Inventory on EPAH health status in CSS

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1. Introduction

This deliverable is part of WP2 entitled "PPPs' distribution and health status". The aim of this deliverable is to provide an overview on the Plant Protection Product (PPP) concentrations measured in Ecosystem, Plant, Animal, and Human matrices (EPAH). This study will serves as a platform for the development of an inventory of PPP distribution and accumulation in EPAH, for the development of an inventory of PPPs' exposure and validation of the model used in WP3 (D3.4), as well as for the development of health risk assessment toolbox (D5.1). In addition, the outcomes of this deliverable will feed into D6.2 - Health damages and external costs at the regional level.

For human health, most evidence is available on reproductive and developmental effects indicating that, mainly, maternal PPP exposure can lead to anomalies in birthweight, malformations, fertility and deviations from normal cognitive and behavioral development in early life. PPP exposure may also be involved in the onset of neurodegenerative and cognitive diseases (autism, ADHD, Alzheimer's disease or Parkinson's disease). Evidence is still limited on the effects of PPPs on cancer, respiratory symptoms/disease and chronic kidney disease. Effects on aquatic ecosystem are mostly studied under controlled conditions in toxicity bioassays. For all the species studied, there is strong evidence supporting connections between PPP residues exposure and effects on non-target aquatic species. Distinct endpoints were impaired, including lethal and sub-lethal effects at distinct levels of biological organization. The effects on terrestrial ecosystem were mostly studied using controlled laboratory experiments. For the different species and endpoints reported, evidence was provided for PPP effects, especially on enzymatic activity in microbiota in controlled laboratory testing. Microcosm studies confirmed these effects and additionally suggested effects on plant growth inhibition, reproduction and community abundance in soil invertebrates. There is a lack of understanding of the effects of mixtures of PPP residues on terrestrial ecosystem. In this deliverable, we aim to link the PPP residue to potential adverse effects on EPAH health. We will identify the sources and sinks of PPP contamination, accumulation across CSS, the exposure of different matrices, and the toxicity of these compounds and examine the association between possible determinants of PPP exposure among humans and animals.

This deliverable is structured as follows:

Chapter 1 – Identifying pesticides of high concern for ecosystem, plant, animal, and human health

This chapter aimed (1) to identify the 20 substances of higher concern for ecosystem, animal and human health based on detection frequency (DF) and median concentrations (MC); (2) to compare results from conventional and organic farming systems (FS); and (3) to provide indicative information on the identified substances' potential hazard to health. In this chapter, we present the hazard profile of the detected residues in the environment, animals, and humans.

Chapter 2 – Occurrence and risk assessment of pesticide residues in ecosystems across Europe and Argentina

The objectives of this chapter are (i) to list the 20 most frequently detected substances in soil, water, sediment, and crops- of 10 European and one Argentinian case study sites, (ii) to find out which of these substances are simultaneously present in these matrices, and (iii) to select pesticide residues of high concern to surface water living species, sediment-dwelling species, earthworms, and humans. In this chapter, we present a short list of compounds having moderate to high risk and their corresponding hazard categories.

