Exposure of workers to pesticide residues during re-entry activities: A Review

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ABSTRACT

Workers may be exposed to pesticide residues when they enter an area that has been previously treated in order to realize different tasks (e.g. for pruning, cutting, picking, harvesting, pest scouting) or to handle a contaminated crop commodity (e.g. sorting, bundling, packing). A review of the scientific literature on workers exposed to pesticide residues during re-entry tasks provides a comprehensive view of possible exposure routes and a better understanding of the risk assessment context, threshold values and calculation methodology. Methods assessing the risk to workers health are also reported and discussed. The impact of re-entry activities on health and factors affecting workers exposure are examined. Finally, solutions and mitigation measures aiming to reduce their exposure to pesticide residues are recommended.

Key Words: pesticide residues, workers, re-entry, risk assessment

INTRODUCTION

Pesticides (fungicides, herbicides, insecticides, etc.) have undoubtedly helped to control pests and diseases (Aktar *et al.* 2009) in order to increase agricultural production qualitatively and quantitatively over decades (Alexandratos and Bruinsma 2012). Pesticide exposure of the human body, which occurs

through ingestion, inhalation and skin contact, can result in either acute or chronic effects on health. Despite all provided advantages and extensive use, some pesticides can be associated with increased risks and human illness (Blair *et al.* 2014; Sarwar 2015), including neurological disorders (Van Maele-Fabry *et al.* 2013; Hernández *et al.* 2016), reproduction problems (Flocks *et al.* 2012; Hossain *et al.* 2010), development of many types of cancers (Koutros *et al.* 2013; Alavanja *et al.* 2012) and metabolic diseases (Kim *et al.* 2014). Therefore effort are made to prevent and reduce exposure and the most toxic pesticides are no more approved in Europe, USA and many other countries thanks to an extended risk assessment and more restrictive regulation.

Main source of exposure of the general population to pesticides occurs primarily through eating food and drinking water contaminated with pesticide residues (Damalas and Eleftherohorinos 2011). Several groups can be identified based on their directly or indirectly exposure to pesticides, like occupational pesticide users (farmers, sprayers and field workers), but also families of occupational pesticide users, bystanders and residents. Workers are defined as persons who, as part of their employment, enter an area that has been treated previously with a plant protection product (PPP) ((Dong and Beauvais 2013), or who handle a crop that has been treated with a PPP (Krol *et al.* 2005; EFSA 2014), or who come into contact with pesticide residues remaining on work surfaces (Kasiotis *et al.* 2017). Physical contact with branches, leaves, fruit or vegetables in previously treated crops is responsible for the transfer of pesticides to the worker's skin during re-entry tasks such as irrigating, scouting, thinning, pruning, weeding, roguing, transplanting, staking, tying, swathing and harvesting (Baldi *et al.* 2014). The vast majority of available studies concern operators who are exposed during loading and mixing operations or during application of the mixture, while reviews about workers are scarcely reported despite their high level of exposure to pesticide residues. However workers may be more at risk: they are working in sprayed areas during several hours compared to the operators who may finish their task within an hour. Operators are trained to prevent their exposure and wear personal protective equipment, while workers may not be informed about the risk of contamination, usually do not wear protective clothes and may not

respect re-entrance intervals. Baldi *et al.* (2014) reported that during re-entry tasks their bodies can enter in contact with levels of pesticide residues that exceed those measured during application. Therefore this review focus on identification of the main issues related to pesticide residues during re-entry activities.

The objectives of such a review were to present and discuss: (1) the risk assessment steps; (2) the possible exposure routes for workers; (3) the risk assessment methods for workers; (4) the health effects on workers following re-entry activities; (5) the exposure of workers to pesticides and factors affecting exposure; and (6) the preventive and mitigation measures able to reduce workers exposure to pesticide residues.

RISK ASSESSMENT STEPS

Risk assessment can be defined as a systematic process for generating a probability distribution or similar quantification that describes uncertainty about the magnitudes, timing or nature of possible health consequences associated with possible exposure to pesticide residues (Covello *et al.* 2013). The definition includes quantitative risk assessment, which emphasises reliance on numerical expressions of risk, and also qualitative expressions of risk, as well as an indication of the attendant uncertainties (WHO/FAO 1995). The risk assessment process includes four steps: hazard identification, hazard characterisation (dose-response assessment), exposure assessment and risk characterisation (figure 1). In the first step (hazard identification) pesticide residues of active substances which can generate detrimental consequences on the health of farm workers after exposure during re-entry activities, according to their biological activity, their mode of action and their toxicity are identified. In the second step (hazard characterisation) the potential adverse health effects and the toxicological profile of the relevant active substances are described with mechanisms by which agents exert their toxic effects, the associated dose, route, duration and timing of exposure (Ferrario *et al.* 2014; OCED 2003). This should, where possible, include a dose–response assessment and its attendant uncertainties (Ferrario *et al.* 2014). For workers, the Health Based Guidance value (HBGV) of each active substance (metabolite included) is the Acceptable Operator Exposure Level (AOEL, in mg/kg bw/day)) defined in the Directive 97/57/EC as "the maximum

amount of active substance to which the operator may be exposed without any adverse health effects'' (European Commission, 2006). In the Directive, the AOEL specifically refers to operators but it can also be used for workers exposed during re-entry and for residents or bystanders non-intentionally exposed (European Commission, 2006). In the third step (exposure assessment), the intensity, the frequency and the duration of workers exposure to pesticide residues are measured or evaluated in relation to the observed re-entry activities. The exposure assessment will consider realistic and high exposure (or even worst case) scenarios for the proposed good agricultural practices and then non-dietary systemic exposure values can be compared with the appropriate toxicological reference values (AOEL) (EFSA 2014). In the last step (risk characterisation), the results of the exposure assessment (step 3) are compared to the HBGV values to determine the risk level for health of workers (expressed in % of the AOEL).

