide were diluted so the remaining response was within the linear range. The concentrations in the filter/XAD extracts were converted into ng/m^3 air using the actual, measured, volume of air loaded onto the filter/XAD combination. Setting of the LC-MS/MS set up are provided in Table 1.

[1] In all cases XAD-2 was used.

In-house validation and on-going analytical quality control was done according to EU guidance document SANTE/11945/2015 (currently SANTE/11813/2017). LODs were 0.003 ng/m3 for most pesticides, 0.006-0.03 ng/m^3 for six pesticides, four pesticides could only be determined reporting an indicative result (Table 2) based upon the average sample volume of air used in field sampling. Trueness was assessed through recovery. The average recoveries of the pesticides were typically in the range 50-150%. Within laboratory reproducibility (relative standard deviation, RSD_{wl}) was generally around 20% at the 0.05 ng/m^3 level. All measurements were carried out using our quality system that satisfies ISO 9001.

Table 1: LC-MS/MS settings determination of pesticides in air.

Eluents	A: 5 mM ammonium formate in ultra pure water + 20 µl/ L 100% formic acid B: 5 mM ammonium formate in methanol + 20 µl/ L 100% formic acid	
Gradient	0	10% B
	10	90% B
	13	90% B
	13.1	10% B
	15	10% B
Flow	0.5 mL/min	
Column	Phenomenex Kinetex 2.6 µm Biphenyl 100 Ă 100x2.1 mm	
Column temperature	60 °C	
Injection volume	5 µl	

MS/MS settings

Source parameters Agilent Jet Stream ESI:

Parameter	**Value (+)**	**Value (-)**
Gas Temp (°C)	300	300
Gas Flow (l/min)	7	7
Nebulizer (psi)	45	45
SheathGasHeater	400	400
SheathGasFlow	12	12
Capillary (V)	3500	-3500
VCharging	0	0

dMRM settings Agilent 6460

Pesticide Name		Precursor	Product (V)	Frag (V)	CE Acc (V)	Cell (min)	Rt Window (min)	Rt	Polarity
acetamiprid	Quan	223	126	106	20	2	6.66	2	Positive
acetamiprid	Qual	223	90.1	106	40	2	6.66	2	Positive
acetamiprid-d4	Quan	226	126	100	20	2	6.65	2	Positive
acetamiprid-d4	Qual	226	90	100	40	2	6.65	2	Positive
asulam	Qual	231	155.9	106	8	2	1.6	2	Positive
asulam	Qual	231	92.1	106	24	2	1.6	2	Positive
asulam-d3	Qual	234	155.8	106	8	2	1.6	2	Positive
asulam-d3	Qual	234	92.1	106	24	2	1.6	2	Positive
azoxystrobin	Qual	404	372.1	106	12	2	10.4	2	Positive
azoxystrobin	Qual	404	344.1	106	24	2	10.4	2	Positive
boscalid	Qual	343	306.9	126	20	2	9.63	2	Positive
boscalid	Qual	343	139.8	126	20	2	9.63	2	Positive
carbendazim	Quan	192	160	106	16	1	5.5	2	Positive
carbendazim	Qual	192	132	106	36	1	5.5	2	Positive
carbendazim-d4	Qual	196	163.9	106	16	1	5.49	2	Positive
carbendazim-d4	Qual	196	135.9	106	36	1	5.49	2	Positive
chloridazon	Qual	222	77.1	126	40	1	5.59	2	Positive
chloridazon	Qual	222	65.1	126	44	1	5.59	2	Positive
chlorpropham	Quan	214	172	60	4	2	8.7	2	Positive
chlorpropham	Qual	214	153.9	60	16	2	8.7	2	Positive
cyhalotrin-lambda (NH4)	Qual	467	224.8	86	12	1	11.9	2	Positive
cyhalotrin-lambda (NH4)	Qual	467	140.9	86	52	1	11.9	2	Positive
cyprodinil	Qual	226	93.1	146	40	1	10.1	2	Positive
cyprodinil	Qual	226	77.1	146	56	1	10.1	2	Positive
deltamethrin (NH4)	Qual	523	280.7	106	12	1	12.4	2	Positive
deltamethrin (NH4)	Qual	523	180.9	106	44	1	12.4	2	Positive
desisopropylatrazine-d5	Qual	179	101.1	126	20	1	3.47	2	Positive
desisopropylatrazine-d5	Qual	179	69.1	126	36	1	3.47	2	Positive
dichloorvos-d6	Quan	227	115	106	16	2	6.78	2	Positive
dichloorvos-d6	Qual	227	83	106	32	2	6.78	2	Positive
difenoconazol	Quan	406	251	126	28	1	11.3	2	Positive
difenoconazol	Qual	406	188	126	52	1	11.3	2	Positive
dimethenamid-P	Quan	276	244	80	12	1	9.52	2	Positive
dimethenamid-P	Qual	276	168	80	24	1	9.52	2	Positive
dimethomorph	Quan	388	301	146	20	1	10	3	Positive
dimethomorph	Qual	388	165	146	36	1	10	3	Positive
diuron-d6	Qual	239	78.1	106	24	1	7.7	2	Positive
diuron-d6	Qual	239	52.1	106	16	1	7.7	2	Positive
flonicamid	Qual	230	148	106	28	2	2.9	3	Positive
flonicamid	Qual	230	98.1	106	44	2	2.9	3	Positive

floupyram-benzamide	Qual	190	170	80	8	1	4.08	2	Positive
floupyram-benzamide	Qual	190	130.1	80	20	1	4.08	2	Positive
fludioxonil	Quan	247	180	-146	28	1	8.62	2	Negative
fludioxonil	Qual	247	126	-146	32	1	8.62	2	Negative
fluopicolide	Qual	385	174.9	106	24	2	9.64	2	Positive
fluopicolide	Qual	385	146.9	106	60	2	9.64	2	Positive
fluopyram	Quan	397	173	106	32	1	9.4	2	Positive
fluopyram	Qual	397	145	106	60	1	9.4	2	Positive
flutolanil	Qual	324	262.1	106	16	1	9.3	2	Positive
flutolanil	Qual	324	242.1	106	24	1	9.3	2	Positive
fosthiazate	Qual	284	228	80	4	2	8.51	2	Positive
fosthiazate	Qual	284	104.1	80	20	2	8.51	2	Positive
imidacloprid	Qual	256	209.1	80	12	1	6.2	2	Positive
imidacloprid	Qual	256	175.1	80	16	1	6.2	2	Positive
imidacloprid-d4	Quan	260	213	100	12	1	6.19	2	Positive
imidacloprid-d4	Qual	260	179.1	100	16	1	6.19	2	Positive
isoproturon-d6	Qual	213	78.1	106	20	1	7.99	2	Positive
isoproturon-d6	Qual	213	52.1	106	16	1	7.99	2	Positive
kresoxim-methyl	Qual	314	267.1	80	4	1	10.6	2	Positive
kresoxim-methyl	Qual	314	222.1	80	12	1	10.6	2	Positive
linuron	Qual	249	159.9	86	16	2	8.46	2	Positive
linuron	Qual	249	133	86	36	2	8.46	2	Positive
mepanipyrim	Qual	224	106.1	126	28	1	9.71	2	Positive
mepanipyrim	Qual	224	77.1	126	44	1	9.71	2	Positive
metamitron	Qual	203	175.1	106	16	1	5.54	2	Positive
metamitron	Qual	203	42.1	106	36	1	5.54	2	Positive
metamitron-desamino	Quan	188	160	106	16	1	4.73	2	Positive
metamitron-desamino	Qual	188	77.1	106	36	1	4.73	2	Positive
metolachlor-S	Qual	284	252.1	100	12	1	10.1	2	Positive
metolachlor-S	Qual	284	176.1	100	28	1	10.1	2	Positive
oxamyl	Qual	237	90.1	60	4	1	4.36	2	Positive
oxamyl	Qual	237	72.1	60	12	1	4.36	2	Positive
pendimethalin	Quan	282	212	80	8	1	11.6	2	Positive
pendimethalin	Qual	282	43.1	80	32	1	11.6	2	Positive
pendimethalin-d5	Qual	287	213.1	80	8	1	11.6	2	Positive
pendimethalin-d5	Qual	287	46.1	80	36	1	11.6	2	Positive
pirimicarb-d6	Qual	245	185.1	100	12	2	8.54	2	Positive
pirimicarb-d6	Qual	245	78.1	100	20	2	8.54	2	Positive
pirimicarb	Qual	239	182.1	106	12	2	8.55	2	Positive
pirimicarb	Qual	239	72.1	106	24	2	8.55	2	Positive
prochloraz	Quan	376	308	80	8	1	10.9	2	Positive
prochloraz	Qual	376	70.1	80	28	1	10.9	2	Positive
propamocarb	Qual	189	102.1	80	16	1	3.5	3.5	Positive
propamocarb	Qual	189	74.1	80	28	1	3.5	3.5	Positive

propamocarb-d7	Qual	196	103.1	100	16	1	3.3	3.5	Positive
propamocarb-d7	Qual	196	75.1	100	28	1	3.3	3.5	Positive
propyzamid-d3	Quan	260	194	80	12	2	8.74	2	Positive
propyzamid-d3	Qual	260	44	80	28	2	8.74	2	Positive
prothioconazol	Quan	344	326	80	8	1	9.86	2	Positive
prothioconazol	Qual	344	125.1	80	44	1	9.86	2	Positive
prothioconazole-desthio	Qual	312	124.9	146	40	1	9.79	2	Positive
prothioconazole-desthio	Quan	312	70	146	24	1	9.79	2	Positive
pymetrozine	Qual	218	105.1	106	20	1	4.99	2	Positive
pymetrozine	Qual	218	78.1	106	48	1	4.99	2	Positive
pyraclostrobin	Qual	388	194.1	100	8	1	11.2	2	Positive
pyraclostrobin	Qual	388	163	100	28	1	11.2	2	Positive
simazine-d10	Qual	212	105	126	28	2	6.84	2	Positive
simazine-d10	Quan	212	44	126	44	2	6.84	2	Positive
spirotetramat	Qual	374	302.2	106	16	1	10.1	2	Positive
spirotetramat	Qual	374	216.1	106	36	1	10.1	2	Positive
spirotetranat-enol	Qual	302	270.1	164	20	2	7.73	2	Positive
spirotetranat-enol	Qual	302	216.1	164	28	2	7.73	2	Positive
sulcotrione	Qual	329	138.9	146	16	2	5	3	Positive
sulcotrione	Qual	329	110.9	146	32	2	5	3	Positive
tebuconazole	Qual	308	125	106	40	1	9.82	2	Positive
tebuconazole	Qual	308	70.1	106	24	1	9.82	2	Positive
tebuconazole-d9	Qual	317	125.3	126	48	1	9.81	2	Positive
tebuconazole-d9	Quan	317	70	126	24	1	9.81	2	Positive
terbutylazine	Quan	230	174	106	16	2	8.71	2	Positive
terbutylazine	Qual	230	79.1	106	28	2	8.71	2	Positive
terbutylazine-d5	Qual	235	179.1	106	16	2	8.7	2	Positive
terbutylazine-d5	Qual	235	69.1	106	44	2	8.7	2	Positive
thiacloprid	Quan	253	126	106	20	2	7.4	2	Positive
thiacloprid	Qual	253	90.1	106	44	2	7.4	2	Positive
thiophanate-methyl	Quan	343	151	100	20	2	8.01	2	Positive
thiophanate-methyl	Qual	343	118.1	100	60	2	8.01	2	Positive
toclofos-methyl	Qual	301	174.6	126	20	1	10.7	2	Positive
toclofos-methyl	Qual	301	124.9	126	12	1	10.7	2	Positive
trifloxystrobin	Quan	409	186	106	16	2	11.1	2	Positive
trifloxystrobin	Qual	409	145	106	52	2	11.1	2	Positive
trifloxystrobin acid	Quan	395	186	100	16	2	8.78	2	Positive
trifloxystrobin acid	Qual	395	145	100	52	2	8.78	2	Positive

Table 2: List of pesticides/metabolites determined in air samples and reporting Limits.

Component	LOQ (ng/m3)	Component	LOQ (ng/m3)
acetamiprid	0.01	mepanipyrim	0.01
asulam	Qual	metamitron	0.01
azoxystrobin	0.01	metamitron-desamino	0.01
boscalid	0.01	metolachlor-S	0.02
carbendazim	0.01	oxamyl	0.01
chloridazon	0.01	pendimethalin	0.01
chlorpropham	0.03	pirimicarb	0.01
cyhalotrin-lambda (NH4)	0.10	prochloraz	0.01
cyprodinil	0.01	propamocarb	0.01
deltamethrin (NH4)	0.02	prothioconazol	Qual
difenoconazol	0.01	prothioconazole-desthio	0.01
dimethenamid-P	0.01	pymetrozine	0.01
		pyraclostrobin	0.01
dimethomorph	0.01	spirotetramat	0.03
flonicamid	0.01	spirotetranat-enol	0.01
floupyram-benzamide	0.01	sulcotrione	Qual
fludioxonil	0.03	tebuconazole	0.01
fluopicolide	0.01	terbutylazine	0.01
fluopyram	0.01	thiacloprid	0.01
flutolanil	0.01	thiophanate-methyl	Qual
fosthiazate	0.01	toclofos-methyl	0.01
imidacloprid	0.01	trifloxystrobin	0.01
kresoxim-methyl	0.01	trifloxystrobin acid	0.01
linuron	0.01		

qual = not fit for quantitative analysis.

Appendix 3: Analyses of other environmental samples

Determination of the pesticides in dust samples.

For determination of the pesticides in the dust samples, a multi-residue method was used based on QuEChERS extraction (Lehotay 2007) and liquid chromatography with tandem mass spectrometry. This way, all 46 selected pesticides and relevant metabolites could be measured simultaneously by one analysis.

Analytical reference standards were purchased from LGC or Sigma. Stock solutions were prepared in methanol or acetonitrile at concentrations of 2 mg/ml. A pesticide mix solution of 1 µg/ml was prepared in methanol. Intermediate dilutions for spiking of the samples, extracts, and preparation of working standards were made in methanol. A series of calibration standards for assessment of linearity of response was prepared by dilutions of the intermediate solutions in water: acetonitrile/1% acetic acid (50:50), concentrations 0, 0.125, 0.25, 0.50, 0.75, 2.5, 6.25, 12.5 ng/ml, corresponding to 0.5-50 µg/kg dust).

With each batch of samples, a reagent blank and a positive control were included. The positive control was prepared by spiking a 1 g subsample from a batch of control dust at 10 or 50 µg/kg.

For analysis, the dust material from the sample sock was transferred into an extraction tube. For extraction, 2 ml water/g dust and 4 ml of acetonitrile/1% acetic acid/g dust were added. The pesticides were extracted from the dust by mechanical shaking for 30 min. Then 0.8 g magnesium sulfate and 0.2 g sodium acetate per g dust material were added and the mixture thoroughly shaken to induce phase partitioning. Two ml of the acetonitrile layer was concentrated to 1.0 ml under a nitrogen flow at 40°C. From this extract, 0.25 ml aliquots were transferred into two filter vials. To the second vial a mix-standard solution of the 46 pesticides was added such that a concentration in final extract corresponding to 10 or 50 µg/kg dust was obtained. To both vials water was added to reach a total extract volume of 0.50 ml.

LC-MS/MS analysis was performed on a Waters Acquity UPLC system coupled to a Sciex API6500 Qtrap tandem mass spectrometer by injection of 5 µl onto a 100 x 2.1 mm ID 1.8 µm HSS T3 column (Waters), maintained at 40°C. Gradient elution was performed at a flow rate of 0.4 ml/min, using a water/methanol gradient, containing 5 mM ammonium formate/0.1% formic acid. MS/MS measurement was done using electrospray ionisation (ESI) in positive mode (except fludioxonil, negative mode), acquiring two transitions for each pesticide/metabolite (details see below in Table 1). Quantification was performed using the standard addition method (1-point calibration against the spiked extract of each individual sample, at the level corresponding to 10 or 50 µg/kg) in order to compensate for matrix effects/ion suppression. So, analysis of each sample involved two injections, one of the extract without, and one of the extract with pesticide addition. In case the level of the pesticide in the sample extract

exceeded the standard-addition spike level (response extract + spike less than 2x response extract without spike), or exceeded the linear range of response, dilutions of the remaining concentrated extract were made, again in two vials, one without and one with standard addition.

In-house validation and on-going analytical quality control was done according to EU guidance document SANTE/11945/2015 (currently SANTE/11813/2017). LOQs were 1 µg/kg for most pesticides, 3-20 µg/kg for nine pesticides (see below in Table 2). Trueness was assessed through recovery. The average recoveries of the pesticides were typically in the range 70-110%. RSD_{wl} was generally around 20% at the 10µg/kg level, and <20% at the 50 µg/kg level.

Determination of the pesticides in soil and crops

For determination of the pesticides in the soil and plant material, a multi-residue method was used based on QuEChERS extraction (Lehotay 2007) and liquid chromatography with tandem mass spectrometry. This way, all 46 selected pesticides and relevant metabolites could be measured simultaneously by one analysis.

Analytical reference standards were purchased from LGC or Sigma. Stock solutions were prepared in methanol or acetonitrile at concentrations of 2 mg/ml. A pesticide mix solution of 1 µg/ml was prepared in methanol. Intermediate dilutions for spiking of the samples, extracts, and preparation of working standards were made in methanol. A series of calibration standards for assessment of linearity of response was prepared by dilutions of the intermediate solutions in water:acetonitrile/1% acetic acid (50:50), concentrations 0, 0.125, 0.25, 0.50, 0.75, 2.5, 6.25, 12.5 ng/ml, corresponding to 0.5-50 µg/kg soil or plant material).

With each batch of samples, a reagent blank and a positive control were included. The positive control was prepared by spiking 5 g of a blank soil or plant material sample at 10 µg/kg.

For analysis of soil and plant material, 5 gram was extracted with 10 ml of acetonitrile/1% acetic acid by mechanical shaking for 30 min. Then 4 g magnesium sulfate and 1 g sodium acetate were added and the mixture thoroughly shaken to induce phase partitioning. An aliquot of the upper acetonitrile layer was diluted 1:1 with water in a filter vial.

LC-MS/MS measurement was performed as described above for dust. Quantification was performed using 1-point bracketing matrix-matched calibration (2.5 ng/ml extract, corresponding to 10 µg/kg sample) in order to compensate for matrix effects/ion suppression. In case the response of the pesticide in the sample extract exceeded the linear range, dilutions were made and extracts re-analyzed.

In-house validation and on-going analytical quality control was done according to EU guidance document SANTE/11945/2015 (currently SANTE/11813/2017). LOQs were 1 µg/kg for most pesticides, 3-10 µg/kg for some pesticides (see below in Table 2). Trueness was assessed through recovery. The average recoveries of the pesticides were typically in the range 70-110%. Within laboratory reproducibility (relative standard deviation) was generally <20% at the 10 µg/kg level.

Table 1: LC-MS/MS settings determination of pesticides in dust, soil, crops.

Eluents	A: 5 mM ammonium formate in MilliQ water + 0,1% formic acid B: 5 mM ammonium formate in methanol/MilliQ water (95/5 v/v) + 0.1% formic acid	
Gradient	0	0% B
	1	0% B
	2.5	45% B
	8.5	100% B
	11.5	100% B
	12	0% B
	14	0%B
Flow	0.4 mL/min	
Column	Waters HSS T3 (1.7 µm particles, 100 × 2.1 mm)	
Column temperature	40 °C	
Injection volume	5 µl	

MS/MS settings

Source parameters:

Ion Source gas 1: (GS1)	60
Ion Source gas 2: (GS2):	60
Curtain gas (CUR):	35
Ionspray voltage (IS):	4000
Source temperature (TEM):	500

MRM settings 6500 Qtrap

Pesticide name	tr (min)	Precursor	Product	DP	EP	CE	CXP
Acetamiprid (qn)	4.3	223	126	51	10	29	10
Acetamiprid (ql)	4.3	223	73	51	10	79	12
Asulam (qn)	3.0	231	156	60	10	15	12
Asulam (ql)	3.0	231	92	60	10	34	12
Azoxystrobin (qn)	6.2	404.2	372.3	66	10	21	10
Azoxystrobin (ql)	6.2	404.2	344.1	66	10	35	20
Boscalid (qn)	6.4	343.1	306.8	96	10	29	18
Boscalid (ql)	6.4	343.1	139.9	96	10	29	12
Carbendazim (qn)	3.8	192	160	106	10	25	16
Carbendazim (ql)	3.8	192	132	106	10	45	18
Chloridazon (qn)	4.4	222	65	116	10	53	14
Chloridazon (ql)	4.4	222	51	116	10	93	20
Chlorpropham (qn)	6.5	214	171.9	25	10	13	6
Chlorpropham (ql)	6.5	214	153.9	25	10	25	14
Cyhalothrin-Lambda (qn)	7.7	467.1	225	36	10	23	12
Cyhalothrin-Lambda (ql)	7.7	469.1	227	36	10	23	12
Cyprodinil (qn)	7.0	226.2	77	96	10	67	12
Cyprodinil (ql)	7.0	226.2	93	96	10	47	36
Deltamethrin (qn)	7.8	522.9	280.7	36	10	23	25
Deltamethrin (ql)	7.8	524.9	282.7	36	10	23	25
Difenoconazole (qn)	7.2	406	251	136	10	39	26
Difenoconazole (ql)	7.2	406	337	136	10	25	26
Dimethenamid (qn)	6.4	276.1	168.1	66	10	35	10
Dimethenamid (ql)	6.4	276.1	244	66	10	41	34
Dimethomorph (qn)	6.4	388	301	60	10	37	12
Dimethomorph (ql)	6.4	388	165	60	10	37	12
Flonicamid (qn)	3.5	230.1	203.1	55	10	35	4
Flonicamid (ql)	3.5	230.1	174	55	10	35	4
Fludioxonil (qn)	6.3	247	179.9	-60	-10	-40	-9
Fludioxonil (ql)	6.3	247	169	-60	-10	-42	-12
Fluopicolide (qn)	6.5	383	173	60	10	60	37
Fluopicolide (ql)	6.5	383	145	60	10	75	12
Fluopyram (qn)	6.6	396.9	207.9	56	10	29	14
Fluopyram (ql)	6.6	396.9	172.9	56	10	37	12
Fluopyram benzamide (qn)	4.0	190	129.8	60	10	27	8
Fluopyram benzamide (ql)	4.0	190	169.9	60	10	15	10
Flutolanil (qn)	6.4	324.2	242.1	60	10	37	12
Flutolanil (ql)	6.4	324.2	262.1	60	10	26	12
Fosthiazate (qn)	5.7	284	104.1	61	10	27	13
Fosthiazate (ql)	5.7	284	227.8	61	10	27	15
Imidacloprid (qn)	4.0	256.1	209	41	10	21	14
Imidacloprid (ql)	4.0	256.1	175.1	41	10	25	12
Kresoxim-Methyl (qn)	6.9	314.1	115.9	36	10	21	25
Kresoxim-Methyl (ql)	6.9	314.1	206.1	36	10	13	25
Linuron (qn)	6.3	249	160	101	10	27	16

Linuron (ql)	6.3	249	182	101	10	23	18
Mepanipyrim (qn)	6.7	224	106.3	60	10	37	12
Mepanipyrim (ql)	6.7	224.1	77.3	60	10	37	12
Metamitron (qn)	4.3	203	175	60	10	30	12
Metamitron (ql)	4.3	203	104	60	10	30	12
Metamitron-desamino (qn)	4.3	188	160	41	10	25	12
Metamitron-desamino (ql)	4.3	188	103.9	41	10	31	8
Metolachlor (qn)	6.8	284	252	60	10	26	12
Metolachlor (ql)	6.8	284	176	60	10	37	20
Oxamyl (qn)	3.3	237	72	21	10	25	30
Oxamyl (ql)	3.3	237	90	21	10	13	16
Pendimethalin (qn)	7.7	282.2	212.1	61	10	17	12
Pendimethalin (ql)	7.7	282.2	194.1	61	10	27	12
Pirimicarb (qn)	5.4	239.2	72	71	10	37	12
Pirimicarb (ql)	5.4	239.2	182.1	71	10	23	12
Prochloraz (qn)	7.1	376	308	36	10	17	25
Prochloraz (ql)	7.1	376	265.9	36	10	23	25
Propamocarb (qn)	3.0	189.3	102	76	10	25	18
Propamocarb (ql)	3.0	189.3	144	76	10	19	14
Prothioconazole	6.9	344	125	66	10	39	12
Prothioconazole (ql)	6.9	344	189.1	66	10	27	12
Prothioconazole-desthio (qn)	6.8	311.9	125	36	10	57	10
Prothioconazole-desthio (ql)	6.8	311.9	70	36	10	83	55
Pymetrozine (qn)	3.0	218	105	80	10	27	12
Pymetrozine (ql)	3.0	218	79	80	10	47	12
Pyraclostrobin (qn)	7.1	388	194	81	10	19	10
Pyraclostrobin (ql)	7.1	388	163	81	10	33	16
Spirotetramat (qn)	6.7	374	216	60	10	49	12
Spirotetramat (ql)	6.7	374.2	330	60	10	22	12
Spirotetramat-enol (qn)	5.8	302.1	216	71	10	39	13
Spirotetramat-enol (ql)	5.8	302.1	270.1	71	10	29	13
Sulcotrione (qn)	5.0	331	139	60	10	33	12
Sulcotrione (ql)	5.0	329	139	60	10	45	12
Tebuconazole (qn)	6.9	308.1	70	41	10	39	14
Tebuconazole (ql)	6.9	308.1	124.9	41	10	47	25
Terbutylazine (qn)	6.4	230	174	60	10	23	12
Terbutylazine (ql)	6.4	232	176	60	10	23	12
Thiacloprid (qn)	4.6	253	126	90	10	29	15
Thiacloprid (ql)	4.6	253	90	90	10	49	12
Thiophanate-methyl (qn)	5.3	343	151	96	10	30	14
Thiophanate-methyl (ql)	5.3	343	268	60	10	15	12
Tolclofos-methyl (qn)	7.1	301	125	60	10	27	12
Tolclofos-methyl (ql)	7.1	301	175	60	10	42	12
Trifloxystrobin(qn)	7.2	409.1	186.1	31	10	23	25
Trifloxystrobin (ql)	7.2	409.1	206.1	31	10	21	25
Trifloxystrobin acid (qn)	6.8	394.9	185.9	60	10	23	4
Trifloxystrobin acid (ql)	6.8	394.9	144.9	60	10	61	4

Table 2: List of pesticides/metabolites determined in crops, soil, dust and reporting Limits.

	Reporting limit (RL) in µg/kg		
Pesticide	**crop (veg/fruit)**	**soil**	**dust**
acetamiprid	1	1	1
asulam	1	1	1
azoxystrobin	1	1	1
boscalid	1	1	1
carbendazim	1	1	1
chloridazon	1	1	1
chlorpropham	10 (qual 3)	3	~20
cyprodinil	1	1	3 (qual 1)
deltamethrin	10	10	qual 10
difenoconazole	1	1	1
dimethenamide-P	1	1	1
dimethomorph	1	1	1
flonicamid	1	1	3
fludioxonil	1	1	1
fluopicolide	1	1	1
fluopyram	1	1	1
fluopyram-benzamide	1-3	1	1
flutolanil	1	1	1
fosthiazate	1	1	1
imidacloprid	1	1	1
kresoxim-methyl	1-3	3 (qual 1)	10 (qual 3)
lambda-cyhalothrin	10 (qual 3)	3	~20 (qual 10)
linuron	1	1	1
mepanipyrim	1	1	1
metamitron	1	1	10 (qual 3)
metamitron-desamino	1	1	1
metolachlor-S	1	1	1
oxamyl	1	1	1
pendimethalin	1	1	1
pirimicarb	1	1	1
prochloraz	1	1	1
propamocarb	1	1	1
prothioconazole	not suited	only qual	not suited
prothioconazole-desthio	1	1	3
pymetrozine	1	1	1
pyraclostrobin	1	1	1
spirotetramat	1	1	1
spirotetramat-enol	1	1	1
sulcotrione	1-3	1	10 (qual 3)
tebuconazole	1-3	1	1
terbuthylazine	1	1	1
thiacloprid	1	1	1
thiophanate-methyl	1	only qual	3 (qual 1)
tolclofos-methyl	1	1	10
trifloxystrobin	1	1	1
trifloxystrobin acid	1	1	1

*reporting limit is LOQ (lowest successfully validated level) and LOD where 'qual' is mentioned.

Appendix 4: Analysis methods for pesticide biomarkers in urine

Determination of TEB-OH (biomarker for tebuconazole)

Stock solutions of TEB-OH and the internal standard (D6-TEB-OH) were prepared in methanol at concentrations of 2 mg/mL. Working solutions of 1000 ng/mL and 100 ng/mL were prepared in 95% of water and 5% of methanol (% v/v). All standards were stored at -20 °C in the dark. A calibration curve of TEB-OH, ranging from 0.05 to 25 ng/mL, including a blank urine, was prepared in a mixture of three randomly provided urine samples, by adding suitable amounts of the working solutions to aliquots of the urine. Each calibration standard was prepared equally as samples were, including addition of the internal standard.
With each batch of samples, the calibration curves, and blank acetonitrile and milliQ were freshly prepared and measured three times during the batch analysis to conform the stability of the system.

All specimens were thawed at room temperature prior to sample preparation. An aliquot of 5 mL of urine was transferred to an Erlenmeyer, and 50 µL of the internal standard working solution was added, resulting in a 1 ng/mL concentration of D6-TEB-OH in urine. For deconjugation purposes, 5 µL of *Helix pomatia* β-glucuronidase/arylsulfatase was dissolved per 2.5 mL acetic acid solution in H2O (0.25 M, pH 4.75), and 2.5 mL of this mixture was added to each sample. The samples were incubated overnight for at least 16 h at 37 °C under gentle agitation, and then a subzero-temperature liquid-liquid extraction was performed as previously described by Yoshida and Akane (1999). Briefly, the samples were first centrifuged at 1800 RCF, and 1 mL of the supernatant was transferred to a test tube. An aliquot of three mL of acetonitrile was added, mixed and placed at -20 °C for 20 min to separate the organic layer from the aqueous layer. One mL of the organic layer was transferred to a vial for subsequent LC-MS/MS analysis.

For the quantification of TEB-OH, an aliquot of 2.5 µL of each sample was analyzed on a Waters Acquity LC-MS/MS system via positive electrospray ionization. The chromatographic separation was performed on a Waters BEH C18 column. The MS was operated in multiple reaction monitoring (MRM) mode. The mass transition selected for quantification of TEB-OH was 325.02 -> 69.96 (collision energy (CE) 20 eV), and for qualification 325.02 -> 124.97 (CE 40eV). The LOQ for TEB-OH was 0.05 ng/mL.

In-house validation and on-going analytical quality control was done according to SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for TEB-OH was 0.05 ng/ml in urine. As for the other pesticides/biomarkers quantification was matrix-matched based on the calibration curve, and matrix-effects were found to vary considerable for different urine samples, these could only be semi-quantitatively determined. Moreover, no labelled standards were included for these compounds. Estimated LODs were 0.05 ng/ml for, metamitron-desamino, spirotetramat-enol, trifloxystrobin-acid and boscalid-OH (M150F01).

Determination of 4-HSA (biomarker for chlorpropham)

4-HSA is a sulfate-conjugate of chlorpropham and most sensitively detected as such, so without deconjugation. The analytical standard (4-HSA potassium salt) was an existing standard available at RIKILT (previously obtained through TNO, Zeist, originally synthesised by Mercachem BV, the Netherlands). The internal standard was D7-4-HSA sodium salt purchased from Toronto Research Chemicals (Toronto, Canada). The boscalid metabolite (M150F01) was a kind gift of CVUA Stuttgart, Germany. Hydroxy-carbendazim (5-HBC) was purchased as custom synthesized compound through Akos (Steinen, Germany). The other pesticides/biomarkers and D3-asulam were purchased from LGC and Sigma. Stock solutions were prepared in methanol at concentrations of 2 mg/ml. A pesticide/biomarker mix solution of 10 µg/ml was prepared in milliQ water. A mix internal standard solution of 0.1 µg/ml isotope labels of 4-HSA and asulam was prepared in milliQ water. Working standards were prepared by further dilution in water. Procedural calibration standards, undergoing the same procedures as the samples, were prepared in blank urine, by addition of 5-100 µl of (intermediate) mix standard and isotope standard to 0.8-0.9 ml of urine (0, 0.05, 0.1, 0.5, 1, 2, 5, and 10 ng/ml urine; isotope labels at 10 ng/ml).

With each batch of samples, a reagent blank (milliQ water) and a positive control were included. The positive control was prepared by spiking one of the samples from the batch with the pesticide/biomarker mix at 2 ng/ml urine.

For sample analysis, urine was thawed and re-homogenized by vortex mixing. A 0.9 ml aliquot was mixed with 0.1 ml of internal standard solution and transferred into a Amicon 30kDa Ultra-centrifuge filter (10 min, 3500xg). The filtrate was transferred into an auto sampler filter vial for LC-MS/MS analysis.

LC-MS/MS analysis was performed on a Waters Acquity UPLC system coupled to a Waters Xevo TQS tandem mass spectrometer by injection of 20 µl onto a 100 x 2.1 mm ID 1.7 µm HSS T3 column (Waters), maintained at 45°C. Gradient elution was performed at a flow rate of 0.4 ml/min, using a water/methanol gradient, containing 2 mM ammonium formate, 1 mM ammonium fluoride, and 20 µl/l formic acid. MS/MS measurement was done using ESI in both negative and positive mode (time-segmented), acquiring two transitions for each pesticide/ biomarker. 4-HSA was measure as [M-H]- using transitions m/z 308>141 and 310>143 (for D7-4-HSA 315>141 and 317>143). The response of 4-HSA in samples and calibrants in blank urine was normalised to the response of the D7-4-HSA internal standard. Quantification was then done using 1-point (2 ng/ml) bracketing matrix-matched calibration. Concentrations outside the linear range, as established with each batch of analysis through the procedural calibration standards, were diluted and re-analysed.

In-house validation and on-going analytical quality control was done according to SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for 4-HSA was 0.1 ng/

ml urine. With this method, asulam could also be quantitatively determined, with an LOQ of 1 ng/ml (for more sensitive determination of asulam see the dedicated method described below). As for the other pesticides/biomarkers quantification was matrix-matched based on one urine sample, and matrix-effects were found to vary considerable for different urine samples, these could only be semi-quantitatively determined. Estimated LODs were 0.1 ng/ml for imidacloprid, flonicamid, metamitron-desamino, trifloxystrobin-acid, spirotetramat-enol; 0.5 ng/ml for metamitron, boscalid-OH (M150F01), 5-HBC.

The average recovery and within-laboratory precision (RSD_{wl}) as obtained for 2 ng/ml 4-HSA spikes analyzed together with the field samples were 97% and 11%, respectively.

Note: since this method does not include a deconjugation step, it will only determine non-conjugated forms of pesticides metabolites, which in certain cases (especially for boscalid-OH (M150F01) and 5-HBC) are minor urinary metabolites.

Determination of 2,4,6-TCP (biomarker for prochloraz)

Stock solutions of 2,4,6-TCP and the internal standard ($^{13}C_6$-2,4,6-TCP) were prepared in acetonitrile at concentrations of 2 mg/mL. Working solutions of 1000 ng/mL and 100 ng/mL were prepared in pure acetonitrile. All standards were stored at -20 °C in the dark. A calibration curve of 2,4,6-TCP, ranging from 0.25 to 25 ng/mL, including a blank urine, was prepared in a mixture of three randomly provided urine samples, by adding suitable amounts of the working solutions to aliquots of the urine. Each calibration standard was prepared equally as samples were, including addition of the internal standard. With each batch of samples, the calibration curves, and blank acetonitrile and milliQ were freshly prepared and measured three times during the batch analysis to conform the stability of the system.

All specimens were thawed at room temperature prior to sample preparation. An aliquot of 5 mL of urine was transferred to an Erlenmeyer, and 5 µL of the internal standard working solution was added, resulting in a 1 ng/mL concentration of 6C13-2,4,6-TCP in urine. For deconjugation purposes, 5 µL of *Helix pomatia* β-glucuronidase/arylsulfatase was dissolved per 2.5 mL acetic acid solution in H2O (0.25 M, pH 4.75), and 2.5 mL of this mixture was added to each sample. The samples were incubated overnight for at least 16 h at 37 °C under gentle agitation, and then a solid phase extraction (SPE) was performed. Briefly, the SPE column was prepared by washing with 10 mL of 0.1% formic acid in acetonitrole (eluent B) and subsequent with 10 mL of 5% acetonitrile, 0.1% formic acid in water (eluent A). The column was loaded with the deconjugated urine, and the column was washed , in two steps, first with 10 mL of eluent A followed by a solution of 10% eluent B in A. The column was eluted with 5 mL of eluent B. The eluted sample was dried and dissolved in 1 mL of 50% eluent A and 50% eluent B and transferred to a vial for subsequent LC-MS/MS analysis.

For the quantification of 2,4,6-TCP, an aliquot of 2.5 µL of each sample was analyzed on a Waters Acquity LC-MS/MS system via negative electrospray ionization. The chromatographic separation was performed on a Waters BEH C18 column. The MS was operated in MRM mode. The mass transition selected for quantification of 2,4,6-TCP was 252.84 -> 194.81 (CE 10 eV), and for qualification 254.84 -> 196.81 (CE 40eV). The LOQ for 2,4,6-TCP was 0.25 ng/mL.

In-house validation and on-going analytical quality control was done according to SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for 2,4,6-TCP was 0.25 ng/ml in urine. Other pesticides/biomarkers could not be determined with this method as the SPE washing steps, buffers and LC conditions were fully optimized for 2,4,6-TCP to reach an acceptable LOQ.

Determination of asulam (biomarker for asulam)

Asulam is mainly excreted through urine unmetabolized. Therefore, similar as for 4-HSA, no deconjugation step is required. The 4-HSA method turned out to be less sensitive and lacked robustness for determination of asulam, and therefore a separate method needed to be developed.

Stock solutions of the analytical standards (for suppliers see description of the 4-HSA method) were prepared in methanol at concentrations of 2 mg/ml. A pesticide/biomarker mix solution of 10 µg/ml was prepared in milliQ water. A mix internal standard solution of 0.1 µg/ml isotope labels of 4-HSA and asulam was prepared in milliQ water. Working standards were prepared by further dilution in water. Calibration standards were prepared in acetonitrile/1% acetic acid, by addition of 5-100 µl of (intermediate) mix standard and isotope standard to 0.8-0.9 ml to this solvent (0, 0.05, 0.1, 0.5, 1, 2, 5, and 10 ng/ml solvent; isotope labels at 10 ng/ml).

With each batch of samples, two reagent blanks (milliQ water) and two positive controls were included. The positive control was prepared by spiking two samples from the batch with the pesticide/biomarker mix at 2 ng/ml urine.

For sample analysis, urine was thawed and re-homogenized by vortex mixing. The extraction method was based on the QuEChERS approach (Lehotay 2007). An aliquot of 1.8 ml of urine was transferred into a polypropylene extraction tube, 0.2 ml of internal standard solution and 2 ml acetonitrile/1% acetic acid were added. After vortex mixing for 2 min, 1 gram magnesium sulfate and 0.25 g of sodium acetate were added and the tube shaken for phase separation. An aliquot of 0.5 ml of the upper acetonitrile layer was transferred into an auto sampler filter vial for LC-MS/MS analysis.

LC-MS/MS analysis was performed on a Waters Acquity UPLC system coupled to a Waters Xevo TQS tandem mass spectrometer by injection of 5 µl onto a 100 x 2.1 mm ID 1.7 µm HSS T3 column (Waters), maintained at 45°C. Gradient elution was

performed at a flow rate of 0.4 ml/min, using a water/methanol gradient, containing 5 mM ammonium formate/0.1% formic acid. MS/MS measurement was done using ESI in both negative and positive mode (time-segmented), acquiring two transitions for each pesticide/ biomarker. Asulam was measured as [M+H]+ using transitions m/z 231>156 and 231>92 (for D3-asulam: m/z 234>156, 234>92). The response of asulam in samples and calibrants in solvent was normalized to the response of the D3-asulam internal standard. Quantification was then done using 1-point (2 ng/ml) bracketing calibration.

In-house validation and on-going analytical quality control was done according to SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for asulam was 0.1 ng/ml urine. As for the other pesticides/biomarkers quantification was done against solvent standards, and matrix-effects were found to vary considerable for different urine samples, these could only be semi-quantitatively determined. Estimated LODs were 0.1 ng/ml for 4-HSA, imidacloprid, flonicamid, metamitron-desamino, trifloxystrobin-acid, and 0.5 ng/ml for 5-HBC, spirotetramat-enol, metamitron, and boscalid-OH (M150F01).