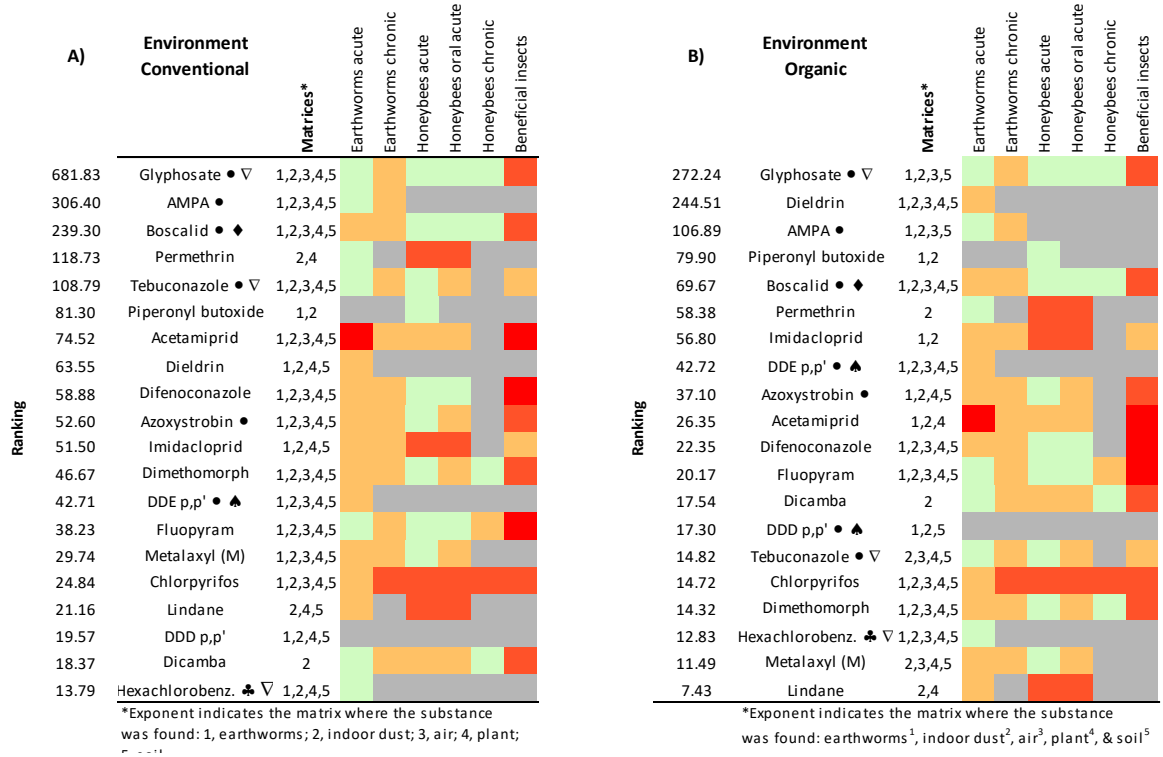
Both chapters are intended for publication in international journals. The first, presented in chapter 1, has been submitted to the journal STOTEN and is under review. The second is being finalised and will be submitted on 20 April 2024.

2. Chapter 1 – Hazard profile of the detected residues

2.1. Hazard to Environment species

In the environmental compartment, in conventional FS, the 20 most frequently detected and highly ranked substances are: glyphosate, AMPA, boscalid, permethrin, tebuconazole, piperonyl butoxide, acetamiprid, dieldrin, difenoconazole, azoxystrobin, imidacloprid, dimethomorph, DDE p,p', fluopyram, metalaxyl (M), chlorpyrifos, lindane, DDD p,p', dicamba, and hexachlorobenzene. Acetamiprid is highly hazardous for earthworms (acute) and chlorpyrifos for earthworms (chronic), honeybees (acute, oral acute, chronic), and for beneficial insects. Three substances are hazardous for honeybees (acute). Nine other substances are hazardous for beneficial insects (glyphosate, boscalid, azoxystrobin, acetamiprid, difenoconazole, fluopyram, dicamba, chlorpyrifos, and dimethomorph) (**Fig. 1A**).

In organic FS, eight substances are detected in all matrices: dieldrin, boscalid, DDE p,p', difenoconazole, fluopyram, chlorpyrifos, dimethomorph, and hexachlorobenzene (**Fig. 1B**). Of the nine most hazardous substances for beneficial insects, five of them are detected in all matrices (boscalid, difenoconazole, dimethomorph, fluopyram, acetamiprid, and chlorpyrifos).