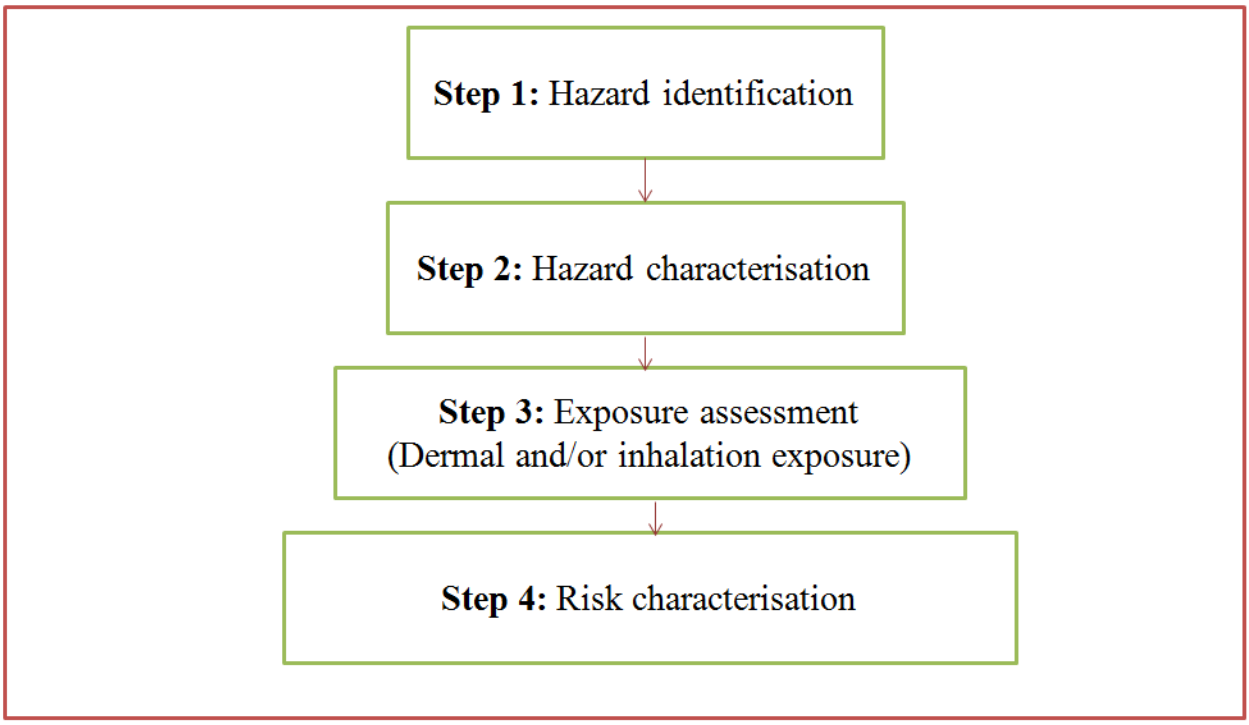

Figure 1. The 4 steps of the risk assessment process

POSSIBLE EXPOSURE ROUTES FOR WORKERS

The routes of exposure during activities performed by a worker in the field after the application of PPP are the same as those of the operator. Dermal exposure is the most important route of exposure (Brouwer *et al.* 1992 a, b and c; Van Hemmen and Brouwer 1997; Jurewicz *et al.* 2009) but other routes (inhalation and ingestion) can also contribute to the total worker exposure (Aprea 2001; Cherrie *et al.* 2006). Therefore, workers may be exposed to pesticide residues by various routes during working in treated fields:

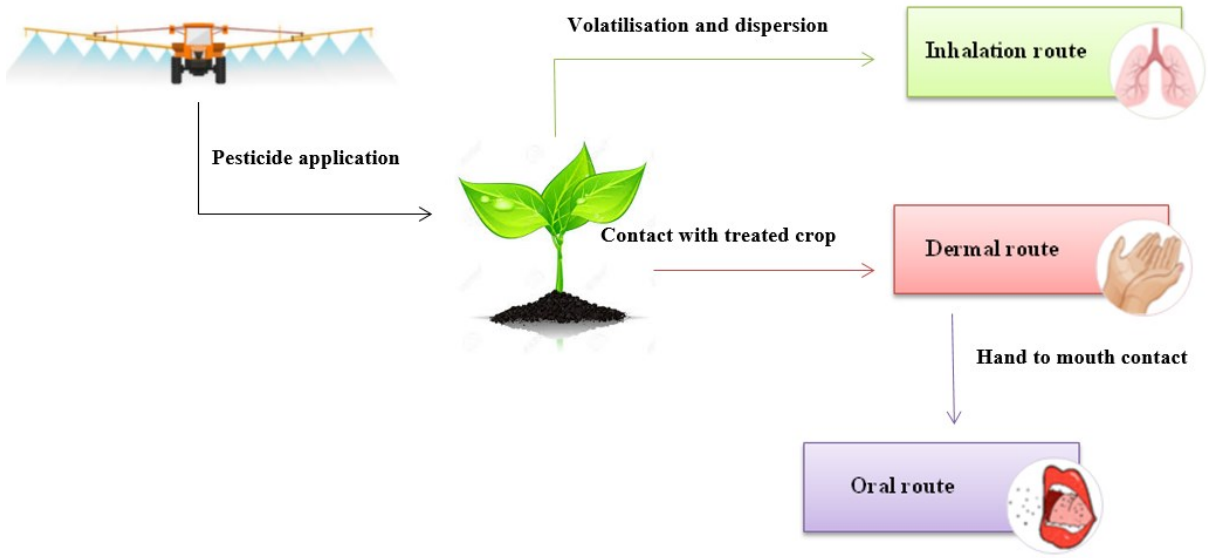

Figure 2. Possible exposure routes for workers

Dermal route

Dermal exposure occurs by direct and physical contact with the contaminated crop. Pesticides residues on branches, leaves, fruit or vegetables previously treated can be transferred to the skin of workers. Many actives substances are persistent, fat-soluble and therefore could be dislodged by contact with the skin (Toumi *et al.* 2016a and b; 2017a and b; Toumi *et al.* 2018). The main dermal routes result from re-entry tasks such as harvesting, bending, leaf pulling and tying, etc. During some other activities, a part of the dermal exposure can result from a contact with a contaminated soil. The intensity of the contact

with the treated foliage, the amount of residues on the foliage, the duration of the re-entry activity and the port of personal protective equipment are considered to be the main factors influencing the dermal exposure (Sankaran *et al.* 2015; Kasiotis *et al.* 2017).