The average RSD_{wl} as obtained for asulam 2 ng/ml analyzed together with the field samples were 104% and 13%, respectively.

Note: since this method does not include a deconjugation step, it only determines non-conjugated forms of pesticides metabolites, which in certain cases (especially for boscalid-OH (M150F01) and 5-HBC) are minor urinary metabolites.

Determination of 5-HBC (biomarker for carbendazim and thiophanate-methyl)

Thiophanate-methyl is used for bulb disinfection and degrades into carbendazim in the environment. 5-HBC is a urinary biomarker for both thiophanate-methyl and carbendazim. Hence, 5-HBC found in urine may come from either thiophanate-methyl or carbendazim exposure. In urine, 5-HBC is (partially) excreted as conjugates. For the determination of total 5-HBC, a method involving an enzymatic deconjugation step was developed.

Stock solutions of the analytical standards (for source see description of the 4-HSA method) were prepared in methanol at concentrations of 2 mg/ml. A pesticide/ biomarker mix solution of 10 µg/ml was prepared in methanol. Further intermediate dilutions were prepared in milliQ water. A mix internal standard solution of 1 µg/ml isotope labels was prepared in water and contained: 5-HBC (^{13}C-^{15}N; purchased as custom synthesized compound through Akos, Steinen, Germany), D3-asulam, D6-tebuconazole-OH (purchased as custom synthesized compound from Alsachim, Illkirch Graffenstaden, France) and D3-carbendazim. Procedural calibration standards, undergoing the same procedures as the samples, were prepared in blank urine, by addition of 6-600 µl of intermediate mix standard standards and mix-isotope standard

to 3 ml of urine (0, 0.01, 0.05, 0.1, 0.5, 2, 5, and 10 ng/ml urine; isotope labels at 5 ng/ml).

With each batch of samples, one reagent blank (milliQ water) and two positive controls were included. The positive control was prepared by spiking two samples from the batch with the pesticide/biomarker mix at 2 ng/ml urine.

For sample analysis, urine was thawed and re-homogenised by vortex mixing. The extraction method was based on the QuEChERS approach (Lehotay 2007). An aliquot of 3 ml of urine was transferred into a polypropylene extraction tube, 15 µl of internal standard, 1.5 ml of a 0.2 M acetate buffer (pH 4.5), and 15 µl β-glucuronidase/aryl sulfatase Helix Pomatia (Merck, 2 ml solution, 30 U/ml / 60 U/ml, respectively). The mixture was incubated overnight (at least 16 h) in a water bath at 37°C for deconjugation. After cooling to room temperature, the biomarkers were extracted with 6 ml acetonitrile/1% acetic acid by shaking end-over-end for 10 min. Then 4 gram magnesium sulfate and 1 gram sodium acetate were added for phase partitioning, the tube was shaken immediately, and centrifuged 5 minutes at 3500xg.

A 5 ml aliquot of the acetonitrile phase was transferred to a clean tube and evaporated to dryness at 40°C under a flow of nitrogen gas. The residue was reconstituted by subsequent addition of 100 µl of methanol and 400 µl of milliQ water (vortex after each addition). The concentrated extract was transferred into an auto sampler filter vial for LC-MS/MS analysis.

LC-MS/MS analysis was performed on a Waters Acquity UPLC system coupled to a Waters Xevo TQS tandem mass spectrometer by injection of 20 µl onto a 100 x 2.1 mm ID 1.7 µm HSS T3 column (Waters), maintained at 45°C. Gradient elution was performed at a flow rate of 0.4 ml/min, using a water/methanol gradient, containing 5 mM ammonium formate/0.1% formic acid. MS/MS measurement was done using ESI in positive mode, acquiring two transitions for each pesticide/ biomarker. 5-HBC was measured as [M+H]+ using transitions m/z 208>176 and 208>148 (for ^{13}C-^{15}N-5-HBC: m/z 210>178, 210>150). The response of 5-HBC in samples and calibrants in blank urine was normalized to the response of the ^{13}C-^{15}N-5-HBC internal standard. Quantification was then done using 1-point (2 ng/ml) bracketing matrix-matched calibration.

In-house validation and on-going analytical quality control was done according to EU guidance document SANTE/11945/2015 (currently SANTE/11813/2017). The LOQ for 5-HBC was 0.05 ng/ml urine. For the other pesticides/biomarkers, the method was suboptimal and/or quantification was matrix-matched based on one urine sample, and as matrix-effects were found to vary considerable for different urine samples, these could only be semi-quantitatively determined. Estimated LODs were 0.05 ng/ml for acetamiprid, carbendazim, flonicamid, metolachlor-mercapturate, prothioconazole-desthio, thiacloprid, and trifloxystrobin-acid (CGA321113); 0.1 ng/ml for boscalid-

hydroxy M510F01 and tebuconazole-OH; 0.5 ng/ml for asulam, fluopyram benzamide, imidacloprid, metamitron, metamitron-desamino, propamocarb.

The average RSD_{wl} as obtained for 5-HBC 2 ng/ml analyzed together with the field samples were 102% and 11%, respectively.

Appendix 5: Analysis of hand wipes

The hand wipes were analyzed in a multi-method for the five target substances, i.e. tebuconazole, chlorpropham, prochloraz, asulam and carbendazim. The sample extraction was performed in the plastic container in which the wipe was stored. This reduces the extraction losses.

Stock solutions of the five target substances were prepared in methanol at concentrations of 1 mg/mL, except for carbendazim which was dissolved in DMSO. Additional working solutions of 1000 ng/mL and 100 ng/mL were prepared in 50% methanol and 50% water. Next, a combination calibration curve of tebuconazole, prochloraz, asulam and carbendazim in the range of 0.1 to 10 ng/mL, including a blank, was constituted in 50% methanol and 50% water. For chlorpropham a separate calibration curve was prepared in the range of 1 to 20 ng/mL, including a blank. In addition, blank wipes were added to the measurement protocol to check if the wipes were free from the analytes of interest.

All specimens were thawed at room temperature prior to sample preparation. The wipes were cut in 64 small pieces and these were put back in the same container. 80 mL of methanol was added, and the container was placed in an ultrasonic bath for 1 h, followed by 10 min on a mechanical shaker. 8 mL of methanol extracted was transferred to a test tube and dried at 40°C under a gentle flow of nitrogen. The dried extract was dissolved in 1 mL of 50% methanol and 50% water and was centrifuged at 2000 RCF to remove remaining fibers. The supernatant was transferred to a vial for subsequent LC-MS/MS analysis.

For the quantification of tebuconazole, chlorpropham, prochloraz, asulam and carbendazim, an aliquot of 1.0 µL of each sample was analyzed on a Waters Acquity LC-MS/MS system via positive electrospray ionization. The chromatographic separation was performed on a Waters CSH C18 column. The MS was operated in MRM mode. The mass transitions selected for quantification are provided in Table 1 below. Chlorpropham was analyzed with the same conditions, but with a lower desolvation temperature of 300°C instead of 600°C.

Table 1: Mass transitions and LOQ's of the five pesticides selected for hand wipe analyses.

Pesticide	Quantification	Qualification	LOQ (ng/wipe)
Tebuconazole	308.03 -> 69.94	308.03 -> 124.87	0.25
Chlorpropham	214.1 -> 171.9	214.1 -> 154.1	2.5
Prochloraz	375.97 -> 307.88	375.97 -> 69.94	1.0
Asulam	231.09 -> 155.96	231.09 -> 91.98	0.5
Carbendazim	192.09 -> 160.01	192.09 -> 132.04	0.5

Appendix 6: Pesticides and application periods

All pesticides analyzed in OBO samples and used on the target fields and additional field (both registered and schemes) were plotted (Figure 1) to determine the period of use. Per pesticide, applications reported during the study were grouped per month (see graphs). Based on this information, the periods for use and non-use were determined.

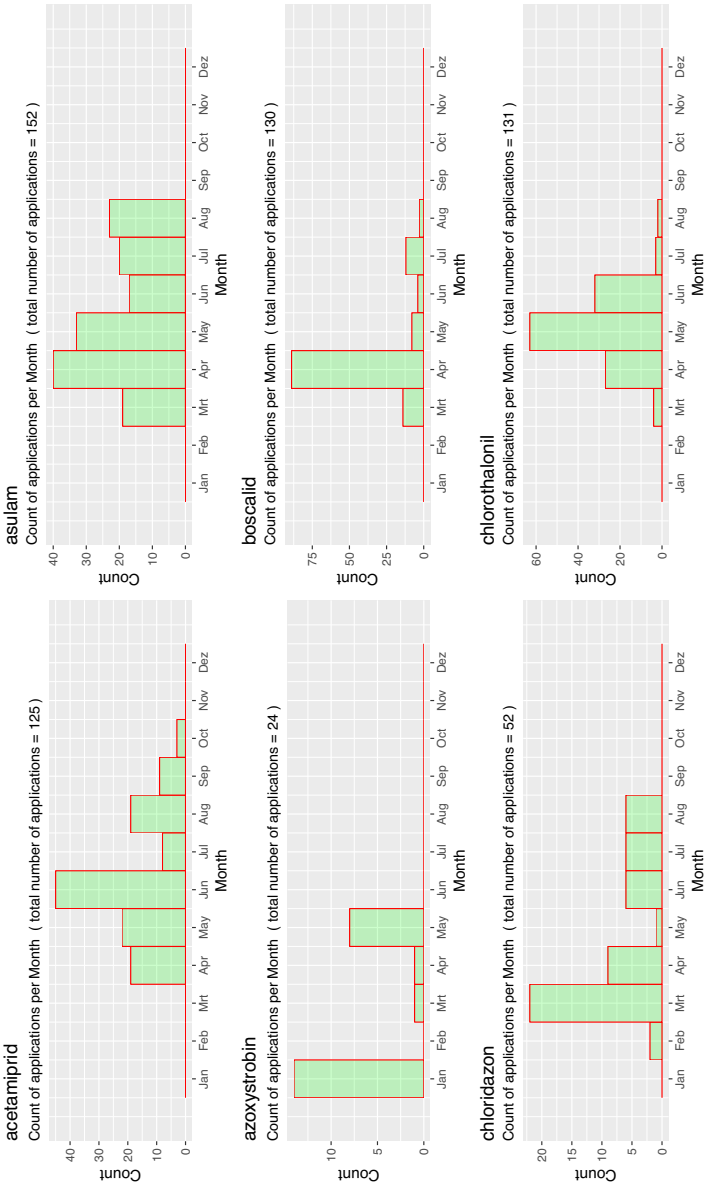

Figure 1: Count of pesticides applied in both target and additional fields.
x axis is the month that application occurred, in the y axis is the total number of spraying events (counts).
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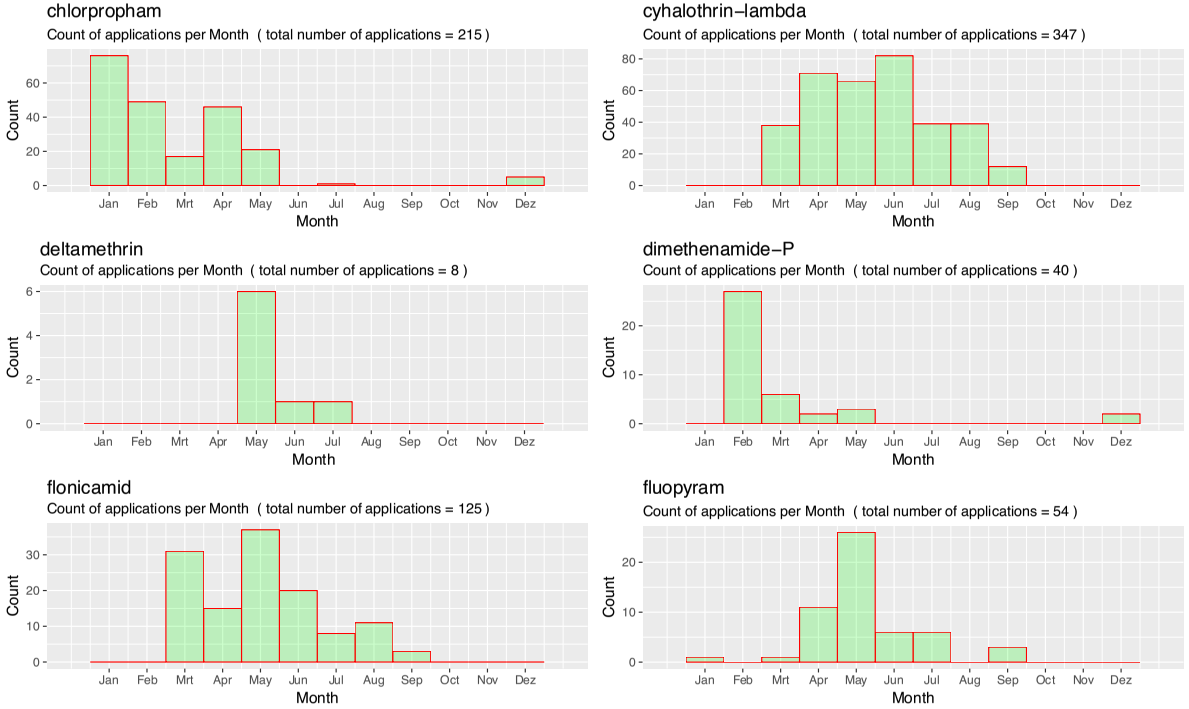

Figure 1: Count of pesticides applied in both target and additional fields.
x axis is the month that application occurred, in the y axis is the total number of spraying events (counts).
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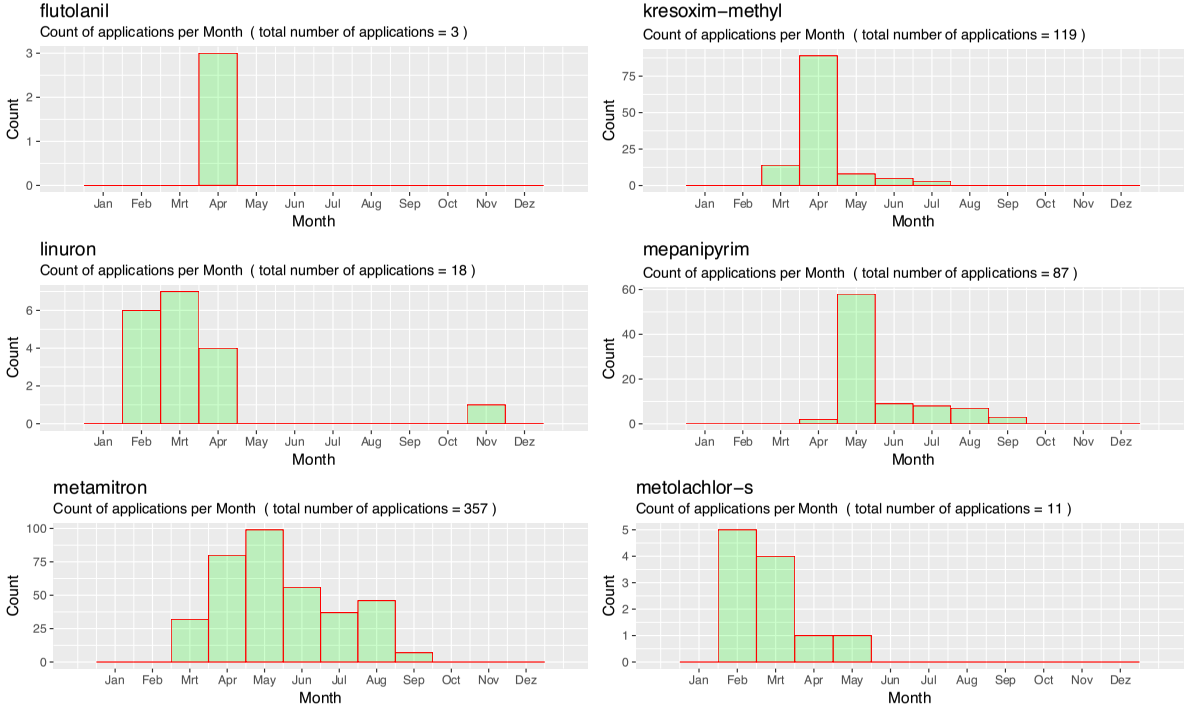

Figure 1: Count of pesticides applied in both target and additional fields.
x axis is the month that application occurred, in the y axis is the total number of spraying events (counts).
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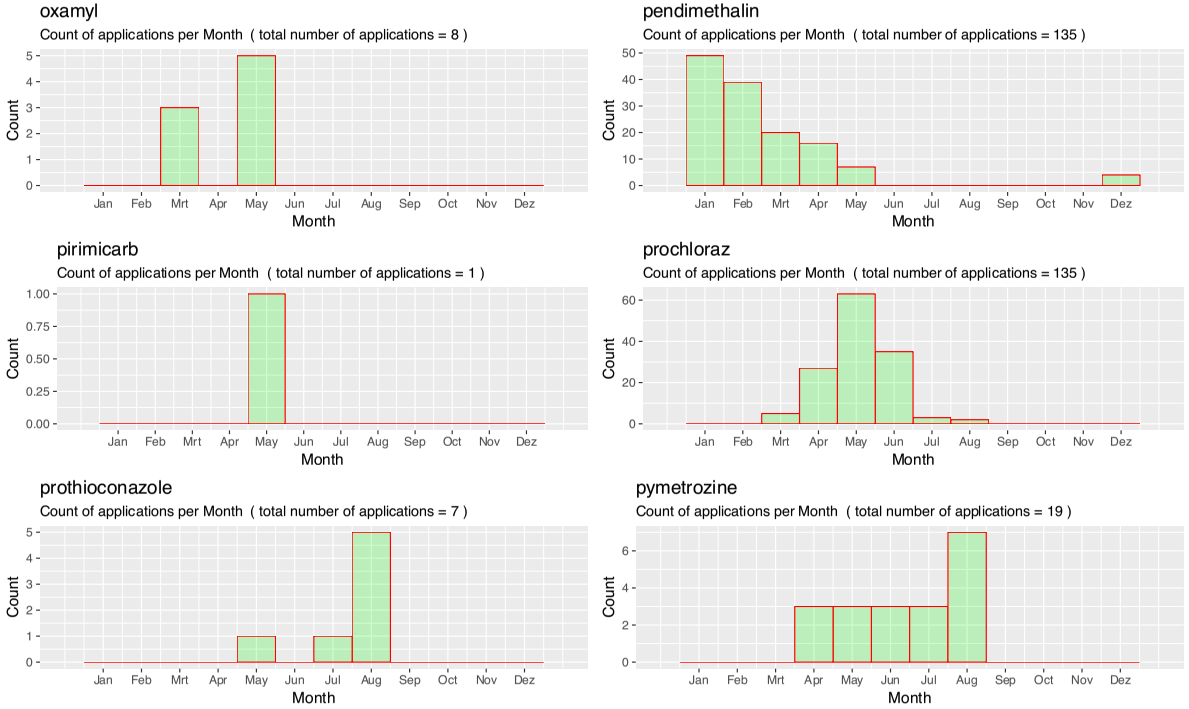

Figure 1: Count of pesticides applied in both target and additional fields.
x axis is the month that application occurred, in the y axis is the total number of spraying events (counts).
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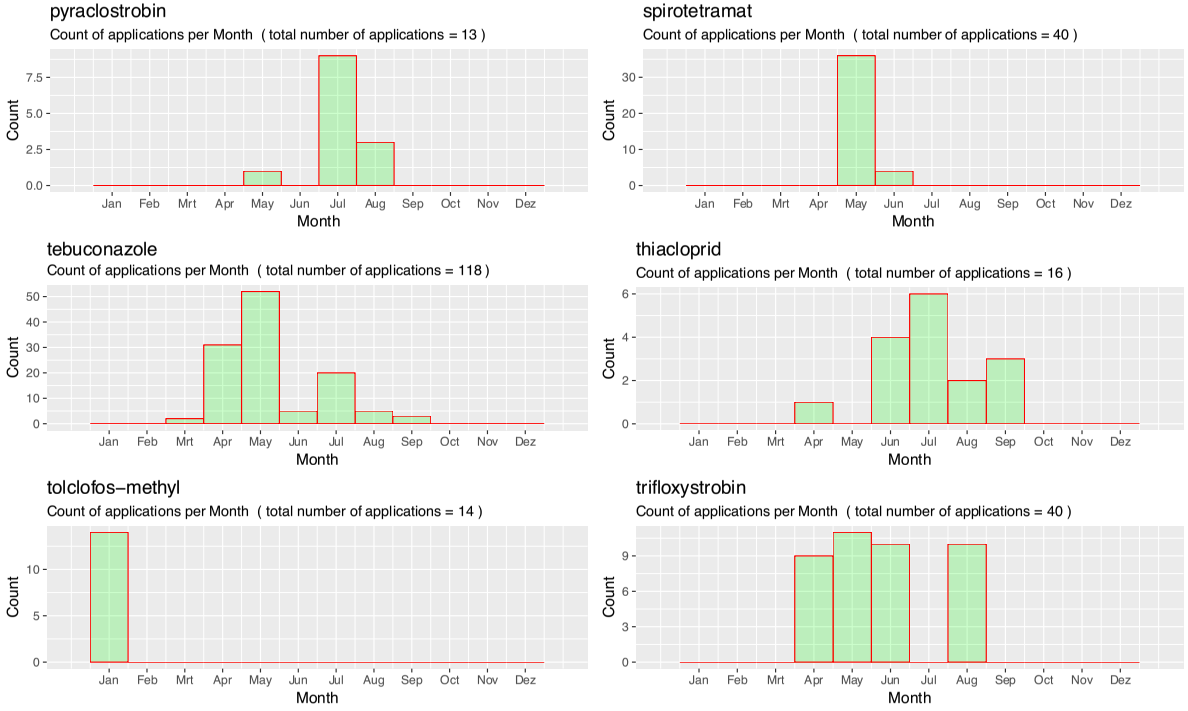
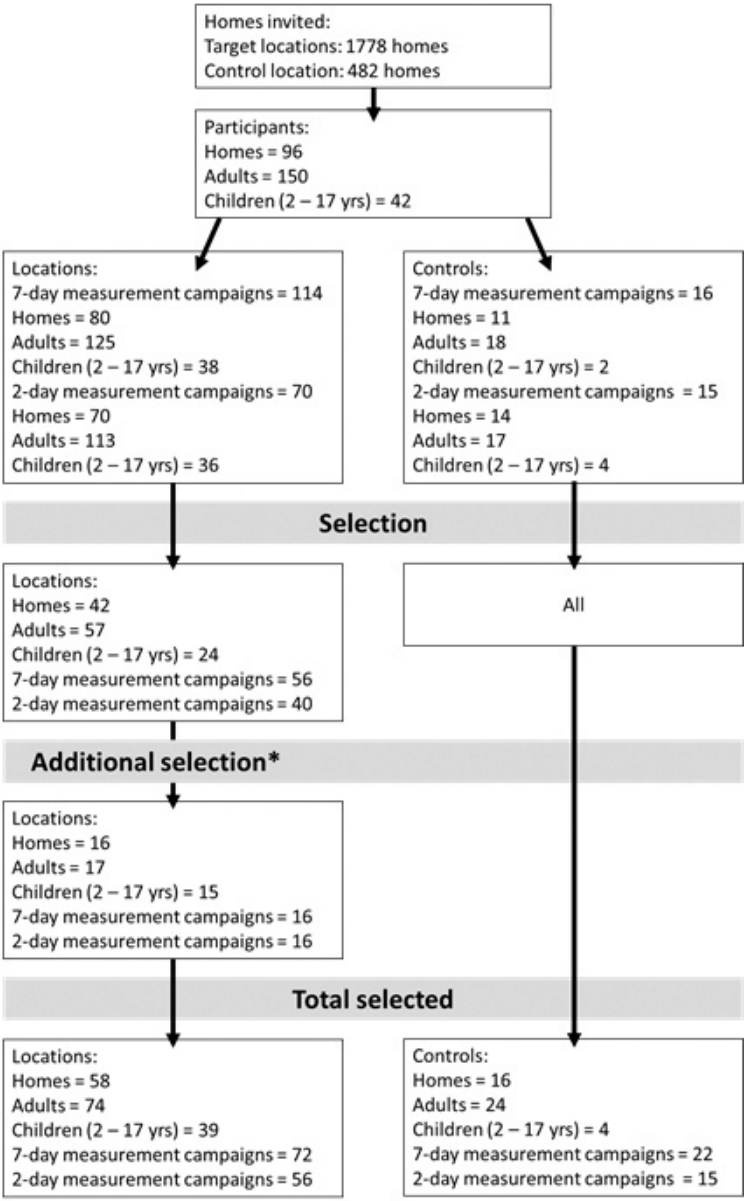


Figure 1: Count of pesticides applied in both target and additional fields.
x axis is the month that application occurred, in the y axis is the total number of spraying events (counts).

Appendix 7: Flow of the residents' field study and overview of the number of analysed samples



*Additional selection was done for air samples and urine samples (see chapter 4)

Not all selected samples were allegeable for analysis (due to pump failure, urine samples not collected etc). In the table below the number of analysed samples is shown.

Table: Total number of analysed samples

Type	Number
Outdoor air	628
Indoor air	43
VFD	128
DDM	125
Soil	124
Urine-Morning	791
Urine-Day	311
Handwipes	112

Appendix 8: Results of farm homes and farm residents

Farm homes: environmental samples

For the main analyses we excluded results from farm homes from the group of residential homes at a location as growers may influence their home exposure. In this appendix we show the results of farm homes in comparison to the location homes. Not all samples were above the LOD and we only show the Figures for those with at least one type of sample with >40% above the LOD. Figure A1 of this appendix shows the measured concentrations of pesticides applied on the target fields and additional fields for location homes and farm homes in the use and non-use period. Figure A2 of this appendix shows the measured concentrations of pesticides applied on the target fields and additional fields for location homes within 50 meters from a field and farm homes in the use and non-use period. Also the pesticides not reported to be applied during our measurement campaign and secondary products of pesticides are shown. Results of outdoor air, vacuumed floor dust (VFD) and dust from the doormat are shown.

The differences between location homes and farm homes is statistically tested by t-tests, whose p-values are shown in Table A. Overall, farm homes have higher levels compared to location homes. For outdoor air during the use period, results from half of the pesticides reach significant difference while this is less often reached for the non-use period and for the two types of indoor dust measures.

Personal samples: morning urines

As exposure may be higher in farm homes due to the occupation of at least one resident, morning urines from growers' families were analyzed separately from the rest of the study population. In Table B we show results from growers' families (both adults and children) compared to residents (adults). Levels of biomarkers of pesticide in urine are corrected for creatinine levels. For the 2 markers with results imputed below the LOD, graphs are shown in Figure B. Significant differences are observed for both chlorpropham and tebuconazole in growers' families between the use and non-use period (Table C).

Personal samples: hand wipes

Hand wipes were collected from residents in protocol B. In total, we collected 27 hand wipes from growers' families (both adults and children), 16 in the use period and 11 in the non-use period. Results from these hand wipes are in Table D. Pesticide levels on the hand wipes are high and except for prochloraz, higher than in residents.

I. Pesticides applied on target fields:

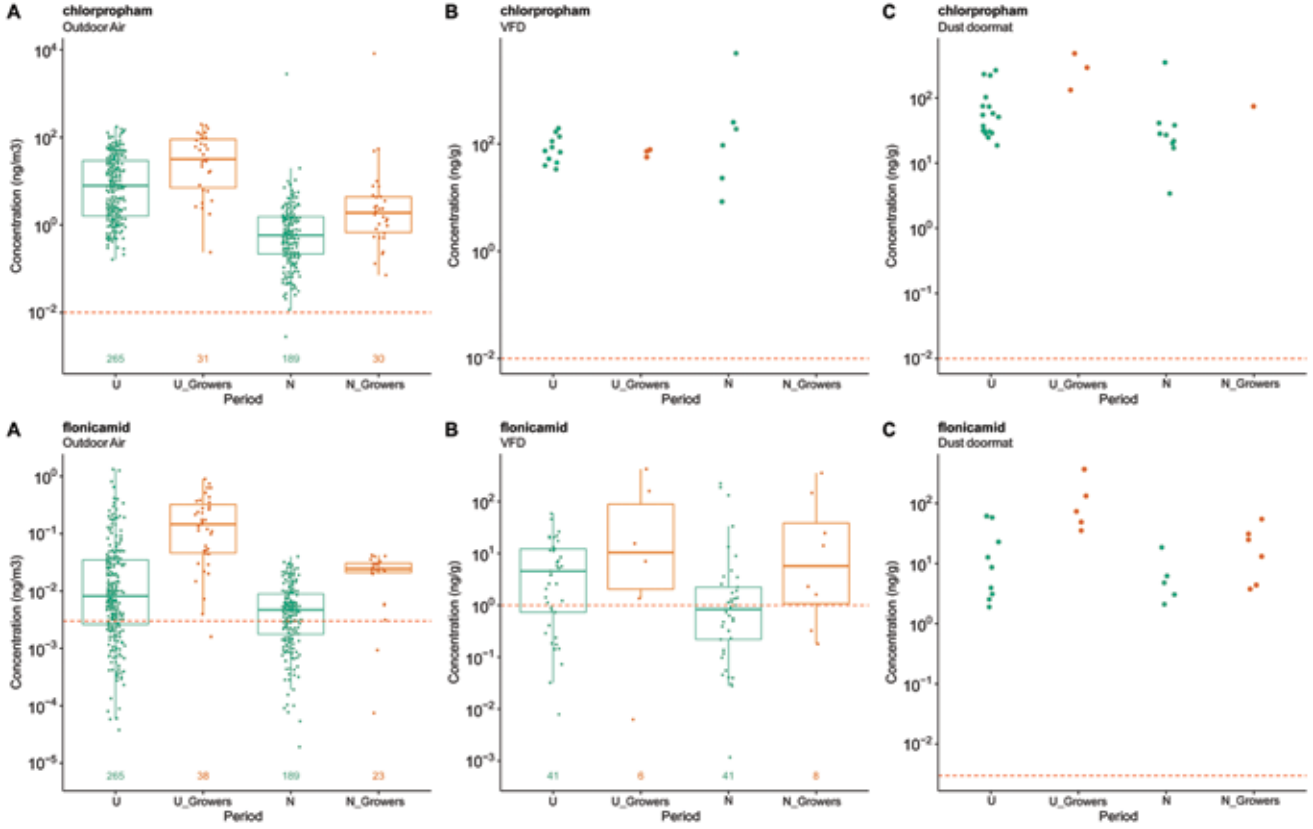


Figure A: Pesticide levels in location homes and farm homes.
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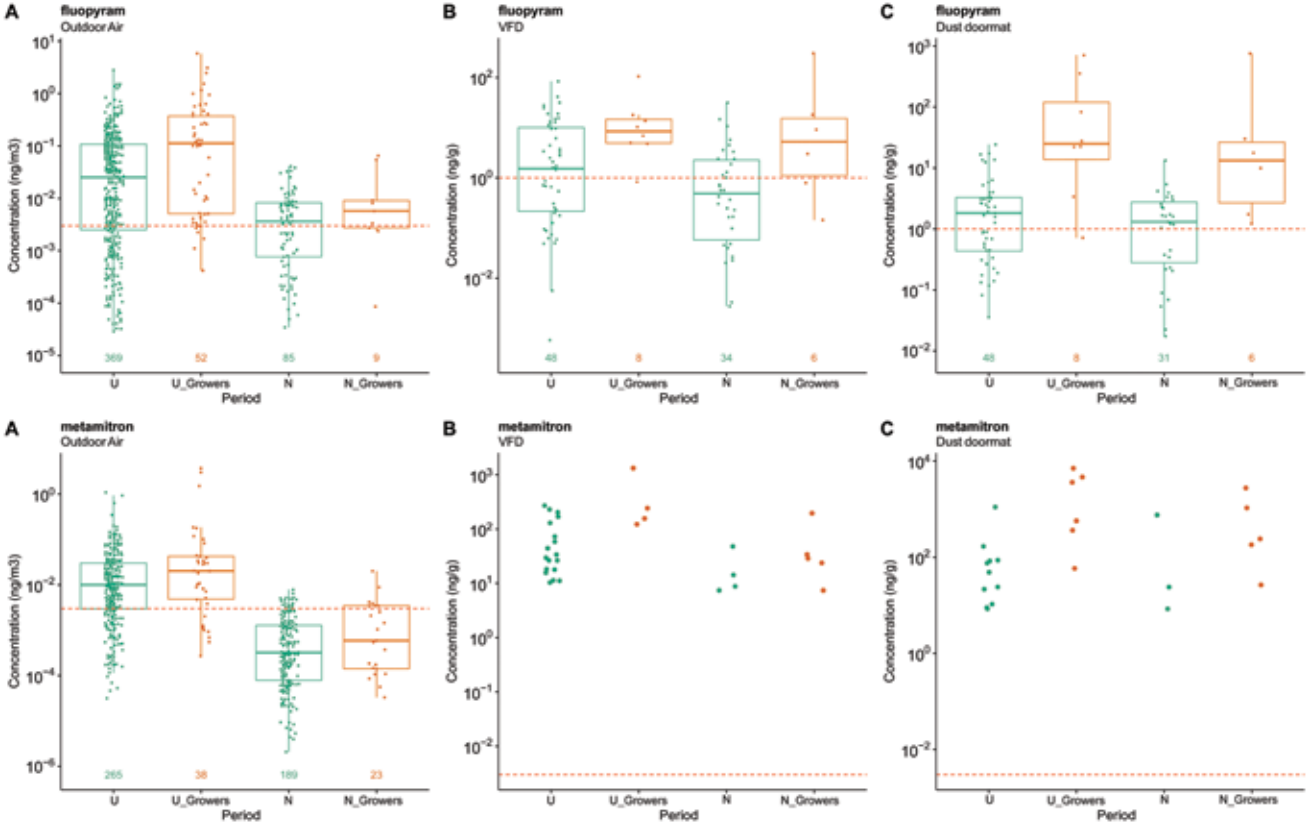

Figure A: Pesticide levels in location homes and farm homes.
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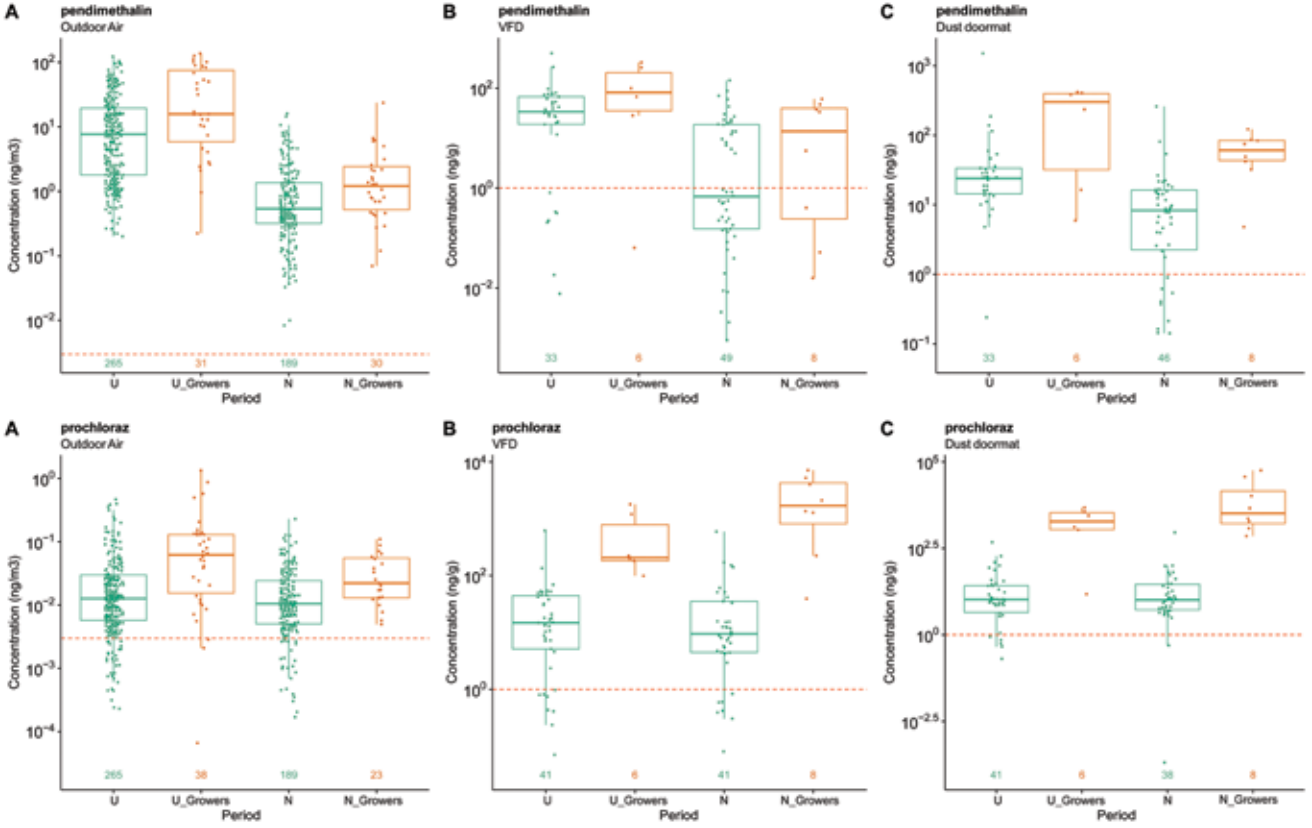

Figure A: Pesticide levels in location homes and farm homes.
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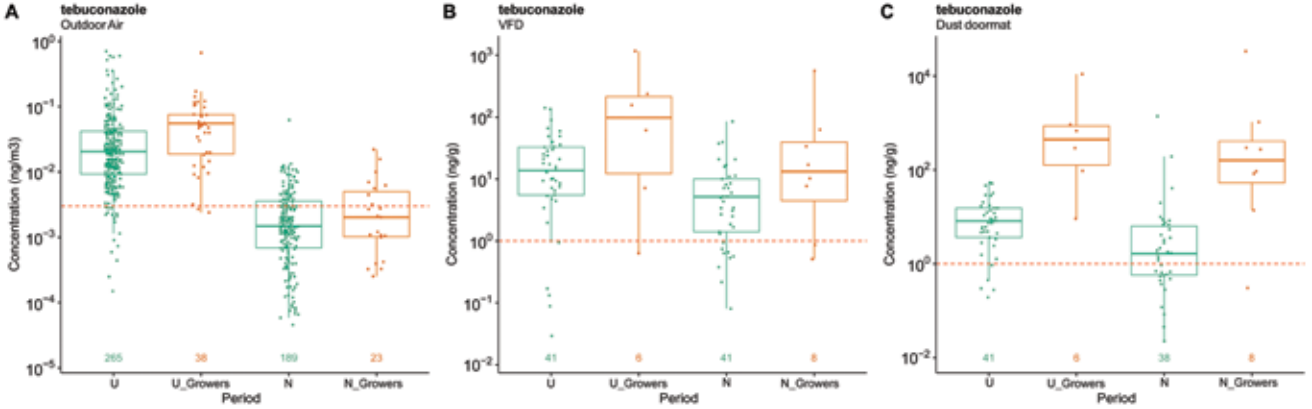

Figure A: Pesticide levels in location homes and farm homes.
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II. Pesticides applied on additional fields