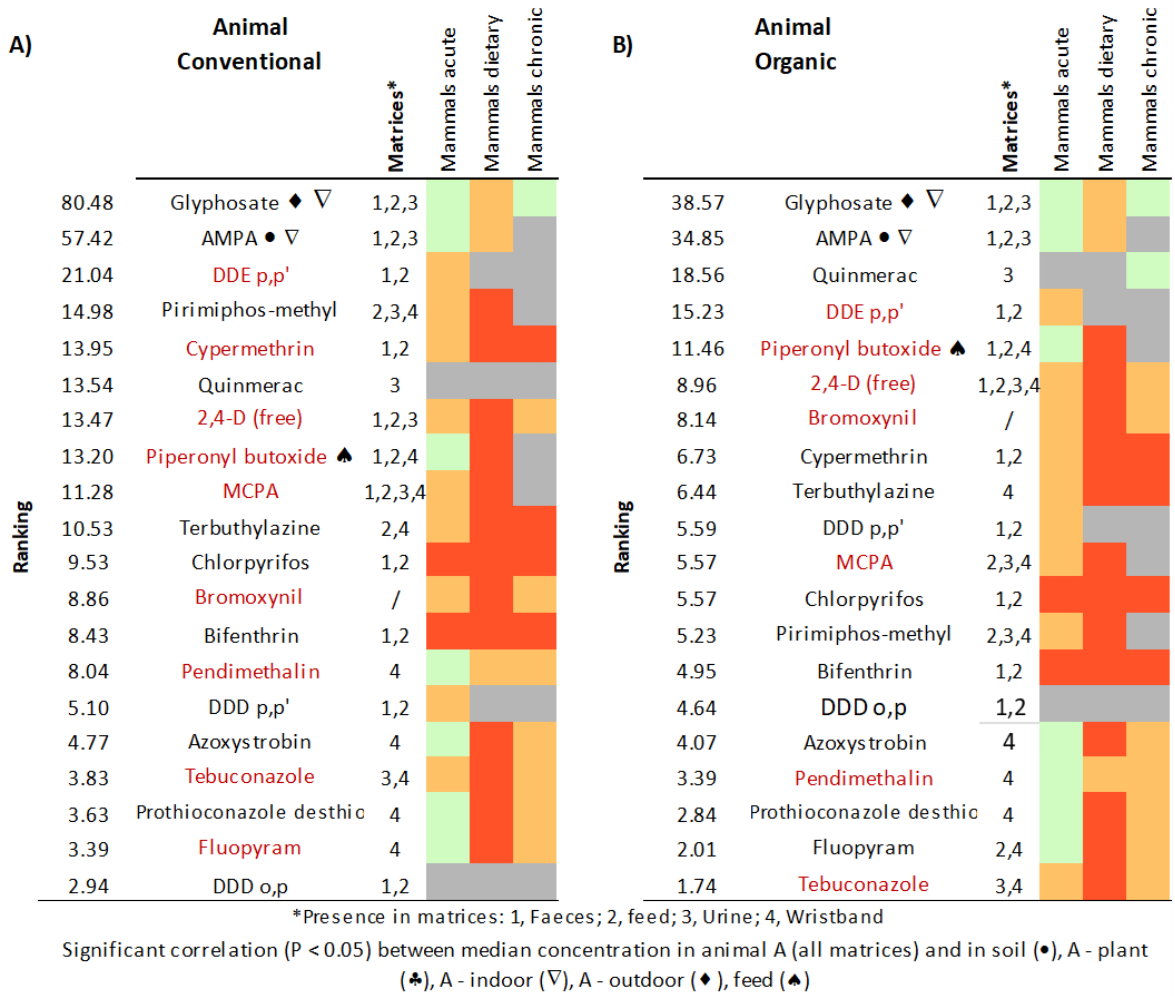
Significant correlation (P<0.05) between median concentration in earthworms E and in soil (●), E - plant (♣), and E - feed (♠), E - indoor (∇), E - outdoor (♦)
Correlations were calculated based on median concentrations in both farming systems.

Figure 1. The 20 substances most frequently detected in the environmental compartment, by farming system: (A) conventional, (B) organic. The figures given in the ranking column represent DF x MC. Cell colors represent the level of evidence according to the PPDB: red, confirmed evidence (yes); orange, possible evidence; green, no evidence; grey, no data available.

2.2. Hazard to Animals

In the animal compartment, looking at conventional FS, the 20 most frequently detected and highly ranked substances are: glyphosate, AMPA, DDE p,p', pirimiphos-methyl, cypermethrin, quinmerac, 2,4-D (free), piperonyl butoxide, MCPA, terbuthylazine, chlorpyrifos, bromoxynil, bifenthrin, pendimethalin, DDD p,p', azoxystrobin, tebuconazole, prothioconazole desthio, fluopyram, and DDD o,p'. Nine of them were detected in animal blood plasma: piperonyl butoxide, cypermethrin, 2,4-D (free), pendimethalin, MCPA, bromoxynil, tebuconazole, DDE p,p', and fluopyram (**Fig. 2A**). MCPA was detected in all matrices, including blood plasma. Five substances were detected in three matrices, with two of them present in blood plasma; and nine substances were detected in two matrices, also with two of them present in blood plasma. Among the 20 substances, two are hazardous for mammals (acute); thirteen are hazardous for mammals (dietary), with seven of these detected in blood plasma; and 4 are hazardous for mammals (chronic).