Inhalation route

Inhalation exposure may result from a concentration of pesticide in the air (vaporization indoor or outdoor) or from airborne particles contaminated with pesticides (Brouwer *et al.* 1992b). Exposure occurs during re-entry activities by inhalation of contaminated air (e.g. dust) or vapours (e.g. volatile or semi-volatile compounds). After application, pesticide droplets are usually dispersed in the air (Stearns *et al.* 1952). When the spray has dried, the dust has settled and the vapours are dissipated, most of the particles can be found on the foliage and soil (Krieger *et al.* 2007). The inhalation exposure mainly depends on the concentration of the substance in the air, the breathing rate and the duration of exposure. Greenhouse temperature, ventilation rate, the vapour pressure of the substance and the ratio between adsorption and volatilisation processes were identified as important factors influencing volatilisation in greenhouses (Doan Ngoc *et al.* 2015). Nevertheless, during re-entry activities inhalation exposure is very low compared to the dermal exposure (Popendorf *et al.* 1979; Spear *et al.* 1977; Aprea *et al.* 2002), but a good correlation exist between levels of airbone pesticides and levels of dislogeables foliar dust (Popendorf *et al.* 1975, 1980). The inhalation exposure to dusted pesticides after re-entry is about of the same order of magnitude as during the application itself when adjusted for exposure time (Brouwer et al. 1992a). When the duration of re-entry tasks increases than the exposure of workers through inhalation may probably be still much higher and, in some situations, may also result in health risks.

Oral route

Oral exposure is the third possible route but is generally considered the least important in a worker exposure scenario. Skin contamination may sometimes lead to oral non-dietary exposure (Aprea *et al*. 2000). This can happen through hand to mouth transfer after facial contact or when pesticide residues on hands contaminate food or tobacco products (Ulenbelt *et al.* 1990; Fenske *et al.* 1993). Oral exposure may

also occur secondarily when an air loaded with particles containing active substances enter in the mouth cavity and those are then subsequently ingested. However, the potential exposure by this route is generally assumed to be negligible for workers in comparison with the ones via skin and inhalation (EFSA 2014; Doan Ngoc *et al.* 2014).

RISK ASSESSMENT METHODS FOR WORKERS

Various approaches have been suggested in the scientific literature to assess the risk for the health of workers after exposure to pesticide residues during re-entry activities. The main approaches are summarised in this section.

Direct methods used for exposure assessment

In the direct method the pesticide residues are trapped when they enter in contact with workers (e.g. contact with dried residue of the diluted product on foliage) (Li *et al.* 2011). Dermal and respiratory exposures during re-entry tasks are estimated with the same approach than exposure measurements during mixing and loading or application. Direct methods are considered easier to perform than indirect methods, but the total estimated potential exposure is more difficult to link to the absorbed dose (total exposure) because measurement is limited to the amount of pesticides retained on external clothing, patches or gloves (Li *et al.* 2011). Many practical measurement methods have been developed and are used to estimate the pesticide exposure of workers when re-entering an area after pesticide application. Table 1 presents a list of methods that cover a range of approaches which were reviewed by various authors over time to increase their performance.

Table 1. Direct methods used to estimate the exposure of workers during re-entry activities, sampling method, measured compartment and the references

Dermal exposure of workers			
Method	**Measured compartment**	**Sampling method**	**References**
	Skin	**Gloves** Glove exposure assessment methods measure dermal exposure to hands by analyzing the residues on gloves (cotton, rubber latex, etc.) worn during manual activities in treated crops. At the end of the trial, pesticide residues on gloves are extracted and the amount of pesticide is measured.	Brouwer *et al.* 1992 a,b, c Aprea *et al.* 1999 Fenske *et al.* 1999 Aprea *et al.* 2002 Jurewicz *et al.* 2009 Ramos *et al.* 2010 Li *et al.* 2011 Sankaran *et al.* 2015 Kasiotis *et al.* 2017 Toumi *et al.* 2018

Dosimetry : **Surrogate skin (passive)**	Skin	**Patches/pads** Method of measurement using patches (mainly tissues or absorbent substances like cotton or cellulose) distributed over different regions of the worker's body (shoulders, neck, chest, forearm, lower arm, upper and lower thigh) or on work clothes. The patches are attached to clothing before workers enter in the treated area. At the end of the trial, pesticide residues on patches are extracted and the amount of pesticide/cm² is measured. The deposits are then converted to a distribution on the whole body using a table. The method allows a semi-quantitative estimate of the external skin contamination of the workers.	Ware *et al.* 1973 Spencer *et al.* 1991 Aprea *et al.* 1999 Aprea *et al.* 2001 Aprea *et al.* 2002 Aprea *et al.* 2005 Aprea *et al.* 2009 Jurewicz *et al.* 2009 Bradman *et al.* 2009 Baldi *et al.* 2014
	Skin	**Whole body (coverall)** Cotton or polyester whole body dosimeters are long-sleeved shirts and long-legged pants worn by workers (sometimes internal and external coveralls) to collect by contact the pesticide residues during the tasks. At the end of the trial, the coverall is cut in various pieces on which pesticide residues are extracted, analysed and quantified for each part of the body.	McCurdy *et al.* 1994 Ramos *et al.* 2010 Kasiotis *et al.* 2017