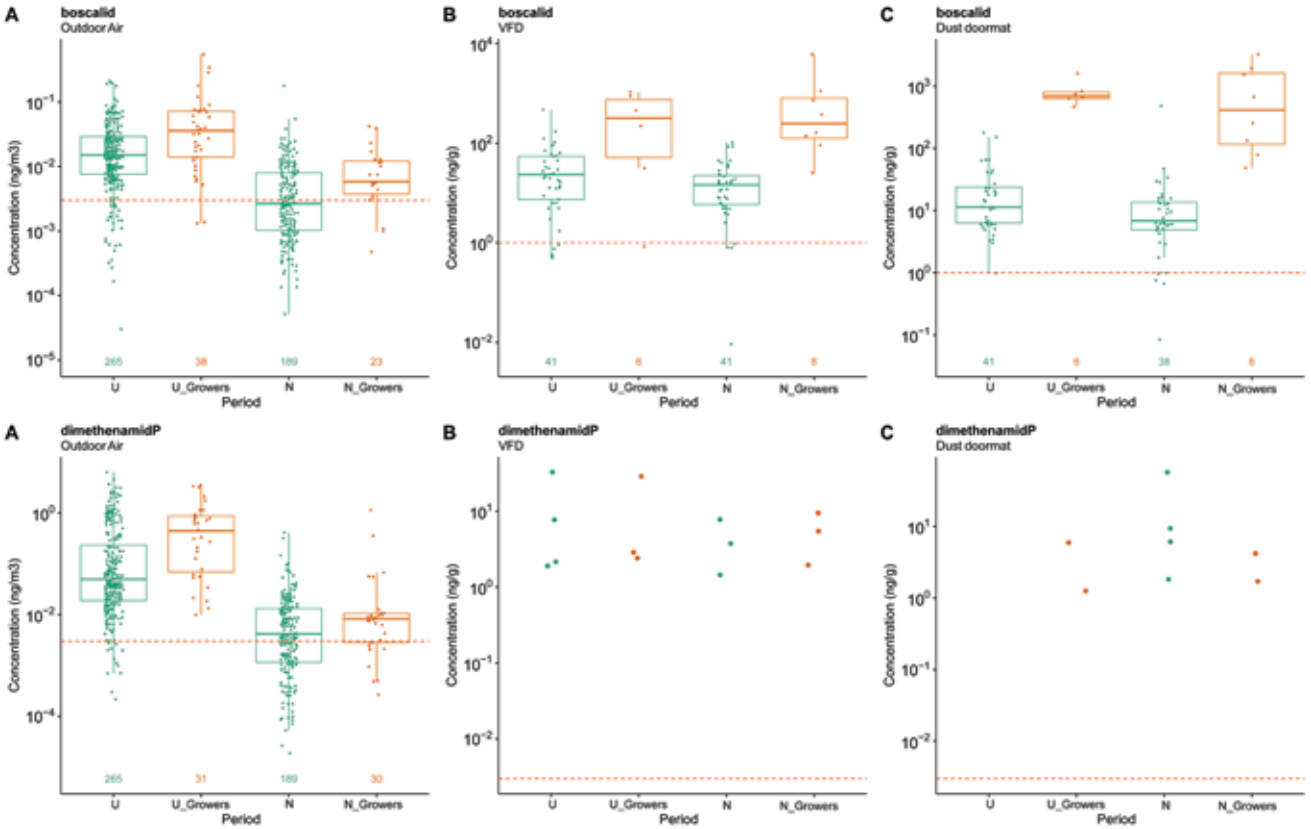

Figure A: Pesticide levels in location homes and farm homes.
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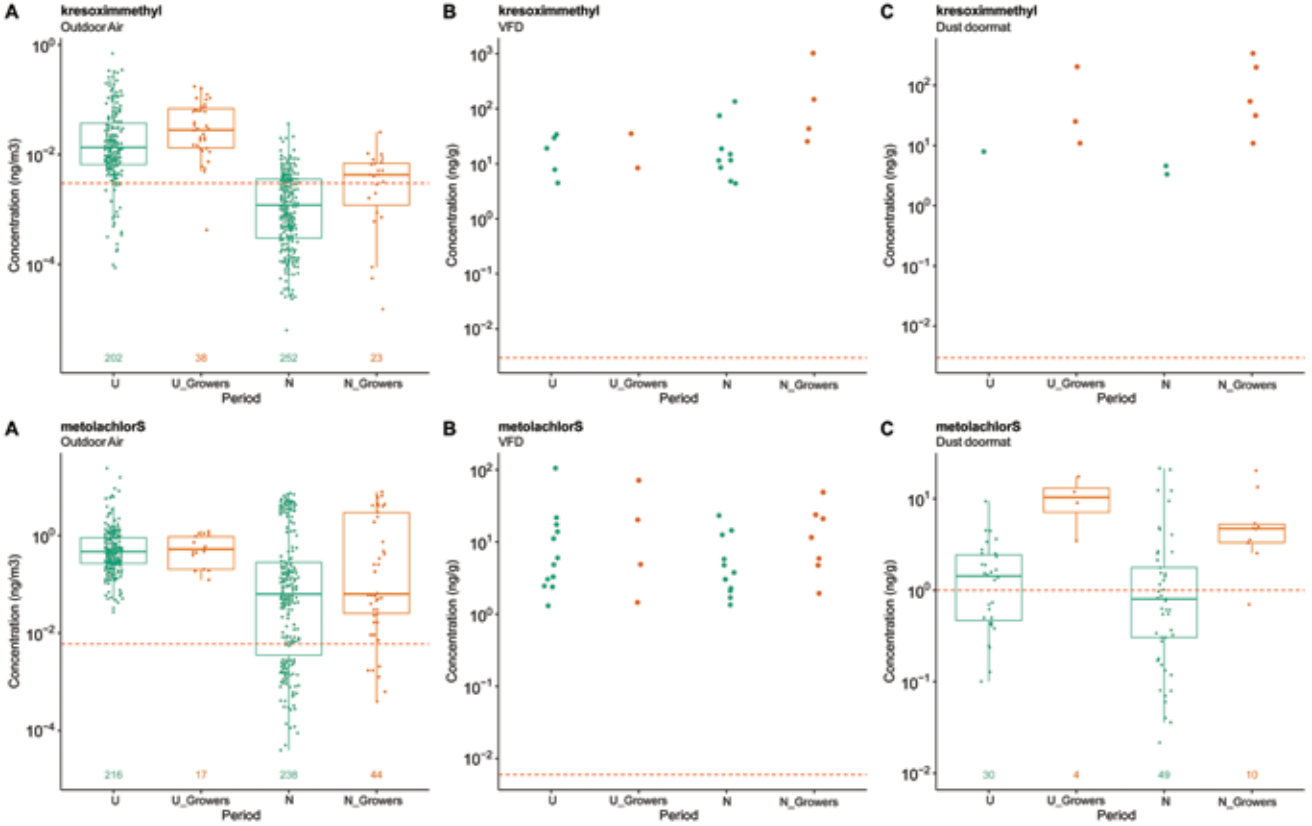

Figure A: Pesticide levels in location homes and farm homes.
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III. Pesticides not applied or secondary-products

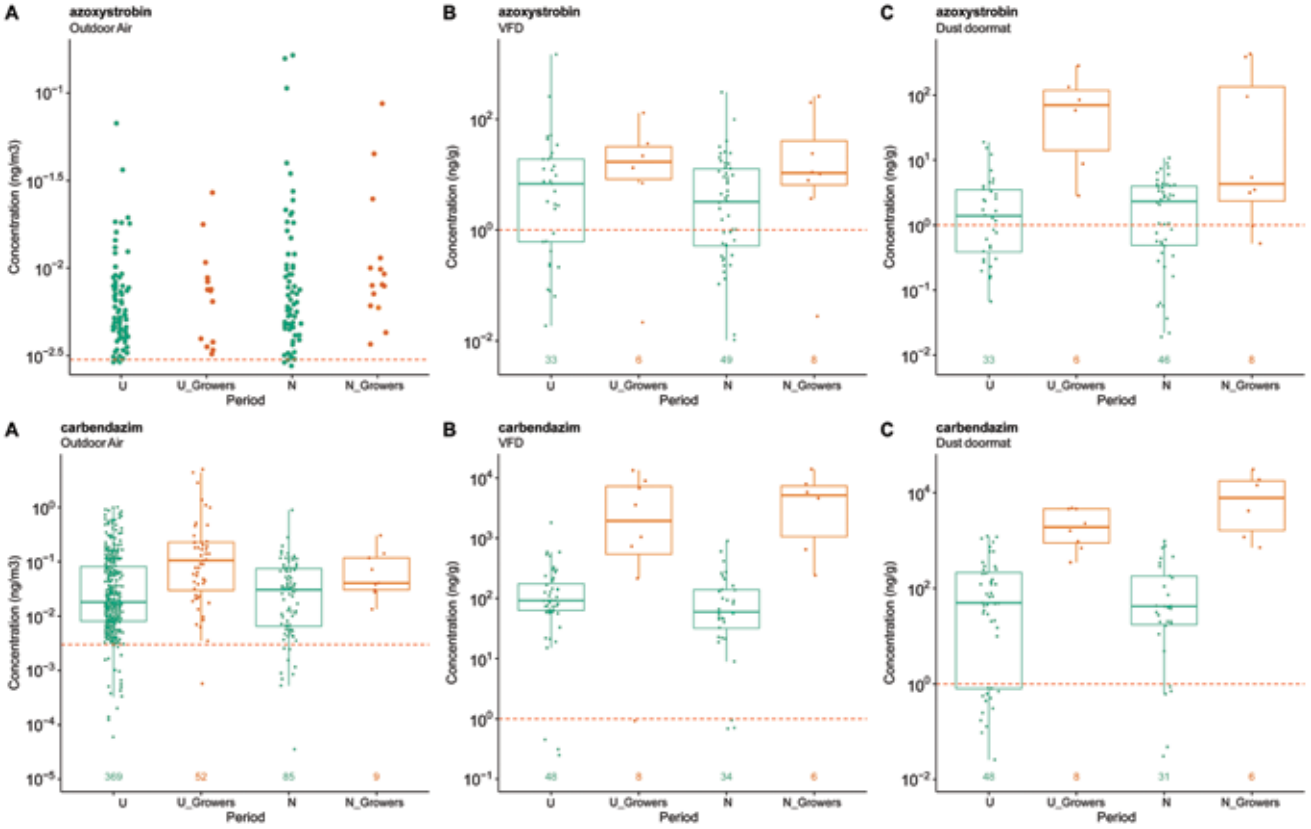

Figure A: Pesticide levels in location homes and farm homes.
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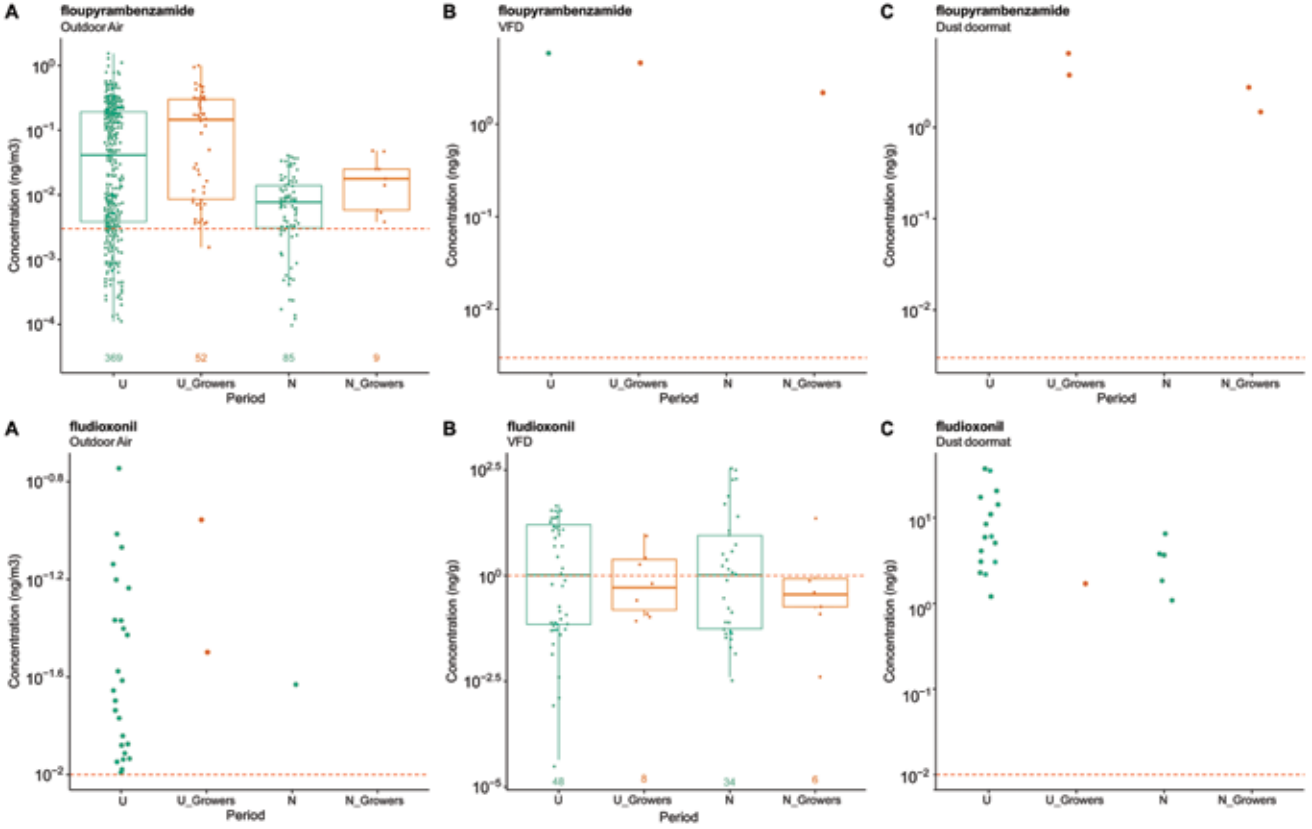

Figure A: Pesticide levels in location homes and farm homes.
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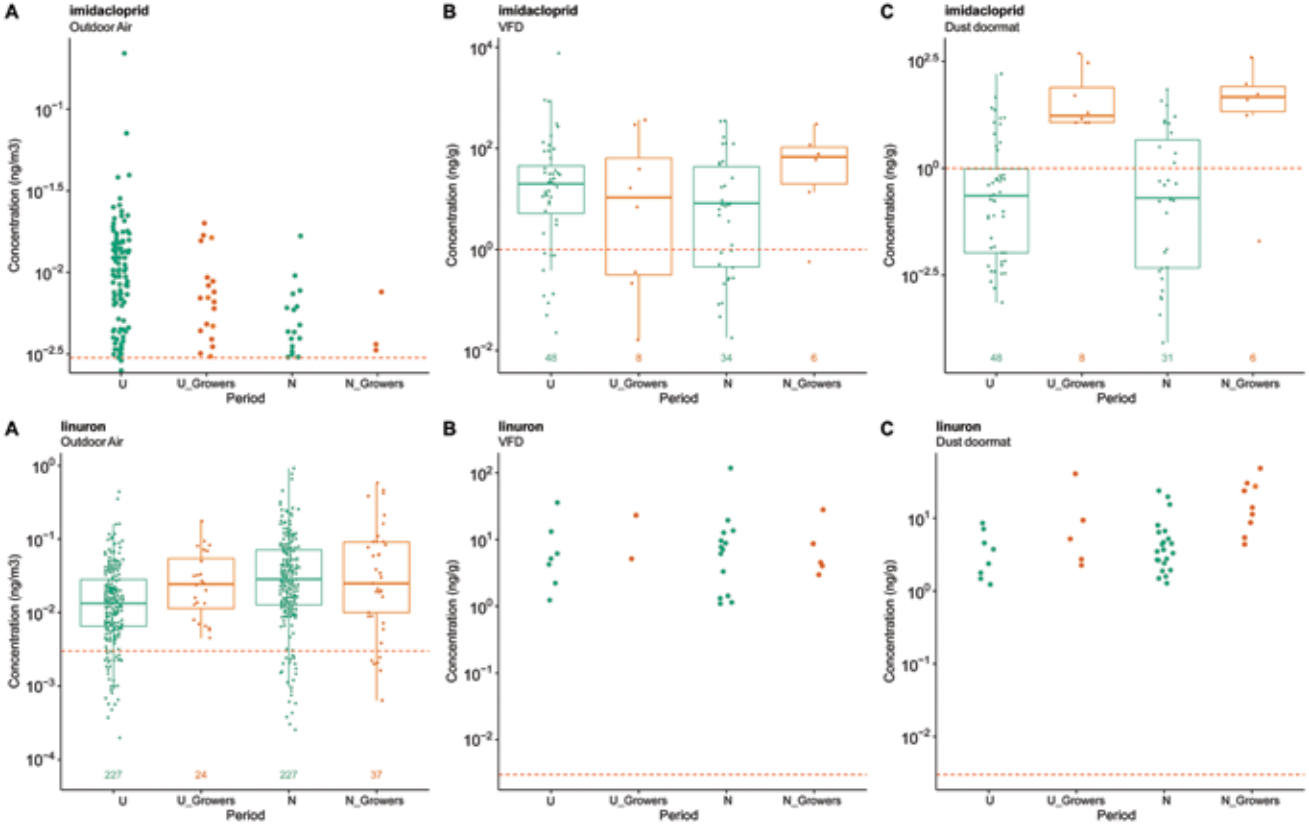

Figure A: Pesticide levels in location homes and farm homes.
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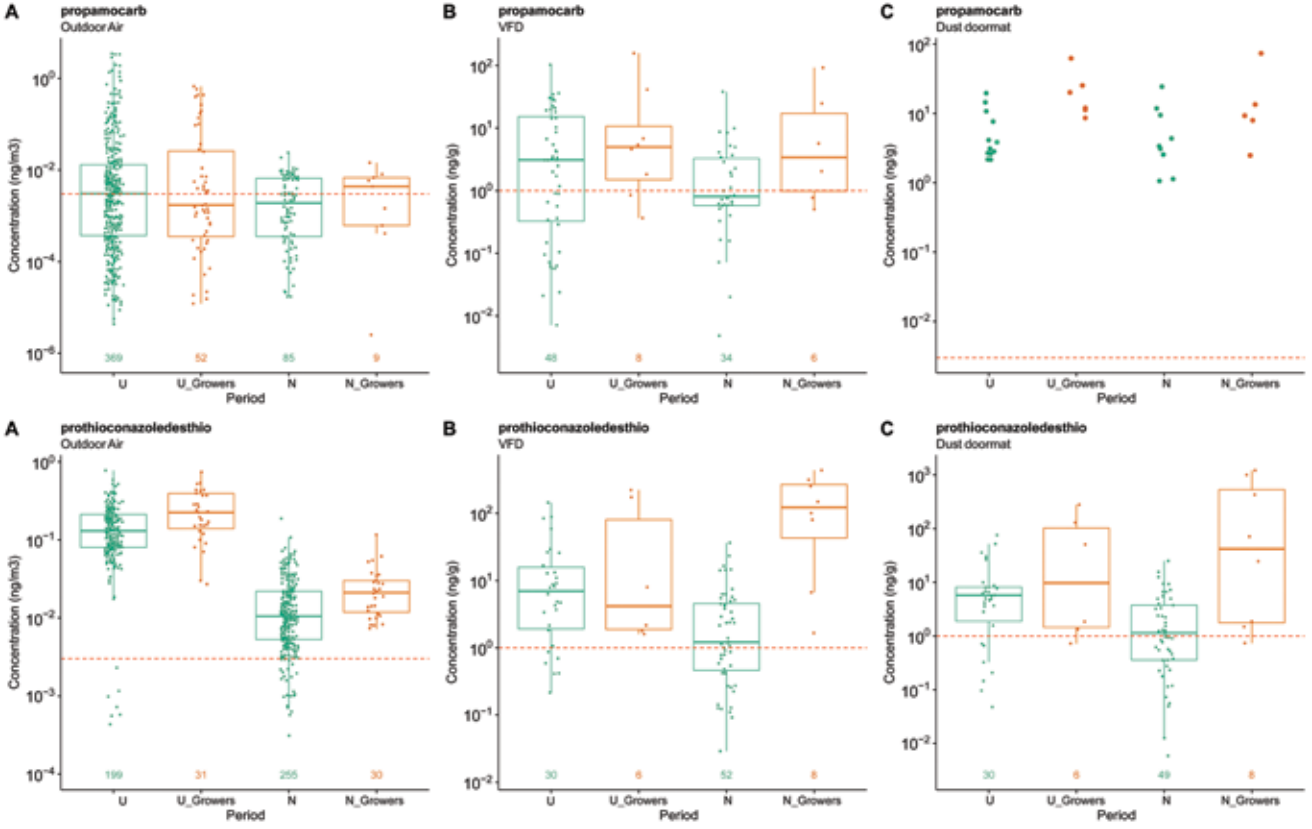

Figure A: Pesticide levels in location homes and farm homes.
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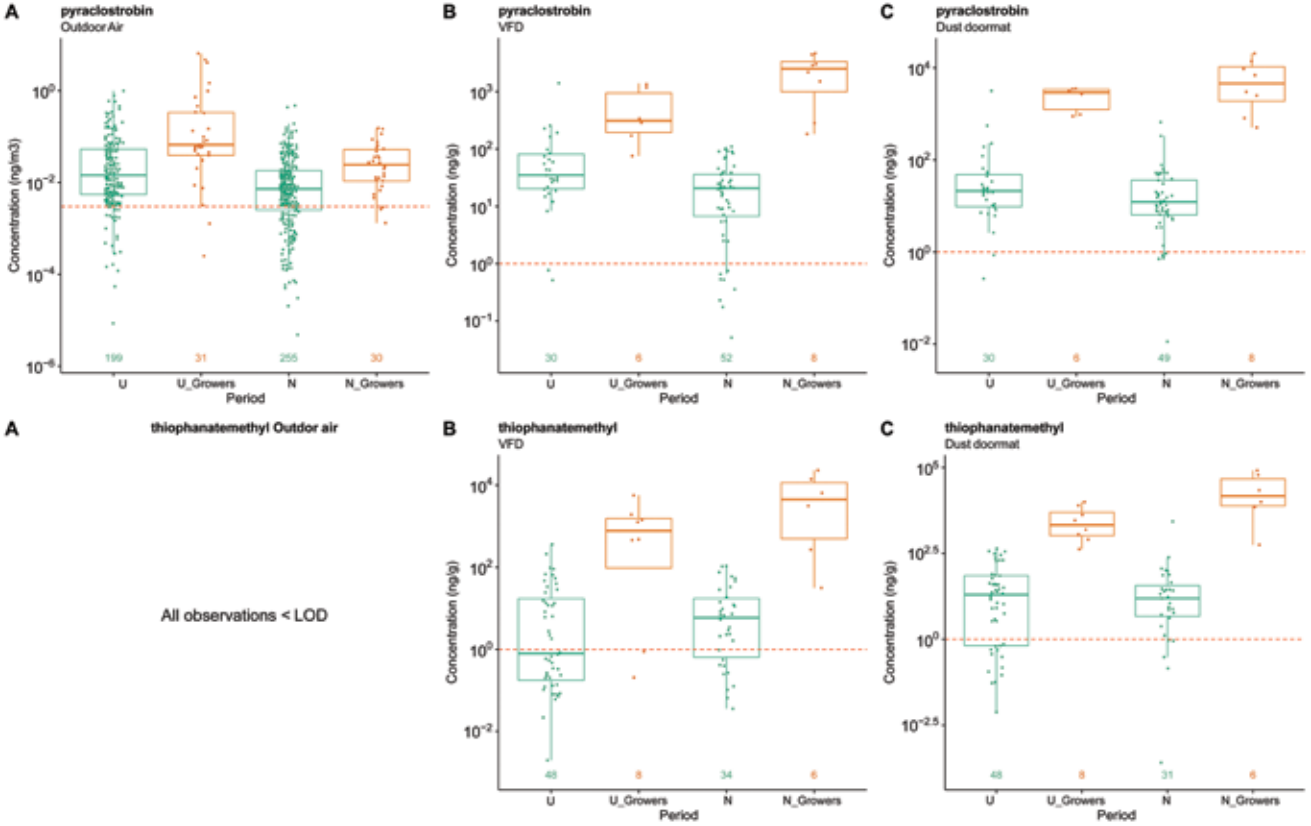

Figure A: Pesticide levels in location homes and farm homes.
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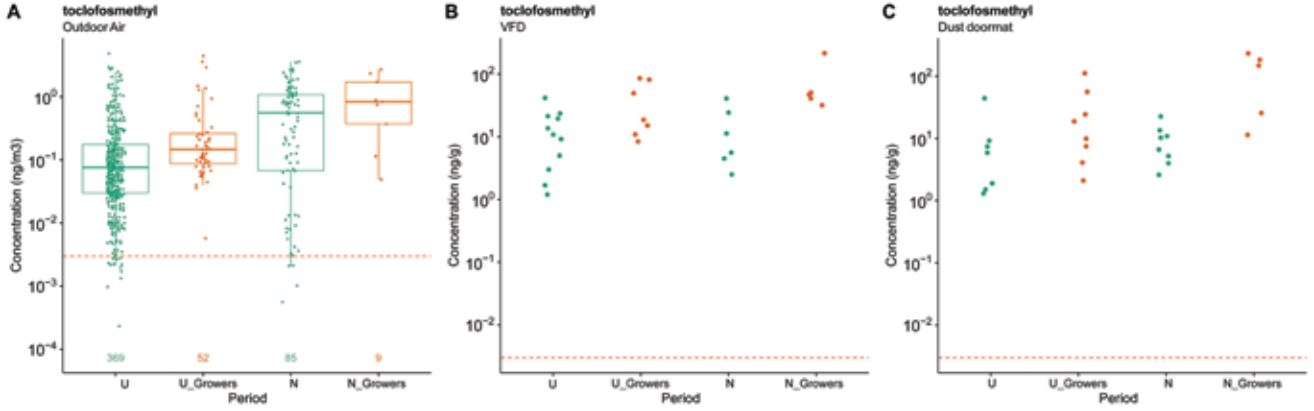


Figure A: Pesticide levels in location homes and farm homes.
We show concentrations of pesticides applied on the target fields (I) and additional fields (II) for location homes and farm homes in the use and the non-use period. Also the pesticides not reported applied during our measurement campaign and secondary products of pesticides are shown (III). On the x-axis is the period: U: location homes in use period; U_Growers: farm homes in use period; N: location homes in non-use period; N_Growers: farm homes in non-use period. In the box plot figures, the number of observations is shown above the x-axis. The red line represents the LOD. If imputation was not possible, there is no box plot shown. In panel A are results for outdoor air, in panel B are results for vacuumed floor dust (VFD) and in panel C are results from dust from the doormat.

Table A: p-values for comparison between location homes and farm homes (t-test).

	Use Period			Non-use Period		
t-test - pvalue	Outdoor air	VFD	DDM	Outdoor air	VFD	DDM
Applied in the target fields						
acetamiprid	0.654	0.976	-	-	-	-
asulam	0.380	0.014	0.010	0.411	-	0.032
chlorpropham	2.39E-04	-	-	0.002	-	-
cyhalotrin-lambda	0.012	-	-	-	-	-
flonicamid	3.58E-13	0.583	0.002	1.60E-04	0.072	0.107
fluopyram	3.22E-04	0.004	0.006	0.275	0.064	0.027
floupyram-benzamide	0.004	-	-	0.009	-	-
mepanipyrim	0.109	-	-	-	-	-
metamitron	0.039	-	0.007	0.053	-	-
metamitron-desamino	0.003	-	0.007	0.129	-	-
pendimethalin	0.003	0.571	0.113	0.010	0.411	1.47E-04
prochloraz	1.85E-04	1.28E-04	0.003	1.65E-04	2.68E-05	3.21E-07
prothioconazole-desthio	-	-	-	-	-	-
prothioconazole-desthio	7.72E-04	0.531	0.316	2.30E-05	5.90E-04	0.012
pymetrozine	-	-	-	-	-	-
tebuconazole	0.003	0.216	0.008	0.294	0.181	0.008
thiacloprid	0.759	-	-	0.831	0.416	-
trifloxystrobin	0.002	-	-	0.966	-	-
trifloxystrobin-acid	0.272	-	-	0.003	-	-
Applied in the additional fields						
boscalid	4.69E-04	0.155	2.14E-12	0.002	3.91E-04	6.07E-05
chloridazon	0.145	0.041	0.001	0.429	-	-
dimethenamid-P	5.07E-05	-	-	0.047	-	-
kresoxim-methyl	0.009	-	-	0.047	-	-
S-metolachlor	0.835	-	-	0.049	0.121	5.37E-05
spirotetramat	0.894	-	-	-	-	-
spirotetramat-enol	-	-	-	-	-	-
Not applied during measuring week						
azoxystrobin	0.479	0.610	0.003	0.317	0.207	0.039
cyprodinil	0.072	-	-	-	-	-
deltamethrin	0.504	-	-	0.089	-	-
difenoconazole	0.005	-	-	-	-	-
dimethomorph	-	-	-	-	-	-
fludioxonil	-	0.843	-	-	0.482	-
fluopicolide	0.139	-	-	-	-	-
flutolanil	0.034	0.071	0.035	-	0.032	0.003
fosthiazate	0.217	-	-	-	-	-
imidacloprid	0.021	0.498	4.20E-07	-	0.087	0.020
linuron	0.011	-	0.197	0.999	0.883	5.78E-04
oxamyl	-	-	-	0.327	-	-
primicarb	-	-	-	-	-	-
propamocarb	0.883	0.198	0.003	0.920	0.119	0.165
pyraclostrobin	3.21E-04	0.002	2.32E-10	6.37E-06	4.01E-07	2.25E-07
sulcotrione	-	-	-	-	-	-
terbuthylazine	3.86E-04	-	-	-	-	-
thiophanate-methyl	-	0.011	3.80E-10	-	0.001	8.89E-06
carbendazim	2.33E-06	0.063	6.07E-09	0.013	7.87E-04	2.93E-05
toclofos-methyl	6.51E-06	0.027	0.103	0.064	0.009	0.021

Legend	
	< 0.001
	< 0.01
	< 0.05
	> 0.05
-	Not enough observations

Table B: Results from morning urines of residents and farm home residents.

	Markers of pesticides with imputed values < LOD			
	U (Residents)	U (FarmHomeR)	N (Residents)	N (FarmHomeR)
	Biomarker of chlorpropham			
N	76	25	39	8
mean	7.95	9.32	3.29	0.67
median	0.74	1.12	0.52	0.26
min	4E-04	9E-03	0.10	0.15
max	177.87	101.83	47.76	3.54
	Biomarker of tebuconazole			
N	99	41	45	14
mean	0.19	0.61	0.10	0.24
median	0.56	0.35	0.22	0.05
min	2E-03	9E-03	1E-03	6E-03
max	7.38	6.71	1.94	1.36
	Markers of pesticides with not imputed values < LOD			
	U (Residents)	U (FarmHomeR)	N (Residents)	N (FarmHomeR)
	Biomarker of carbendazim			
N	118	18	60	8
N > LOD	25	20	11	4
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD
max	7.38	12.46	1.94	12.20
	Biomarker of prochloraz			
N	30	15	22	8
N > LOD	0	13	2	6
mean	NA	NA	NA	NA
median	< LOD	0.88	< LOD	0.09
min	< LOD	< LOD	< LOD	< LOD
max	NA	3.89	0.06	0.53
	Biomarker of Asulam			
N	71	21	25	2
N > LOD	2	1	0	0
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	NA
min	< LOD	< LOD	< LOD	NA
max	0.18	0.09	NA	NA

U (Residents): results from morning urines of adult residents from locations, during pesticides usage. period; N (Residents): results from morning urines of residents from locations, outside pesticides usage period.

U (FarmHomeR): results from morning urines of farm home residents from locations, during pesticides usage period; N (FarmHomeR): results from morning urines of farm home residents, outside pesticides usage period.

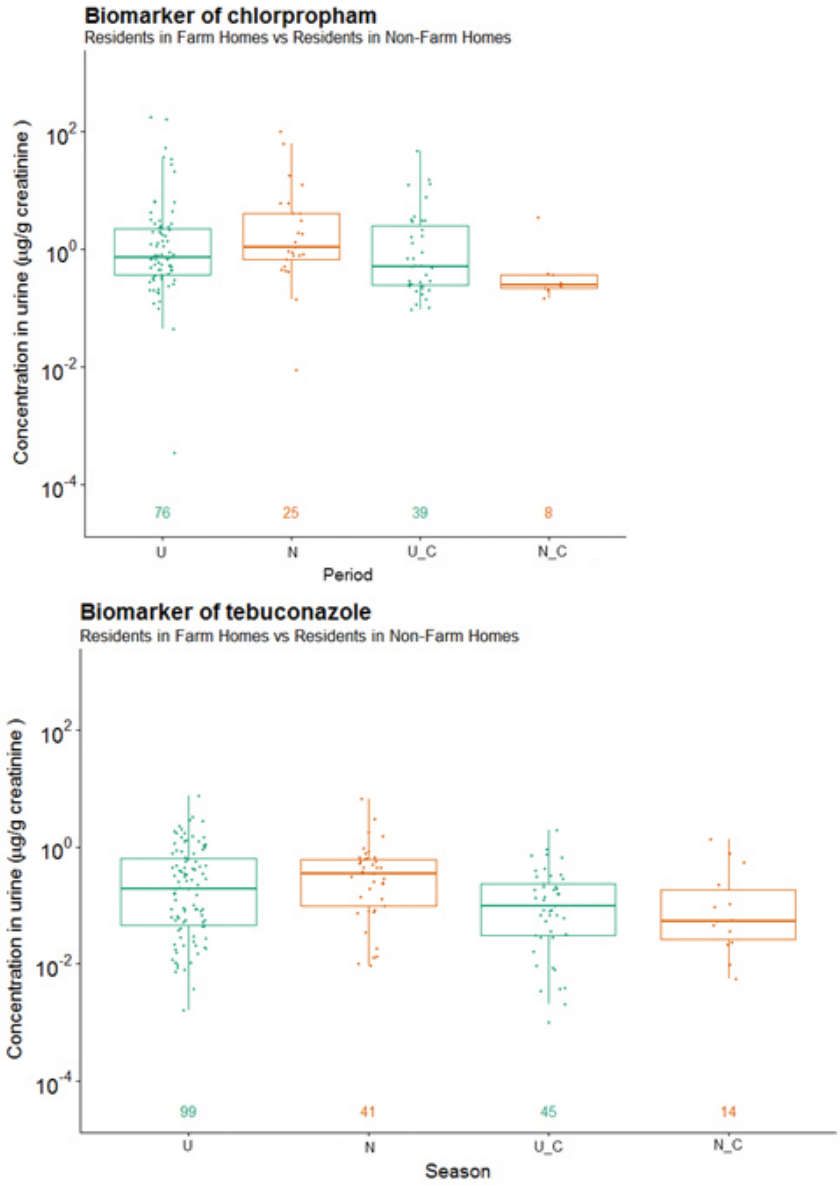


Figure B: Levels of biomarkers of chlorpropham and tebuconazole morning urines of residents and farm home residents.

Concentrations of biomarkers are shown corrected for creatinine. On the x-axis is the period: U: location homes in use period; U_Growers: farm homes in use period; N: location homes in non-use period; N_ Growers: farm homes in non-use period.

Table C: p-values for biomarkers of chlorpropham and tebuconazole in urines of growers' families vs residents.

	T-test P-values		
	U vs U_Growers	N vs N_Growers	U_Growers vs N_Growers
Chlorpropham	0.306	0.115	0.006
Tebuconazole	0.126	0.920	0.027

Legend	
	< 0.001
	< 0.01
	< 0.05
	> 0.05
-	Not enough observations

U: results from morning urines of adult residents from locations, during pesticides usage period;
N: results from morning urines of residents from locations, outside pesticides usage period;
U_Growers: results from morning urines of growers' families, during pesticides usage period;
N_Growers: results from morning urines of growers' families , outside pesticides usage period.

Table D: Hand wipe results of growers' families.

		Residents		Growers' families	
	Period:	Use	Non-use	Use	No-use
Number of hand wipes		34	20	16	17
Asulam	LOD	0.5 ng/wipe			
	% > LOD	9	5	50	35
	median	< LOD	< LOD	19.4	< LOD
	mean	NA	NA	550.0	22.6
	min	< LOD	< LOD	< LOD	< LOD
	max	5.2	887.7	3499.5	117.9
Carbendazim	LOD	0.5 ng/wipe			
	% > LOD	82	95	100	100
	median	42.4	11.5	1199.2	295.1
	mean	4155.9	71.3	10682.5	10578.4
	min	0.08	0.20	31.1	28.9
	max	136147	892	114864	163321
Chlorpropham	LOD	2.5 ng/wipe			
	% > LOD	26	35	25	41
	median	< LOD	< LOD	< LOD	< LOD
	mean	NA	NA	171.8	12.6
	min	< LOD	< LOD	< LOD	< LOD
	max	1723.9	149.1	641.6	45.5
Prochloraz	LOD	1 ng/wipe			
	% > LOD	15	25	69	82
	median	< LOD	< LOD	64.0	55.3
	mean	NA	NA	197.6	4115.0
	min	< LOD	< LOD	< LOD	< LOD
	max	761.2	48.1	1034.8	53932.9
Tebuconazole	LOD	0.25 ng/wipe			
	% > LOD	44	30	81	35
	median	< LOD	< LOD	1.8	< LOD
	mean	0.9	0.8	148.8	1.9
	min	0.0006	0.0002	0.0052	0.0002
	max	7.9	7.5	1793.6	14.8

Values are in ng/handwipe.
Residents: adult residents of location homes; growers' families: adults and children living in farm homes.

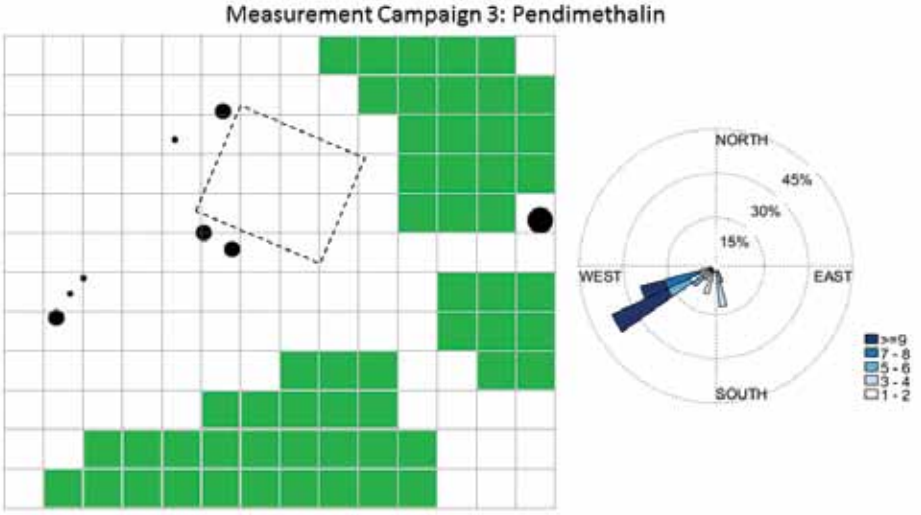
Appendix 9: Results of fruit and vegetables

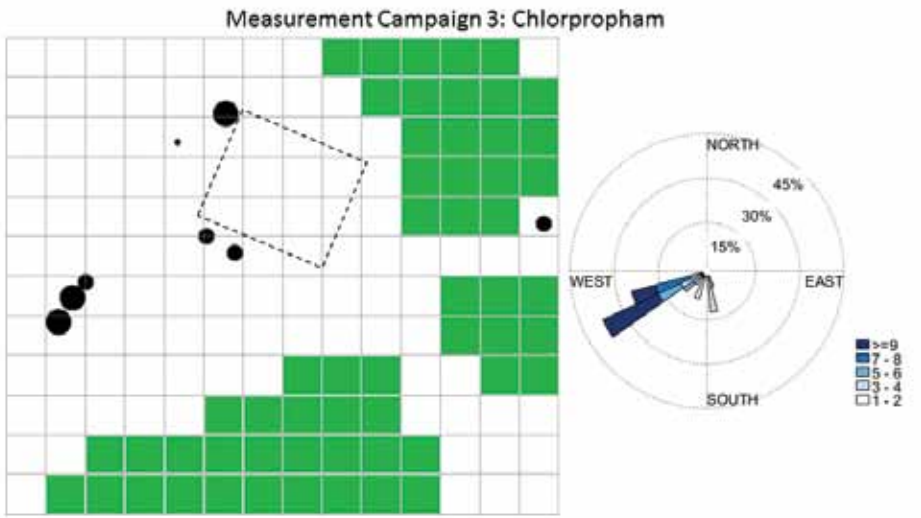
In the entire study, 27 samples were taken from 12 location homes, of which 20 were analyzed. Not analyzed were: one single egg sample and crop samples from 2 not selected homes. For a number of crop samples, the amounts available were very small, only 2-65 gram, and, consequently, cannot be considered representative for human consumption. In addition, some of the samples were non-edible (immature crop, leaves of crops). Generally, no or only small traces of pesticides (below 10 µg/kg, the default EU-MRL for non-registered pesticides) were present. Overall, pesticides exceeding 10 µg/kg were found in six samples. These pesticides were boscalid (37 µg/kg), chlorpropham (59 µg/kg), lambda-cyhalothrin (15 µg/kg), pendimethalin (5x, 12-71 µg/kg), prochloraz (18 µg/kg) and pyraclostrobin (31 µg/kg). Five out of these ten residues were found in samples from the garden of a farm home.