In organic FS, seven of the 20 most frequently detected substances were detected in blood plasma: DDE p,p', piperonyl butoxide, 2,4-D (free), bromoxynil, MCPA, pendimethalin, and tebuconazole. 2,4-D (free) was detected in all matrices. Five substances were detected in 3 matrices, with two of them present in plasma (deltamethrin, tebuconazole). Bromoxynil was not detected in any other matrices apart from blood plasma in either FS. Among the 20 substances, two are hazardous for mammals (acute). Five of those detected in animal blood plasma in organic FS (against seven in animal blood plasma in conventional FS) are hazardous for mammals (dietary), namely piperonyl butoxide, 2,4-D (free), bromoxynil, MCPA, and tebuconazole; and no data exists for DDD o,p' (**Fig. 2B**).



*Presence in matrices: 1, Faeces; 2, feed; 3, Urine; 4, Wristband

Significant correlation ($P < 0.05$) between median concentration in animal A (all matrices) and in soil (•), A - plant (♣), A - indoor (∇), A - outdoor (♦), feed (♠)

Correlations were calculated based on median concentrations in both farming systems.

Figure 2. The 20 substances most frequently detected in the animal compartment, by farming system: (A) conventional, (B) organic. Substances shown in red were detected in animal blood plasma. The figures given in the ranking column represent DF x MC. Cell colors represent the level of evidence according to the PPDB: red, confirmed evidence (yes); orange, possible evidence; green, no evidence; grey, no data available; bromoxynil was detected only in blood plasma.

2.3. Hazard to Humans

In the human compartment, in conventional FS, the 20 most frequently detected and highly ranked substances are: DDE p,p', glyphosate, tebuconazole, AMPA, piperonyl butoxide, hexachlorobenzene, deltamethrin, fipronil sulfone, 2,4-D (free), pirimiphos-methyl, azoxystrobin, boscalid, fludioxonil, propiconazole, lambda-cyhalothrin, cypermethrin, propoxur, fipronil, pyrimethanil, and chlorpyrifos TCPy (**Fig. 3A**). Twelve of them are present in conventional farmers' blood plasma, namely DDE p,p', glyphosate, tebuconazole, piperonyl butoxide, hexachlorobenzene, fipronil sulfone, 2,4-D (free), fludioxonil, propiconazole, lambda-cyhalothrin, pyrimethanil, and chlorpyrifos methyl, while five – deltamethrin, boscalid, cypermethrin, propoxur, and fipronil – are present only in the blood plasma of the other stakeholder groups, that is, neighbors and/or consumers. Among the 20 substances, four are hazardous with regard to cancer: DDE p,p' piperonil

butoxide, hexachlorobenzene, and pirimiphos methyl, and ten are classed as probably carcinogen (glyphosate, tebuconazole, deltamethrin, 2.4-D, fludioxonil, propiconazole, cypermethrin, propoxur, fipronil, and pyrimethanil); ten – DDE p,p, tebuconazole, piperonyl butoxide, hexachlorobenzene, deltamethrin, 2,4-D, propiconazole, cypermethrin, propoxur, and chlorpyrifos methyl – are hazardous in terms of endocrine disruption; six – DDE p,p', tebuconazole, 2,4-D (free), Propiconazole, cypermethrin, and chlorpyrifos metabolite TCPy – are hazardous regarding reproduction/development; and eight are neurotoxicants, namely DDE p,p', hexachlorobenzene, deltamethrin, 2,4-D (free), lambda-cyhalothrin, cypermethrin, fipronil, and chlorpyrifos metabolite TCPy.

In organic FS, eleven substances were detected in farmers' blood plasma: DDE p,p', Piperonyl butoxide, Hexachlorobenzene, fipronil sulfone, tebuconazole, cypermethrin, 2,4-D (free), Propiconazole, fipronil, Pyrimethanil, and chlorpyrifos TCPy (**Fig. 3B**). Fludioxonil, lambda-cyhalothrin, and glyphosate, were detected in the blood plasma of conventional farmers, but not in the blood plasma of organic farmers. Conversely, fipronil and cypermethrin were detected only in the blood plasma of organic farmers, but not in that of conventional farmers.