Removal techniques	Skin	**Hand washes and wipes** Pesticide residues deposited on skin can be removed by washing or wiping. Water-surfactant mixture or water-alcohol wash solution are generally used only to assess hand exposure, while wiping techniques can in theory be applied to larger and more diverse skin surfaces. Hand washes and skin wipes have been used for dermal exposure sampling since they collect residues that are potentially available for skin absorption.	Ware *et al.* 1974 Ware *et al.* 1975 Spencer *et al.* 1991 McCURDY *et al.* 1994 Aprea *et al.* 1994 Aprea *et al.* 1999 Fenske *et al.* 1999 Aprea *et al.* 2001 Aprea *et al.* 2002 Curwin *et al.* 2003 Aprea *et al.* 2005 Aprea *et al.* 2009 Bradman *et al.* 2009 Baldi *et al.* 2014 Sankaran *et al.* 2015
Tracer	Skin	**Video imaging technique (Video Imaging Technique to Assess Exposure (VITAE))** A fluorescent imaging system provides an illuminated image of an object that has been subjected to a fluorescent dye, as well as a fluorescence image of the object. This technique can be used to measure transfer of pesticide residues	Archibald *et al.* 1994a Archibald *et al.* 1994b

techniques		from surfaces to hands during re-entry activities.	
Inhalation exposure of workers			
Personal air sampling	Air (inhalated)	**Personal air sampler** Personal air sampling is a technique for personal monitoring. The sampling equipment is carried around by the worker during re-entry activities and pesticide in the air is filtered and fixed on an absorbent. Air concentrations of pesticides, measured after desorption with a solvent, are used to calculate the actual respiratory dose and inhalation exposure on the basis of lung ventilation.	Ware *et al.* 1973 Ware *et al.* 1974 Ware *et al.* 1975 Spencer *et al.* 1991 Brouwer *et al.* 1992a and b Brouwer *et al.* 1993 Aprea *et al.* 1999 Aprea *et al.* 2001 Aprea *et al.* 2002 Aprea *et al.* 2005 Aprea *et al.* 2009

Indirect methods used for exposure assessment

Indirect methods provide indirect indication of potential for skin exposure, included environmental monitoring (plant surface-sampling techniques and determination of the Dislodgeable Foliar Residue) and biological monitoring (measurement of a pesticide, its metabolite(s) or reaction product(s) in various biological matrices) (van Hemmen *et al.* 2006; Li *et al.* 2011).

Environmental monitoring : the Dislodgeable Foliar Residue (DFR)

Currently the most widely used technique for calculating worker exposure during re-entry activities is by quantifying the dislodgeable foliar residues (DFR), which are indirect estimates of total surface foliar residues "available" after spraying for transfer from leaf and other vegetative surfaces to workers bodies (Chowdhury *et al.* 2001; Korpalski *et al.* 2005; Dong and Beauvais 2013; EFSA 2014; Sankaran *et al.* 2015). The dislodgeable foliar residue (DFR) is defined as the amount of pesticide residue that can be removed from both sides (the top and the bottom) of the treated leaves using an extraction procedure with an aqueous surfactant (Iwata *et al.* 1977). The DFR value is reported in amount of residue per unit of leaf area (µg/cm²). Based on the DFR measurement it is possible to approximate the potential dermal exposures to pesticide residues for workers re-entering treated crops. Re-entry exposures were estimated using the DFR values for many active substances applied to many different crops over the time (Table 2). In absence of specific data, a default value of 3 $\mu g/cm^2$/kg active substance/ha is used (EFSA 2014), based on the 90th percentile of DFR data extracted from literature (Van Hemmen *et al.* 2002).

Table 2. DFR (µg/cm^2) of different actives substances reported by many studies over the time, with the crops, the region, the re-entry activities and time since application and the exposure period (presented in chronological order from 1973 to 2017)

Active Substances	Crop	Country (Region)	DFR (µg/cm^2)	Re-entry Activity	Re-Entry Time (Since Application)	Exposure duration	References
Azinphos-methyl	Peach	USA (Washington)	2.62	Thinning	-	-	Foster 1973
	Apple						
	Peach	USA (California)	2.10	Thinning	-	-	Kraus *et al.* 1977
			2.63		-	-	Richards *et al.* 1978
Carbofuran	Citrus		0.16	-	8.1	-	Iwata *et al.* 1983
3-Hydroxy-carbofuran			0.03		12		
Chlorothalonil	Tomato	-	1.13	Harvesting	-	-	Spencer *et al.* 1991
Azinphos-methyl	Peach	USA (California)	0.82-1.72	Harvesting, Sorting	-	-	Schneider *et al.* 1991
Abamectin	Rose	The Netherlands	0.0081	Cutting, Sorting And Bundling	27h	73 min	Brouwer *et al.* 1992c
Dodemorph	Rose		0.26				
Bupirimate	Rose		0.64				

Chlorothalonil	Carnations	The Netherlands	4.22		35h	74 min	Brouwer *et al.* 1992b
Thiophanate-methyl			4.47				
Thiram			1.10				
Zineb			1.21				
Propoxur			0.3	Cutting	-	-	Brouwer *et al.* 1993
			0.2	Sorting/Bundling	-	-	
Azinphos-Methyl	Peach	USA (California)	0.64	Thinning	30 Day	21 days	McCurdy *et al.* 1994
Malathion	Strawberry		0.074	Harvesting	-	-	Hernandez *et al.* 1997
Azinphos-Methyl	Apple	USA (Washington)	0.5	Thinning	-	-	Simcox *et al.* 1999
Captan	Strawberry	USA (California)	0.037	Harvesting	-	-	Krieger and Dinoff, 2000
Chlorothalonil	Ornamental Plants	Italy	2.62	-	41h	-	Aprea *et al.* 2002
			2.15		65h		
			1.66		89h		
			1.44		137h		
Malathion	Strawberry	USA (California)	0.39	-	12h	-	Hernandez *et al.* 2002
Tetradifon		Italy (Bracciano)	0.109	-	1 day	-	Cafferli *et al.* 2005
			0.018		15 day		
Chlorpyrifos-ethyl	Tomato		0.092		1 day		