Appendix 10: Plots of day 1 with wind roses

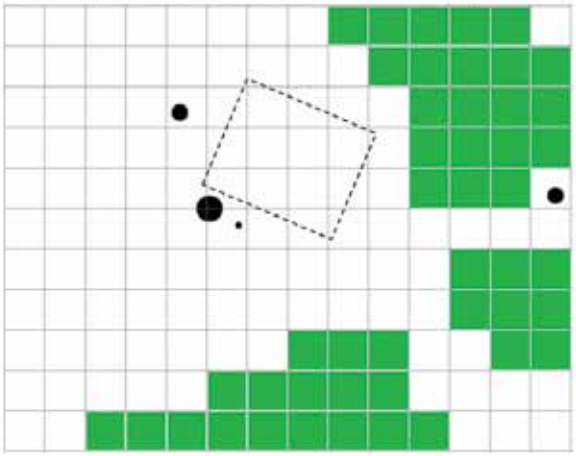
Wind and pesticide concentrations in air during the first 24h.

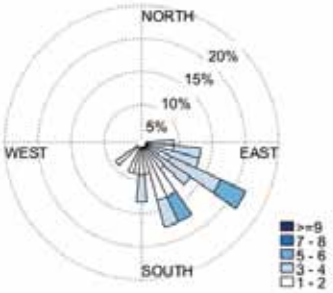
Graphic display of the location of a specified measuring campaign. Each cell is 50 by 50 meters. The target field is situated in the box with the dotted line. The wind rose next to the display represents wind direction and wind speed (measured at 10 m height) during the first 24h after application. Green cells are cells with additional fields. Dots are location homes (farm homes excluded) and the dot size represents the measured exposure to the specified pesticide in quantiles. Legends for wind speed are given on the right side of the display. Wind direction is represented as the direction the wind originates from.



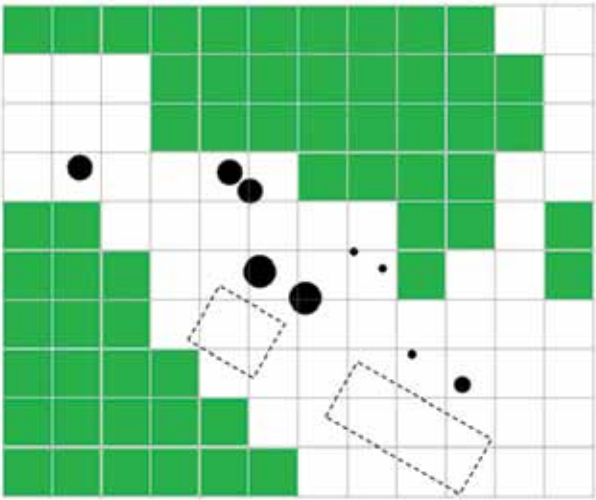


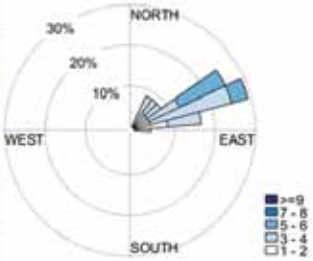
Measurement Campaign 4: Tebuconazole



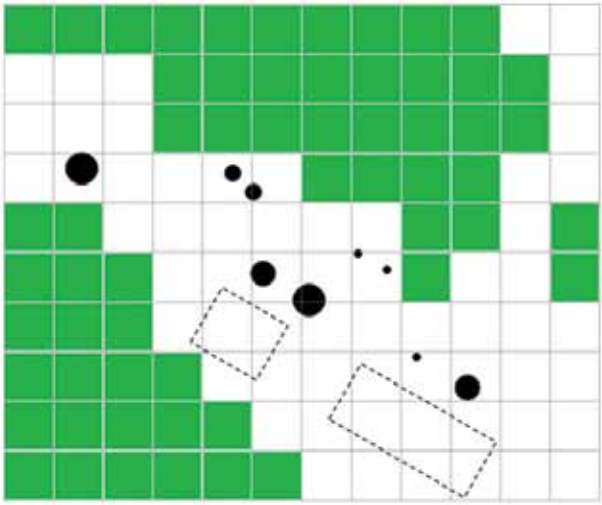


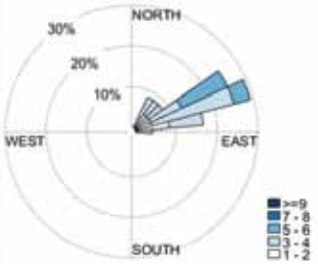
Measurement Campaign 5: Chlorpropham



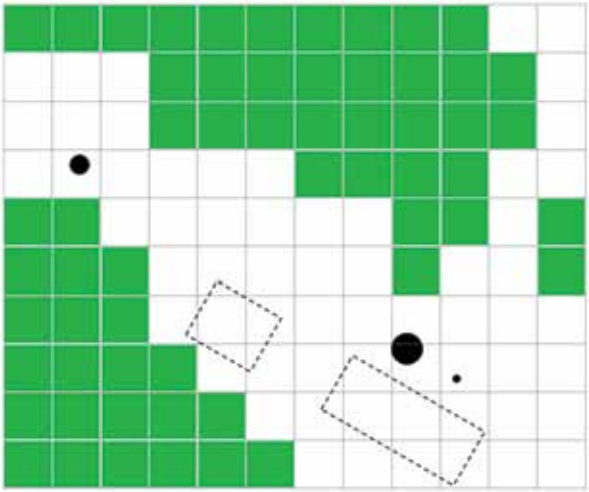


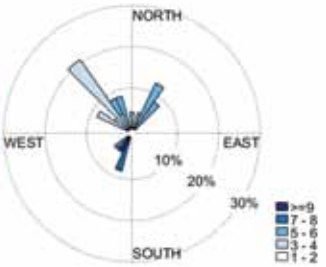
Measurement Campaign 5: Pendimethalin



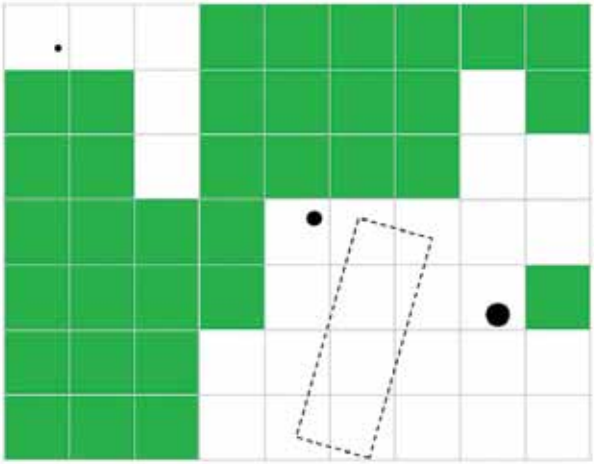


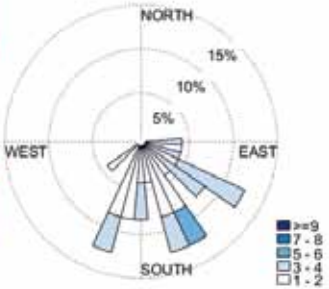
Measurement Campaign 6: Prochloraz



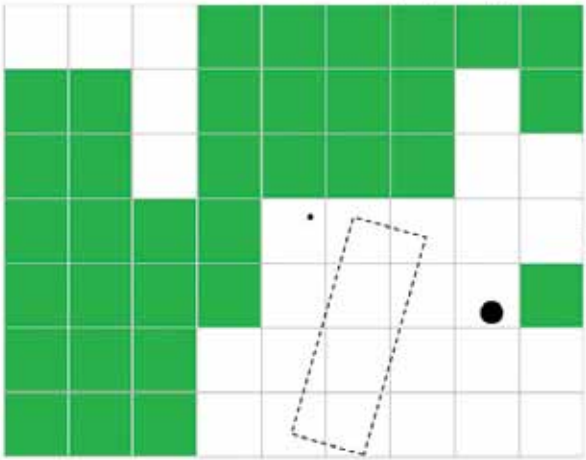


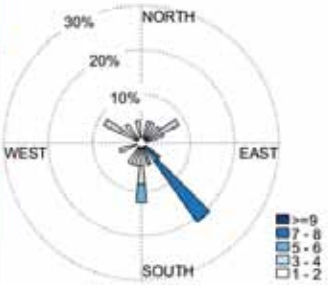
Measurement Campaign 7: Mepanipyrim



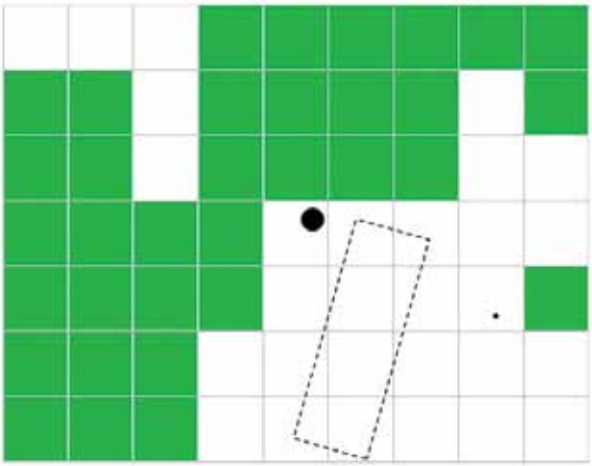


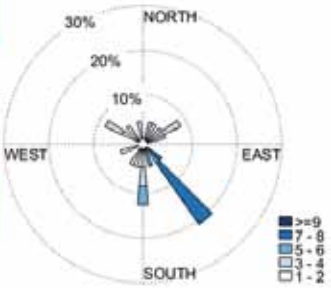
Measurement Campaign 8: Cyhalotrin-Lambda



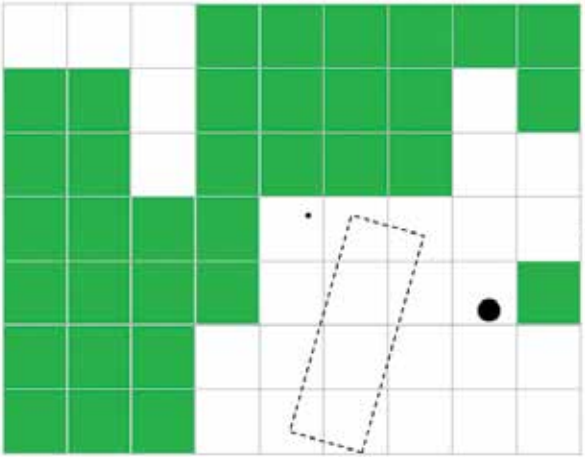


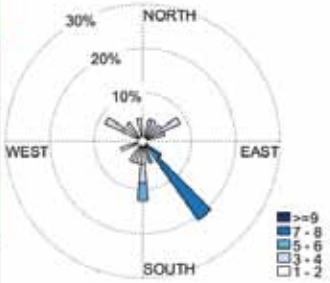
Measurement Campaign 8: Flonicamid



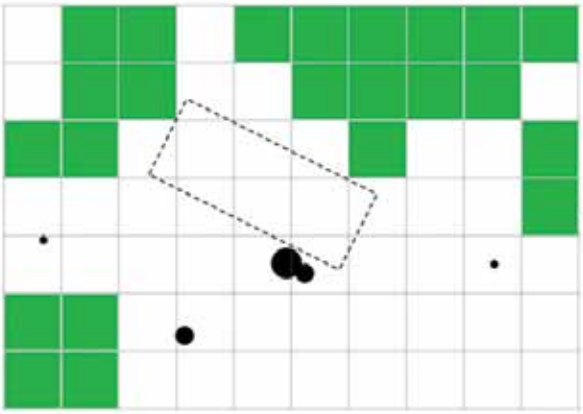


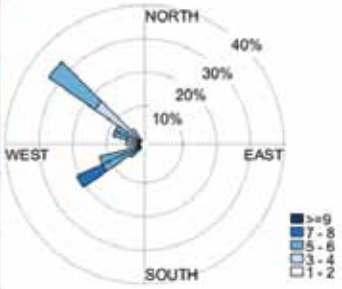
Measurement Campaign 8: Tebuconazole



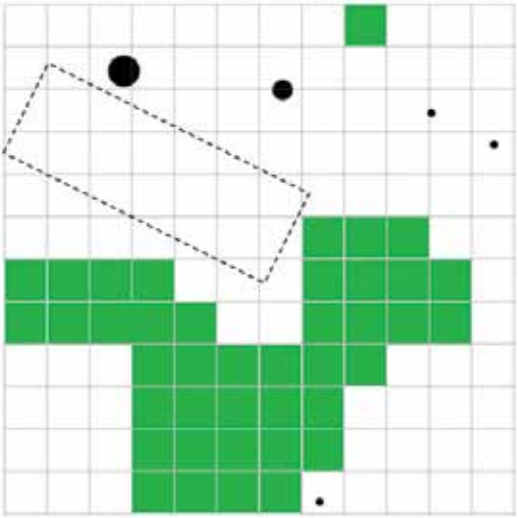


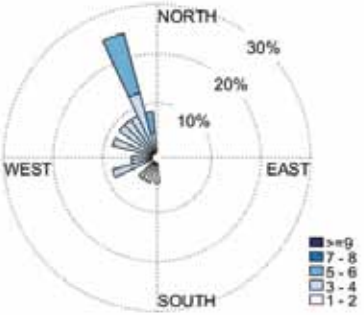
Measurement Campaign 9: Tebuconazole



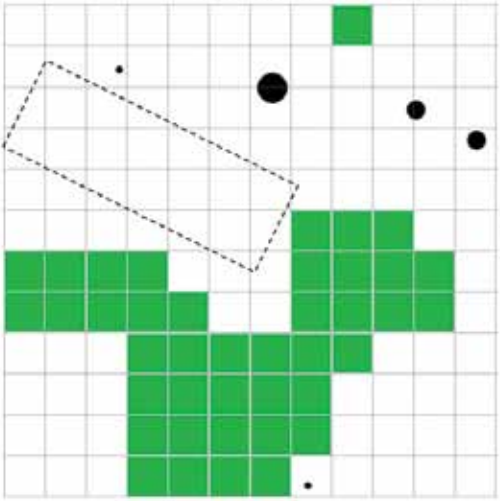


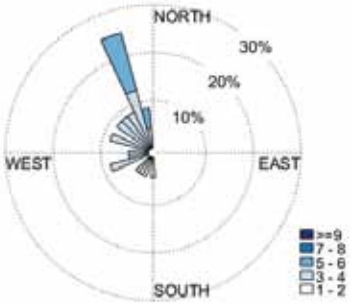
Measurement Campaign 11: Cyhalotrin-Lambda



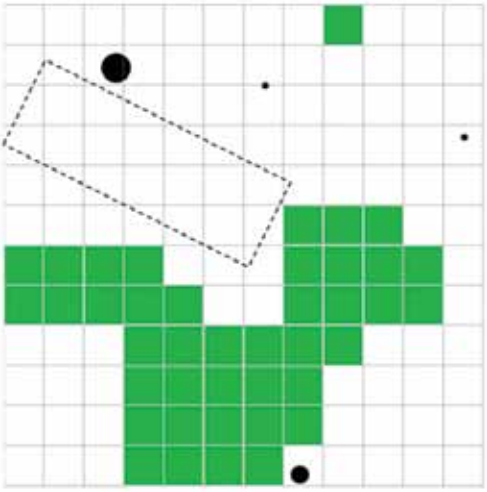


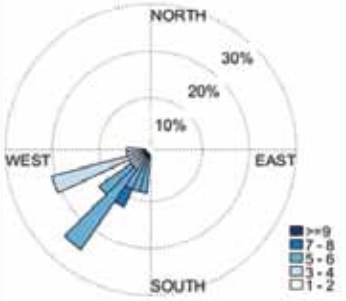
Measurement Campaign 11: Metamitron



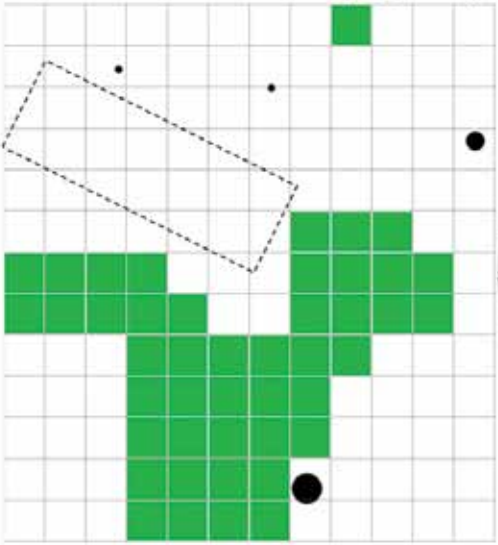


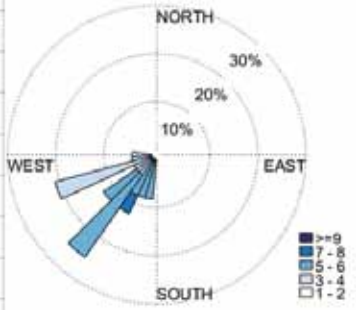
Measurement Campaign 12: Asulam



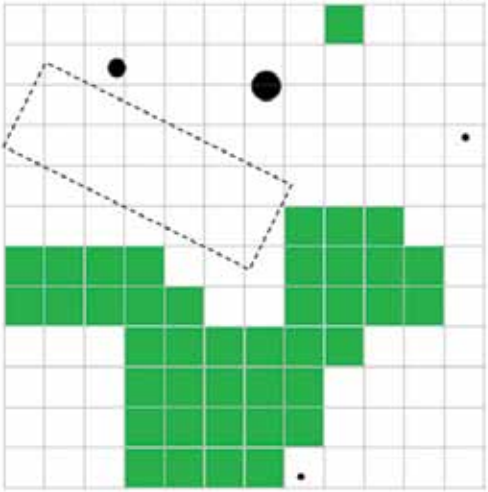


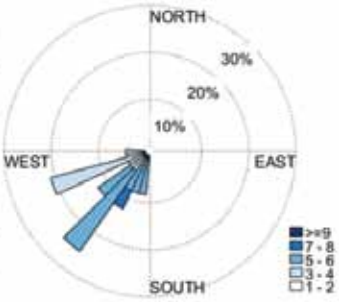
Measurement Campaign 12: Cyhalotrin-Lambda



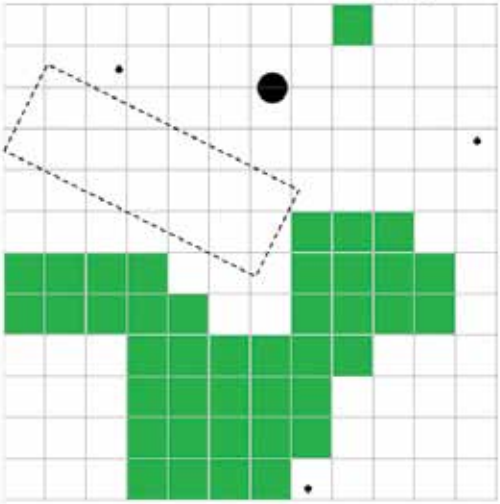


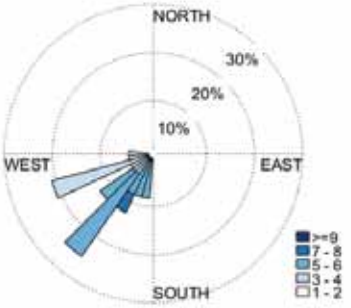
Measurement Campaign 12: Metamitron



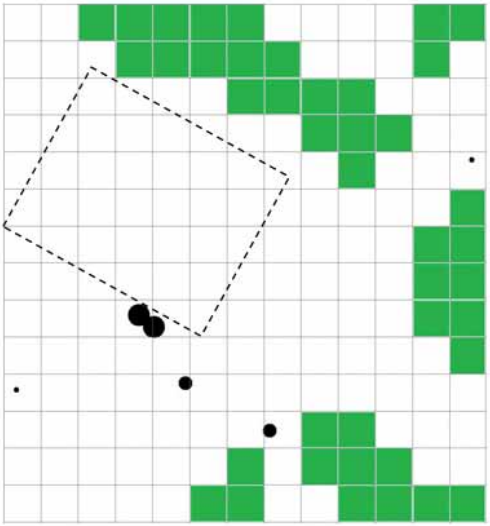


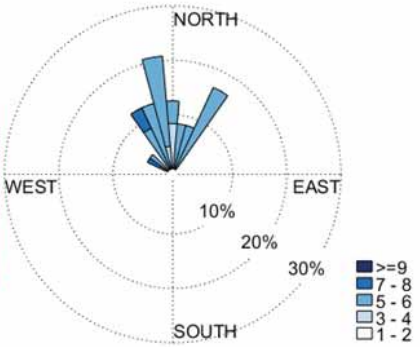
Measurement Campaign 12: Pymetrozine



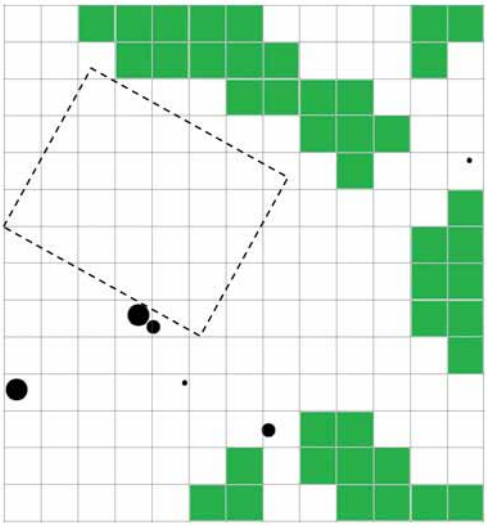


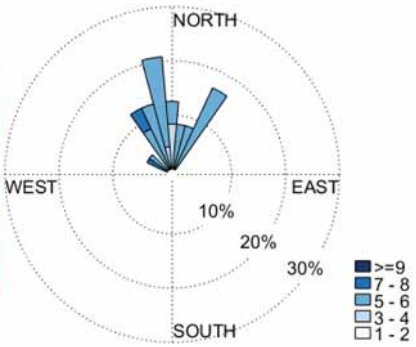
Measurement Campaign 13: Fluopyram



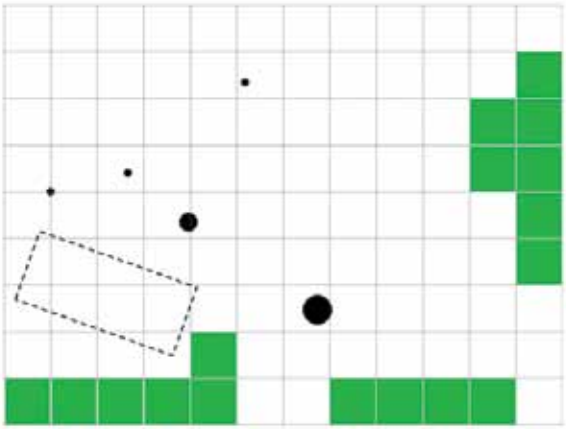


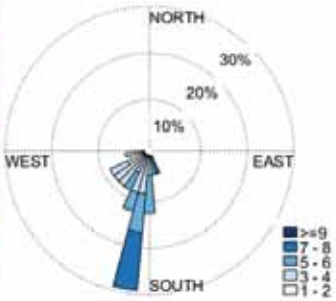
Measurement Campaign 13: Trifloxystrobin





Measurement Campaign 14: Trifloxystrobin





Appendix 11: Means and ranges of outdoor air, VFD and DDM

Table 1: Means and ranges of outdoor air collected during the OBO measurement campaign.

	Outdoor Air							
	N	Use period Locations	N	Non-use period Locations	N	Use period Controls	N	Non-use period Controls
Applied in the target field(s)								
acetamiprid	26	NA (<LOD,0.02)	5	NA (<LOD,0.01)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
asulam	29	NA (<LOD,0.05)	21	NA (<LOD,0.01)	7	NA (<LOD,0.05)	5	NA (<LOD,6E-3)
chlorpropham(i)	265	6.92 (0.16,173.78)	189	0.55 (3E-3,2818.38)	41	NA (<LOD,57.54)	72	0.11 (3E-3,2.19)
cyhalotrin-lambda	67	NA (<LOD,0.32)	44	0.04 (0.03,0.13)	7	NA (<LOD,0.12)	10	NA (<LOD,0.08)
flonicamid(i)	265	0.01 (4E-5,1.32)	189	4E-3 (2E-5,0.04)	55	6E-3 (2E-4,0.07)	58	2E-3 (1E-5,0.04)
fluopyram(i)	369	0.01 (0,2.82)	85	2E-3 (3E-5,0.04)	68	5E-3 (3E-5,0.30)	45	2E-3 (1E-6,0.24)
floupyram-benzamide (i)	369	0.03 (1E-4,1.51)	85	5E-3 (1E-4,0.04)	68	7E-3 (3E-5,0.63)	45	4E-3 (2E-5,0.54)
mepanipyrim	127	NA (<LOD,0.65)	2	NA (<LOD,0.01)	9	NA (<LOD,0.025)	8	NA (<LOD,0.02)
metamitron(i)	265	0.01 (3E-5,1.1)	189	3E-4 (2E-6,0.01)	55	1E-3 (2E-6,0.05)	58	5E-4 (4E-6,0.04)
metamitron-desamino	135	NA (<LOD,0.26)	36	NA (<LOD,0.01)	17	NA (<LOD,0.02)	9	NA (<LOD,0.03)
pendimethalin(i)	265	6.31 (0.20,123.02)	189	0.60 (0.01,15.85)	41	0.44 (0.01,40.74)	72	0.11 (2E-3,2.29)
prochloraz(i)	265	0.01 (2E-4,0.47)	189	0.01 (2E-4,0.23)	55	4E-3 (2E-4,0.35)	58	4E-3 (2E-4,0.58)
prothioconazole-desthio(i)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
prothioconazole-desthio (i)	199	0.11 (4E-4,0.78)	255	0.01 (3E-4,0.19)	41	0.04 (4E-4,0.32)	72	0.01 (1E-4,0.48)
pymetrozine	12	NA (<LOD,0.03)	7	NA (<LOD,0.01)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,3E-3)
tebuconazole(i)	265	0.02 (2E-4,0.71)	189	1E-3 (5E-5,0.06)	55	5E-3 (1E-4,0.22)	58	2E-3 (4E-5,0.05)
thiacloprid	42	NA (<LOD,0.11)	23	NA (<LOD,0.06)	2	NA (<LOD,6E-3)	6	NA (<LOD,0.06)
trifloxystrobin	147	NA (<LOD,1.07)	32	NA (<LOD,0.03)	20	NA (<LOD,0.02)	9	NA (<LOD,0.05)
trifloxystrobin-acid	113	NA (<LOD,0.54)	76	NA (<LOD,0.06)	0	<LOD (<LOD,<LOD)	20	NA (<LOD,0.06)
Applied in the additional fields								
boscalid(i)	265	0.01 (3E-5,0.20)	189	3E-3 (5E-5,0.19)	55	8E-3 (1E-4,1.45)	58	2E-3 (6E-5,0.2)
chloridazon	101	NA (<LOD,0.26)	24	NA (<LOD,0.12)	16	NA (<LOD,0.26)	5	NA (<LOD,9E-3)
dimethenamidP(i)	265	0.07 (2E-4,6.31)	189	4E-3 (2E-5,0.41)	41	6E-3 (6E-5,1.02)	72	1E-3 (6E-6,0.07)
kresoxim-methyl(i)	202	0.01 (9E-5,0.70)	252	1E-3 (6E-6,0.04)	48	1E-3 (3E-6,0.08)	65	1E-3 (2E-6,0.06)
S-metolachlor(i)	216	0.49 (0.03,23.99)	238	0.05 (0,7.41)	34	NA (<LOD,0.22)	79	8E-3 (6E-5,5.25)
spirotetramat	51	NA (<LOD,0.14)	6	NA (<LOD,0.10)	6	NA (<LOD,0.21)	6	NA (<LOD,0.04)
spirotetramat-enol	1	NA (<LOD,0.01)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
Not applied during measuring week								
azoxystrobin	87	NA (<LOD,0.07)	71	NA (<LOD,0.17)	12	NA (<LOD,0.03)	13	NA (<LOD,0.05)
cyprodinil	128	NA (<LOD,0.15)	13	NA (<LOD,0.01)	27	NA (<LOD,0.18)	1	NA (<LOD,4E-3)
deltamethrin	47	NA (<LOD,0.08)	121	NA (<LOD,0.04)	7	NA (<LOD,0.02)	14	NA (<LOD,0.01)
difenoconazole	115	NA (<LOD,0.17)	39	NA (<LOD,0.02)	28	NA (<LOD,0.04)	4	NA (<LOD,0.01)
dimethomorph	26	NA (<LOD,0.01)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,0.01)	0	<LOD (<LOD,<LOD)
fludioxonil	25	NA (<LOD,0.18)	1	NA (<LOD,0.02)	6	NA (<LOD,0.02)	0	<LOD (<LOD,<LOD)
fluopicolide	72	NA (<LOD,0.06)	0	<LOD (<LOD,<LOD)	11	NA (<LOD,0.09)	0	<LOD (<LOD,<LOD)
flutolanil	43	NA (<LOD,0.12)	25	NA (<LOD,0.08)	15	NA (<LOD,0.11)	1	NA (<LOD,8E-3)
fosthiazate	102	NA (<LOD,0.11)	0	<LOD (<LOD,<LOD)	7	NA (<LOD,0.01)	0	<LOD (<LOD,<LOD)
imidacloprid	111	NA (<LOD,0.22)	18	NA (<LOD,0.02)	25	NA (<LOD,0.05)	4	NA (<LOD,0.01)
linuron(i)	227	0.01 (2E-4,0.44)	227	0.03 (3E-4,0.91)	53	0.005 (3E-4,0.12)	60	3E-3 (2E-4,0.05)
oxamyl	35	NA (<LOD,0.35)	12	NA (<LOD,0.04)	1	NA (<LOD,0.02)	0	<LOD (<LOD,<LOD)
primicarb	10	NA (<LOD,0.02)	5	NA (<LOD,0.01)	9	NA (<LOD,0.33)	3	NA (<LOD,5E-3)
propamocarb(i)	369	3E-3 (4E-6,3.55)	85	1E-3 (2E-5,0.02)	89	0.002 (2E-6,2.63)	24	2E-3 (3E-4,0.01)
pyraclostrobin(i)	199	0.02(9E-6,1.0)	255	6E-3 (5E-6,0.47)	41	0.004 (2E-4,0.54)	72	2E-3 (5E-5,1.18)
sulcotrione	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
terbuthylazine	219	NA (<LOD,0.60)	3	NA (<LOD,4E-3)	53	NA (<LOD,0.43)	3	NA (<LOD,0.01)
thiophanate-methyl	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
carbendazim#(i)	369	0.02 (6E-5,1.0)	85	0.02 (4E-5,0.89)	89	0.005 (1E-4,6.31)	24	5E-3 (3E-4,0.07)
toclofos-methyl(i)	369	0.07 (2E-4,4.90)	85	0.22 (1E-3,3.55)	89	0.011 (7E-5,2.63)	24	0.03 (2E-3,1.62)

All results are in ng/m3. "(i)" in front of a pesticide name means that values < LOD were imputed.

Table 2: Means and ranges of VFD collected during the OBO measurement campaign.

	VFD							
	N	Use period Locations	N	Non-use period Locations	N	Use period Controls	N	Non-use period Controls
Applied in the target field(s)								
acetamiprid	7	NA (<LOD,26.92)	5	NA (<LOD,77.63)	3	NA (<LOD,6.31)	1	NA (<LOD,1.20)
asulam	15	NA (<LOD,72.44)	1	NA (<LOD,1.15)	1	NA (<LOD,1.29)	0	<LOD (<LOD,<LOD)
chlorpropham	13	NA (<LOD,194.98)	6	NA (<LOD,4897.79)	2	NA (<LOD,20.89)	1	NA (<LOD,29.51)
cyhalotrin-lambda	1	NA (<LOD,39.81)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
flonicamid(i)	41	2.40 (8E-3,58.88)	41	0.79 (1E-3,223.87)	13	0.09 (1E-3,9.33)	19	0.27 (1E-3,7.59)
fluopyram(i)	48	1.15 (1E-3,83.18)	34	0.39 (3E-3,31.62)	16	0.09 (1E-3,2.63)	16	0.15 (1E-3,3.16)
floupyram-benzamide	1	NA (<LOD,6.03)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
mepanipyrim	3	NA (<LOD,204.17)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
metamitron	19	NA (<LOD,269.15)	4	NA (<LOD,47.86)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
metamitron-desamino	15	NA (<LOD,120.23)	4	NA (<LOD,13.18)	1	NA (<LOD,11.75)	2	NA (<LOD,7.94)
pendimethalin(i)	33	14.13 (0.01,501.19)	49	1.02 (1E-3,144.54)	9	0.15 (3E-3,28.18)	23	0.30 (6E-3,15.49)
prochloraz(i)	41	10.47 (0.07,616.60)	41	9.12 (0.08,588.84)	13	0.26 (8E-3,4.07)	19	2.51 (0.05,602.56)
prothioconazole(i)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
prothioconazole-desthio (i)	30	5.75 (0.21,144.54)	52	1.38 (0.03,36.31)	11	1.12 (0.15,8.51)	21	0.40 (4E-3,7.94)
pymetrozine	5	NA (<LOD,87.10)	3	NA (<LOD,57.54)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
tebuconazole(i)	41	9.77 (0.03,141.25)	41	3.80 (0.08,85.11)	13	3.39 (0.24,22.39)	19	1.82 (9E-3,67.61)
thiacloprid	11	NA (<LOD,74.13)	10	NA (<LOD,151.36)	1	NA (<LOD,2.04)	0	<LOD (<LOD,<LOD)
trifloxystrobin	5	NA (<LOD,16.22)	2	NA (<LOD,23.99)	2	NA (<LOD,5.50)	0	<LOD (<LOD,<LOD)
trifloxystrobin-acid	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
Applied in the additional fields								
boscalid(i)	41	17.78 (0.49,467.74)	41	10 (9E-3,102.33)	13	2.00 (0.09,81.28)	19	2.14 (7E-3,134.90)
chloridazon	12	NA (<LOD,162.18)	2	NA (<LOD,7.59)	1	NA (<LOD,1.59)	0	<LOD (<LOD,<LOD)
dimethenamidP	4	NA (<LOD,33.11)	3	NA (<LOD,7.76)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
kresoxim-methyl	5	NA (<LOD,33.88)	9	NA (<LOD,134.90)	1	NA (<LOD,4.68)	2	NA (<LOD,28.18)
S-metolachlor	13	NA (<LOD,104.71)	11	NA (<LOD,22.91)	1	NA (<LOD,1.82)	2	NA (<LOD,1.82)
spirotetramat	1	NA (<LOD,31.62)	1	NA (<LOD,4.90)	0	<LOD (<LOD,<LOD)	2	NA (<LOD,4.90)
spirotetramat-enol	0	<LOD (<LOD,<LOD)	2	NA (<LOD,28.84)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,1.38)
Not applied during measuring week								
azoxystrobin(i)	33	3.80 (0.02,1479.11)	49	2.46 (0.01,309.03)	9	3.24 (0.15,61.66)	23	1 (0.04,22.91)
cyprodinil	10	NA (<LOD,37.15)	6	NA (<LOD,50.12)	0	<LOD (<LOD,<LOD)	2	NA (<LOD,37.15)
deltamethrin	0	<LOD (<LOD,<LOD)	4	NA (<LOD,70.80)	0	<LOD (<LOD,<LOD)	3	NA (<LOD,12.02)
difenoconazole	13	NA (<LOD,72.44)	6	NA (<LOD,4.57)	2	NA (<LOD,15.85)	2	NA (<LOD,6.61)
dimethomorph	13	NA (<LOD,426.58)	7	NA (<LOD,38.02)	2	NA (<LOD,10.47)	2	NA (<LOD,35.48)
fludioxonil(i)	48	0.79 (0,48.98)	34	0.96 (4E-3,354.81)	16	0.12 (1E-3,169.82)	16	0.46 (0.02,75.86)
fluopicolide	5	NA (<LOD,10.23)	3	NA (<LOD,10.97)	1	NA (<LOD,2.40)	1	NA (<LOD,1.55)
flutolanil	16	NA (<LOD,16.60)	9	NA (<LOD,6.166)	3	NA (<LOD,3.63)	0	<LOD (<LOD,<LOD)
fosthiazate	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
imidacloprid(i)	48	13.49 (0.02,7585.78)	34	4.47 (0.018,346.74)	16	89.13 (0.06,26915.35)	16	70.80 (0.12,50118.72)
linuron	7	NA (<LOD,35.48)	14	NA (<LOD,117.49)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
oxamyl	4	NA (<LOD,25.12)	4	NA (<LOD,10.97)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
primicarb	5	NA (<LOD,63.10)	3	NA (<LOD,10.47)	2	NA (<LOD,5.62)	1	NA (<LOD,5.01)
propamocarb(i)	48	1.82 (7E-3,102.33)	34	0.96 (5E-3,38.02)	16	0.96 (1E-3,114.82)	16	0.53 (8E-3,26.92)
pyraclostrobin(i)	30	37.15 (0.51,1412.54)	52	10.97 (0.05,109.65)	11	0.29 (0.03,8.51)	21	0.71 (0.01,15.14)
sulcotrione	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,25.12)	0	<LOD (<LOD,<LOD)
terbuthylazine	2	NA (<LOD,7.59)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,7.08)	0	<LOD (<LOD,<LOD)
thiophanate-methyl(i)	48	1.70 (2E-3,363.08)	34	3.63 (0.04,107.15)	16	0.31 (2E-3,15.14)	16	0.55 (0,46.77)
carbendazim#(i)	48	77.63 (0.25,1819.70)	34	53.70 (0.68,891.25)	16	3.02 (0.09,100)	16	3.31 (0.11,64.57)
toclofos-methyl	12	NA (<LOD,41.69)	6	NA (<LOD,40.74)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,75.86)

All results are in ng/m3. "(i)" in front of a pesticide name means that values < LOD were imputed.

Table 3: Means and ranges of DDM collected during the OBO measurement campaign.