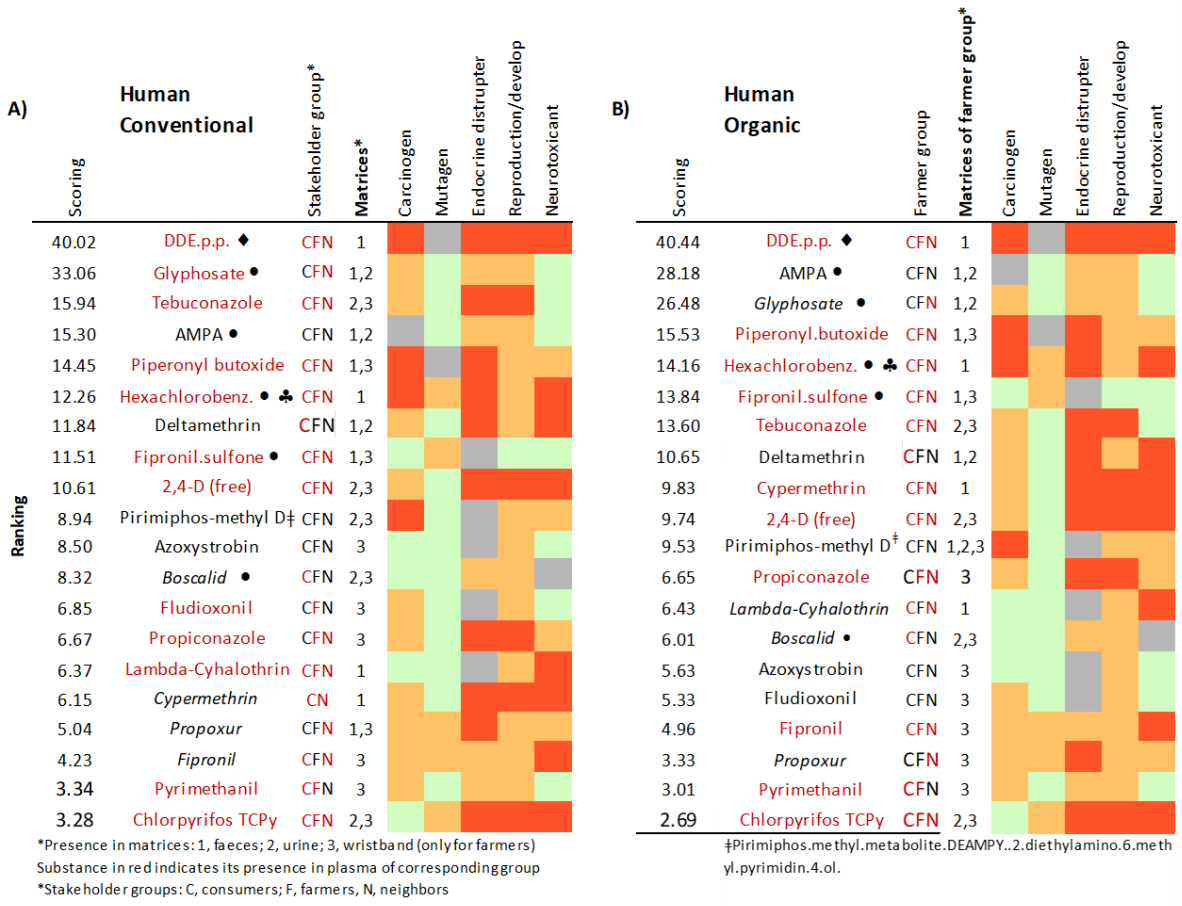


Figure 3. The 20 substances most frequently detected in the human compartment, by farming system: (A) conventional, (B) organic. Substances shown in red were detected in the respective groups' blood plasma; those shown in black italic were detected in the blood plasma only of consumers and/or neighbors. The figures given in the ranking column represent DF x MC. Cell

3. Chapter 2 – List of compounds having moderate to high risk

By neglecting the low and negligible risk and considering only the medium and high risk with a sum greater than or equal to 50%, these substances were detected among the 20 most frequently detected in each matrix (**Table 4**).

Figure 4. List of substances with the sum of the frequencies of occurrence of moderate and high risks greater than 50%; this concerns the conventional fields only except in the case of lindane gamma