			0.001		16 day		
Azoxystrobin			0.107		1 day		
			0.117		16 day		
Achrinathrin			0.115		3 day		
			0.008		16 day		
Fenarimol	Cucumber		0.082		1 day		
			0.002		16 day		
Metalaxyl			0.116		1 day		
			0.001		16 day		
Azoxystrobin			0.126		1 day		
			0.002		20 day		
Malathion	Strawberry	USA (California)	0.22	-	1 Day		Zhang 2005
			0.014	-	10 Day		
Profenofos	Jasmine	Inde (Tamil Nadu)	6.04	Picking	0 Day	-	Suganthi *et al.* 2008
			3.87		1day		
			1.53		3 Day		
Malathion	Strawberry	-	0.2	Harvesting	-	-	Salvator *et al.* 2008
			1	Harvesting		72 hours	Bradman *et al.* 2009
Imidacloprid	Ornamental Plants	Italy	0.00102- 0.80937	Stapling	-	-	Aprea *et al.* 2009

			0.09987-1.13363				
Malathion	Strawberry	USA (California)	0.132	Harvesting	3 Day		Li *et al.* 2011
Methidathion	Cucumber	-	0.0121-0.2225	Harvesting	7 Days	44 hours	Choi et al. 2013
Fenpropathrin	Strawberry	USA (California)	0.023	Harvesting	4 Days	-	Sankaran *et al.* 2015
			0.003		14 Days		
Malathion			0.248		4 Days		
			0.003		14 Days		
Tebufenozide	Tomato	Greece	0.11	Pruning	3.5h	60 min	Kasiotis *et al.* 2017
	Pepper		0.085	Tying	14.7h		
Bupirimate	Tomato		0.0115	Pruning	3h		
	Pepper		0.1358		16.5h		

Biological monitoring

Biomonitoring involves the measurement of a pesticide and its metabolite(s) or reaction product(s) in various biological matrices (urine, hair, nails, blood or blood components and tissues). This approach is often preferred because it allows an integration of all possible sources and routes of exposure and provides a complete picture of the internal dose with a better assessment of the possible associated risks (He 1993, 1999; Anwar 1997; Barr *et al.* 1999, 2006; Albertini *et al.* 2006; Ferland *et al.* 2015). Table 3 summarises a list of active substances biomonitored for the workers during re-entry activities over time.

Table 3: Active substances biomonitored for the workers during re-entry activities (presented in chronological order from 1973 to 2015), their CLP classification (according the EU Pesticides database), their chemical family, their urinary metabolites and the crop, the limit of detection and the mean concentrations ± standard deviation (range) when available

Active substance	CLP classification	Chemical family	Crop	Urinary metabolites	LOD	Mean concentration ± standard deviation (range) when available	References
Azinphos-methyl	H300, H311, H317, H330	Organophosphorus	Peach	DMTP	-	830 µg/L	Foster, 1973
			Apple				
Methyl parathion	H300, H311, H330, H373	Organophosphorus	Cotton	PNP	-	no detectable residues	Ware *et al.* 1973
Ethyl parathion	H300, H311, H330, H372						
Methyl parathion	H300, H311, H330, H373	Organophosphorus	Cotton	PNP	-	0.50±0.49 (0.15-1.20) mg/48h	Ware *et al.* 1974
Ethyl parathion	H300, H311, H330, H372				-	0.89±0.14 (0.74-1.01) mg/48h	
Methyl parathion	H300, H311, H330, H373	Organophosphorus	Cotton	PNP	-	1.76±0.47 (1.13-2.31) mg/48h	Ware *et al.* 1975

Ethyl parathion	H300, H311, H330, H372					0.14±0.07 (0.09-0.25) mg/48h 0.12±0.03 (0.09-0.16) mg/48h	
Azinphos-methyl	H300, H311, H317, H330	Organophosphorus	Peach	DMTP	-	2850±2490 µg/L 2430±2730 µg/L 2280±2430 µg/L 2080±2080 µg/L 1020±1390 µg/L	Kraus *et al.* 1977
Azinphos-methyl	H300, H311, H317, H330	Organophosphorus	Peach	DMTP	-	14100 µg/L	Richards *et al.* 1978
NA	-	Organophosphorus	Citrus	DMTP DMDTP DMP DEP DETP DEDTP	20 µg/L (occasionaly 30 or 40 µg/L)	500 µg/L 600 µg/L 1,650 µg/L 650 µg/L 75 µg/L 60 µg/L	Duncan & Griffith 1985
				DMTP DMDTP DMP DEP DETP DEDTP	20 µg/L (occasionaly 30 or 40 µg/L)	150±83 µg/L 250±106 µg/L 390±198 µg/L 90±7µg/L 70±6 µg/L 60±6 µg/L	Griffith & Duncan 1985
Propoxur	H301	Carbamates	Carnation	IPP	6 µg/L	158.3±4.4(10.3-1231.1) µg/24h*	Brouwer *et al.* 1993
Chlorpyrifos methyl Azinphos methyl	H317 H300, H311, H317, H330	Organophosphorus	Peach	DMP DMDTP DMTP	-	3990±2035.1(1658-8833) nmol/g creatinine	Aprea *et al.* 1994
Pirimicarb	H301, H317, H331, H351	Carbamates	Chrysanthemum	DDHP MDHP	0.05 µg/L[¥]	no detectable residues	Archibald *et al.* 1994b