	DDM							
	N	Use period Locations	N	Non-use period Locations	N	Use period Controls	N	Non-use period Controls
Applied in the target field(s)								
acetamiprid	3	NA (<LOD,26.30)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
asulam	15	NA (<LOD,234.42)	6	NA (<LOD,6.92)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
chlorpropham	18	NA (<LOD,263.03)	9	NA (<LOD,346.74)	3	NA (<LOD,52.48)	0	<LOD (<LOD,<LOD)
cyhalotrin-lambda	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
flonicamid	9	NA (<LOD,61.66)	5	NA (<LOD,18.62)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,2.34)
fluopyram(i)	48	1.35 (0.04,24.55)	31	0.79 (0.02,13.18)	16	0.22 (0.01,2.57)	16	0.8 (2E-3,2.95)
floupyram-benzamide	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
mepanipyrim	9	NA (<LOD,20.89)	2	NA (<LOD,3.55)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
metamitron	11	NA (<LOD,1096.48)	3	NA (<LOD,758.58)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
metamitron-desamino	10	NA (<LOD,223.87)	1	NA (<LOD,6.03)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
pendimethalin(i)	33	23.99 (0.24,1513.56)	46	5.25 (0.14,257.04)	9	0.85 (0.06,12.02)	23	0.28 (0.01,5.01)
prochloraz(i)	41	10.23 (0.20,478.63)	38	9.55 (2E-4,912.011)	13	1.12 (0.09,24.55)	19	0.93 (6E-3,60.26)
prothioconazole	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
prothioconazole-desthio (i)	30	3.63 (0.05,75.86)	49	0.98 (6E-3,25.12)	11	0.21 (9E-3,3.90)	21	0.12 (1E-3,1.86)
pymetrozine	6	NA (<LOD,41.69)	8	NA (<LOD,16.98)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
tebuconazole(i)	41	6.31 (0.20,53.70)	38	1.86 (0.02,1380.38)	13	3.55 (0.32,19.06)	19	0.87 (0.01,30.20)
thiacloprid	1	NA (<LOD,1.48)	1	NA (<LOD,6.31)	1	NA (<LOD,2.042)	1	NA (<LOD,2.40)
trifloxystrobin	4	NA (<LOD,12.88)	3	NA (<LOD,8.32)	1	NA (<LOD,3.39)	1	NA (<LOD,1.86)
trifloxystrobin-acid	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
Applied in the additional fields								
boscalid(i)	41	13.50 (0.98,177.83)	38	6.92 (0.08,478.63)	13	3.47 (0.76,15.14)	19	1.55 (0.03,52.48)
chloridazon	5	NA (<LOD,34.67)	2	NA (<LOD,33.88)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
dimethenamidP	0	<LOD (<LOD,<LOD)	4	NA (<LOD,57.54)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
kresoxim-methyl	1	NA (<LOD,7.94)	2	NA (<LOD,4.57)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
S-metolachlor(i)	30	1.07 (0.1,9.33)	49	0.71 (0.02,21.38)	7	NA (<LOD,0.42)	25	0.12 (5E-3,1.45)
spirotetramat	2	NA (<LOD,2.82)	1	NA (<LOD,2.19)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
spirotetramat-enol	1	NA (<LOD,1.48)	1	NA (<LOD,1.02)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
Not applied during measuring week								
azoxystrobin(i)	33	1.26 (0.07,19.06)	46	1.12 (0.02,10.72)	9	NA (<LOD,6.92)	23	0.17 (6E-3,18.62)
cyprodinil	8	NA (<LOD,15.14)	4	NA (<LOD,17.78)	2	NA (<LOD,12.59)	0	<LOD (<LOD,<LOD)
deltamethrin	2	NA (<LOD,18.20)	2	NA (<LOD,52.48)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,37.15)
difenoconazole	3	NA (<LOD,19.95)	4	NA (<LOD,1.32)	1	NA (<LOD,3.02)	1	NA (<LOD,1.91)
dimethomorph	9	NA (<LOD,41.69)	3	NA (<LOD,4.57)	1	NA (<LOD,2.40)	3	NA (<LOD,2.24)
fludioxonil	16	7.08 (<LOD,38.02)	5	NA (<LOD,7.08)	4	NA (<LOD,7.76)	1	NA (<LOD,2.51)
fluopicolide	1	NA (<LOD,4.47)	1	NA (<LOD,1.23)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
flutolanil	20	NA (<LOD,66.07)	12	NA (<LOD,12.30)	2	NA (<LOD,4.27)	0	<LOD (<LOD,<LOD)
fosthiazate	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
imidacloprid(i)	48	0.19 (1E-3,162.18)	31	0.17 (8E-5,69.18)	16	20.89 (0.06,14454.40)	16	0.69 (3E-5,977.24)
linuron	8	NA (<LOD,8.32)	23	NA (<LOD,23.99)	0	<LOD (<LOD,<LOD)	1	NA (<LOD,13.80)
oxamyl	2	NA (<LOD,2.04)	1	NA (<LOD,43.65)	1	NA (<LOD,1.15)	0	<LOD (<LOD,<LOD)
primicarb	4	NA (<LOD,40.74)	2	NA (<LOD,13.49)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
propamocarb	14	NA (<LOD,19.50)	9	NA (<LOD,24.547)	1	NA (<LOD,6.03)	4	NA (<LOD,5.25)
pyraclostrobin(i)	30	22.39 (0.26,3162.28)	49	11.48 (0.01,660.69)	11	3.16 (0.42,16.60)	21	1.18 (0.01,35.48)
sulcotrione	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
terbuthylazine	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)
thiophanate-methyl(i)	48	8.51 (8E-3,426.58)	31	9.55 (3E-4,2691.54)	16	0.29 (5E-3,15.14)	16	0.15 (1E-3,87.10)
carbendazim#(i)	48	23.99 (0.03,1258.93)	31	29.51 (0.03,977.24)	16	17.38 (0.28,363.08)	16	1.74 (0.06,295.12)
toclofos-methyl	8	NA (<LOD,44.67)	9	NA (<LOD,22.39)	0	<LOD (<LOD,<LOD)	0	<LOD (<LOD,<LOD)

All results are in ng/m3. "(i)" in front of a pesticide name means that values < LOD were imputed.

Appendix 12: Uncorrected urine values

In this appendix we show morning urine values not corrected for creatinine (ug/L) for adults (Table 1) and children (Table 2).

Table 1: Uncorrected urine results for adults.

	Residents (adults)		Controls (adults)	
	U	N	U	N
Biomarker of asulam				
N	71	25	64	36
N > LOD	2	0	10	5
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD
max	0.16	< LOD	0.79	0.22
Biomarker of carbendazim				
N	118	60	64	36
N > LOD	25	11	7	4
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD
max	12.84	1.74	0.62	0.16
Biomarker of chlorpropham				
N	76	39	58	34
mean	5.11	3.48	1.85	0.69
median	0.80	0.37	0.30	0.10
min	1E-03	0.06	4E-03	4E-03
max	124.75	73.47	21.16	7.57
Biomarker of prochloraz				
N	30	22	64	34
N > LOD	0	2	0	0
mean	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD
max	NA	0.16	NA	NA
Biomarker of tebuconazole				
N	99	45	64	34
mean	0.46	0.17	0.12	0.14
median	0.16	0.09	0.10	0.10
min	2E-03	1E-03	2E-03	8E-03
max	9.35	1.71	1.81	2.79

Table 2: Uncorrected urine results for children.

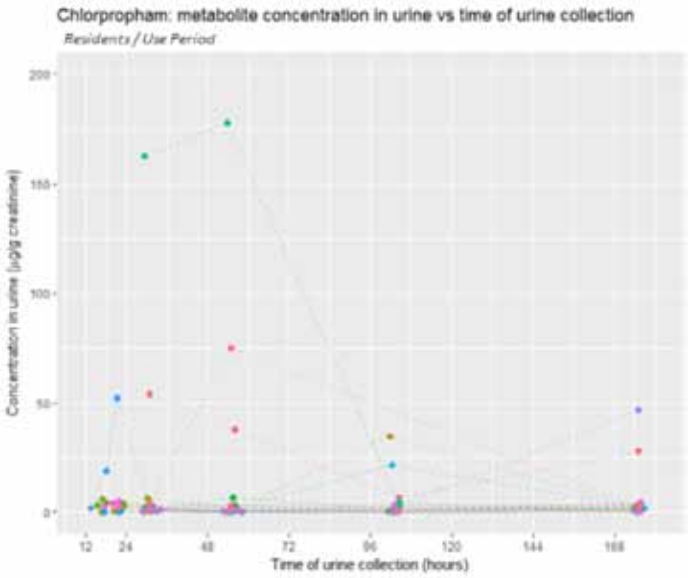
	Diapers (age: 2-4 yrs)		Age 2 to 12				Age 13 to 17			
	U	N	U	N	U_C	N_C	U	N	U_C	N_C
Biomarker of asulam										
N	7	1	11	5	3	2	9	4	3	2
N > LOD	1	0	0	0	0	0	0	0	0	1
mean	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
max	0.16	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	0.20
Biomarker of carbendazim										
N	7	1	27	17	3	2	9	5	3	2
N > LOD	0	0	9	5	0	0	1	1	1	0
mean	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
max	< LOD	< LOD	1.66	0.90	< LOD	< LOD	0.09	0.35	1.38	< LOD
Biomarker of chlorpropham										
N	7	1	4	2	3	2	16	7	3	2
mean	8.27	2.00	0.34	0.16	0.06	4.05	1.77	0.53	1.18	2.84
median	0.87	2.00	0.27	0.16	0.07	4.05	1.68	0.27	0.38	2.84
min	0.14	2.00	0.22	0.13	0.03	0.53	0.34	0.07	0.24	1.15
max	52.50	2.00	0.82	0.19	0.10	7.57	68.77	10.91	17.97	4.53
Biomarker of prochloraz										
N	12	1	4	2	3	2	-	3	3	1
N > LOD	0	1	0	0	0	0	NA	2	0	0
mean	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
median	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	< LOD	< LOD	< LOD
min	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	< LOD	< LOD	< LOD
max	< LOD	0.20	< LOD	< LOD	< LOD	< LOD	NA	0.20	< LOD	< LOD
Biomarker of tebuconazole										
N	12	1	30	15	3	2	17	9	3	1
mean	0.41	NA	0.09	0.05	0.11	0.06	0.20	0.16	0.08	0.17
median	0.34	< LOD	0.09	0.05	0.06	0.06	0.16	0.20	0.06	0.17
min	0.12	< LOD	3E-03	2E-03	0.05	0.02	0.05	0.02	0.02	0.17
max	0.88	< LOD	1.24	0.30	0.44	0.10	1.39	0.52	0.47	0.17

Appendix 13: Urine result per measuring campaign

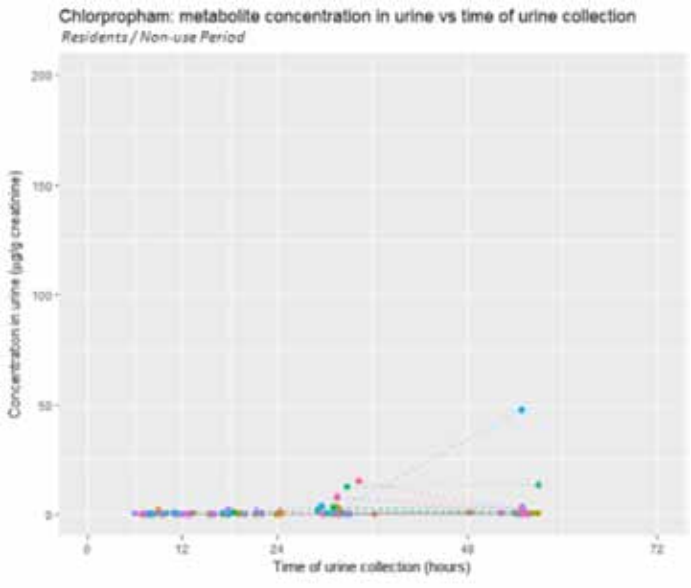
Urine results for all participants, independent of age. Biomarker results in urine grouped for the 6 measuring campaigns that included tebuconazole or chlorpropham. These graphs show the concentrations of biomarkers of chlorpropham and tebuconazole in the urines collected on the first day AND the morning urines from the following days (day 1, 2, 4 and 7). Each colored line represents one person (over time). De connecting lines are dotted as the dynamics of the biomarkers in the urine may be different from the expressed line.

Chlorpropham

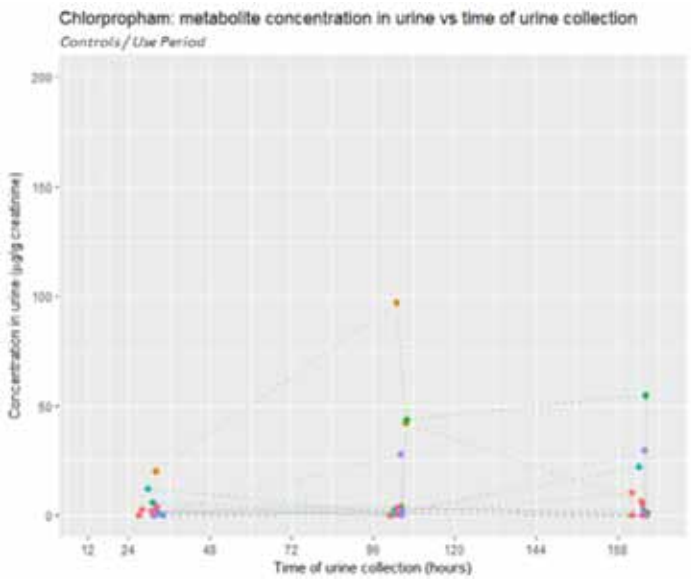
Residents: use period in-season



Residents: non-use period



Controls: use period



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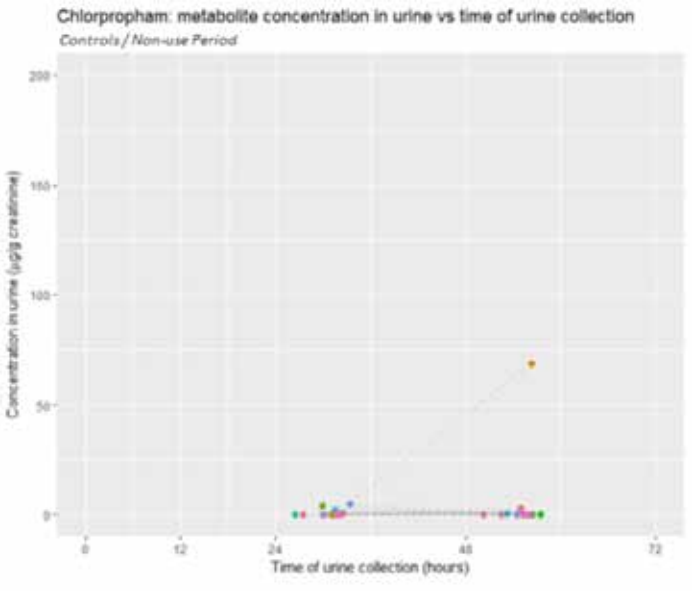
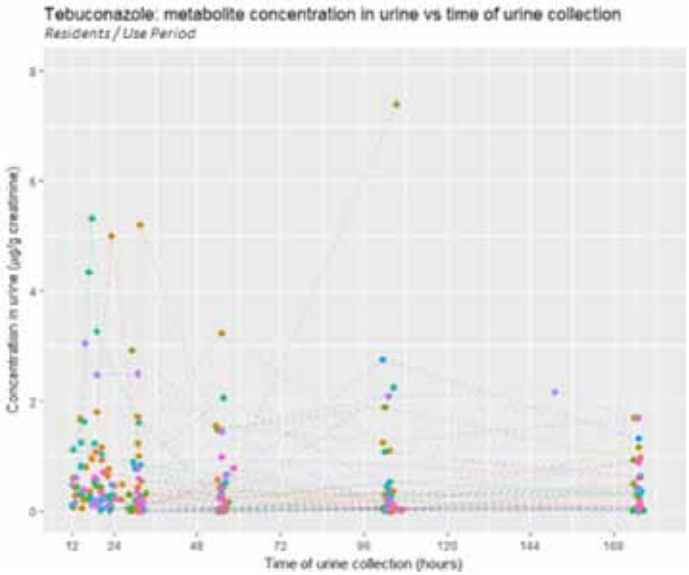
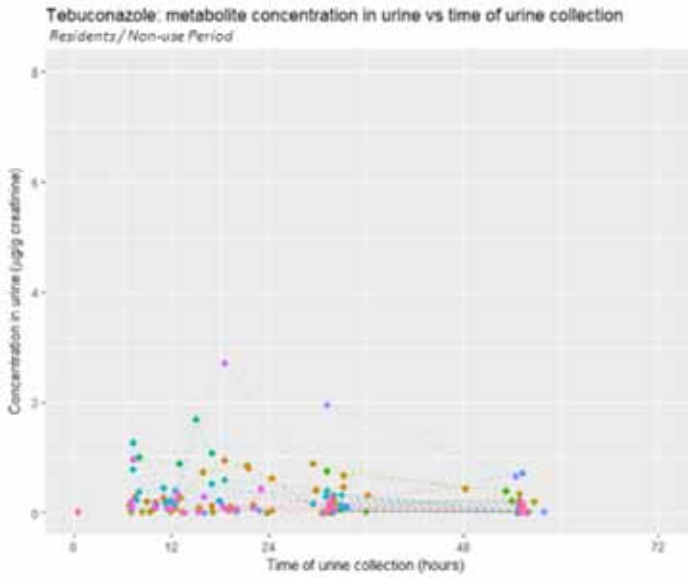


Tebuconazole

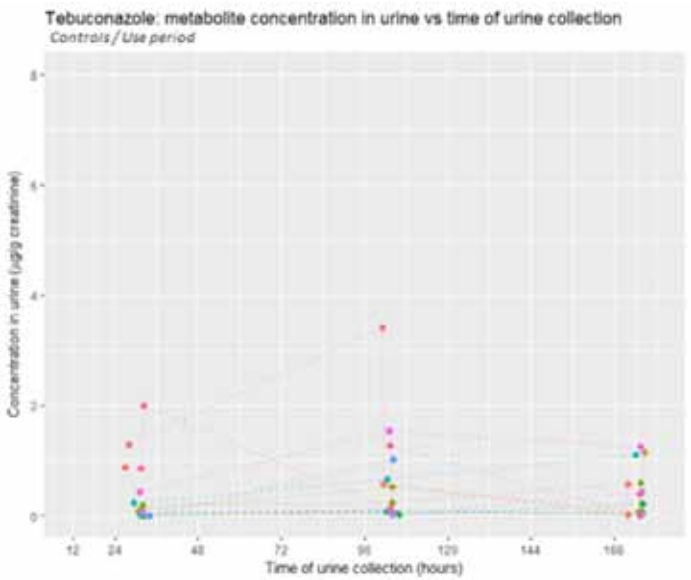
Residents: use period



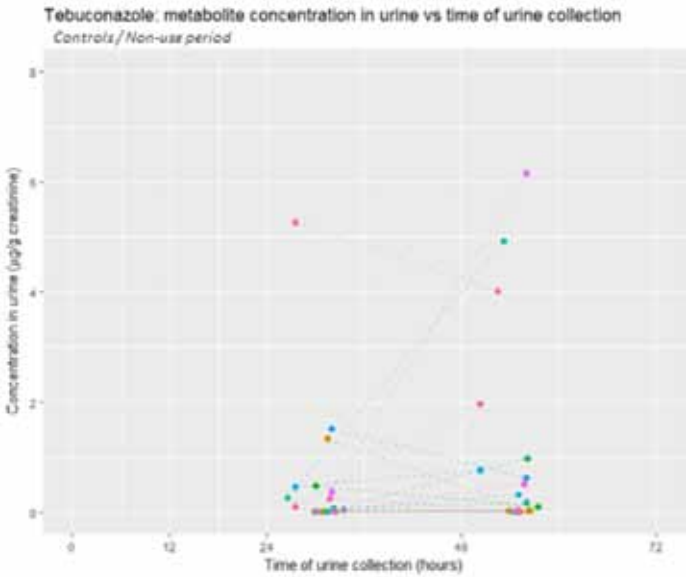
Residents: non-use period



Controls: use period



Controls: non-use period



Appendix 14: Lateral and vertical fluctuations in wind speed

The dispersion coefficients affect the extension of the plume containing contaminants due to atmospheric turbulence which results in a dilution of the contamination. The dilution in the horizontal and vertical direction perpendicular to the wind direction is affected by turbulence in the atmospheric boundary layer. This turbulence can be described using data on fast lateral and vertical fluctuations in the wind speed. Usually these fluctuations are scaled to the friction velocity using a procedure described by Stull (1988). The basic rules for these calculations have been derived from measurements above undisturbed, homogeneous surfaces. In most cases the variance is divided by the square of the friction velocity. According to Stull (1988) this ratio ranges for a neutral atmospheric boundary layer from 1.0 to 2.5 for vertical fluctuations and from 2.9 to 6.1 for lateral fluctuations.

Figure 1 shows the friction velocity-scaled lateral and vertical wind speed fluctuations for the measurements at OBO location “A” , together with the lower and upper boundary values for this scaled parameter as given by Stull (1988) for the period of 19 May (Day-of-Year 140) until 27 June (Day-of-Year 179). These results show that the scaled fluctuations are mostly more pronounced than the maximum value based on the procedure proposed by Stull (1988). This could be explained by the effect of obstacles in the vicinity of the measurement site, but the atmospheric stability also plays a role. This should be investigated further, because this higher scaled variable suggests a greater dispersion coefficient, hence more dilution of the contaminant plume perpendicular to the plum direction. This does not mean that concentrations will be lower overall. Depending on the local conditions maxima in the concentrations in air could occur as a result of quasi-stationary eddies, so-called lee eddies. Such effects are not taken into account by the dispersion coefficients as used in the standard atmospheric dispersion models.

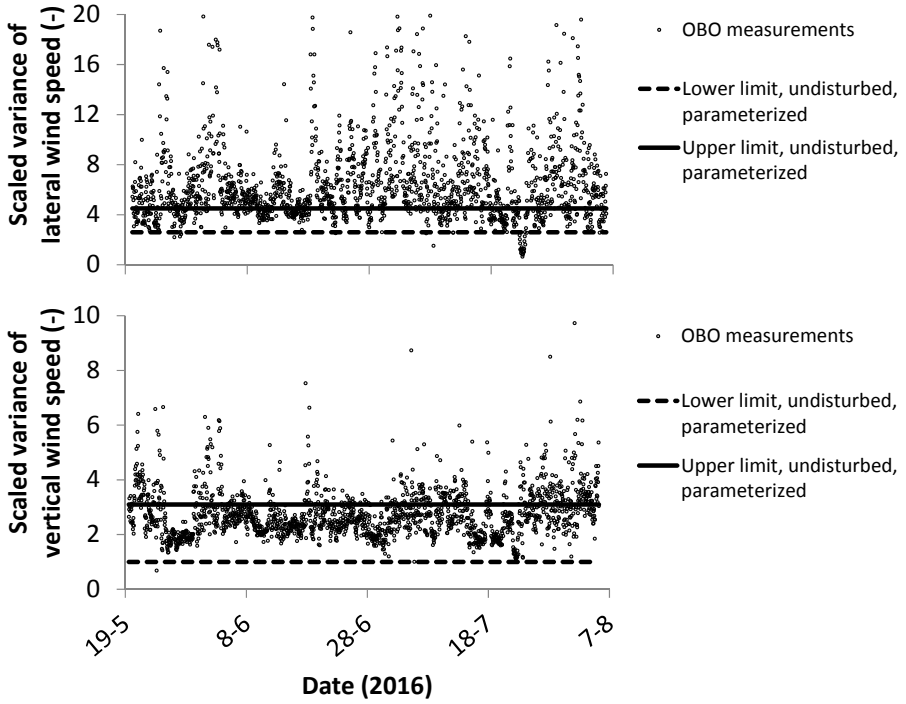


Figure 1: Lateral and vertical fluctuations in wind speed calculated according to Stull (1988).

Appendix 15: Footprint calculations for volatilization measurement at field research site

Application of the flux-gradient relationships requires the flux and gradient to be in equilibrium. This is the case if the so-called fetch or source area is large enough. Given the measurement heights applied at the field research site this is expected to be the case in general (see Garratt, 1992). Footprint calculations (Schuepp et al., 1990) based on the turbulence measurements indicate that the footprint for measurements at a height of 2.5 m was well below 300 m during most volatilization measurements. This is shown in Figure 1.

The footprint distance, defined as the distance over which 80% of the flux originates varied between 100 m and 264 m during sampling times 1-2 and 4-7. Sampling time 3 was performed around dawn during stable conditions (see above). In this case the computed footprint was much longer and varied between 634 m and 5408 m. During sampling time 8 the footprint could not be computed from the turbulence measurements because of the instrument failure.

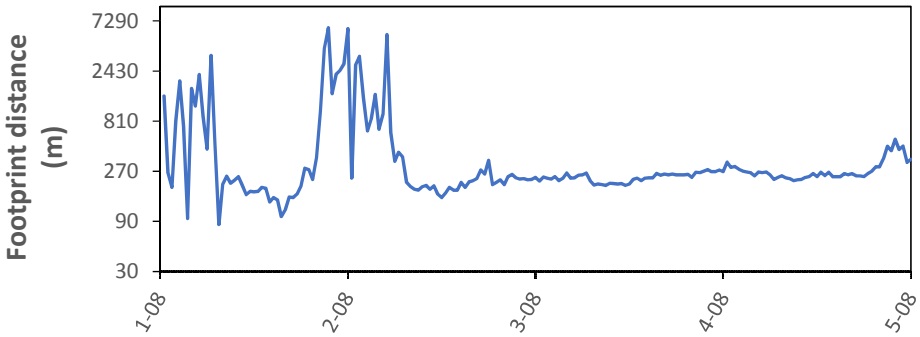


Figure 1: Computed footprint distance during the OBO volatilization measurements. 80% of the flux originates from an area between the location of the measurements and the upwind distance given in the figure. Calculations have been based on the model described by Schuepp et al. (1990). Note that the y-axis has a logarithmic scale with base 3.

Appendix 16: Meteorological equipment and Gap-filling technique for missing meteorological data

Meteorological observations

Meteorological observations were done in support of the volatilization measurements. An overview of the measurements and instruments applied is given in Figure 1. All instruments were powered by means of solar energy.

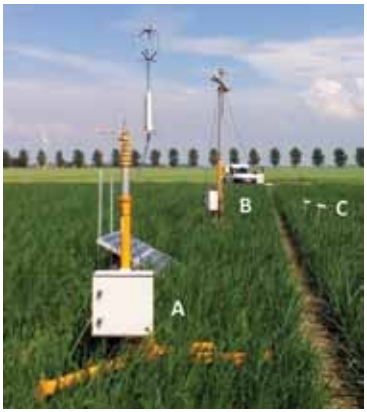


Figure 1: Meteorological equipment applied during the OBO volatilization experiment in July and August 2017.
The labels in the photo indicate A) mast with 3-D sonic anemometer; B) mast with equipment for "slow" meteorological observations; C) sensors for leaf wetness and leaf temperature measurements. See Table 1 for a list of the equipment.

Table 1: Overview of meteorological measurements.

Parameter	Instrument	Height of measurement (m)
Incoming shortwave radiation	Kipp&Zonen CM11	4.0
Incoming longwave radiation	Kipp&Zonen CG3	4.0
Reflected shortwave radiation	Kipp&Zonen CM11	4.0
Outgoing longwave radiation	Kipp&Zonen CG3	4.0
Incoming direct PAR†	Delta-T BF3	4.0
Incoming diffuse PAR†	Delta-T BF3	4.0
Reflected PAR†	Li-Cor 190SZ	4.0
Air temperature	Vaisala HMP45A	1.5
Relative humidity	Vaisala HMP45A	1.5
Precipitation	EM ARG100	0.4
Leaf surface temperature (2x)	Campbell Scientific IR100	0.4
Leaf wetness (2x)	Decagon LWS	0.4
Air pressure	Vaisala PTB101C	1.0
Turbulent wind speed fluctuations (3-D) and air temperature fluctuations	Gill Instruments R3-50 ultrasonic anemometer	2.5

† PAR: photo-synthetically active radiation.

Gap-filling technique for missing meteorological data at field research site

The gap-filling technique consists of looking for similar weather conditions in the meteorological records and related turbulence measurements that are available. “Similar weather” should be understood as similar regarding the main drivers of turbulence: wind speed, temperature and solar radiation. For the best result, the conditions should be found in a period of time as close as possible to the time of the data gap. Here, we also use wind direction as a criterion, since spatial differences in roughness may also have an impact on the turbulence parameters.

In order to find such conditions the observations of the KNMI station at Lelystad were investigated. For wind speed and wind direction, half-hourly OBO measurements are compared with the hourly observations at the KNMI station in Lelystad in order to be able to cover the entire period with these quantities as well. Wind speed from the OBO site was observed at a height of 2.5 m and has been corrected to a height of 10 m assuming near-neutral conditions in the atmosphere and using the friction velocity observed at the OBO site. The wind speed and direction of the two sites correspond quite well, although at the OBO sites somewhat lower wind speeds are observed under the conditions of stronger winds on 3 August (see main text).

During sampling time 8, the wind speed at Lelystad varied between 210 and 220 degrees, the wind speed between 4 and 7 m s-1, the temperature between 18.6 and 20.2 °C and the global radiation between 530 and 708 W m-2. We required similar conditions to be within the same range for wind direction, wind speed and global radiation. We required the temperature to be within 2 °C from the average. A match was found on 2 August 2017, 12-13 MEWT. During these hours, the wind speed was 5 m s-1, the wind direction 220 degrees, the temperature 21.0-21.2 °C and the global radiation 544 631 W m 2. The conditions are summarized in Table 2, along with the relevant turbulent parameters derived from the measurements at 2 August, 12-13 MEWT.

Table 2: Estimated turbulence parameters for sampling time 8. Numbers in bold are the estimated turbulence parameters used to compute volatilization from concentration observations during sampling time 8, when these parameters were unavailable (N/A).

	7-8-2017, 10-12 MEWT	2-8-2017, 12-13 MEWT
Wind Direction (°)	210-220	220
Wind Speed (m s^{-1})	4-7	5
Temperature (°C)	18.6-20.2	21.0-21.2
Solar radiation (W m^{-2})	531-708	544-631
u_* (m s^{-1})	N/A	**0.39**
Footprint (m)	N/A	**169**

Appendix 17: Measurement methods and results for volatilization experiment on location A

Measurement of concentration in the air

Concentrations in air were determined using the polystyrene adsorbent XAD-2 (SERDOLIT, Serva, research grade). The particle diameter of the grains varies from 0.3 to 1.0 mm and the surface area of XAD is 300 m2/g. The sampling units are made of glass tubes (inner diameter 35 mm) with screw thread on both ends (see Figure 1). Inside the glass tube a stainless-steel gauze was placed (mesh width 0.1 mm). The tube was filled with 10 g XAD-2 adsorbent, resulting in a layer of approximately 1.5 cm. The tube for breakthrough check was filled with 5 g XAD-2 adsorbent. The tube with adsorbent was placed vertically in a connection unit bound with one of the gas meters in the sampling unit. A copper cap with crack-shaped openings on two sides (approximately perpendicular to the wind direction) prevented the adsorbent to be blown out and rain drops to enter the sampling unit.

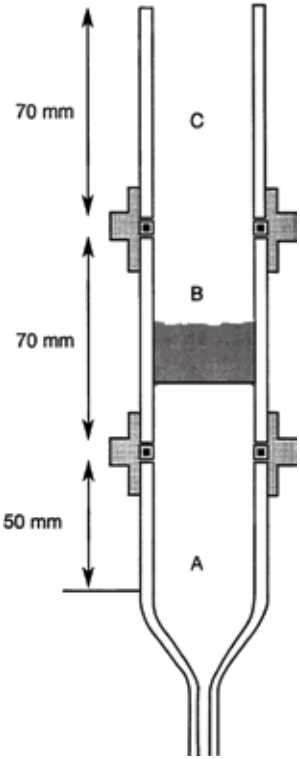


Figure 1: Sampling unit.
Scheme (right) air sampling unit and photo of the unit with copper cap (left). B = XAD-2 layer on gauze with removable glass tube (internal diameter 35 mm).

Determination of concentrations in the spraying solutions

The amounts of tebuconazole and thiacloprid in the spraying tank is specified in Table 1. Using the mass of active substances and the volume of water the nominal concentrations in the spraying solutions were calculated. These concentrations are listed in Table 2.

The samples of the spraying solution were analyzed by RIKILT. The average concentrations measured were 337 mg/L for tebuconazole and 573 mg/L for thiacloprid. The concentrations measured were higher than those calculated from the amounts added to the mixing tank and the volume of water.

The volume of the spraying solution that had been applied was taken from the volume indicator on the mixing tank. The volume at the beginning was 1220 L and at the end it was 804 L, so the volume sprayed amounted to 416 L. The applied mass of tebuconazole is calculated to be 140 g. The areic application rate (including the paths) was 75.2 g/ha. The amount of thiacloprid applied is calculated to be 238 g, which results in an application rate of 128 g/ha.

Table 1: Amount of active ingredient in the tank.

Product name	Volume of product	Active substance
Spirit Adama	2,5 L from container of 10 L	tebuconazole 100 g/L folpet 450 g/L
Calypso Bayer	1,250 L from 5 L container	thiacloprid 480 g/L
Epso Microtop	1 bag of 10 kg	'bitterzout' 75% granules

Table 2: Nominal concentration in the spraying solution calculated from the amounts of active ingredient added and the volume of water. Volume of water added: 1220 L.

Active ingredient	Concentration in product (g/L)	Volume of product (L)	Amount added to the mixing tank (g)	Concentration in the mixing tank (mg/L)
tebuconazole	100	2.5	250	205
thiacloprid	480	1.25	600	492

Measurement of pesticide residue on plant leaves

The treated field was divided into 4 rectangular sections of similar size. In each section 10 leaves of the hyacinth plants (5 inner leaves and 5 outer leaves) were collected from 5 flower-bulb beds with different hyacinth variety. The leaves were extracted within one hour after sampling. Each set of 10 leaves was transferred into a 500 mL flask to which 200 mL methanol was added. During the extraction period of about 30 minutes the flasks were shaken manually a few times. Next 3 mL of the methanol solvent was taken and transferred into a glass vial with a screw cap (with aluminum foil inlay). The procedure for the extraction of the leaves sampled at one hour after application was somewhat different. The plant leaves were transferred to an aluminum tray to which methanol was added until the plant leaves were entirely submerged in this solvent. Next the trays were put into plastic bags and these bags were sealed. The plastic bags with the trays were shaken gently by hand at regular intervals. After 30 min the solvent of each plastic bag was transferred into a glass flask of 250 mL. The plant leaf extracts were transported to the laboratory and stored at -18 °C until transfer to the analytical laboratory of RIKILT.

The surface of the plant leaves were measured at Unifarm (Wageningen University & Research). The plant leaves sampled at each sampling time were stored in a closed vessel in a refrigerator at about 4 °C. After the end of the field experiment the total surface of each set of 10 leaves was measured.

The recovery of tebuconazole and thiacloprid from plant leaves was measured by adding 1 mL of the spraying solution (obtained from spraying solution prior to application) on 18 hyacinth leaves using a syringe. After 10 minutes the plant leaves were partitioned over two 250 mL flasks, to which 200 mL methanol was added. During the subsequent 30 min the flasks were shaken manually regularly. Next the methanol was transferred to 250 mL flasks. The contents of both flasks were mixed and a 3 mL aliquot was taken from this mixture and transported to RIKILT for analysis. Only a single measurement of the recovery was done. The recovery of tebuconazole and thiacloprid was measured to be 35.7% and 77.8%, respectively. It should be noted that the droplets of the spraying solution containing tebuconazole did not spread out over the leaf surface, instead the shape of the droplets did not change much after their deposit on the plant leaves. Further, the comparatively high vapor pressure for tebuconazole may have resulted in a higher loss by volatilization and consequently a lower recovery than was measured for thiacloprid.

Concentrations of tebuconazole and thiacloprid in air

The results of the measurements of the concentrations in air are presented in Table 3 for tebuconazole and in Table 4 for thiacloprid. During the first air sampling period just after the end of the application the wind direction changed. Therefore the status of the upwind sampling point was no longer upwind and the fetch of the sampling unit at the downwind side of the field was reduced to below 100 m. However, the concentration measured at the upwind sampling point was below the LOD.

On the day of application, the concentration of tebuconazole in air during the first sampling period was measured to be 0.42 ng m^{-3} at a height of 0.75 m and 0.29 ng m^{-3} at a height of 1.50 m. At sampling heights between these two levels the concentrations were measured to be below the LOD. At three hours after application, only the concentration at a level of 0.75 m could be quantified, i.e. 0.55 ng m^{-3}. At two days after the day of application a concentration of 0.55 ng m^{-3} was measured at the upwind sampling site, which indicates that another field had been treated with this substance in upwind direction from this sampling point. On the fourth day after the day of application, the concentrations of tebuconazole in air at sampling heights of 1.0 and 1.25 m could be quantified, although these concentrations were close to the LOD. It should be noted that the duration of the sampling on this day was longer than that on the preceding days, so a greater volume of air was sampled, about 6 m^3 instead of 3 m^3.

For thiacloprid the concentrations for the first air sampling period after application were below the LOQ of this substance at all 4 measurement heights. At 3 hours after application the concentration measured at a height of 0.75 m was 0.88 ng m^{-3}. On the second day after the day of application, the concentration of thiacloprid measured at the upwind side of the field was 0.31 ng m^{-3}. This may have been due to the volatilization of this substance from another field treated with this substance upwind of the air sampling point.

The vertical concentration gradient of tebuconazole above the crop could not be quantified. Therefore, the rate of volatilization of this substance could not be quantified. For thiacloprid, the concentrations in air were almost all below the level of detection, so for this substance the rate of volatilization could not be quantified either. Therefore, no effort was made to collect data on other applications of these compounds upwind of the field at location A during the period of measurement.

Table 3: Concentration of tebuconazole in air above the hyacinth crop.

Time	Day	Concentration (ng/m3)				
		upwind	0.75 m	1.00 m	1.25 m	1.50 m
1	1	<	0.42	<	<	0.29
2	1	<	0.55	<	<	<
3	1	<	<	<	<	<
4	2	<	<	<	<	<
5	2	<	<	<	<	<
6	3	0.55	<	<	<	<
7	3	<	<	<	<	<
8	5	<	<	0.15	0.15	<

< : measurement is below level of quantification of about 0.3 ng/m3 (LOQ).

Table 4: Concentration of thiacloprid in air above the hyacinth crop.

Time	Day	Concentration (ng/m3)				
		upwind	0.75 m	1.00 m	1.25 m	1.50 m
1	1	<	<	<	<	<
2	1	<	0.88	<	<	<
3	1	<	<	<	<	<
4	2	<	<	<	<	<
5	2	<	<	<	<	<
6	3	0.31	<	<	<	<
7	3	<	<	<	<	<
8	5	<	<	<	<	<

< : measurement is below level of quantification of about 0.3 ng/m3 (LOQ).

Residues of tebuconazole and thiacloprid on leaves

The results of the analysis of tebuconazole and thiacloprid in the leaf extracts are shown in Table 5. In this table the average mass of each substance is given for the leaf samples taken from each section as well as the standard deviation for the measured values.

Table 5: Deviation of the residue of tebuconazole and thiacloprid on hyacinth leaves as measured on all four sections.

Sampling time (days after application)	Residue on leaves (µg/cm2)	
	tebuconazole	thiacloprid
0.06	0.100 ±0.029	0.243 ±0.034
0.88	0.061 ±0.008	0.167 ±0.037
0.89	0.033 ±0.004	0.095 ±0.015

Appendix 18: Measurement methods and results for volatilization experiment on field research site

Description of field site and the application

The height of the crop above the bed surface was measured in each quadrant in five different beds on 2 August 2017. The results are given in Table 1. The average of the 20 measurements was 47±9 cm. In some places the onion leaves were lying flat on the field (see Figure 1 B), giving some low values for the crop height.

(A) (B)

Figure 1: Onion crop.
Onion crop at 1 August 2017 (A) (quadrant I) and (B) example of spot in the field where onion leaves lay flat (left side of photo) (quadrant III).

Table 1: Crop height, density and soil cover for each quadrant of the onion field.

Quadrant	Height (cm)	Density (number of plants per 0.5 m2)	Soil cover (%)
I	48 ± 6	48 ± 3	61 ± 6
II	50 ± 5	51 ± 8	66 ± 4
III	43 ± 13	50 ± 7	58 ± 6
IV	47 ± 11	45 ± 2	55 ± 3
Average	47 ± 9	49 ± 6	60 ± 5

The density of the crop was determined by counting the number of plants in a rectangle of 0.5 m^2 (1 x 0.5 m) on a bed. This was done in each quadrant in five different beds on 1 August 2017. The densities per quadrant are given in Table 2. The average number of plants from counting was 49 per 0.5 m^2 bed, hence 98 plants per m^2 bed. The onion beds including path are 2.28 m wide; 8 rows of onions with 0.25 m in between: 1.75 m and path 0.53 m (S. de Lange, Personal communication, December 2017). Considering the area taken by the paths of 23% of the area (0.53/2.28), the density was 100/123 * 98 plants per m^2 = 82 plants per m^2 field, or 820 000 plants per ha. This agrees roughly with 900 000 plants per ha expected.

Soil cover was determined from photos made in the field of the 0.5 m^2 rectangle also used for determination of crop density, on 1 August 2017. The area inside the rectangle was selected, and then the number of green pixels and the total number of pixels in the square were counted using Image-J software. The average soil cover for the beds in the field was 60%.

The LAI was determined by determining leaf area of 20 onion plants taken at random from the field. The number of leaves per plant varied from four to seven.
The average plant leaf area (n=20) was 393.2 cm^2 (sd 192.1) and the number of plants per m^2 was 49.

The composition of the spray solution is given in Table 2.

Table 2: Dosage of pesticide in spray tank.

Product	Registration number	Active ingredient	Volume of product
Allure	11585 N	chlorothalonil 333 g/L prochloraz 105 g/L	20 L, two bottles of 10 L
Milcozeb	13586 N	mancozeb 75% water dispersible granulate	28 kg
Certain	-	alcoxylated alcohol 100%, wetting agent	3.2 L from bottle of 5 L

The products were dissolved and mixed in 4000 L of water. The nominal concentrations in the tank solution were calculated on the basis of the mass of active ingredient added (see Table 3) in the volume of 4000 L. The concentrations calculated are given in Table 3. Samples were taken from the spray solution in the tank using a beaker connected to a rod. Duplo samples were taken at three times; before (4000 L in the tank), halfway (2200 L) and after spraying (200 L) of the 13.8 ha field. As 200 L of spray solution remained in the tank, the 13.8 ha was sprayed with 3800 L of the spray solution (275 L/ha).

The samples of the tank solution were analyzed by RIKILT. The average measured concentration were 1450 mg/L for chlorothalonil and 410 mg/L for prochloraz. The measured concentrations are lower than the nominal concentrations that were calculated from the mass of active ingredients added to the tank solution (see Table 3).

The volume of the tank solution that was applied on the onion is read from the meter of the tank. On the plot 3800 L (start 10:45 4000 , end 11:45 200 L) is sprayed. The mass of chlorothalonil applied was 5510 g (3800 L x 1450 mg/L). The area of the crop (including paths) of the onion plot was 13.8 ha,

Table 3: Nominal concentration in tank solution calculated from mass of active ingredient added and the volume of water in the tank (4000 L).