Substance	Soil	Crop	Water	Sed.	Type	Status	Found in x matrices
Diflufenican		50	100	50	Herbicide	App	3
Difenoconazole	67	8		100	Fungicide	App	
Terbuthylazine		100	7	100	Herbicide	App	
Chlorpyrifos	70	44	100		Insecticide	**NA**	2
Lambda cyhalothrin	70	8		100	Insecticide	App	
Permethrin		100	100		Insecticide	**NA**	
Acetamiprid	67	25			Insecticide	App	
Deltamethrin	100	13			Insecticide	App	
Hexachlorobenzene		60			Fungicide	**NA**	
Atrazine	20	100			Herbicide	**NA**	
Lindane gamma*		50			Insecticide	**NA**	
Prosulfocarb	14	100			Insecticide	App	
Fludioxonil			100	8	Insecticide	App	1
Spiroxamine			17	67	Fungicide	App	
Zoxamid			100		Fungicide	App	
Bifentrin		29	100		Insecticide	**NA**	
Terbutryn			63		Herbicide	**NA**	
Cypermethrin		30		50	Insecticide	App	
Folpet PHI				100	Fungicide (M)	App	

*Occurring in both farming systems; otherwise

Considering the pesticide residues with moderate to high risk (sum of the frequencies of occurrence of moderate and high risks greater than 50%), we provided the relationship between hazard level and hazard category of the compounds selected. Among the 18 substances selected for their risk profile, twelve compounds with high hazard levels for multiple categories for environment and human, are listed below. Diflufenican in crop is hazardous for humans as an endocrine disrupter and neurotoxicant. It is also hazardous in water for algae (acute and chronic). Chlorpyrifos is hazardous for earthworms (chronic) in soil, fish (acute and chronic), for aquatic invertebrates (acute and chronic), for aquatic crustaceans (acute) in water systems, and dwelling organisms (acute and chronic) in sediment. Permethrin has a high hazard level for humans when consumed in crops, as a carcinogen, endocrine disrupter, reproduction/Development, and as neurotoxicant, and for fish and algae (acute and chronic), aquatic invertebrates and crustaceans (acute). Acetamiprid is hazardous for earthworms (acute). Hexachlorobenzene has highly severe effects on humans as it is classified as carcinogenic, endocrine disrupter, and neurotoxicant. Atrazine and lindane gamma are both hazardous for humans and act as an endocrine disrupter, in addition to the neurotoxicant effect of the second compound, while Prosulfocarb is hazardous for humans too as a neurotoxicant. Fludioxonil and zosamide have highly severe effects on aquatic invertebrates (chronic), and fish (chronic), respectively. Bifenthrin is hazardous for fish and aquatic invertebrates (acute and chronic),

and for aquatic crustaceans (acute). Cypermethrin has a highly severe effect on dwelling organisms (acute), while no data exist for folpet PHI.

Among the substances with a moderate effect on the environment and humans, 16 out of 18 affect earthworms (Difenoconazole, chlorpyrifos, lambda-cyhalothrin, acetamiprid, and deltamethrin), humans (diflufenican, terbuthylazine, hexachlorobenzene, atrazine, and lindane gamma), aquatic organisms (diflufenican, chlorpyrifos, permethrin, fludioxonil, zoxamide, bifenthrin, and terbutryn), and finally 5 are hazardous for dwelling organisms: diflufenican, difenoconazole, terbuylazine, chlorpyrifos, and spiroxamine.

Among the 20 top-frequency substances having moderate to high RQ, 7 are not approved, among which 5 are used for industrial issues: chlorpyrifos, permethrin, hexachlorobenzene, bifenthrin, and terbutryn; lindane is used for veterinary drugs, while atrazine is used for both veterinary drugs and industrial issues.

4. Conclusions

In this study, we showed that most of the pesticide residues detected in soil, water, indoor dust, outdoor air, sediment, and crop samples are hazardous for non-target organisms, including animals and humans. We have also shown that humans are mainly exposed to substances from the environment and, to a certain extent, to dual-use substances, evidenced by the presence of a set of common pesticide residues across all matrices suggesting exposure to mixtures of multiple pesticides. The toxic effect of such exposure is unknown, especially over a longer period. This study provides a useful basis for selecting the pesticide residues to be considered in the investigation of mixtures, as it highlights the top-frequency substances across all matrices. With so many substances omnipresent in the environment, it would be judicious to consider the mixtures of substances already present in animal and human bodies, including those found in blood plasma, and to include biocides in the mixture studies. The association between exposure to certain pesticides and their hazardous effects has been thoroughly proven and cannot be ignored. Given that the negative effects of health hazards on humans depend on both the individual and the wider environmental context, it is imperative to take a comprehensive approach and use integrative and interdisciplinary methods.

Acknowledgments

All Case Study Sites Leaders contribute to this work. There are 11 CSS in total, 10 covering Europe and one in Argentina.

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