Azinphos-methyl	H300, H311, H317, H330	Organophosphorus	Peach	DMP DMTP DMDTP	-	3.84 µmoles/day**	McCurdy *et al.* 1994
Chlorpyrifos methyl	H317	Organophosphorus	Vine	TCPy	5 nmol/L	92.4 ± 162.5 (4.5-748.8) nmol/g creatinine	Aprea *et al.* 1997
				DMP	18 nmol/L	123.0 ±79.0 (22.1-302.6) nmol/g creatinine	
				DMTP	12 nmol/L	489.3 ± 288.3 (139.0-1237.7) nmol/g creatinine	
Fenitrothion	H302	Organophosphorus	Ornamental plants	DMP DMTP	LOD_{DMP} = 18 nmol/L, LOD_{DMTP} = 12 nmol/L	278.8 ± 143.5 (80.0–270.0) nmol/g creatinine	Aprea *et al.* 1999
						206.4 ± 117.2 (128.0–444.7) nmol/g creatinine	
						387.4 ± 178.9(219.8–629.9) nmol/g creatinine	
Azinphos-methyl	H300, H311, H317, H330	Organophosphorus	Apple	DMTP	40 µg/L	530 µg/L	Simcox *et al.* 1999
						290 µg/L	
						900 µg/L	
				DMDTP	-	(40-290) µg/L	
Captan	H317, H318, H331, H351	Phtalimides	Strawberry	THPI	5 µg/L[¥]	5.3 ± 4.0 (0.4–13.8) µg captan /person/day	Krieger & Dinoff, 2000
Omethoate	H301, H312	Organophosphorus	Ornamental plants	DMP DMTP	LOD_{DMP} = 18 nmol/L, LOD_{DMTP} = 12 nmol/L	92±27 (60-130) nmol/g creatinine	Aprea *et al.* 2001
Fenitrothion	H302					122±33 (72-166) nmol/g creatinine	
						212±108 (101-335) nmol/g creatinine	

Tolclofos Methyl	H317					223±54(153-291) nmol/g creatinine 123±59 (59-188) nmol/g creatinine	
N.A	-	Organophosphorus	Apple	DMP	0.15 µg/L	33.1 ± 3.3 µg /g creatinine* 10.8 ± 3.0 µg /g creatinine*	Ueyma *et al.* 2002
				DMTP	0.05 µg/L	10.1 ± 3.4 µg /g creatinine* 5.8 ± 4.0 µg /g creatinine*	
				DEP	0.07 µg/L	4.2 ± 2.6 µg /g creatinine* 4.7 ± 2.4 µg /g creatinine*	
				DETP	0.05 µg/L	1.6 ± 2.6 µg /g creatinine* 0.8 ± 2.9 µg /g creatinine*	
Mancozeb	H317, H361d	Carbamates	Vine	ETU	0.5 µg /g creatinine	12.5 ± 25.9 µg /g creatinine	Colosio *et al.* 2002[1]
Chlorothalonil	H317, H318, H330, H335, H351	Chloronitriles	Ornamental plants	CHL	0.25 µg/L	1.58 ± 2.13 (0.45-8.3) µg/L	Aprea *et al,* 2002
Azinphos-methyl	H300, H311, H317, H330	Organophosphorus	Apple	DMP DMTP DMDTP	40 µg/L	27 ± 2.4 (3.5- 310) µg/ kg/day*	Fenske *et al.* 2003
Omethoate	H301, H312	Organophosphorus	Ornamental plants	DMP DMTP	-	(8.38–854) nmol/g creatinine (38.3–2496) nmol/g creatinine	Aprea *et al.* 2005
Dichlorvos	H301, H311, H317, H330	Organophosphorus	N.A		0.01 µg/L[¥]	204 (23-582) nmol/g creatinine**	Bouvier *et al.* 2006[2]

Fenthion	H302, H312, H331, H341, H372			DMP DMTP DMDTP			
Malathion	H302, H317						
Methyl parathion	H300, H311, H330, H373						
Chlorpyrifos	H301			DEP DETP DEDTP		15(ND – 107) nmol/g creatinine**	
Diazinon	H302						
Ethyl parathion	H300, H311, H330, H372						
Malathion	H302, H317	Organophosphorus	Strawberry	MDA	0.3 µg/L	44.4 µg/g creatinine*	Salvatore *et al.* 2008
				DMP	0.4 µg/L	215.4 nmol/g creatinine*	
				DMTP	0.3 µg/L		
				DMDTP	0.08 µg/L		
Ethylenebisdithiocarbamates	-	Carbamates	Flower bulbs	ETU	-	1.27 mg/mmol creatinine*	van Amelsvoort *et al.* 2008
Malathion	H302, H317	Organophosphorus	Strawberry	MDA	0.3 µg/L	131.2 µg/g creatinine**	Bradman *et al.* 2009
Permethrin	H302, H332, H335	Pyrethroids	Corn	3-PBA	0.1-0.3 µg/L	0.206 µmol/ mol creatinine**	Ferland *et al.* 2015
						0.449 µmol/ mol creatinine**	
						0.241 µmol/ mol creatinine**	
						0.362 µmol/ mol creatinine**	
						0.072 µmol/ mol creatinine**	
						0.161 µmol/ mol creatinine**	
						0.183 µmol/ mol	

						creatinine**	
						0.273 µmol/ mol creatinine**	
						0.228 µmol/ mol creatinine**	
						0.802 µmol/ mol creatinine**	
				trans-DCCA		0.048 µmol/ mol creatinine**	
						0.146 µmol/ mol creatinine**	
						0.268 µmol/ mol creatinine**	
						0.102 µmol/ mol creatinine**	
						0.08 µmol/ mol creatinine**	
						0.058 µmol/ mol creatinine**	
						0.079 µmol/ mol creatinine**	
						0.197 µmol/ mol creatinine**	
						0.105 µmol/ mol creatinine**	
						0.455 µmol/ mol creatinine**	
Malathion	H302, H317	Organophosphorus	Strawberry	MMA	5 µg/L[¥]	28.3 nmol/g creatinine	Sankaran *et al.* 2015
				MDA″	10 µg/L [¥]		
Fenpropathrin	H301, H312, H330			DMP	1 µg/L[¥]	16.4 nmol/g creatinine	
				DMTP	1 µg/L[¥]		
				DMDTP	1 µg/L[¥]		

3-PBA: 3-phenoxybenzoic acid, CHL: chlorothalonil urinary, DEP: diethylphosphate, DEDTP: diethyldithiophosphate, DETP: diethylthiophosphate, DDHP: 2-dimethylamino-5,6-dimethyl-4-hydroxypyrimidine, DMP: dimethylphosphate, DMDTP: dimethyldithiophosphate, DMTP: dimethylthiophosphate, ETU: Ethylenethiourea, IPP: 2-isopropoxyphenol, MMA: malathion monoacid, MDA″ : malathion diacids, MDA: malathion dicarboxylic acid, MDHP : 2-methylamino-5,6-dimethyl-4-hydroxypyrimidine, PNP: p-nitrophenol, TCPy : 3,5,6-trichloro-2-pyridinol, THPI: tetrahydrophalimide, Trans-DCCA: trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanel-carboxylic acid metabolites.