Active ingredient	Concentration in product (g/L)	Volume of product (L)	Mass of active ingredient in tank (g)	Concentration of active ingredient in tank water volume of 4000 L (mg/L)
chlorothalonil	333	20	6660	1665
prochloraz	105	20	2050	512.5

Measurement of concentrations in air

The recovery was tested in 2016 before the first volatilization experiment. To determine recovery and breakthrough of the XAD-2 in the sampling unit a mixture of the compounds selected for protocol B measurements was spiked in a high dosage of approximately 5 µg of each compound (except chlorpropham: 10 µg) at the XAD-2 of the unit. Then for one hour at a rate of 3 m^3/h air was sucked through the sampling unit, with behind it a clean unit ("breakthrough" unit). The XAD-2 in the two sampling units (including a breakthrough unit) were extracted and the total recovery and reproducibility was determined by TNO. The recovery of prochloraz was 96±4% and breakthrough of prochloraz was not observed. Chlorothalonil was not included in the test. Therefore TNO tested recovery of extraction of chlorothalonil separately, giving a recovery > 80% (M. Noteboom, personal communication, November 2017). However, whilst checking the recovery alongside the extraction and analysis of the field samples, the recovery was much lower: 35±15%. Therefore, to reduce the effect of this uncertainty the measured masses were corrected for recovery using the recovery samples of the day of extraction.

Measurement of pesticide residue on plant leaves

The leaves were extracted within one hour after sampling. Each set of five leaves were cut in short pieces of approximately 5 cm. The pieces of the upper half were put in a flask of 500 mL, and the pieces of the lower half of the leaves were put in another flask of 500 mL. To each flask 200 mL methanol was added. During the next half hour the flasks were shaken regularly by hand. Thereafter the flasks with the leaves were put a cold room. The flasks were transported to Wageningen Environmental Research (WENR) on 7 August 2017. There approximately 3 mL of the methanol was transferred to a 4-mL WISP vial. The samples, the flasks with remaining extract and leaves were stored in refrigerator at WENR. During transport all samples were stored in a cooling box. At WENR the samples were stored at -18 °C until transport to RIKILT on 8 August 2017.

The surface area of the leaves was measured at Unifarm (Wageningen University & Research). The leaves of the three sampling times were stored at WENR in a refrigerator at approximately 4°C. After finalizing the field measurements the surface area of the ten leaf halves was determined for each quadrant and each sampling time on 8 August 2017.

Recovery of chlorothalonil and prochloraz from onion leaves was determined by sprinkling 1 mL of the spraying solution (subsample from sample taken halfway the application) using a syringe on five onion leaves (sections of leaves) lying in an aluminum dish. The solution is sprinkled all over the leaves, but it was observed that the little drops clustered then. After 20 minutes the leave sections were put in a 500 ml flask, and 100 mL of methanol was added. The dish was rinsed with another 100 mL of methanol, and this methanol was also added to the 500 mL flask. Thereafter the

bottles were shaken by hand regularly and 3 mL samples were taken from the extract. For the further procedure see the description of determining areic mass on the onion leaves.

The recovery measurement was performed in triplicate, using the sample taken in middle of application as dosing solution. The concentrations in the spraying solution were: chlorothalonil 1.43 g/L; and prochloraz 0.383 g/L. Applying of 1 mL of the solution to the leaves resulted in dosages: chlorothalonil 1.43 mg; and prochloraz 0.383 mg. The recovery of chlorothalonil from the onion leaves could not be determined because the concentration in the extract was below 10 µg/L. The mass of prochloraz measured after extraction was 0.583 mg. Hence the recovery determined for prochloraz was 152% (0.583 mg/0.383 mg), which is rather high. This can be due to matrix effects or residues present on the leaves from a former application. These effects cannot be excluded because blanc leaves were not analyzed. Although the recovery is rather high, the results can be used to show the decline in the residue on the plant leaves.

Concentrations of chlorothalonil and prochloraz in air

The results of the measurements of chlorothalonil concentration in air are given in Table 4. The concentrations in the upwind samples and in the breakthrough samples were all below LOQ. The LOQ of chlorothalonil of 25 ng on the adsorbent assuming 3 m^3 of air sampled means a LOQ of approximately 8 ng/m^3.

The measured concentrations of chlorothalonil in air are presented in Figure 2. At sampling times 6 and 7 (both day 4) all concentrations in air were below LOQ. The concentrations measured at day 1, sampling time 1 and 2 are highest, except for the sample taken at 2.5 height at t =2 that was below LOQ. The concentrations at 1.5 m were higher than at 1 m, which is not expected; it would mean a downward flux, i.e. deposition instead of volatilization. The uncertainty in the measured concentration is high (see paragraph “Measurement of concentrations in air”); hence we assume that the unexpected flux direction is attributed to this uncertainty.

The concentrations measured on day 2, at 5 a.m., were lower than those measured on day 1. The concentration measured at 2 m height is higher than at 1.5 m, which is attributed to the uncertainty discussed above. The concentrations measured at day 2, at 9 a.m. were below LOQ, except at 1.5 m height. The concentrations measured at day 2, at 12:30 at 1 m height was lower than at 5 a.m. The concentrations at other heights were higher than at 5 a.m.

The concentrations measured at day 7 were lower than measured at day 1 and day 2 and similar for 1, 1.5 and 2 m height, and below LOQ for 2.5 m height.

Note that the uncertainty in the chlorothalonil results is relatively large (see paragraph “Measurement of concentrations in air”).

Table 4: Concentration chlorothalonil in air measured above an onion crop after application at a rate of 399 g active substance per ha on 1 August 2017 (10:45 -11:45).

Sample time	Date and time start sampling	Day nr	Concentration in air (ng/m3)			
			1.00 m	1.50 m	2.00 m	2.50 m
1	1 Aug 13:00	1	81.9	110.4	81.1	73.7
2	1 Aug 16:00	1	97.5	126.6	83.1	<
3	2 Aug 5:00	2	73.2	31.9	40.7	11.9
4	2 Aug 9:00	2	<	23.5	<	<
5	2 Aug 12:30	2	54.0	39.1	49.6	29.2
6	4 Aug 9:00	4	<	<	<	<
7	4 Aug 12:47	4	<	<	<	<
8	7 Aug 9:46	7	15.4	15.6	19.9	<

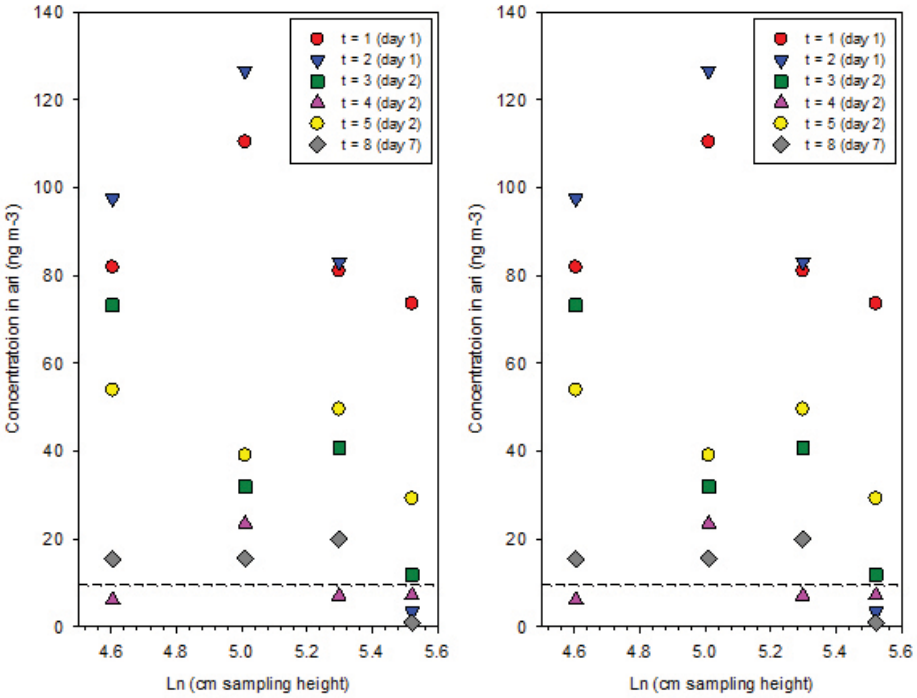


Figure 2: Concentration of chlorothalonil in air.
Concentration of chlorothalonil in air as a function of the natural logarithm of the sampling height (in cm). Note that samples for t = 6 and for t =7 (both at day 4) are not given, because all measurements at those sampling times were below LOQ. Measurement below the horizontal dashed line were < LOQ, and are given as 0.5* LOQ-value.

Residues of chlorothalonil and prochloraz on leaves

The results of extractions of chlorothalonil from the leaves, averages and standard deviations on the basis of measurements of four quadrants are given in Table 5. Mass on leaves is expected to decrease in time. However, chlorothalonil mass determined for first sampling time was below 0.0032 µg/cm2, based on the limit of quantification (LOQ) in the extraction solution, and then increased in time. Chlorothalonil is not stable in homogenized leaf material, especially for crops with sulphur components (cabbage, onion and leak) (H. Mol, personal communication December 2017). Samples were taken from the extraction solution on 8 August 2017, hence leaves sampled on day 1 had been in the solution for seven days, leaves sampled at day 2 for six days and leaves sampled at day 7 for one day. The observation that the measured mass on leaves of chlorothalonil increases with shorter stay of the leaves in methanol supports the assumption of degradation of chlorothalonil with the leaves. The masses of chlorothalonil were not corrected for its recovery because the recovery could not be determined.

The results of extractions of prochloraz from the leaves, averages and standard deviations on the basis of measurements of four quadrants are given in Table 6. The masses of prochloraz were corrected for its recovery of 152% (see above). Because of these high recoveries there is a substantial uncertainty in the values calculated for the mass remaining on the plant leaves.

Table 5: Mass of chlorothalonil on onion leaves for each sampling time; average and standard deviation for the four quadrants in the field.

Sampling time	Mass on leaves (µg/cm2)
t = 1, day 1 13:30	< 0.0032
t = 2, day 2 9:15	0.065 ±0.057
t = 3, day 7 10:05	0.192 ±0.092

Table 6: Mass of prochloraz on onion leaves for each sampling time; average and standard deviation for the four quadrants in the field.

Sampling time	Mass on leaves (µg/cm2)
t = 1, day 1 13:30	0.106±0.023
t = 2, day 2 9:15	0.062 ±0.007
t = 3, day 7 10:05	0.0025 ±0.001

Appendix 19: List of screened models

- The Composite Box Model (Knight et al. 1995 - Knight, A., McTainsh, G. & Simpson, R. (1995). Sediment loads in an Australian dust storm: Implications for present and past dust processes. CATENA 24, pp 195-213)
- FDM model (Winges et al. 1991 - Winges, K.D. (1991) User's guide for the fugitive dust model (FDM) revised epa-910/9-88-20 2r Ed., US Environmental Protection Agency: Seattle,WA)
- HOTSPOT (Homann and Aluzzi, 2014 - Homann, S.G., Aluzzi, F. (2014). HotSpot Health Physics Codes, Version 3.0. User's Guide. Lawrence Livermore National Laboratory.)
- Improved Gaussian-MLA (Ma et al. 2016 - Ma, D., & Zhang, Z. (2016). Contaminant dispersion prediction and source estimation with integrated Gaussian-machine learning network model for point source emission in atmosphere. Journal of Hazardous Materials, 311(28), 237–245.)
- LEACHP – Leaching estimation and chemistry model for pesticides (Hutson & Wagenet 1989 - HUTSON J.L. and WAGENET R.J., 1989, LEACHM: Leaching Estimation And Chemistry Model. A process-based model of water and solute movement, transformations, plant uptake and chemical reactions in the saturated zone, Department of Soil, Crop and Atmospreric Sciences, Cornell University, Ithaca, New York)
- MIN3P Extended (Bao et al. 2015 - Bao, Z., Haberer, C., Maier, U., Beckingham, B., Amos, R. T., & Grathwohl, P. (2015). Science of the Total Environment Modeling long-term uptake and re-volatilization of semi-volatile organic compounds (SVOCs) across the soil – atmosphere interface. Science of the Total Environment, The, 538, 789–801.)
- Nema (Velthof et al. 2012 - Velthof, G.L., C. van Bruggen, C.M. Groenestein, B.J. de Haan, M.W. Hoogeveen, J.F.M. Huijsmans (2012) A model for inventory of ammonia emissions from agriculture in the Netherlands. Atmospheric Environment 46, 248-255)
- RICEWQ (Williams et al. 1999 - Williams W.M., Ritter A.M., Cheplick J.M., Zdinak C.E. (1999) RICEWQ: Pesticide runoff model for rice crops – user's manual and program documents version 1.6.1. Waterborne Environmental, S.E Leesburg, VA)
- SESOIL (Bonazountas & Wagner 1981 - Bonazountas, M., Wagner, J. M. (1981). "SESOIL" A seasonal soil compartment model, Arthur D. Little, Inc., Cambridge, Massachusetts 02140)
- Source model (Butler et al. 1995 - Butler, H. J. and Hogarth, W. L. and McTainsh, G. H. (1995) Towards a simple Gaussian model to describe multiple source areas during wind erosion events. In: International Congress on Modelling and Simulation (MODSIM 1995), 27-30 Nov 1995, Newcastle, Australia)
- SURFAtm pesticide model (Bedos et al. 2011 - Bedos C., Personne E., Lichiheb N., Magandji-Douckagha G., Barriuso E. , 2011. Modelling Pesticide volatilization from crop at the field scale. XIII Symposium Pesticide Chemistry - Environmental Fate and Ecological Effects (Piacenza, Italy, sept. 2011)).
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- ASIMD (Pekar & Van Pul 1998 - Pekar, M. and Van Pul W.A.J. (1998). Modeling of lindane and PCBs transport in the European region. Proceedings EUROTRACK symposium 1998)
- AUSTAL (Janicke 2002 - AUSTAL 2000, Programmbeschreibung, Dunum, 2002)
- ATSTEP (Ievdin et al., 2012 - Ievdin, I.O., Khalchenkov, O.V., Kovalets, I.V., Rakob, W., Trybushnyi, D., Zheleznyak, M., 2012. Application of decision support system JRODOS for assessments of atmospheric dispersion and deposition from Fukushima Daiichi nuclear power plant accident. Int. J. Energy a Clean Environ. 13, 179-190)
- Cambridge 2-D atmospheric chemistry transport model (Law & Pyle 1993 - Law, K. S., and J. A. Pyle (1993), Modelling trace gas budgets in the troposphere: 1. Ozone and odd nitrogen, J. Geophys. Res., 98, 18,377 – 18,400)
- CTDM-PLUS(Perry 1992 - Perry SG. CTDMPLUS: a dispersion model for sources near complex topography. Part I: technical formulations. J Appl Meteorol 1992;31: 633–45)
- DMU (Zlatev et al. 1996 - Z. Zlatev, I. Dimov and K. Georgiev: "Three-dimensional version of the Danish Eulerian Model". Zeitschrift für Angewandte Mathematik und Mechanik, Vol. 76 (1996) S4, 473-476)
- ECHAM (Roelofs & Lelieveld 1995 - Roelofs, G.-J. & Lelieveld, J. 1995 Distribution and budget of O$ in the troposphere calculated with a chemistrygeneral circulation model. J. geoph's. Res. 100, 20 983– 20 998)
- HARM (Metcalfe & Whyatt 1995 - Metcalfe, S.E., Whyatt, J.D. (1995). Modelling future acid deposition with HARM. In: Acid rain and its impact: the critical loads debate (Battarbee, R.W. (Ed)), 27-37. ENSIS Publishing, London)
- HAR-WELL (Hough 1991 - Hough, A. M.: Development of a 2-dimensional global tropospheric model – model chemistry, J. Geophys. Res.-Atmos., 96, 7325– 7362, 1991)
- IMAGES (Müller & Brasseur 1995 - Müller, J.-F., and BRASSEUR, G. (1995), IMAGES: A threedimensional chemical transport model of the global troposphere, J. Geophys. Res. 100, 16455–16490)
- INPUFF 2.0 (Petersen and Lavdas, 1986 - Petersen, W. AND L. Lavdas. INPUFF 2.0 - A MULTIPLE SOURCE GAUSSIAN PUFF DISPERSION ALGORITHM. USER'S GUIDE. U.S. Environmental Protection Agency, Washington, D.C., EPA/600/8-86/024 (NTIS PB86242450))
- Landform model (Ma et al. 2016 - Ma, X., Zhong, W., Feng, W., Li, G. Modelling of pollutant dispersion with atmospheric instabilities in an industrial park, Powder Technol. (2016))
- Liège uni and bidimensional model (Hauglustaine 1992 - Hauglustaine D. (1992). Modelisation de l;evolution de la composition chimique atmospherique et due climat: approches uni et bi-dimensionnelles. These de doctorat en Sciences Physiques, University of Liege, Belgium.)
- LOTOS (Schaap et al. 2005 - Schaap, M., Timmermans, R., Roemer, M., Boersen, G., and Builtjes, P. J. (2005). The LOTUS-EUROS model: description, validation and latest developments. Int. J. Environment and Pollution.)
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- OML Model (Olesen et al. 2007 - Olesen, H.R., Berkowicz, R.B, Løfstrøm, P. (2007): OML: Review of model formulation. National Environmental Research Institute, Denmark. 130pp. NERI Technical Report No. 609)

- OpenFOAM (Fiates et al. 2016 - Fiates, J., & Vianna, S. S. V. (2016). OpenFOAM. Process Safety and Environmental Protection, 104, 277–293)
- Oslo CTM2 (Eleftheratos et al. 2011 - Eleftheratos, C. S. Zerefos, E. Gerasopoulos, I. S. A. Isaksen, B. Rognerud, S. Dalsøren, C. Varotsos, A note on the comparison between total ozone from Oslo CTM2 and SBUV satellite data, International Journal of Remote Sensing, 2011, 32, 9, 2535)
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- Steady-state plume model (Ellis et al. 2010 - Ellis, B., & Miller, P. C. H. (2010). The Silsoe spray drift model: a model of spray drift for the assessment of non-target exposures to pesticides. Biosystems Engineering, 107(3), 169e177)
- STOCHEM (Khan et al. 2015 - Khan, M. A. H., Cooke, M. C., Utembe, S. R., Archibald, A. T., Maxwell, P., Morris, W. C., Shallcross, D. E. (2015). A study of global atmospheric budget and distribution of acetone using global atmospheric model STOCHEM-CRI. Atmospheric Environment, 112, 269–277.)
- TMK (Velders et al. 1994 - Velders, G. J. M., L. C. J. Heijboer, and H. Kelder, The simulation of the transport of aircraft emissions by a three-dimensional global model, Ann. Geophys., 12, 385-393, 1994)
- TVM – Tridimensional vorticity model (Schayes et al. 1996 - Schayes, G, P. Thunis, R. Bornstein, 1996: Topographic Vorticity-Mode Mesoscale-B (TVM) Model. Part I: Formulation, J. Appl. Meteor., 35, 1815-1823)
- UK-ADMS (Carruthers et al. 1991 - Carruthers, D.J., Holroyd, R.J., Hunt, J.C.R., Weng, W.S., Robins, A.G., Apsley, D.D., Smith, F.B., Thomson, D.J., Hudson, B. 1991. UK Atmospheric Dispersion Modelling System. Proc. 19th International Technical Meeting on Air Pollution Modelling and its Applications. Crete.)
- BREAM (Kennedy et al. 2012 – Kennedy, M., Butler Ellis, C., Miller, P.C.H. BREAM: A probabilistic Bystander and Resident Exposure Assessment Model of spray drift from an agricultural boom spraye. October 2012. Computers and Electronics in Agriculture 88:63–71)
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- EUTREND (Van Jaarsveld et al. 1994 - Van Jaarsveld J.A., Van Pul W.A.J., De Leeuw F.A.A.M. (1994). Modelling the long-range transport and deposition of persistent organic pollutants over Europe and its surrounding marine areas In: Air Pollution Modeling and its application X, edited by S-E. Gryning and M. M. Millán, 143-157. Plenum Press, New York.)
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- ISCST3 (US EPA 1995 - U.S. EPA, 1995. User's Guide for the Industrial Source Complex (ISC) Dispersion Model – Volume I User Instructions, U.S. Environmental Protection Agency, Office of Air Quality, Planning and Standards, Research Triangle Park, NC. September.)
- EVA 1.1 (Winkler et al. 2002 - Winkler, R., Binner, R., Gottschild, D., Koch, W. and Siebers, J. (2002). Bewertungskonzept zum Nahtransport von Pflanzenschutzmitteln infolge Exposition über den Luftpfad (Abtrift, Verflüchtigung und Deposition). Berichte aus der Biologischen Bundesanstalt für Land- und Forstwirtschaft, Heft 110 (2002).)
- PESTDEP (Asman 1998 - Asman, W.A.H. (1998) Factors influencing dry deposition of gases with special reference to ammonia. Atmospheric Environment 12, 415-421.)
- PELMO (Klein 1995 - Klein, M.: PELMO(1995): Pesticide Leaching Model, User manual version 2.01. Fraunhofer-Institut für Umweltchemie und)
- EXAMS (US EPA 2000 - U.S. EPA (2000) Exposure Assessment Modelling System (EXAMS): User Manual and System Documentation. Research Triangle Park, NC, US Environmental Protection Agency (EPA/600/R-00/081, Revision B).)
- PRZM (Carsel et al. 1998 - Carsel, R.F., Imhoff, J.C., Hummel, P.R.,Cheplick, J.M. and Donigian, A.S. (1998). PRZM-3, A Model for Predicting Pesticide and Nitrogen Fate in the Crop Root and Unsaturated Soil Zones: User's Manual for Release 3.0. National Exposure Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Athens, GA 30605 – 2720)
- PEM (Scholtz et al. 2002 – Scholtz, M.T., Voldner, E., Mcmillan, A., Van Heyst, B.J. A pesticide emission model (PEM) Part I: Model development October 2002 Atmospheric Environment 36(32):5005-5013)
- BROWSE (EU 7th Framework Programme, ref. 265307)

Appendix 20: Additional routes

Dragging of pesticides

This process is important to be taken into account an as exposure route, as concluded by Hyland & Laribi 2017 in their review: "The studies evaluated provided evidence that the take-home exposure route is one source of pesticide exposure for children of farmworkers and those living in agricultural communities". However dragging of pesticides is a very difficult process to tackle/assess. In literature most of the studies focus mainly on the type of clothing material, surface or activity than the actual drag of different substances by those means (e.g. Fogh et al. 1999; McDonagh et al. 2012, 2014). Nevertheless, there are recent studies that focus on dragging and its impact on different scientific fields (e.g. Murray et al. 2016).

Emission of particle-phase pesticides due to crop erosion

To study the flux of pesticides bound to soil particles, the APEX model (Wang et al. 2011) was used to simulate different scenarios based on the meteorological conditions presented on sub-chapter 6.3.2. It can be concluded that under the studied conditions there is no expected erosion of PM10; hence, this route can be neglected.

The abovementioned is due to the low wind speed registered on the day of the applications, the wind was not strong enough to erode the soil in the field. Additionally, in The Netherlands the soil is known for having high water content which is also a contributing factor to very low erosion rates. Finally, for the studied fields plant canopy also plays an important part on blocking smaller particles from escaping.

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Appendix 21: Home Characteristics

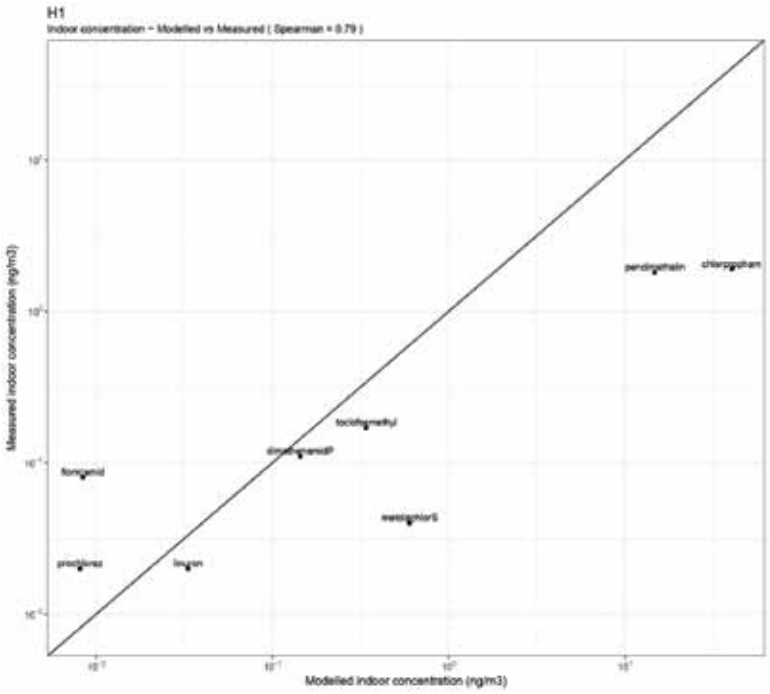
Home Characteristics - Summary Table				
Parameter	Answers	Percentage	Parameter	Mean (min,max)
Home - Type	Corner home	14%	Volume (m3)	364 (100,715)
	Duplex	19%	Surface area (m2)	114 (40,200)
	Row home	22%	Height	8 (3,15)
	Detached	42%	Year of construction	1970 (1900,2016)
	Apartment	2%	Age of the floor	15 (0.5,70)
Roof angle	Angled	87%		
	Angled & Flat	7%		
	Flat	6%		
Kitchen - Open/Closed	Closed	31%		
	Open	69%		
Visable holes/cracks	No	93%		
	Yes	7%		
House Sealed agains draught	No	38%		
	Yes	63%		
Flooring - Type	SMOOTH	78%		
	RUG or CARPET	22%		

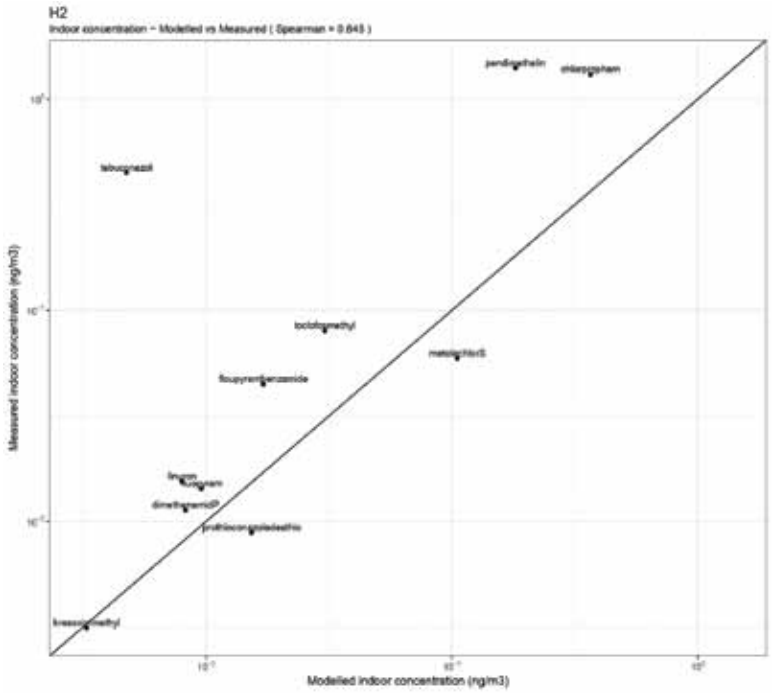
Appendix 22: Population characteristics

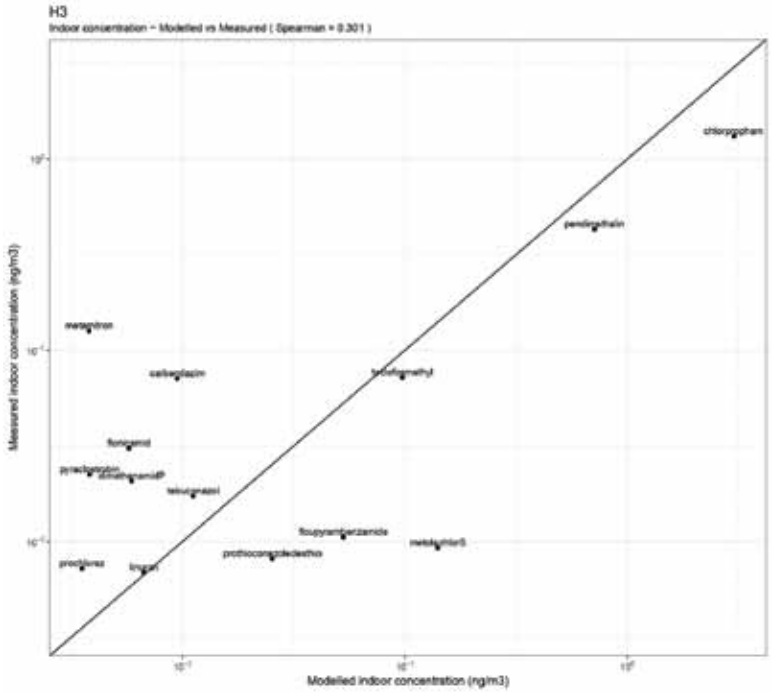
	Residents (N=164)	Controls (N=28)
Demographic charactheristics		
Age (Years - mean (range))	44 (2-88)	50 (12-76)
Females (%)	54	43
Height* (cm	163 ± 37	173 ± 11.4
Weight* (kg)	64 ± 31.7	75 ± 15.6
Self-reported charactheristics		
Time spent indoors* (hours)	14.6 ± 3.9	13.6 ± 3.7
Use pesticides at home (%)	50	51
Consume food from own garden (%	30	30
Have pets (%)	49	78
Hang laundry outside (%)	69	81

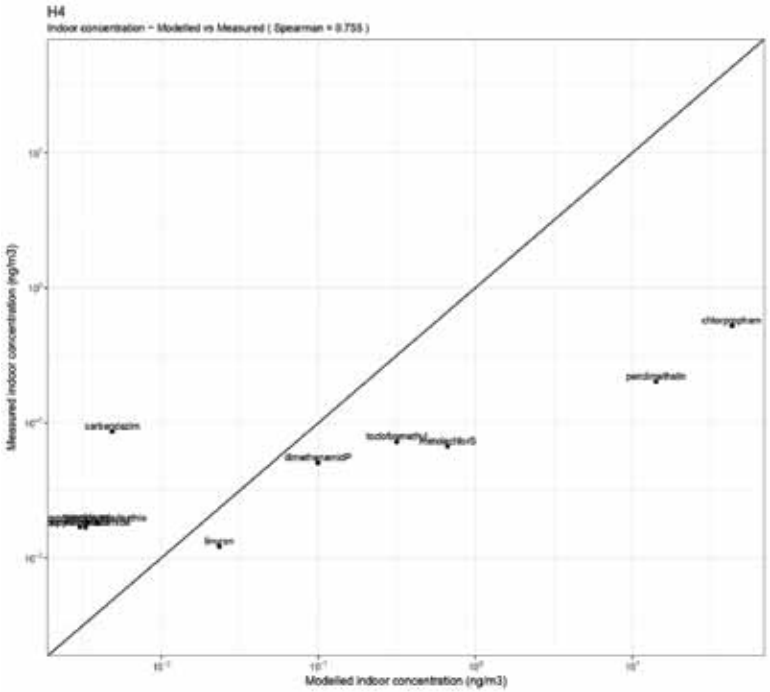
** All values Mean ± SD*

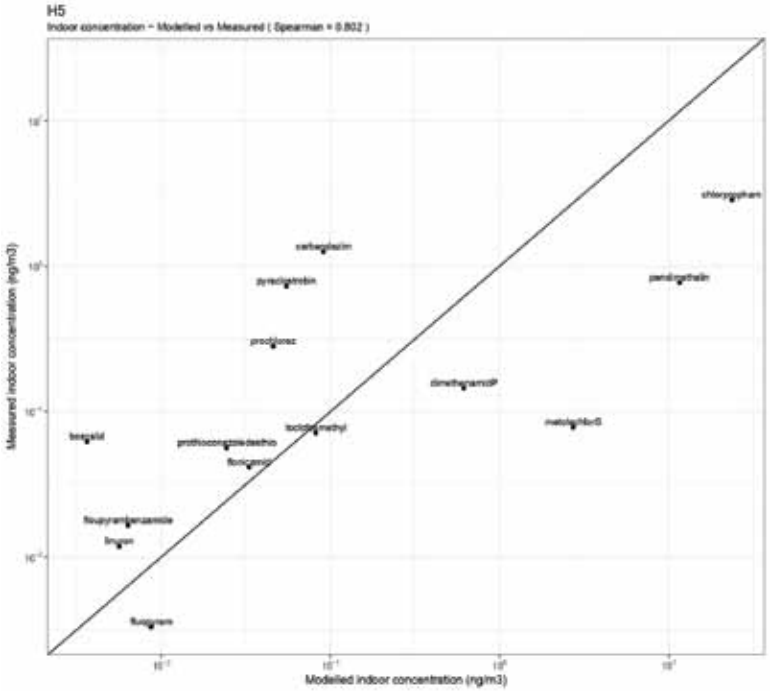
Appendix 23: gComis verification plots

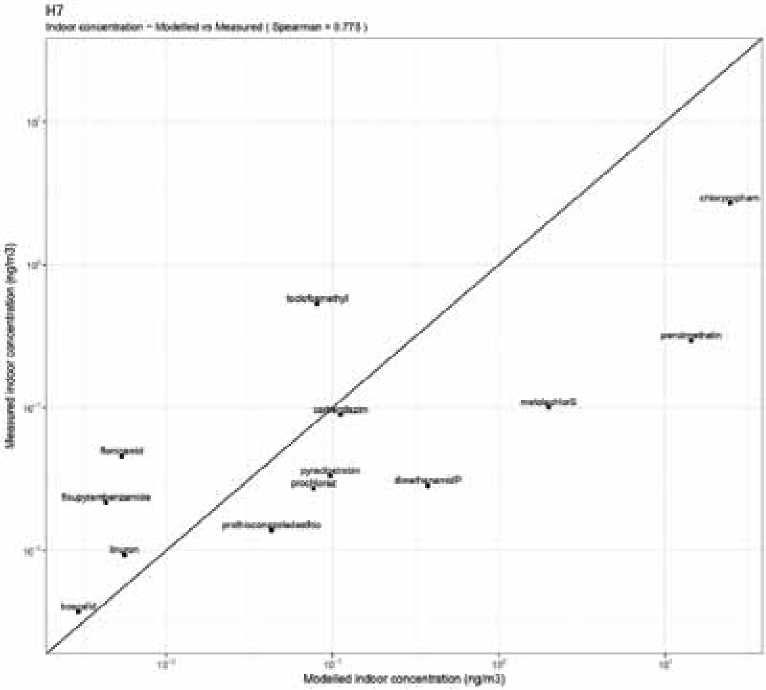


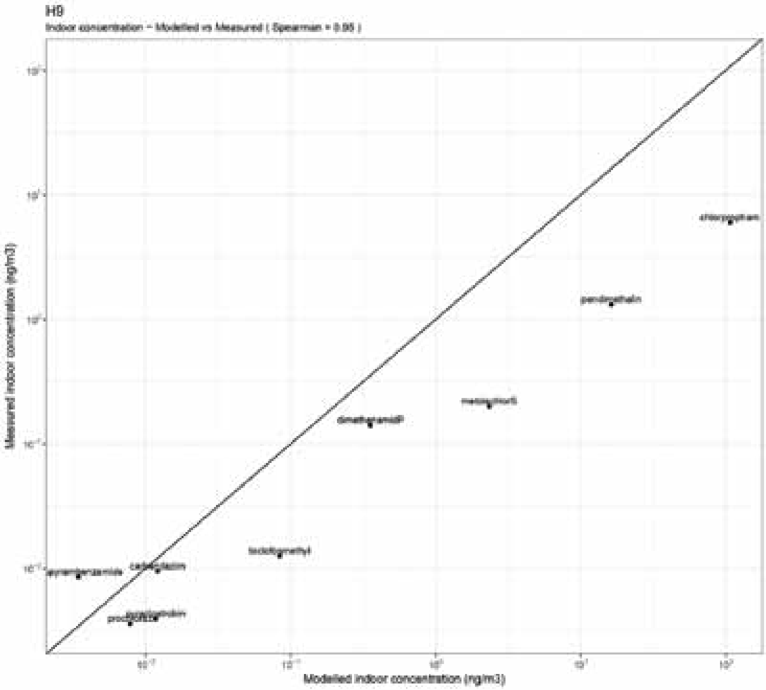

H2
Indoor concentration ~ Modelled vs Measured (Spearman = 0.643)
pendimethalin
chlorpyrifos
tebufenozid
tolclofos-methyl
metolachlor-S
fluopyram
benzamide
imazalil
dimethenamid-P
prothioconazole-desthio
kresoxim-methyl
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)

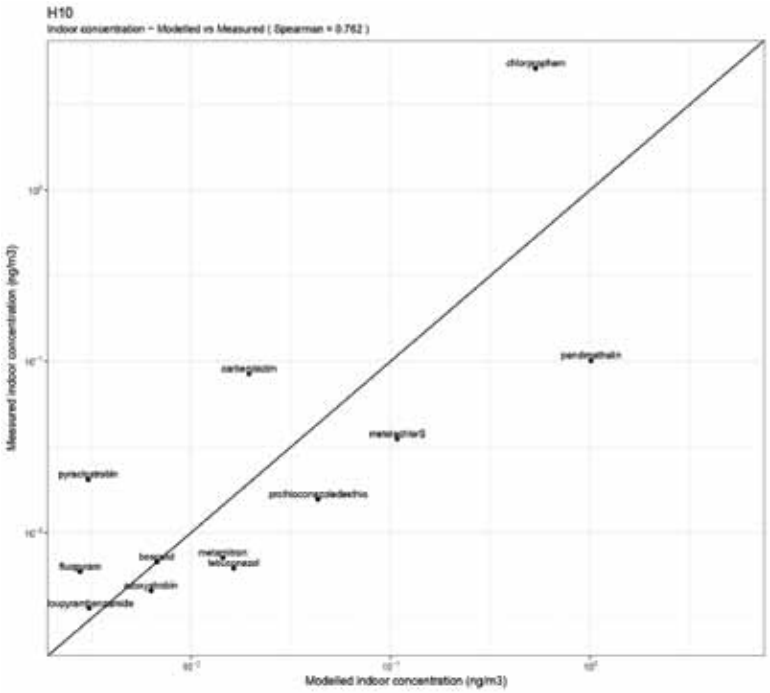

H3
Indoor concentration ~ Modelled vs Measured (Spearman = 0.301)
chlorpyrifos
pendimethalin
metazachlor
carbendazim
tolclofos-methyl
fluopyram
pyraclostrobin
dimethenamid-P
tebufenozid
fluopyram
benzamide
metolachlor-S
prothioconazole-desthio
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)

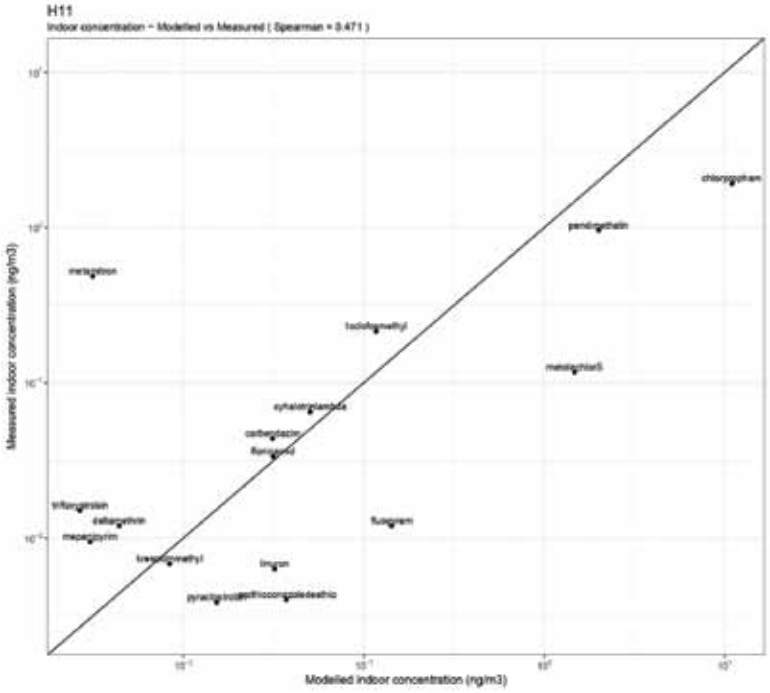

H4
Indoor concentration ~ Modelled vs Measured (Spearman = 0.755)
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)
chlorpyrifos
pendimethalin
carbendazim
tolclofos-methyl
dimethomorph
metolachlor-S
fipronil