[1] study conducted among 12 operators and 1 worker

[2] study conducted among 12 workers from different occupational places (two greenhouses, three florist shops)

NA: Non applicable

ND : Non detectable

*Geometric mean ± Geometric standard deviation (range) when available

** Median (range) when available

¥ LOQ

H300: Fatal if swallowed; H301: Toxic if swallowed; H302: Harmful if swallowed ; H311: Toxic in contact with skin; H312: Harmful in contact with skin; H317: May cause an allergic skin reaction; H318: Causes serious eye damage; H330: Fatal if inhaled; H331:Toxic if inhaled; H332: Harmful if inhaled; H335: May cause respiratory irritation; H341: Suspected of causing genetic defects; H351: Suspected of causing cancer; H361d: suspected of damaging the unborn child; H372: Causes damage to organs through prolonged or repeated exposure; H373: May cause damage to organs through prolonged or repeated exposure

Risk assessment for workers

Dermal exposure

According to the EFSA Guidance Document (EFSA 2014), dermal exposure from contact with residues on foliage should be estimated as the product of the dislodgeable foliar residue (DFR), the transfer coefficient (TC) and the task duration (T):

Potential dermal exposure (PDE) in mg a.s./day = (DFR [$\mu g/cm^2$] × TC [cm^2/h] × T [h/day])/1 000

The default value for time of exposure should be taken as eight hours a day for harvesting and maintenance type activities and two hours for crop inspection (scouting or certification) and irrigation-type activities.

The actual dermal exposure is defined as the exposure to the skin that would occur in the presence of clothing and/or personal protective equipment (EFSA 2014). In contrast to potential and actual exposures, which are external exposures, the internal dose, absorbed dose or systemic dose is the fraction of the external dose that has been absorbed and enters the general circulation (EFSA 2016).

To convert estimated dermal exposures to corresponding systemic exposures, potential dermal exposure should be multiplied by a dermal absorption factor. This factor is based on absorption values obtained in dermal absorption studies performed on the formulation or on default values (EFSA 2012, 2017).

Inhalation exposure

According to the EFSA Guidance Document (EFSA 2014), the potential exposure to a volatile substance decreases with time as its concentration decreases by absorption in plants, degradation or losses in the environment. Although in many cases, exposure by inhalation contributes far less to the total potential exposure compared to the dermal route, in some situations (e.g. orchards or greenhouses) the inhalation route is significant and needs to be calculated. For this purpose, task-specific inhalation factors

should be used for first tier exposure assessments (e.g. relating to harvesting tasks indoors and to re-entering in greenhouses where pesticide droplets may remain airborne after the treatment). Inhalation exposure for these re-entry scenarios may be predicted by the following:

Potential inhalation exposure [mg a.s./h inhaled] = Application Rate [kg a.s./ha] × Task Specific Factor [ha/h × 10^{-3}]

The Task Specific Factors can be used in the first tier of the exposure and risk assessment: they have been estimated for a small set of exposure data for harvesting and re-entry in ornamental greenhouses.

Oral exposure

According to the BROWSE (Bystanders, Residents, Operators and Workers Exposure) models for plant protection products (BROWSE 2014) and the EFSA Guidance Document (EFSA 2014), the dermal exposure on the hands may become ingested through hand-to-mouth contact. During this contact, a certain amount of PPP is transferred from the hands to the mouth. Oral exposure may be predicted by the following equation:

$$OE = DE_{HANDS} \times A_M/A_H \times SE \times (N \times T)$$

Where OE : Oral exposure (µg/d), DE : hands Dermal exposure of the hands (µg/d), A_M/A_H : Fraction of hand area making contact with the mouth, input on assessment tab of the BROWSE software (default = 7%), SE : Skin-to-mouth transfer factor (%), input on assessment tab (default = 43%), N : Number of hand-to-mouth contacts (contacts/h), fixed at 1 contact/hour and T : Duration of exposure (h/d).

HEALTH EFFECTS OF WORKERS FOLLOWING RE-ENTRY ACTIVITIES

The health risk for the agricultural worker using pesticides is an important aspect to consider during the registration procedure of plant protection products. Health effects may resulting from pesticide

exposure will vary with the pesticide involved and the route of exposure (dermal, oral or inhalation) (MacFarlane *et al.* 2013) and can be observed despite that these chemical products are developed under a very strict regulation process which aims to reduce the risk with reasonable certainty and to minimise the negative impacts on human health and the environment (Damalas and Eleftherohorinos 2011). Despite their popularity and extensive use, previous studies showed that pesticide exposure often induces acute (short-term) health effects, as well as chronic (long-term) health effects on workers that entered in treated fields. Adverse effects of pesticide residues on field workers were already recognised more than fifty years ago (Carman 1952; Quinby and Lemmon 1958). Frequent dermal contact with foliage treated with organophosphorous pesticides have led to incidents of illness among fieldworkers in citrus crops in USA (Gunther *et a1*. 1977). Local effects such as contact dermatitis due to heavy foliar contact and cutaneous exposure to crop associated materials have been reported among California table grape workers (Maddy and Smith 1985; O'Connell *et al.* 1987). Over the past decades, several studies have pointed exposure to pesticide residues as a potential cause of reproductive problems. Male fecundity (sperm concentration, morphology and viability) may be endangered after repeated exposure to pesticide residues by handling products in greenhouses (Abell et al. 2000a). Other studies underlined the probability that re-entry tasks entail a risk for reduced fecundity in increasing the time to pregnancy (Abell *et al.* 2000b; Bretveld *et al.* 2006). In addition, Lander *et al.* (2000) showed some effects on chromosome aberration after an exposure during re-entry activities (such as nipping, cutting, pricking, and potting) to low pesticide concentrations among workers in Denmark. Moreover, neurological disorders could be associated to re-entry tasks in greenhouses or field previously treated with pesticides (Kamel *et al.* 2003; Baldi *et al.* 2011). Further toxicologic and epidemiologic research is needed to confirm these results and assess the impact on public health. Pesticide residues can also be related to an increase in bladder cancer (Boulanger *et al.* 2016) and breast cancer (Lemarchand *et al.* 2016) even if more studies are needed for confirmation. Consequently, serious concerns have been raised about health risks resulting from exposure of workers during re-entry activities. These health effects are different depending on the contamination level, the type of exposure, the frequency and duration of tasks and the behaviour of the worker (Andersson *et al.* 2014).