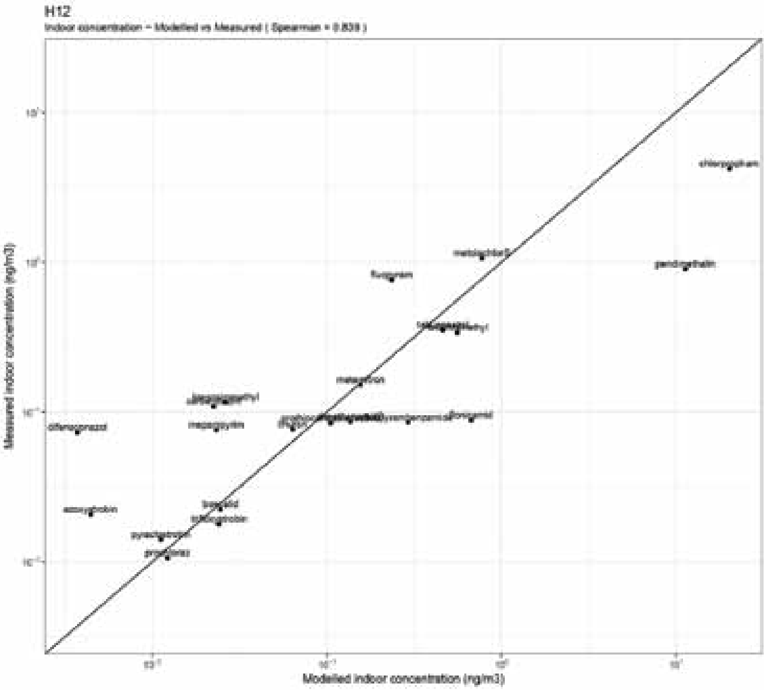

H5
Indoor concentration ~ Modelled vs Measured (Spearman = 0.802)
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)
chlorpyrifos
carbendazim
pendimethalin
dimethomorph
metolachlor-S
tolclofos-methyl
fipronil
flupyram
fluopyram

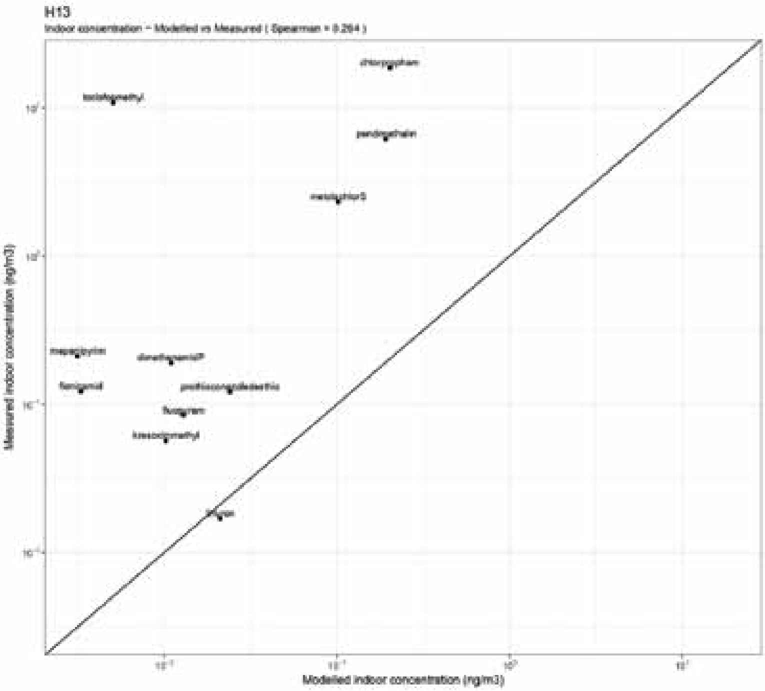

H7
Indoor concentration ~ Modelled vs Measured (Spearman = 0.773)
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)


H9
Indoor concentration ~ Modelled vs Measured (Spearman = 0.95)
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)


H10
Indoor concentration ~ Modelled vs Measured (Spearman = 0.762)
chlorpyrifos
pendimethalin
carbendazim
metalaxyl-M
pyraclostrobin
prothioconazole-desthio
fluopyram
boscalid
metalaxyl
tebuconazole
azoxystrobin
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)

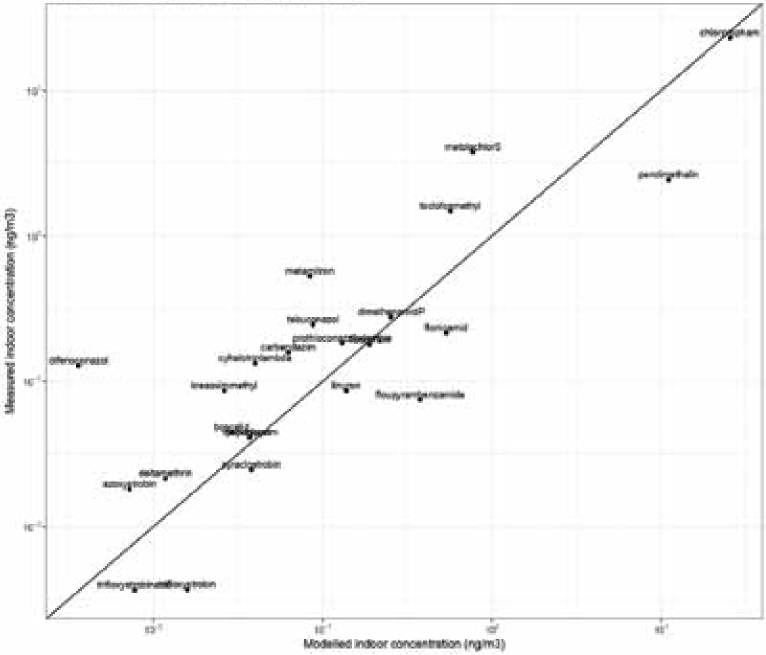

H11
Indoor concentration ~ Modelled vs Measured (Spearman = 0.471)
chlorpyrifos
pendimethalin
metalaxyl
tolclofos-methyl
metalaxyl-M
cyhalothrin-lambda
carbendazim
fludioxonil
trifloxystrobin
diflufenican
fluopyram
mepanipyrim
tebuconazole
linuron
pyraclostrobin
prothioconazole-desthio
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)


H12
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)


H13
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)

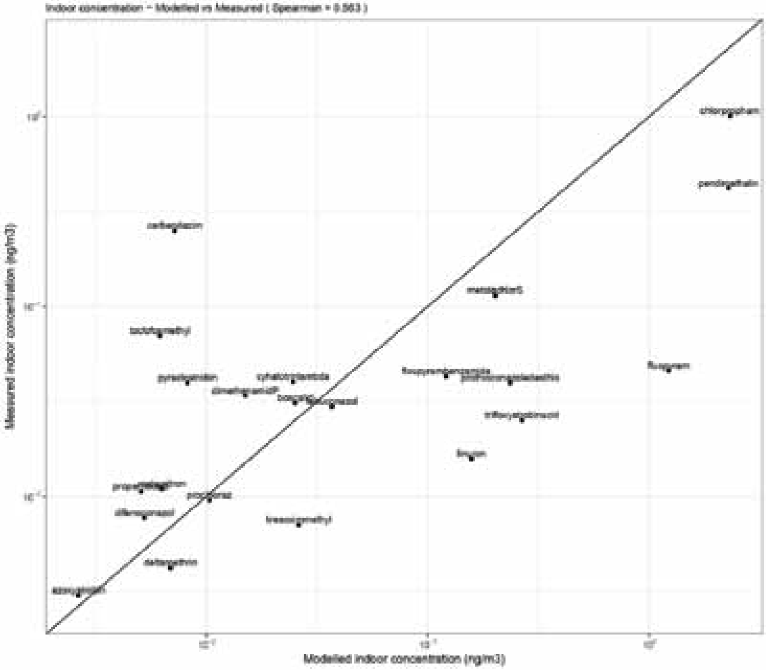
H14

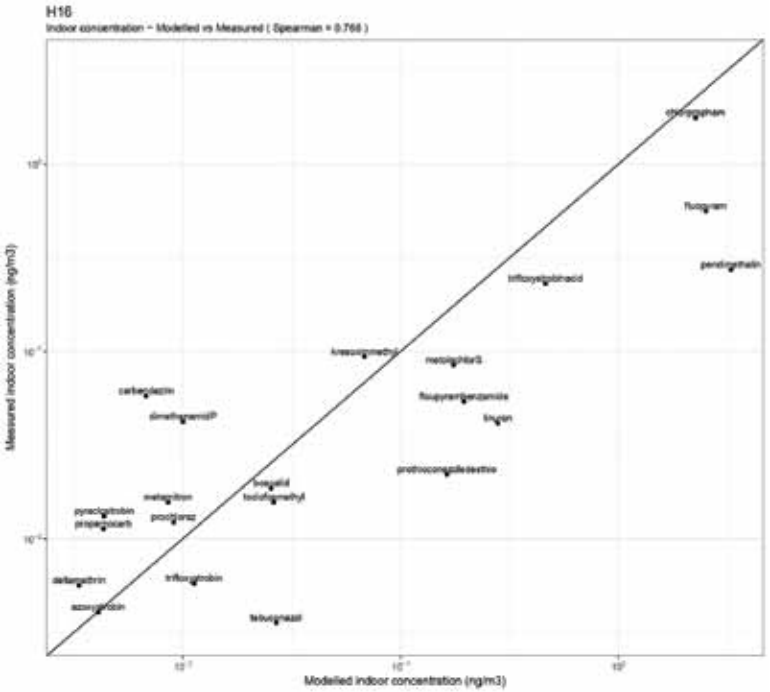
Indoor concentration – Modelled vs Measured (Spearman = 0.825)



H15

Indoor concentration – Modelled vs Measured (Spearman = 0.563)




H16
Indoor concentration ~ Modelled vs Measured (Spearman = 0.768)
Measured indoor concentration (ng/m3)
Modelled indoor concentration (ng/m3)
chlorpyrifos
flutolanil
pendimethalin
trifloxystrobin acid
kresoxim-methyl
metalaxyl
carbendazim
fluopyram
benzamide
dimethomorph
tebuconazole
prothioconazole-desthio
pyraclostrobin
propiconazole
deltamethrin
trifloxystrobin
azoxystrobin
tebuconazole

Appendix 24: Resuspension

Different studies indicate resuspension rates range between 10^{-5} to 10^{-2}. (e.g. Table 1, Qian et al. 2014). Resuspension was added in the gComis model as an indoor source for concentration of pesticides in air. The main conclusion was that resuspension can serve as an additional input to gComis, as a continuous variable with input in kg/s per zone. For larger concentrations in dust or high resuspension rates (> 0.001), resuspension can have an effect on pesticides daily average concentration in indoor air.

References

Qian, J., Peccia, J., Ferro, A.R. (2014). Walking-induced particle resuspension in indoor environments. Atmospheric Environment, Volume 89, 2014, Pages 464-481.

Appendix 25: Predictors tested in model selection

List of independent variables		Source	Variable type
Environment			
Concentration	Pesticide in outdoor air	Measured data	Numerical or Binary (<LOD/>LOD)
	Pesticide in dust vacuumed	Measured data	Numerical or Binary (<LOD/>LOD)
	Pesticide in dust doormat	Measured data	Numerical or Binary (<LOD/>LOD)
Meteorological data	Temperature	Weather station	Numerical
	Humidity	Weather station	Numerical
	Rainfall	Weather station	Binary (Y/N)
	Wind Speed	Weather station	Numerical
	Wind direciton	Weather station	Categorical
Home Specific			
Home characteristics	Year house was built	Questionnaire	Numerical
	Air leakage	Calculated	Numerical
	Type of flooring	Questionnaire	Categorical
	Age of the floor	Questionnaire	Numerical
	Volume	Questionnaire	Numerical
	Distance to applying field	ArcGIS	Categorical
Resident Specific			
General information	Age	Questionnaire	Numerical
	Height	Questionnaire	Numerical
	BMI	Calculated	Numerical
	Gender	Questionnaire	Binary (M/F)
	Inhalation rate - mean	Questionnaire	Numerical
	Average time spent indoors	Questionnaire	Numerical
	Consumption of food from home garden	Questionnaire	Binary (Y/N)
	Use of pesticides indoor	Questionnaire	Binary (Y/N)
	Use of pesticides outdoor	Questionnaire	Binary (Y/N)
Time spent	inside own home	Diary	Numerical
	inside work / company	Diary	Numerical
	inside stable, barn or shed	Diary	Numerical
	in vehicle (car or bus)	Diary	Numerical
	on tractor or other agricultural vehicle	Diary	Numerical
	on bike or walking	Diary	Numerical
	outside in own garden or the street	Diary	Numerical
	outside work / company	Diary	Numerical
	on agricultural field or in orchard	Diary	Numerical
Contact	with pets / poultry cattle today	Diary	Binary (Y/N)
	with substance against fleas or ticks of pets	Diary	Binary (Y/N)
	with substance against head lice	Diary	Binary (Y/N)
	with insecticides	Diary	Binary (Y/N)
	with substance against weeds, green deposits or moss	Diary	Binary (Y/N)
	with fungicides	Diary	Binary (Y/N)
	with substance against snails	Diary	Binary (Y/N)
	with substance against rats and mice	Diary	Binary (Y/N)
	with preserved wood	Diary	Binary (Y/N)
Action	Barbecued today	Diary	Binary (Y/N)
	Barbecue or fire basket lighted in garden / nearby	Diary	Binary (Y/N)
	Lighted fireplace today	Diary	Binary (Y/N)
	Taken medication today	Diary	Binary (Y/N)
	Which medication taken today	Diary	Binary (Y/N)
	Child wearing diaper	Diary	Binary (Y/N)

List of independent variables		Source	Variable type
Resident Specific			
Consumed	endive	Diary	Binary (Y/N)
	eggplant	Diary	Binary (Y/N)
	broccoli	Diary	Binary (Y/N)
	celery	Diary	Binary (Y/N)
	cauliflower	Diary	Binary (Y/N)
	beans	Diary	Binary (Y/N)
	mushroom	Diary	Binary (Y/N)
	courgette	Diary	Binary (Y/N)
	peas	Diary	Binary (Y/N)
	mixed vegetable	Diary	Binary (Y/N)
	cucumber	Diary	Binary (Y/N)
	cabbage	Diary	Binary (Y/N)
	corn	Diary	Binary (Y/N)
	pepper	Diary	Binary (Y/N)
	leek	Diary	Binary (Y/N)
	salad	Diary	Binary (Y/N)
	spinach	Diary	Binary (Y/N)
	tomato	Diary	Binary (Y/N)
	onion	Diary	Binary (Y/N)
	chicory	Diary	Binary (Y/N)
	carrot	Diary	Binary (Y/N)
	strawberries	Diary	Binary (Y/N)
	apple	Diary	Binary (Y/N)
	banana	Diary	Binary (Y/N)
	berries	Diary	Binary (Y/N)
	blackberries	Diary	Binary (Y/N)
	citrus fruit	Diary	Binary (Y/N)
	grape	Diary	Binary (Y/N)
	raspberries	Diary	Binary (Y/N)
	cherries	Diary	Binary (Y/N)
	kiwi	Diary	Binary (Y/N)
	nectarine	Diary	Binary (Y/N)
	pear	Diary	Binary (Y/N)
	peach	Diary	Binary (Y/N)
	potato	Diary	Binary (Y/N)
	bread	Diary	Binary (Y/N)
	eggs	Diary	Binary (Y/N)
	cereals	Diary	Binary (Y/N)
	pasta	Diary	Binary (Y/N)
	rice	Diary	Binary (Y/N)
	superfood	Diary	Binary (Y/N)
	soft drink	Diary	Binary (Y/N)
	juice (prepacked)	Diary	Binary (Y/N)
	juice (fresh)	Diary	Binary (Y/N)
	coffee	Diary	Binary (Y/N)
	milk	Diary	Binary (Y/N)
	tea	Diary	Binary (Y/N)
	water	Diary	Binary (Y/N)
	wine and/or beer	Diary	Binary (Y/N)

Appendix 26: Summary results of statistical modelling

All estimates shown in the following tables are in the log10 scale.

Log-linear mixed effect models – **Across** all season

Tebuconazole – model for urine.

Independent variables	Estimate (ß)	P-value
Intercept (Floor type = Rug or Carpet)	-1.082587	1.55e-6
Creatinine (mmol/l)	0.022158	0.01428
Age (years)	0.005165	0.03492
Floor Type = Smooth	-0.426440	0.00537
Consume Strawberries = Yes	0.386955	0.00218
Consume Pears = Yes	0.542728	0.00206
Consume Peas = Yes	0.751398	0.01528

Chlorpropham – model for urine.

Independent variables	Estimate (ß)	P-value
Intercept (Resident ID)	0.03707	0.883
Creatinine (mmol/l)	-0.0025	0.859
Age (years)	-0.007497	0.03037
Concentration in outdoor air (ng/m3)	0.003707	0.002569
Time spent outside in own garden or street (hours)	0.002269	0.00029

Log-linear mixed effect models – **During** spraying season

Tebuconazole – During spraying season - model for urine.

Independent variables	Estimate (ß)	P-value
Intercept (Floor type = Rug or Carpet)	-0.737676	9.54e-5
Creatinine (mmol/l)	0.037076	0.001029
Consume food items from own garden = Yes	0.560997	0.000899
Floor Type = Smooth	-0.777604	0.01199
Consume Peas = Yes	0.701323	0.013329

Chlorpropham – During spraying season - model for urine.

Independent variables	Estimate (ß)	P-value
Intercept (DDM Above LOD)	0.844378	0.00295
Creatinine (mmol/l)	-0.014525	0.32591
Age (years)	-0.008995	0.00667
DDM Below LOD = Yes	-0.423893	0.01199

Log-linear mixed effect models – **Outside** spraying season

Tebuconazole – Outside spraying season - model for urine.

Independent variables	Estimate (ß)	P-value
Intercept (Contact w/ Fungicide = No)	- 0.78853	1.36e-7
Creatinine (mmol/l)	- 0.02390	0.0478
Contact with fungicide (s) = Yes	0.53586	0.0138

Chlorpropham – Outside spraying season - model for urine.

No statistically significant finding was found between the different independent variables and the outcome.

Logistic mixed effect models – **Across** all season

Carbendazim –model for urine.

Independent variables	Estimate (ß)	P-value
Intercept (Consume onions = No)	- 2.38029	0.00223
Creatinine (mmol/l)	- 0.59764	0.04061
VFD (ng/g)	0.22623	0.02250
Number of people living in the home (-)	0.32576	0.04677
Consume Onions = Yes	0.61781	0.08924

Prochloraz and Asulam

No statistically significant finding was found between the different independent variables and the outcome.

Logistic mixed effect models – **During** spraying season

Carbendazim – During spraying season - model for urine.

Independent variables	Estimate (ß)	P-value
Intercept (Consume Superfoods = No)	- 3.2914	0.00279
Creatinine (mmol/l)	- 0.4843	0.22088
VFD (ng/g)	0.2808	0.04088
Number of people living in the home (-)	0.4215	0.05140
Consume Superfoods = Yes	3.8059	0.01037
Contact with pets = Yes	1.6119	0.01760

No statistically significant finding was found for carbendazim outside spraying season.

Appendix 27: Add-on - Personal sampling with wristbands

Introduction - Silicone wristbands

In their search for new passive sampling devices (PSDs), O'Connell et al. (2014) modified commercial silicone wristbands, enabling them to adsorb chemicals with a wide range of physical properties. Like other PSDs, they work by accumulating organic compounds on its silicone matrix. While worn on the wrist, silicone wristbands adsorb compounds from any medium or surface that it comes in contact with. Organic compounds permeate through the silicone matrices and increase in concentration until the compounds reach equilibrium (Anderson et al., 2017).
Silicone wristbands have been used to sample compounds from various classes (e.g. PAHs and flame retardants), including pesticides (e.g. Aerts et al., 2018). Since the silicone sampler is worn on the wrist, it detects chemicals that expose its wearer.

Add-on to the OBO study

In the OBO study, exposure to pesticides is measured via different sampling methods (e.g. active air sampling, biomonitoring – urine, collection of dust samples) across different mediums. These are collected during the different measurement campaigns to understand residents exposure to pesticides applied in the surrounding bulb fields.
The wristbands are a valuable addition to the OBO study to passively measure personal exposure between measurement campaigns, as well as during measurement campaigns. Unlike the active air samplers, their non-invasive nature allow them to be worn for long periods of time, thereby capturing episodic exposures and improve detection limits. Furthermore, in contrast with biological samples like urine or blood, concentrations on wristbands are not subject to metabolism, and therefore reflect accurate levels of external exposure.
During the time that the wristband is used by the participant, the silicone is expected to naturally absorb and retain various pesticides it comes in contact with, and the type and quantity of these pesticides will later be measured. Anticipated advantages of this exposure matrix are that:

1. It is less invasive than biological sample collection and is expected to yield measurements of pesticides which are not yet measurable in bio-samples.
2. Their chemical and physical properties mimic the uptake of a cell or an organism. The lipophilicity of the devices matches that of biological membranes and can capture many but not all bioavailable compounds.
3. They will continuously bind and sequester the compounds that they are effective for, providing a time weighted average for exposure during the study period. This allows for the detection of chemicals at low environmental concentrations and will capture less frequent acute exposures.

Wristbands are not part of the main study, but is has been agreed that 'add-on' results will be reported for information.

Methodology

Recruitment and consent

All participants of OBO over the age of 4 years, were asked to also wear a wristband. Children younger than 4 could not participate in this part of the study due to small wrists. Wearing the wristband was not an obligated part of the study and participants could participate in OBO without wearing the wristband. Upon participation in OBO, participants will be informed by an information letter. There was a separate box on the informed consent form to tick if they were willing to wear a wristband.

Collection and storage

Wristbands were worn continuously (even during showering and sleeping) during the first sampling week and a new one worn between sampling week 1 and 2, to capture all potential exposure events. The bands were stored in Teflon bags labelled with the participant's code once the deployment period finished.

Wristband Analyses

Wristbands were extracted in acetonitrile. Extracts were treated the same way air sample extracts were treated in the OBO-project (appendix 2 of the OBO report). Pesticide levels were determined using LC-MS/MS. Results are expressed in ng pesticide per gram wristband.

Statistical Analyses

For calculation purposes, levels below the LOD were imputed when the pesticide was detected (>LOD) in at least 40% of the measured wristband samples. Fixed imputation was performed, using two thirds (2/3) of the LOD has fixed imputed value.

Results

Wristband samples

The total number of wristband samples analyzed was 20. This was due to the late stage of introducing wristband sampling into the OBO study. In addition, wristband sampling was optional for the participants of the OBO study. Five wristbands belonged to residents living within 50 meters from a bulb field.

Descriptive analysis

The individual analysis results are provided in Table 2, at the end of this appendix. In total, 38 out of the 45 targeted pesticides were detected in the wristbands. In Table 1, a summary of findings is shown.

Various pesticides can be found in almost all wristband samples (>=75%). These pertain to pesticides applied in different fields during the measurement campaigns (marked with an asterisk in Table 1), but also to other pesticides that were not applied during

measurement campaigns, such as, for example, carbendazim, fludioxonil, azoxystrobin and terbuthylazine.
Some of these pesticides are also not used in bulb disinfection, but can be found in various wristbands. This is a strong indication that exposure occurring between campaign periods can be well captured using wristband samplers. Additionally, some pesticides (terbuthylazine and fludioxinil) found in wristbands were found less frequently in samples taken from air and dust during the measurement campaigns.

Conclusion

A total of 20 wristband samples from 20 residents were analyzed for 45 pesticides. 38 pesticides were detected. Pesticides commonly found in various mediums during the OBO-study were also found in the add-on wristbands (e.g. chlorpropham and pendimethalin). Some pesticides (terbuthylazine and fludioxinil) were more frequently found in wristbands than other mediums, this can indicate that exposure to these pesticides occurred between measurement periods and most likely result from field applications, since these are not used in bulb disinfection.

Finally, wristbands seem a viable way to detect and quantify resident's exposure to pesticides and the fact that are cost-friendly, easily deployable and non-invasive, might be a future substitute of other samplers applied to collected data in larger populations.

Table 1: Summary of pesticides in wristbands collected in the frame of the OBO project.

Active Ingredient	% > LOD	median	mean	min	max
acetamiprid	25%	< LOD	NA	< LOD	1.20
asulam	0%	< LOD	NA	< LOD	0.00
azoxystrobin	100%	5.19	9.29	0.30	59.47
boscalid	90%	1.32	2.68	0.09	10.07
carbendazim	100%	4.43	28.69	1.02	414.37
chloridazon	30%	< LOD	NA	< LOD	2.03
chlorpropham	95%	8.06	11.23	0.09	32.82
cyhalotrin-lambda	25%	< LOD	NA	< LOD	18.61
cyprodinil	40%	< LOD	NA	< LOD	2.71
deltamethrin	15%	< LOD	NA	< LOD	0.99
difenoconazole	5%	< LOD	NA	< LOD	0.32
dimethenamid-P	50%	0.19	0.45	0.09	2.60
dimethomorph	15%	< LOD	NA	< LOD	1.60
flonicamid	45%	< LOD	NA	< LOD	1.66
floupyram-benzamide	10%	< LOD	NA	< LOD	0.47
fludioxonil	90%	1.42	1.97	0.09	7.27
fluopicolide	10%	< LOD	NA	< LOD	0.41
fluopyram	35%	< LOD	NA	< LOD	1.33
flutolanil	10%	< LOD	NA	< LOD	0.31
fosthiazate	5%	< LOD	NA	< LOD	1.73
imidacloprid	80%	0.76	3.00	0.09	39.60
kresoxim-methyl	20%	< LOD	NA	< LOD	2.11
linuron	35%	< LOD	NA	< LOD	1.37
mepanipyrim	80%	0.70	1.01	0.09	4.12
metamitron	55%	0.31	0.39	0.09	1.40
metamitron-desamino	0%	ND	NA	ND	0.00
metolachlor-S	75%	0.94	0.83	0.09	1.68
oxamyl	10%	< LOD	NA	< LOD	0.69
pendimethalin	95%	0.64	0.77	0.09	1.72
primicarb	25%	< LOD	NA	< LOD	1.28
prochloraz	30%	< LOD	NA	< LOD	3.47
propamocarb	0%	< LOD	NA	< LOD	< LOD
prothioconazole	0%	ND	NA	ND	ND
prothioconazole-desthio	90%	0.65	0.80	0.09	2.06
pymetrozine	100%	0.84	2.98	0.29	15.80
pyraclostrobin	55%	0.29	1.55	0.09	17.22
spirotetramat	15%	< LOD	NA	< LOD	3.92
spirotetranat-enol	0%	< LOD	NA	< LOD	0.00
sulcotrione	60%	0.34	5.87	0.09	51.52
tebuconazole	75%	0.40	1.16	0.09	9.21
terbuthylazine	75%	0.42	0.39	0.09	0.87
thiacloprid	15%	< LOD	NA	< LOD	0.83
thiophanate-methyl	0%	ND	NA	ND	ND
toclofos-methyl	10%	< LOD	NA	< LOD	2.59
trifloxystrobin acid	0%	< LOD	NA	< LOD	< LOD
trifloxystrobin	5%	< LOD	NA	< LOD	0.60

Median, mean, min and max in ng/gram of substance found in the wristband.

Table 2: Individual results (ng/gram).

	Distance to field	< 50 m					50 - 250 m														
LOD	Resident ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
0.27	acetamiprid	<	<	<	<	<	1.20	0.28	0.30	<	<	0.57	<	<	<	<	<	<	0.39	<	<
0.27	asulam	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
0.27	azoxystrobin	59.47	0.33	9.89	7.79	3.42	1.92	8.15	0.64	0.32	0.30	8.79	37.01	4.22	7.51	4.08	17.14	1.69	6.17	6.44	0.60
0.27	boscalid	3.83	<	0.31	1.27	0.63	6.14	3.16	0.94	0.87	<	6.65	4.60	0.71	0.71	6.07	1.37	3.74	1.70	0.55	10.07
0.27	carbendazim	3.98	4.38	14.67	2.97	5.71	9.08	16.63	11.35	3.84	1.14	2.73	5.66	414.37	56.44	2.50	8.23	4.49	3.49	1.15	1.02
0.27	chloridazon	<	<	0.29	<	<	0.74	<	0.30	<	<	2.03	0.32	<	<	0.86	<	<	<	<	<
1.60	chlorpropham	8.92	<	2.26	7.21	6.46	32.82	2.52	21.61	25.23	17.06	20.46	4.38	6.24	14.22	18.62	4.46	6.44	9.25	5.64	10.77
2.67	cyhalotrin-lambda	<	<	<	<	<	<	2.70	18.61	4.17	<	<	<	5.68	<	7.62	<	<	<	<	<
0.27	cyprodinil	0.50	<	0.37	<	0.58	<	0.80	0.73	<	<	0.49	2.71	<	<	<	<	<	<	0.32	<
0.53	deltamethrin	<	<	0.58	<	<	<	<	<	0.57	<	<	0.99	<	<	<	<	<	<	<	<
0.27	difenoconazole	<	<	<	<	<	<	<	<	<	<	<	0.32	<	<	<	<	<	<	<	<
0.27	dimethenamid-P	<	<	<	<	0.47	1.66	<	2.60	0.28	<	0.58	0.46	0.34	0.40	<	0.90	<	0.32	<	<
0.27	dimethomorph	<	<	<	<	<	0.84	<	<	<	<	<	2.24	<	<	<	<	3.11	<	<	<
0.27	flonicamid	0.94	<	<	0.27	<	1.30	<	0.77	0.74	<	1.20	0.69	<	<	0.80	1.66	<	<	<	<
0.27	floupyram-benzamide	<	<	<	<	<	0.47	<	<	<	<	<	<	<	<	<	<	<	0.41	<	<
0.27	fludioxonil	2.01	<	1.42	5.57	1.43	1.89	1.32	1.55	7.27	<	1.61	2.90	0.56	0.79	5.89	2.07	1.13	0.50	0.57	0.80
0.27	fluopicolide	0.41	<	<	<	<	<	<	0.41	<	<	<	<	<	<	<	<	<	<	<	<
0.27	fluopyram	<	<	<	<	<	0.54	1.07	1.33	<	<	0.50	1.16	<	<	<	0.60	<	0.67	<	<
0.27	flutolanil	<	<	<	<	<	0.28	<	0.31	<	<	<	<	<	<	<	<	<	<	<	<
0.27	fosthiazate	<	<	<	<	<	1.73	<	<	<	<	<	<	<	<	<	<	<	<	<	<
0.27	imidacloprid	1.66	<	0.93	0.68	0.62	0.61	39.60	2.32	1.77	<	1.42	1.70	0.96	0.83	0.34	<	0.51	0.47	<	5.21
0.27	kresoxim-methyl	<	<	<	<	<	<	<	<	<	<	2.11	1.74	<	<	1.20	0.47	<	<	<	<
0.27	linuron	<	<	<	<	0.67	1.37	<	<	0.78	<	<	1.27	<	<	0.43	0.51	<	0.35	<	<
0.27	mepanipyrim	0.51	<	0.35	0.67	0.92	1.37	3.20	0.68	0.43	<	0.33	0.79	0.78	<	<	0.72	0.90	4.12	0.87	3.18
0.27	metamitron	0.35	<	<	0.45	<	1.40	0.55	0.58	0.67	<	1.31	<	<	<	0.32	<	<	0.50	0.30	0.49
0.27	metamitron-desamino	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
0.53	metolachlor-S	<	<	<	0.81	0.80	1.18	0.94	0.73	0.94	<	1.27	1.68	1.11	1.15	1.12	1.40	<	1.38	0.54	1.02
0.27	oxamyl	<	<	<	<	<	0.69	<	<	<	<	0.33	<	<	<	<	<	<	<	<	<
0.27	pendimethalin	0.43	<	0.33	0.84	1.40	0.47	0.51	1.19	1.72	1.14	0.75	0.42	0.84	0.67	1.16	0.62	0.57	0.54	0.43	1.19
0.27	primicarb	<	<	<	<	<	1.28	0.45	<	<	<	<	1.13	<	<	<	0.56	<	0.96	<	<
0.27	prochloraz	<	0.27	<	<	<	0.34	<	<	<	<	0.79	3.47	<	<	<	0.30	<	<	0.58	<
0.27	propamocarb	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
-	prothioconazole	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
0.27	prothioconazole-desthio	1.21	0.33	<	0.33	0.55	2.06	0.53	0.51	1.88	<	0.74	2.04	0.44	0.45	0.69	0.82	0.71	1.05	0.62	0.96
0.27	pymetrozine	4.51	0.39	0.56	0.54	0.48	15.80	6.36	9.35	4.08	0.98	7.70	2.16	2.79	1.06	0.56	0.69	0.45	0.56	0.29	0.36
0.27	pyraclostrobin	3.87	<	<	<	<	0.38	<	<	3.48	0.55	1.70	17.22	0.28	<	0.97	<	0.62	0.29	<	0.77
0.80	spirotetramat	<	<	<	<	<	1.56	<	<	<	<	3.92	<	<	<	0.88	<	<	<	<	<
0.27	spirotetranat-enol	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
0.27	sulcotrione	6.56	<	0.27	0.29	<	51.52	5.86	10.29	4.30	1.30	33.68	1.44	0.73	0.40	<	<	<	<	<	<
0.27	tebuconazole	0.58	<	1.29	0.50	0.45	1.94	0.31	0.29	0.32	0.61	9.21	5.55	0.38	<	0.49	<	0.35	0.43	<	<
0.27	terbuthylazine	0.41	0.47	0.36	<	0.46	0.57	0.87	<	0.42	0.49	0.42	0.46	<	<	<	0.68	0.40	0.40	0.31	0.55
0.27	thiacloprid	<	<	<	<	<	0.83	0.30	<	<	<	0.42	<	<	<	<	<	<	<	<	<
-	thiophanate-methyl	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
0.27	toclofos-methyl	<	<	<	<	2.59	<	<	<	<	<	<	<	<	<	<	<	<	0.41	<	<
0.27	trifloxystrobin acid	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
0.27	trifloxystrobin	<	<	<	<	<	<	<	<	<	<	<	0.60	<	<	<	<	<	<	<	<

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Appendix 28: Add-on - Outdoor passive sampling with polyurethane foam disks

Introduction

Polyurethane Passive Air Samplers

The Polyurethane Passive Air Samplers (PUF) design is based on accumulation of chemicals on a matrix, and represent a cumulative exposure assessment to determine the concentration of chemicals in the air. Uptake of chemicals is air side controlled and can be described with air-side mass transfer coefficient (MTC) (Shoeib and Harner, 2002). Therefore airflow plays a crucial role in the uptake of chemicals by PUF and can also influence the sampling rate (Rs) of compounds which is typically around 4 ± 2 m^3/day. Consequently, certain meteorological parameters influence the Rs of the PUF disk, most notably temperature and wind. The effect of high wind speed on the sampling rate also depends on temperature and on whether the measured chemicals are in gas phase or particle bound phase (Klanova et al. 2008).

Tendency towards gas or particle bound phase also depends on temperature and is chemical specific due to differences in chemical properties, also differences in prevalence of a pesticide on different sizes of particles are observed (Coscollà et al., 2013). Passive sampling theory doesn't take particle associated chemicals into account, although particles can penetrate into the PUF disk (Chaemfa et al. 2009). Next to wind, molecules with lower molecular weights have a tendency for higher volatility and can in combination with changes in temperature influence accumulation and elimination on the PUF disk (Petrich et al., 2013). Next to meteorological changes, characteristics of the PUF disk like density and surface area should also be considered (Chaemfa et al. 2009).

Multiple studies have successfully used PUF-PAS as alternative for measuring in- and outdoor pollutants (e.g. Bohlin et al. 2010, Gibbs et al. 2016).

Add-on to the OBO study

In the OBO study, the exposure assessment makes use of multiple methods including active air sampling (AAS), passive air sampling (PAS), urine biomarkers, electrostatic dust collectors and questionnaires among others. High volume AAS are used to link specific spraying events to short term exposure (RIVM, 2016). Although highly accurate in measuring air concentrations, disadvantages include costs, size and necessity for electricity (Pozo et al. 2004). Moreover, they tend to make noise which makes them intrusive when conducting a residential housing study.

As an alternative, PUF disks are cost-effective, easy to handle and less invasive and are therefore widely used in large scale long-term sampling studies assessing spatial and long-term temporal or seasonal variability. Despite its widespread use, research is still optimizing the efficiency and precision of PUF-PAS (Bohlin et al. 2014).

As an add-on to the study we assess the long term indoor and outdoor exposure by using PUF-PAS to identify and quantify the pesticides in the homes of residents

living in proximity of a bulb field. Then, compare these results with the AAS to further model the PUF disks into a viable alternative for AAS, contributing to a more complete resident exposure assessment.
PUF-PAS are not part of the main study, but is has been agreed that 'add-on' descriptive results will be reported for information.

Methodology

PUF disk technical information: 14 cm long, 1.35 cm thick, 0.0213 g/cm^3, surface area of 365 cm^2 (Tisch Environmental).

Recruitment

During the OBO study various residences in different locations have been approached to participate in their research. The PUF-PAS where deployed at these residences, however due to time and shortness of equipment it was not possible to place them in all the participating residences. All of the asked participants agreed to partake in this extra study. PUF-PAS deployment was scheduled to cover at least 1 spraying event of the field.

Pre-cleaning and PUF setting

PUF disks were prior to deployment pre-cleaned by Soxhlet extraction for 24 hours with acetone. Next the disks were dried under a fume hood for 6-7 hours, then stored in 2 aluminum foil layers and placed in zipped polyethylene bags in the freezer at -20°C. The PUF disks were deployed indoor and outdoor at sampling sites. Indoor sampler is the TE-300 passive air sampler of Tisch Environmental, a tripod with one stainless steel dome above the PUF disk to maximize airflow but still protect the disk from gravitational deposition of coarse particles. Outdoor sampler is the TE-200 passive air sampler of Tisch Environmental. Composed of 2 stainless steel bowls, the so called flying saucer design, the top bowl is 24 centimeters and the bottom bowl is 20 centimeters in diameter. Air can flow through the gaps on the side and exit through the holes in the bottom of the sampler, see Figure 1. The bowls protect the disk from precipitation, high wind velocities, sunlight and gravitational deposition of coarse particles.

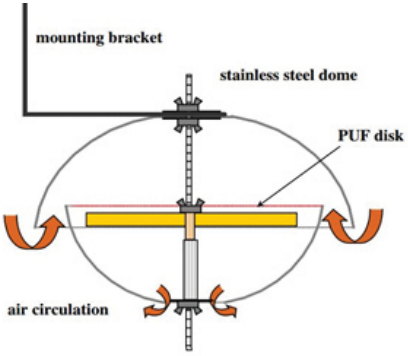

Figure 1: Schematic of a "flying saucer" design of the PUF-PAS.
Showing points of entry for wind and location of the PUF disk. Taken from (Harner et al. 2006).

Deployment and storage

The PUF disk were placed in the sampler housing with clean gloves at the sample site. The outdoor PAS were mounted on a wooden pole, in the ground at a height of 1.80 meter. The outdoor PAS were placed in the backyard, with as much free space surrounding the PAS as possible. The indoor PAS were usually placed between 1.2 and 2 meters on a cabinet in the living room or kitchen depending on availability of free space and in consultation with the residents. Method blanks and field blanks were taken into account. The field blank was taken to the field, taken out of the packing and immediately stored in 2 layers of aluminum foil and a Ziploc bag. From this point it was treated like the other samples.

Upon retrieving the PUF disks from the field, they were stored in a cool box containing cooling elements, after arrival at the laboratory the samples were taken directly to the freezer and stored at -20˚C until further extraction and analysis.