FACTORS AFFECTING WORKER EXPOSURE

Several factors influence the workers' exposure to pesticide residues during re-entry tasks. Dermal exposure is determined by the transfer of the pesticide residue from the surface of the foliage to the skin of the workers resulting from contact with crops previously treated with pesticide residues (Jurweiz *et al.* 2009; Kasiotis *et al.* 2017; Toumi *et al.* 2018). Risk of exposure depends on the amount available for transfer and the frequency and intensity of skin contact with the treated crops (Jurewicz *et al.* 2009). The amount of pesticide on the leaves available (DFR) depends on the formulation (active substance and its physicochemical properties, such as vapour pressure or solubility), application technique, frequency and rate of required pesticide application, crop height and the re-entry intervals (Brouwer et al. 1992a). Potential toxicity of the PPP, dermal absorption, number and duration of contacts with residues persistency (contact or systemic active substances), use of dermal and respiratory protections, all those factors are important and can affect the exposure of workers who re-enter the pesticide-treated fields or greenhouses. Other factors that can also explain variation in exposure levels are the crop nature and characteristics (e.g. physiological proprieties and composition of the cuticles) (Toumi *et al.* 2018), the relative humidity and temperature during the working day, previous rainfall, the worker skills and status (seasonal or not) and the worn clothing (Baldi *et al.* 2014). Temperature and relative humidity seem to be major factors affecting the exposure of workers to pesticide residues. High temperature and humidity facilitate the passage of the pesticide through clothing (Aprea *et al.* 2005; Aprea *et al.* 2009). Many studies reported that these conditions associated with poor ventilation in greenhouses affect significantly the level of risk for their health. Moreover, in greenhouses temperature is maintained at about 18 °C and variations are smaller than in field conditions. Therefore greenhouse workers are exposed to higher levels of pesticide in the air compared to other workers (Kittas *et al.* 2014). Consequently, working in greenhouse increases both dermal and inhalation exposures of workers to pesticide residues during re-entry.

SOLUTIONS AND MITIGATION MEASURES TO REDUCE WORKER EXPOSURE TO PESTICIDE RESIDUES

Previous studies showed that pesticide residues remaining available in crops could be an issue for workers entering an area previously treated. Results of the studies reviewed suggest that behavioural interventions are needed and can be effective in reducing pesticide exposures for workers. Greater precautions should be taken to reduce contamination, in particular of the hands and skin because the dermal exposure is an important source of exposure for workers.

Lots of studies have showed the efficacy of the personal protective equipment. Gloves (even in latex) can offer a powerful protective barrier against surface residues (Sankaran *et al.* 2015). Li *et al.* (2011) reports the use of rubber latex gloves by strawberry harvesters to protect their skin from exposure and to promote food safety. By urine biomonitoring, Krieger and Dinoff (2000) showed that wearing rubber latex gloves reduces harvester exposure to captan by about 40% compared to bare-handed harvesters during harvesting of strawberries. Bradman *et al.* (2008) and Salvatore *et al.* (2009) showed also that wearing gloves results both in lower levels of pesticide residues on worker's hands and lower absorbed dose. Additionally, hand washing (Curwin *et al.* 2003; Salvatore *et al.* 2009) and daily changing of gloves and clothing (Aprea *et al.* 2009) can reduce skin exposure. But, it should be noted that protective equipment such as gloves on which pesticide can accumulate could lead to a secondary exposure. Study results indicate that normal work clothing provides a 90% reduction in dermal exposure to chlorothalonil (Spencer *et al.* 1991). Standard work clothing for re-entry activities such as harvesting may include long-sleeve shirts, long pants, shoes and socks (Franklin and Worgan 2005; Whitmyre *et al.* 2005). For certain worker re-entry activities such as scouting, coveralls may be worn which impart additional protection Franklin and Worgan 2005; Whitmyre *et al.* 2005).

In addition, concerning inhalation exposure, a suggested improvement in worker protection would involve respiratory protection with a face mask to filter out airborne particulates (Aprea *et al.* 2002). As pesticide residues are normally declining during the days following application, pre-harvest intervals and

restricted re-entry intervals indicated on the labels should be strictly respected to lower the potential exposure of workers. The no respect of the period following application before re-entry is illegal and lead to exposure to toxic levels of pesticide residues. Training and education of workers on (personal) hygiene and the use of protective gloves should be advocated in order to reduce exposure (Brouwer *et al.* 1992b). Finally, the use of pesticides with a higher penetration in plants and lower volatilization could also be useful to decrease the risk level.

CONCLUSION

Workers re-entering in treated fields or greenhouses can be highly exposed to pesticide residues which may result in serious risks for their health. The levels of dermal exposure on a working day due to a manual contact with a contaminated crop can be similar to or higher than those observed for people who handle and sprayed a pesticide. Similarly, the inhalation exposure of workers to pesticide residues after re-entry is of the same order of magnitude than during application of a pesticide. In Europe, placing a PPP on the market is only allowed if a safe use is identified, among other, for the worker. However, in some cases the risk is only acceptable for workers wearing gloves or when mitigations measures are applied. Therefore, a greater attention should be given to raise the awareness of workers about the risk for their health and better preventive measures should be taken to reduce the levels of exposure.

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