Extraction and analysis

Extraction

Retrieve the samples from the freezer and let them get to room temperature under a fume hood for ~30 minutes, still within the polyethylene zip lock bags. Next, unpack the samples and put in 100 ml glass jars using either nitrile gloves or acetone rinsed tweezers. When using gloves, replace gloves after each sample. Add 100 ml acetone HPLC grade to the jar and close it. Make sure the PUF is completely submerged in acetone, and let it stand for 10 minutes. Next, place the glass jars in a Sonicator bath for 1.5 hour at ~30˚C. Afterwards let the jars stand for another 10 minutes before extracting the acetone from the PUF. Pour the acetone in an Erlenmeyer, let the jar leak out for a short amount of time before squeezing the PUF with acetone rinsed tweezers to get most of the acetone out of the PUF. When a funnel is used, rinse this with 1 ml of acetone. To assess the amount of acetone extracted, weigh the Erlenmeyer before and after the extraction to calculate the total volume. Let the Erlenmeyer covered with parafilm stand in the freezer overnight. Next let the samples come to room temperature under a fume hood, pour the sample over in flasks, suitable for vacuum evaporation. Rinse the Erlenmeyer with 3 ml of acetone and add it to your sample. Evaporate with a vacuum evaporator, ~400 mbar and 50˚C or Turbovap till ~1 ml. Next quantitatively transfer the sample to a 5-ml glass tube and evaporate to ~1 ml under a gentle stream of nitrogen. Put samples in freezer till further steps. Next, put samples in the centrifuge for 10 minutes at 4000 rounds per minute. And transfer the top fraction of the sample into a 5-ml glass tube. Add 300 µl water and let it stand for 2 hours at room temperature. Put the samples again in the centrifuge for 10 minutes at 4000 rounds per minute. Next 10 µg internal standards of each active compound will be added to the sample. Pipet the top fraction into a 2um nylon filter of 13 mm, once this is passes rinse the bottom fraction with 300 µl water/methanol 1:1 and put it through the filter. Due to the large particulate matter this might take a couple of minutes, this process can be accelerated by adding air pressure with a syringe. Next centrifuge the samples for 10 minutes at 4000 RPM and pipet ~0.5ml of the top fraction into a MS-

vial, if the samples contained less than 0.5 ml an insert was placed in the MS vial and 0.1 or 0.2 ml was added to the insert.

White substance during the process

An unforeseen event during cleaning and extraction process was the appearance of a white substance which seemed to come from the polymers of the PUF itself. The following sections discuss different methods used to try to remove the white substance from the sample.

Solid Phase Extraction

When tackling the white substances, Solid phase extraction (SPE) was used as an alternative. Blanco's with the white substance were tested with the SPE by using Strata X 22u polymeric reversed phase 60 mg/ 3ml columns. The columns were conditioned with 1 ml water and subsequently 2 ml methanol, the column was kept wet. Then the spiked samples and blanks were put on the column and washed with 0.5 ml water or 2 ml hexane. The hexane step was added in the hope that it would wash more white substance of the column but will leave the compounds on the column. For the same spiked samples both were performed. Then the column was dried by a stream of nitrogen. Next 2 ml methanol is added to the column thereby extracting the compounds from the column. Flow through the column was manually performed by adding air pressure. After the first blanks, spiked PUFs and solely spiked methanol (1 µg/ml) and spiked methanol that was completely blown dry were used in recovery experiments to assess the viability of this option. After the SPE, samples were blown dry till ~50 µl methanol, and worked up to 200 µl methanol. Next 1800 µl water was added and vortexed. 1 ml from this mixture was added to a MS vial. Recovery experiments of the solid phase extraction were analyzed on a High-Performance Liquid Chromatography (HPLC) attached to an Ultraviolet-visible spectroscopy (UV-VIS). A Hitachi L-7100 (Tokyo, Japan) low pressure pump was used coupled to an Spark, Holland auto sampler (Emmen, the Netherlands) the column oven, Spark Holland, was set to 40°C and the column itself is a Phenomenex Luna C18(2) 5µ 150 x 4.6 mm (Torrance, California, USA) with a flow of 0.8 ml/min. the UV-Vis is an Applied Biosystems model 785A (Waltham, Massachusetts, USA). The total injection volume was 2 µl. The compounds chosen for recovery experiments with SPE are compounds with the lowest and highest of K_{OA} values of the total list of compounds. The optimum wavelength (nm) of 270, 247, 220, 264, 270 was set for Sulcotrione, Linuron, Metalochlor-S, deltamethrin, λ-cyhalothrin, respectively. For each of the different compounds different eluents were used for the most optimal graph. The eluents differed between concentration methanol, water and acetonitrile.

Gel Permeation Chromatography (GPC)

GPC is a column chromatography method used for the separations of polymers, it is a size exclusion chromatography and could therefore be of interest of the cleaning of the samples. Especially since the hypothesis is that the white substances are

polyurethane foam polymers of different sizes. The aim is that the white substance will be separated from the compounds in the GPC and therefore different fractions can be collected, including a cleaned fraction, without white substance, with the PPPs. The GPC consists of binary Agilent pump G1312A (Santa Clara, California, USA) with two eluents, A; 100% Dichloromethane and B; with tert-Butyl Methyl Ether (MTBE) and pentane, concentration 1:1. The pump had a flow of 2 ml/minute. Sampler Agilent G1329A, with an injection volume of 50 µl and with needle wash. The column was set at a temperature of 35°C. The total run time was 30 minutes and the fractions were collected at 6.6 t/m 21 minutes in a Gilson fraction collector 202 (Middleton, Wisconsin, USA). Unfortunately, the retention time of the white substance overlapped with the retention time of the pesticides, therefore, no separation could be achieved.

Silica Column

In some literature a silica column or similar columns like Florisil columns are used to clean up the samples. (Yao et al., 2008) (Herkert, Martinez and Hornbuckle, 2016) (Degrendele et al., 2016) Therefore a blank sample which was stored after the being blown dry to ~2 ml with nitrogen, thus containing the white substance and acetone was used to try this method. The sample was blown dry and dissolved in 2 ml of 1:1 hexane: dichloromethane. The silica column was made by using 0.5 g of silica and activate it in the oven at 100°C for 1 hour. The silica column was conditioned by 1 ml of 1:1 hexane: dichloromethane solution, next the sample was put on the column and eluted with 20 ml of 1:1 hexane: dichloromethane. This solution was again blown dry and water was added. At this point the solution turned white again, thus the silica column seemed not to work. Although the silica column method was only tried once, there could be a way of making the silica column or a similar column to work.

LC MS/MS

Quantification was performed on an Agilent 6490 liquid chromatography tandem mass spectrometer, with 3 MRM repeats. The ion source was an Electrospray ionization (positive polarity and negative polarity; Gas temperature (300°C), N2, gas flow was 7 L/min, nebulizer 45 psi, capillary voltage 3500) with an Agilent jet stream. An auto sampler (Agilent, G7129A) injected 5 ul volume. Binary pump is Agilent G1312B with solutions A: MilliQ 5mM Ammonium Formate + 20 µl Formic Acid and B: Methanol 5mM Ammonium Formate + 20 µl Formic Acid. The first 13 minutes the ratio of solvents is 90% to 10 %, B to A and after the 13 minutes it changes it to 90% A and 10% B. Both at a flow rate of 0.5 ml/min flow and total run time was 18 minutes.

Quality assurance/control

Laboratory blanks, field blanks and quality control spikes were analyzed, and samples were not corrected for blanks. Recoveries of quality control spikes were 28% on average, with a wide range of 2-50% between compounds. Recovery of the nylon syringe filter alone yielded an average recovery of 90.5% with a range of 69-107% recoveries between compounds. Due to the difference in recovery per compound and

the low recovery in general a compound specific recovery was calculated.

Statistical Analyses

For calculation purposes, levels below the LOD were imputed when the pesticide was detected (>LOD) in at least 40% of the measured wristband samples. Fixed imputation was performed, using two thirds (2/3) of the LOD has fixed imputed value.

Results

PUF-PAS samples

PUF-PAS were deployed indoor and outdoor at 33 homes at 4 different locations within 250 meters of a bulb field and at 6 control homes. Control homes where within the same region as the field, however they were more than 5 km away from the field of interest. At the same time 8 residences where within 50 meters of the field of interest, in these residences two outdoor PUFs were deployed. After 1 week one of these PUFs was collected and the remaining PUF stayed in place until the indoor PAS was collected. Due to a shortness of material there are in total 5 incomplete sets (either missing outdoor or indoor) of PUF-PAS. Once a home terminated the study earlier due to unwillingness to participate further. A quick overview of the above-mentioned information is given in Table 1.

For analyses a selection of samples collected was made. This selection was based on three criteria:

1 Analyze the homes where both an outdoor and indoor PUF-PAS were available (i.e. paired).
2 For each location have at least one parallel outdoor measurement.
3 Have at least one control per location.

Table 1: Overview of residences in the different locations, the sampling period and the amount of controls for that location.

	Location 1	Location 2	Location 3	Location 4
Total residences (excluding controls)	12	10	3	8
<50-meter residences	1 (stopped early)	3	2	2
Incomplete sets	0	1 (no outdoor PAS)	0	4 (no indoor PAS)
Residences that stopped early	1	0	0	0
Average time of sampling*	~13 weeks	~8 weeks	~8 weeks	~6 weeks
Controls for this location	2	2*	2*	2

* Since location 2 and 3 are in close proximity of each other it was chosen to have the same controls. Therefore only 2 controls exist for both location 2 and 3.

Descriptive analysis

The analysis results per home and location are provided in Table 3 at the end of this appendix. Due to difficulties during the extraction process (i.e. white substance) and since it has been proven difficult to calculate the air concentrations from the concentrations in the PUF's, the results are presented in ng/PUF, posing no problem since all PUF's have the same density and surface area. Finally, the results must be seen as semi-quantitative, since they have been corrected for external recovery. Therefore only values above limit of quantification (LOQ) were reported by the lab.

In total, 19 homes and 3 controls were selected for analyses. 46 PUF samples were analyzed, comprising 27 outdoor samples and 19 indoor samples. Out of the 45 targeted pesticides, 11 were detected in the PUFs. The two pesticides detected in almost all PUF samples were chlorpropham and pendimethalin, which are widely applied herbicides in different types of bulb fields across the Netherlands. The other 9 pesticides detected can also be applied in bulb fields. A summary of findings is shown in Table 2.

Due to the low number of control samples a significance test between mean concentrations in homes and controls was not possible to be performed, nevertheless there is a clear difference in concentrations between these two groups, with concentrations in homes being higher than in controls for all the detected pesticides, except for Kresoxym-methyl.

Overall concentrations indoors tend to be lower than outdoor. This finding is not surprising considering the fact that the main driver of pesticides via the PUF is air and air flux indoor tends to be considerably lower than outdoor. This can also indicate, although difficult to verify, that for some indoor samples more deployment time was needed for equilibrium to be reached.

Finally, the pesticides found in the add-on PUFs were also seen across different mediums during the OBO study and are known to be more in gas-phase than particle-phase. Some pesticides that are more commonly seen in particle-phase, such as Fludioxonil and Thiophanate-methyl, were below limit of quantification for all PUF samples but found in various samples collected during the OBO study.

Conclusion

A total of 46 PUF-PAS samples were analyzed for 45 pesticides. 11 pesticides were detected. Two pesticides commonly found in various mediums during the OBO-study were also found in almost all samples (Chlorpropham and Pendimethalin). The remaining pesticides detected in the PUF-PAS are also authorized to be used in bulb fields in the Netherlands and their usage is reported in different locations in the OBO study.

PUF-PAS seems a viable way to detect and quantify residents' exposure to pesticides, since they are cost-friendly and non-invasive, however more research needs to be done to perfect this technique. One of the limitations of this add-on was the white substance found across different samples during extraction, which might induce errors in the final readings, since during its removal some pesticides fractions might have adhered to this material.

Finally, from the results is seems that PUF-PAS creates a limitation when studying exposure of residents to pesticides that are largely in particle-phase, since these group seems to be less captured by this sampling approach.

Table 2: Summary of pesticides in PUF-PAS collected in the frame of the OBO project.

	Location - Homes								Location - Controls							
	Outdoor (N=24)				Indoor (N=16)				Outdoor (N=3)				Indoor (N=3)			
Active Ingredients	Median	Mean	Min	Max	Median	Mean	Min	Max	Median	Mean	Min	Max	Median	Mean	Min	Max
acetamiprid	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
asulam	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
azoxystrobin	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
boscalid	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
carbendazim	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
chloridazon	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
chlorpropham	660	879	111	3197	327	434	111	1772	111	131	111	172	170	151	111	173
cyhalotrin-lambda	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
cyprodinil	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
deltamethrin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
difenoconazole	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
dimethenamid-P	<	NA	<	201	<	<	<	<	<	<	<	<	<	<	<	<
dimethomorph	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
flonicamid	<	NA	<	47	<	<	<	<	<	<	<	<	<	<	<	<
floupyram-benzamide	<	NA	<	122	<	<	<	<	<	<	<	<	<	<	<	<
fludioxonil	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
fluopicolide	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
fluopyram	<	NA	<	69	<	<	<	<	<	<	<	<	<	NA	<	55
flutolanil	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
fosthiazate	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
imidacloprid	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
kresoxim-methyl	<	NA	<	80	<	<	<	<	<	<	<	<	<	NA	<	173
linuron	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
mepanipyrim	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
metamitron	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
metamitron-desamino	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
metolachlor-S	<	NA	<	222	<	NA	<	88	<	<	<	<	<	<	<	<
oxamyl	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
pendimethalin	576	1121	74	5241	89	144	39	425	65	184	39	448	39	124	39	294
primicarb	<	NA	<	269	<	<	<	<	<	<	<	<	<	<	<	<
prochloraz	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
propamocarb	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
prothioconazole	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
prothioconazole-desthio	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
pymetrozine	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
pyraclostrobin	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
spirotetramat	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
spirotetramat-enol	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
sulcotrione	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
tebuconazole	<	NA	<	56	<	<	<	<	<	<	<	<	<	<	<	<
terbuthylazine	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
thiacloprid	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
thiophanate-methyl	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
toclofos-methyl	<	NA	<	237	<	NA	<	209	<	<	<	<	<	<	<	<
trifloxystrobin acid	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
trifloxystrobin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 3: PUF-PAS results per Location.

		Location 1																	
		H11			H12		H13			H14		H15			H16			C1	
Active Ingredient	LOQ (ng/PUF)	In	Out	Out	In	Out	Out	Out	In	In	Out	In	Out	Out	In	Out	Out	In	Out
acetamiprid	54	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
asulam	54	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
azoxystrobin	51	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
boscalid	60	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
carbendazim	51	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
chloridazon	52	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
chlorpropham	166	274	506	1531	420	536	746	1500	<	354	981	949	1440	574	511	1692	992	173	<
cyhalotrin-lambda	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
cyprodinil	58	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
deltamethrin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
difenoconazole	50	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
dimethenamid-P	66	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
dimethomorph A	20	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
dimethomorph B	36	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
flonicamid	44	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
floupyram-benzamide	57	<	84	<	<	63	92	<	<	<	118	<	<	74	<	<	104	<	<
fludioxonil	161	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
fluopicolide	51	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
fluopyram	49	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
flutolanil	51	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
fosthiazate	50	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
imidacloprid	51	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
kresoxim-methyl	56	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
linuron	51	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
mepanipyrim	56	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
metamitron	50	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
metamitron-desamino	55	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
metolachlor-S	87	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
oxamyl	50	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
pendimethalin	58	94	253	1018	208	333	504	1029	87	<	490	71	1085	245	85	1616	648	<	65
primicarb	56	<	266	<	<	<	105	<	<	<	<	<	<	<	<	<	269	<	<
prochloraz	53	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
propamocarb	60	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
prothioconazole	53	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
prothioconazole-desthio	54	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
pymetrozine	52	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
pyraclostrobin	60	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
spirotetramat	59	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
spirotetranat-enol	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
sulcotrione	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
tebuconazole	51	<	<	<	<	<	<	56	<	<	<	<	<	<	<	<	<	<	<
terbuthylazine	45	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
thiacloprid	60	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
thiophanate-methyl	56	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
toclofos-methyl	161	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
trifloxystrobin acid	50	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<	<
trifloxystrobin	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

		Location 2							
		H21		H22			H23		
Active Ingredient	LOQ (ng/PUF)	In	Out	In	Out	Out	In	Out	Out
acetamiprid	54	<	<	<	<	<	<	<	<
asulam	54	-	-	-	-	-	-	-	-
azoxystrobin	51	<	<	<	<	<	<	<	<
boscalid	60	<	<	<	<	<	<	<	<
carbendazim	51	<	<	<	<	<	<	<	<
chloridazon	52	<	<	<	<	<	<	<	<
chlorpropham	166	783	1678	466	1606	1024	1772	3197	1674
cyhalotrin-lambda	-	-	-	-	-	-	-	-	-
cyprodinil	58	<	<	<	<	<	<	<	<
deltamethrin	-	-	-	-	-	-	-	-	-
difenoconazole	50	<	<	<	<	<	<	<	<
dimethenamid-P	66	<	95	<	<	78	<	201	112
dimethomorph A	20	<	<	<	<	<	<	<	<
dimethomorph B	36	<	<	<	<	<	<	<	<
flonicamid	44	<	47	<	<	45	<	<	<
floupyram-benzamide	57	<	122	<	<	92	<	<	94
fludioxonil	161	<	<	<	<	<	<	<	<
fluopicolide	51	<	<	<	<	<	<	<	<
fluopyram	49	<	<	<	<	<	<	<	<
flutolanil	51	<	<	<	<	<	<	<	<
fosthiazate	50	<	<	<	<	<	<	<	<
imidacloprid	51	<	<	<	<	<	<	<	<
kresoxim-methyl	56	<	<	<	<	<	<	<	<
linuron	51	<	<	<	<	<	<	<	<
mepanipyrim	56	<	<	<	<	<	<	<	<
metamitron	50	<	<	<	<	<	<	<	<
metamitron-desamino	55	<	<	<	<	<	<	<	<
metolachlor-S	87	<	222	<	114	<	88	<	<
oxamyl	50	<	<	<	<	<	<	<	<
pendimethalin	58	425	1206	207	2013	685	361	4003	817
primicarb	56	<	<	<	<	<	<	<	<
prochloraz	53	<	<	<	<	<	<	<	<
propamocarb	60	-	-	-	-	-	-	-	-
prothioconazole	53	-	-	-	-	-	-	-	-
prothioconazole-desthio	54	<	<	<	<	<	<	<	<
pymetrozine	52	<	<	<	<	<	<	<	<
pyraclostrobin	60	<	<	<	<	<	<	<	<
spirotetramat	59	<	<	<	<	<	<	<	<
spirotetranat-enol	-	-	-	-	-	-	-	-	-
sulcotrione	-	-	-	-	-	-	-	-	-
tebuconazole	51	<	<	<	<	<	<	<	<
terbuthylazine	45	<	<	<	<	<	<	<	<
thiacloprid	60	<	<	<	<	<	<	<	<
thiophanate-methyl	56	-	-	-	-	-	-	-	-
toclofos-methyl	161	<	<	<	226	<	209	237	<
trifloxystrobin acid	50	<	<	<	<	<	<	<	<
trifloxystrobin	-	-	-	-	-	-	-	-	-

		Location 3												
		H31		H32			H33		H34		H35		C2&C3	
Active Ingredient	LOQ (ng/PUF)	Out	In	In	Out	Out	In	Out	in	Out	In	Out	In	Out
acetamiprid	54	<	<	<	<	<	<	<	<	<	<	<	<	<
asulam	54	-	-	-	-	-	-	-	-	-	-	-	-	-
azoxystrobin	51	<	<	<	<	<	<	<	<	<	<	<	<	<
boscalid	60	<	<	<	<	<	<	<	<	<	<	<	<	<
carbendazim	51	<	<	<	<	<	<	<	<	<	<	<	<	<
chloridazon	52	<	<	<	<	<	<	<	<	<	<	<	<	<
chlorpropham	166	187	190	<	290	229	<	167	<	<	299	<	<	<
cyhalotrin-lambda	-	-	-	-	-	-	-	-	-	-	-	-	-	-
cyprodinil	58	<	<	<	<	<	<	<	<	<	<	<	<	<
deltamethrin	-	-	-	-	-	-	-	-	-	-	-	-	-	-
difenoconazole	50	<	<	<	<	<	<	<	<	<	<	<	<	<
dimethenamid-P	66	<	<	<	<	<	<	<	<	<	<	<	<	<
dimethomorph A	20	<	<	<	<	<	<	<	<	<	<	<	<	<
dimethomorph B	36	<	<	<	<	<	<	<	<	<	<	<	<	<
flonicamid	44	<	<	<	<	<	<	<	<	<	<	<	<	<
floupyram-benzamide	57	<	<	<	<	<	<	<	<	<	<	<	<	<
fludioxonil	161	<	<	<	<	<	<	<	<	<	<	<	<	<
fluopicolide	51	<	<	<	<	<	<	<	<	<	<	<	<	<
fluopyram	49	<	<	<	<	<	<	<	<	<	<	<	<	<
flutolanil	51	<	<	<	<	<	<	<	<	<	<	<	<	<
fosthiazate	50	<	<	<	<	<	<	<	<	<	<	<	<	<
imidacloprid	51	<	<	<	<	<	<	<	<	<	<	<	<	<
kresoxim-methyl	56	<	<	<	<	<	<	<	<	<	<	<	<	<
linuron	51	<	<	<	<	<	<	<	<	<	<	<	<	<
mepanipyrim	56	<	<	<	<	<	<	<	<	<	<	<	<	<
metamitron	50	<	<	<	<	<	<	<	<	<	<	<	<	<
metamitron-desamino	55	<	<	<	<	<	<	<	<	<	<	<	<	<
metolachlor-S	87	<	<	<	<	<	<	<	<	<	<	<	<	<
oxamyl	50	<	<	<	<	<	<	<	<	<	<	<	<	<
pendimethalin	58	113	<	<	4305	5241	266	169	<	196	73	74	<	<
primicarb	56	<	<	<	<	<	<	<	<	<	<	<	<	<
prochloraz	53	<	<	<	<	<	<	<	<	<	<	<	<	<
propamocarb	60	-	-	-	-	-	-	-	-	-	-	-	-	-
prothioconazole	53	-	-	-	-	-	-	-	-	-	-	-	-	-
prothioconazole-desthio	54	<	<	<	<	<	<	<	<	<	<	<	<	<
pymetrozine	52	<	<	<	<	<	<	<	<	<	<	<	<	<
pyraclostrobin	60	<	<	<	<	<	<	<	<	<	<	<	<	<
spirotetramat	59	<	<	<	<	<	<	<	<	<	<	<	<	<
spirotetranat-enol	-	-	-	-	-	-	-	-	-	-	-	-	-	-
sulcotrione	-	-	-	-	-	-	-	-	-	-	-	-	-	-
tebuconazole	51	<	<	<	<	<	<	<	<	<	<	<	<	<
terbuthylazine	45	<	<	<	<	<	<	<	<	<	<	<	<	<
thiacloprid	60	<	<	<	<	<	<	<	<	<	<	<	<	<
thiophanate-methyl	56	-	-	-	-	-	-	-	-	-	-	-	-	-
toclofos-methyl	161	<	<	<	<	<	<	<	<	<	<	<	<	<
trifloxystrobin acid	50	<	<	<	<	<	<	<	<	<	<	<	<	<
trifloxystrobin	-	-	-	-	-	-	-	-	-	-	-	-	-	-

		Location 4						
		H41		H42	H43	H44	C4	
Active Ingredient	LOQ (ng/PUF)	Out	In	In	Out	Out	In	Out
acetamiprid	54	<	<	<	<	<	<	<
asulam	54	-	-	-	-	-	-	-
azoxystrobin	51	<	<	<	<	<	<	<
boscalid	60	<	<	<	<	<	<	<
carbendazim	51	<	<	<	<	<	<	<
chloridazon	52	<	<	<	<	<	<	<
chlorpropham	166	<	371	<	<	<	170	172
cyhalotrin-lambda	-	-	-	-	-	-	-	-
cyprodinil	58	<	<	<	<	<	<	<
deltamethrin	-	-	-	-	-	-	-	-
difenoconazole	50	<	<	<	<	<	<	<
dimethenamid-P	66	<	<	<	<	<	<	<
dimethomorph A	20	<	<	<	<	<	<	<
dimethomorph B	36	<	<	<	<	<	<	<
flonicamid	44	<	<	<	<	<	<	<
floupyram-benzamide	57	<	<	<	<	<	<	<
fludioxonil	161	<	<	<	<	<	<	<
fluopicolide	51	<	<	<	<	<	<	<
fluopyram	49	<	<	<	<	69	55	<
flutolanil	51	<	<	<	<	<	<	<
fosthiazate	50	<	<	<	<	<	<	<
imidacloprid	51	<	<	<	<	<	<	<
kresoxim-methyl	56	<	<	<	<	80	173	<
linuron	51	<	<	<	<	<	<	<
mepanipyrim	56	<	<	<	<	<	<	<
metamitron	50	<	<	<	<	<	<	<
metamitron-desamino	55	<	<	<	<	<	<	<
metolachlor-S	87	<	<	<	<	<	<	<
oxamyl	50	<	<	<	<	<	<	<
pendimethalin	58	334	184	90	94	426	294	448
primicarb	56	<	<	<	<	<	<	<
prochloraz	53	<	<	<	<	<	<	<
propamocarb	60	-	-	-	-	-	-	-
prothioconazole	53	-	-	-	-	-	-	-
prothioconazole-desthio	54	<	<	<	<	<	<	<
pymetrozine	52	<	<	<	<	<	<	<
pyraclostrobin	60	<	<	<	<	<	<	<
spirotetramat	59	<	<	<	<	<	<	<
spirotetranat-enol	-	-	-	-	-	-	-	-
sulcotrione	-	-	-	-	-	-	-	-
tebuconazole	51	<	<	<	<	<	<	<
terbuthylazine	45	<	<	<	<	<	<	<
thiacloprid	60	<	<	<	<	<	<	<
thiophanate-methyl	56	-	-	-	-	-	-	-
toclofos-methyl	161	<	<	<	<	<	<	<
trifloxystrobin acid	50	<	<	<	<	<	<	<
trifloxystrobin	-	-	-	-	-	-	-	-

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Appendix 29: Add-on - Personal sampling using hair

Introduction

In the OBO study, exposure to pesticides at a personal level is measured by biomonitoring using urine as matrix. Urine is a well-established non-invasive matrix. For most pesticides, urine provides information on short-term exposure which is useful to link biomarker levels to a specific exposure event, e.g. such as used in the OBO-protocol following a spray event. Since most pesticides are rapidly metabolized, the biomarkers determined in urine are often specific biomarkers. For many of the active substances from the OBO study, analytical standards of the biomarkers (pesticide biomarkers) are not readily available. This is one of the reasons why the number of active substances included in the assessment of internal exposure has been restricted to five.

We proposed to add hair as an additional matrix to obtain information on exposure at a personal level for a larger number of pesticides over a longer time period. Hair is an alternative and complementary matrix for biomonitoring. It reflects long-term or chronic exposure and in many cases the parent compound is incorporated which eliminates the aforementioned issues related to non-availability of analytical reference standards. Hair analysis is frequently done in forensic analysis (e.g. testing for drug of abuse) and the interest for biomonitoring in (non)occupational exposure is increasing (Appenzeller 2012, Baciu 2015, Kintz 2015). A range of pesticides have been detected in human hair (Salquèbre 2012, Schummer 2012, Hardy 2015). Pesticides in hair have also been investigated to identify associations between indoor air contamination and human exposure (Raeppel 2016). Other advantages of hair are ease of collection, storage (room temperature), transport (mail) and good storage stability. At this stage, however, it should also be mentioned that there are still a number of knowledge gaps. Discrimination between pesticides on the outer hair surface and pesticides incorporated inside the hair is a point of discussion. Furthermore, there is little data on occurrence of pesticides in hair of the general ('control') population and on the variability of levels. At this moment, there is potential to use hair data to compare differences in exposure between two populations (one of the main goals of OBO), but it is not yet possible to translate concentrations in hair to actual exposure (oral/inhalation/dermal intake).

During the design of the OBO study, the inclusion of hair analysis was already proposed. Although it was recognized that hair is a promising additional biological matrix with added value for the study, in the end it was not included in the OBO research protocol because of the knowledge gaps mentioned above and budgetary reasons. This add-on explored the possibilities, using the OBO infrastructure. Hair analysis is not part of the main study, but is has been agreed that 'add-on' results will be reported for information.

Hair sampling

A procedure taking the 'Guidelines from the Society of Hair Testing for drug testing in hair' (Cooper 2012) into account was described in an instruction form for research assistants and participants in the OBO study. Samples were taken using these instructions. The samples were packed in aluminum foil and sent to RIKILT, either directly or through IRAS or Radboudumc. Samples were stored at room temperature in dry/dark conditions until analysis.

The subjects were asked to answer 4 questions about his/her hair (natural color, cosmetic treatments). Several subjects indicated to (regularly) use a form of heat treatment (blow dryer, straightener). One subject indicated to dye the hair. Bleaching was not indicated by any of the subjects.

A) Hair samples from participants in the volunteer studies:

The aim here was to verify whether the two controlled pesticide exposures (oral and dermal) done in the frame of the volunteer studies would result in detectable levels of the administered pesticide in hair. Hair samples were taken under responsibility of Radboudumc. This was done approx. 6 weeks after the last exposure session, close to the scalp. This time lag is required to ensure that pesticides are in the external hair. Participants in the volunteer study were asked to provide a hair sample themselves, using instructions provided through Radboudumc. In short: if possible, hair samples were taken from the posterior vertex region of the head (as this region of the scalp is associated with least variation in growth rates) and as close to the scalp as possible. The amount of hair asked for was a ''lock of hair'' of 0.5 cm diameter, or a pencil thickness of hair (multiple smaller hair strand samples were considered acceptable here in case of baldness or thinning hair). The hair sample obtained was a (combined) lock kept as such with clear indication of scalp side and hair-end side to allow segmentation and to have the option to link results of segments to time periods of exposure.

B) Hair samples from participants in the OBO field study:

The aim here was to verify whether the pattern/levels of pesticides in hair from residents living near bulb fields differ between from residents and the control group (i.e. not living close to bulb fields). Since hair residues cover periods of months, the time of sampling was not very critical. Hair samples were taken under responsibility of IRAS. Initially, it was foreseen that hair samples were taken from residents by a research assistant during one of the visits within the regular OBO sample scheme. However, as this add-on was embedded into the OBO study at a relative late stage, the regular sampling rounds were already finished in many cases. Therefore, instead, residents were asked to take the sample themselves using written instructions as outlined above under A).

Hair analyses

For hair analysis a targeted LC-MS/MS-based multi-method was used. Since hair is a variable and complex matrix, the use of isotopic labelled internal standards for each of the pesticides was considered a pre-requisite for quantitative analysis. Although isotopic labelled analogues are commercially available for many pesticides, this did restrict the scope of analysis. In total, 25 pesticides (in some cases biomarkers/biomarkers) were included in the scope (see Appendix A). The pesticides included the ones selected for biomonitoring in urine, and the ones frequently found in the environmental analysis. Thiabendazole, imazalil and pyrimethanil were not directly related to the OBO study, but included because they have been frequently found in previous work.

Analytical reference standards were purchased from LGC or Sigma. Some of the isotopic labelled biomarkers were custom synthesized (for details see Appendix 3.1 in main OBO report). Stock solutions were prepared in methanol or acetonitrile at concentrations of 2 mg/ml. A pesticide mix solution of 1 µg/ml was prepared in methanol. Intermediate dilutions for spiking of the samples, extracts, and preparation of working standards were made in methanol. A mix stock solution of isotopic labelled pesticides was prepared in methanol for addition as internal standards to the calibrants and each of the hair samples. A series of calibration standards for assessment of linearity of response and quantification was prepared by dilutions of the intermediate solutions in water:acetonitrile/1% acetic acid (50:50), concentrations corresponding to 0, 0.5, 1, 2, 5, 10, 15 and 20 pg/mg hair. The internal standards were added at the level equivalent to 5 pg/mg hair.

Hair samples were analyzed using a method previously developed and validated at RIKILT. The LOQs were 0.5-2 pg/mg hair for most of the pesticides included. The exceptions were chlorpropham (15 pg/mg) and lambda-cyhalothrin (5 pg/mg)
In brief, hair was first decontaminated to remove pesticides from the outer surface of the intact hair. This was done by washing the hair in a vial with 5 ml milliQ water (shaking 5 min), then drying the hair (on filter paper, ambient temperature), then washing with 5 ml of dichloromethane and drying again. Next, hair was pulverized using a ball mill (4 min, 25 Hz). An amount of 100 mg (in five cases less was available, 32-79 mg) was weighed into an extraction tube, isotopically labelled internal standards were added and the hair powder was extracted with 2 ml acetonitrile (overnight, ultrasonication). After centrifugation, an aliquot of 1.5 ml was evaporated to dryness and reconstituted in 300 µl acetonitrile 1% acetic acid/water (1/1).

LC-MS/MS analysis was performed on a Waters Acquity UPLC system coupled to a Waters Xevo TQS tandem mass spectrometer by injection of 10 µl onto a 100 x 2.1 mm ID 1.7 µm HSS T3 column (Waters), maintained at 45°C. Gradient elution was performed at a flow rate of 0.4 ml/min, using a water/methanol gradient, containing 5 mM ammonium formate/0.1% formic acid. MS/MS measurement was done using ESI in positive mode, acquiring two transitions for each pesticide/ biomarker (see Appendix

A). The response of each pesticide (biomarker) was normalized to its isotopic labelled analogue. Quantification was done based on bracketing calibration using standards in solvent.

With each batch of samples, a reagent blank and a positive control were included. The positive control was prepared by spiking 100 mg of pulverized hair material sample at 10 pg/mg.

Results

Hair samples received

The total number of hair samples received was 21, which was rather limited. This was due to the late stage of introducing hair sampling into the OBO study. In addition, hair sampling was optional for the participants of the OBO study.

From the participants in the volunteer studies, 6 samples were received. In one case, the amount provided was insufficient for analysis.

From the residents, 15 hair samples were received, of which one was a too small amount to allow analysis. The samples were from residents living close (<250 m) to bulb fields (12), and included one sample from a grower, and one sample from the control group.

In 6 cases, a hair strand was obtained that allowed segmentation into two or three segments, which were separately analyzed. With this, the total number of hair (segment) samples analyzed was 28.

Analysis results

The individual analysis results are provided in Appendix B.

In total, 13 out of the 25 targeted pesticides were detected in the hair samples. Biomarkers/biomarkers were not detected, also not when the parent pesticide was found in hair. From drug analysis it is known that the concentrations of biomarkers in hair are often much lower compared to the parent compounds.

From the volunteer study, hair samples were received from subjects to which either chlorpropham, asulam, or tebuconazole was administered. None of these pesticides were detected in these samples. For chlorpropham the detection limit was rather high, which compromised detectability. For tebuconazole the measurement failed and therefore no indications on possible transfer of the dosed pesticides to hair could be derived.

In Figure 1, the cumulative findings for the individual subjects are graphically shown. In Table 1 a summary is provided of the pesticides detected in the hair samples. In

case multiple segments were analyzed of a hair strand from the same subject, then the average concentration was used for compilation of Figure 1 and Table 1. In order to enlarge the number of control samples, the results of the hair samples from the volunteer study were combined with the one field control. This was considered justified because none of the subjects of the volunteer study lived close to bulb fields.

The most frequently detected pesticides, boscalid, thiabendazole, imazalil, azoxystrobin, and imidacloprid are all pesticides that have been regularly found in randomly taken hair samples previously analyzed at RIKILT. These are all common in fruit and vegetables, which might explain the observation. Imidacloprid has a lower abundance in food, but exposure may also originate from use as biocide or veterinary drug in pets. In the analysis of environmental samples, it was noted the imidacloprid is frequently detected in both residents and control house dust.

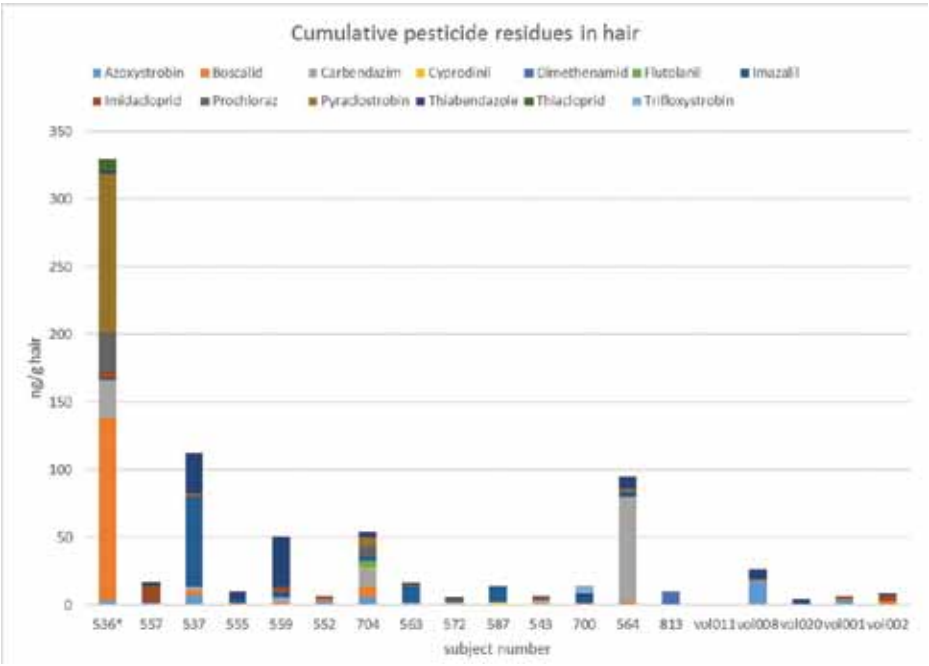

Figure 1: Cumulative concentration of pesticide residues in hair samples from 19 subjects.
In case of multiple segments from the same subject, the average was taken. Subject 536* = grower, 813= field control, volxxx = hair from participants in the volunteer studies. Other subjects are residents <250 m from bulb fields.

Table 1: Summary of pesticides detected in hair samples collected in the frame of the OBO project.

		Grower	Residents (N=12)				Controls (N=6*)			
	total	(N=1)		median	min	max		median	min	max
Pesticide	#detects	pg/mg	% detects	pg/mg			% detects	pg/mg		
Boscalid	15	135	83%	1.3	0.5	7.0	67%	1.0	0.7	2.3
Thiabendazole	14	2.2	83%	3.4	0.8	37.4	50%	1.6	1.1	7.0
Imazalil	13	1.8	83%	3.9	0.7	66.2	33%	1.2	1.0	1.5
Azoxystrobin	10	2.9	42%	3.5	0.7	7.5	67%	2.4	1.0	17.3
Imidacloprid	10	4.8	58%	1.9	0.5	12.1	33%	3.0	2.1	4.0
Carbendazim	8	27.9	58%	3.7	1.2	77.3	0%			
Pyraclostrobin	6	117	42%	0.9	0.9	6.1	0%			
Prochloraz	3	29.2	17%	4.2	0.6	7.8	0%			
Thiacloprid	3	8.4	17%	0.9	0.8	1.1	0%			
Cyprodinil	2		17%	0.8	0.8	0.8	0%			
Dimethenamid	1		0%				17%	9.2	9.2	9.2
Flutolanil	1		8%	5.4	5.4	5.4	0%			
Trifloxystrobin	1		8%	5.9	5.9	5.9	0%			

*1 field control + 5 subjects from volunteer studies.

Carbendazim, pyraclostrobin, prochloraz and thiacloprid were detected in hair from the residents (including the grower) and not in the controls, which might indicate a difference in exposure between residents and controls. However, it is clear that the number of samples analyzed is too small to draw any firm conclusions. In previous analysis of hair samples performed at RIKILT, carbendazim, pyraclostrobin and thiacloprid had also been incidentally found. Prochloraz had not been included in previous analyses and no comparison to existing data from the general population could be made.

In five cases, besides data for the hair samples also data from dust analysis from the house of the resident was available. No obvious links between de results could be observed, again compromised by the small number of data sets. In many cases the pesticides were found in house dust, but not always in the hair from the corresponding subject.
Analysis of multiple hair segments from the same strand of a subject resulted in detection of the same pesticides in the different segments, in many cases also in a similar concentration range which might indicate to exposure over a longer period of time (hair grows approx. 1 cm/month).

In the hair sample from the grower, the concentration of a number of pesticides clearly stood out from that in the residents and controls (see also Figure 1). For carbendazim, pyraclostrobin and prochloraz this clearly links to typical pesticides used in bulbs (field and/or disinfection). Also boscalid was much higher than found in the residents and controls analyzed here, as well as residue levels found previously by RIKILT in the general population.

Although only one hair sample from a grower was included, the higher levels found for some of the pesticides point towards higher exposure. This is consistent with previous analysis of hair from farmers/growers (RIKILT, unpublished results).

Conclusion

A total of 28 hair samples/segments from 19 subjects were analyzed for 25 pesticides. 13 pesticides were detected, of which boscalid, thiabendazole, imazalil, azoxystrobin and imidacloprid are also commonly found in the general population. The number of samples was rather small which makes it difficult to draw any sound conclusions. Nevertheless, the residues found in the hair of a grower are considered to arise from occupational exposure. Some of the residues found in the residents' hair might point to enhanced exposure which is in line with the generally higher levels of these pesticides in the residents' environment. However, a larger number of samples of both residents and controls would be needed to confirm this.

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