1.1 Session Title

Impact of pesticides on ecosystem and human health: risk assessment based on data from the SPRINT large scale monitoring campaign

1.2 Session Date and Time

16th of September 2024 at 5:00 EST (11:00 CEST)

1.3 Convenor name

Prof. dr. Violette Geissen

2 Speakers and Panelists

2.1 Speaker 1

2.1.1 Name: Prof. dr. Violette Geissen

2.1.2 Organisation name: Wageningen University and Research

2.1.3 Type of organisation: Academic institute

2.1.4 Title of the presentation: The SPRINT approach for global health risk assessment

2.1.5 Summary of the presentation (max 200 words):

The SPRINT project aims to develop a global pesticide health risk assessment using monitoring data from across Europe and Argentina. This approach is the first to utilize large-scale field data for assessing risks to both ecosystems and human health. During the 2021 growing season, a monitoring campaign across 10 case study sites revealed that pesticide residue mixtures are almost universally present in terrestrial and aquatic ecosystems, including soils, surface water, sediment, air, and indoor dust, with one farmer's house containing up to 123 residues. Human samples—blood, urine, and feces—from approximately 700 farmers, neighbors, and consumers also showed widespread presence of these pesticide cocktails. The most relevant pesticides at each site were identified based on frequency, concentration, and hazardous characteristics, with these compounds and their mixtures used for risk assessment. The SPRINT project introduces innovative indicators for health risk assessment. This session presents the impact of pesticide residues on ecosystems and human health, focusing on 1) ecotoxicological tests on terrestrial and aquatic ecosystems, 2) organoid and gut microbiome studies, and 3) in vivo experiments with rats and mice. The project contributes to the development of a novel health risk assessment based on real-world data.

2.2 Speaker 2

2.2.1 Name: Kayode Jegede

2.2.2 Organisation name: University of California Davis

2.2.3 Type of organisation: Academic institute

2.2.4 Title of the presentation:

2.2.5 Summary of the presentation (max 200 words):

Soil organisms like earthworms are often exposed to pesticide mixtures due to intentional combinations or cumulative applications in agriculture. Therefore, assessing the cumulative mixture effects of pesticides is a realistic approach to evaluating environmental risks. In this study, two native European earthworms, Lumbricus rubellus and Lumbricus terrestris, were added to soils in the lab. Pesticide formulations were sprayed on the soil surface following real-world spray schemes for five different cropping scenarios. The exposure durations varied from 57 to 98 days, with 4 to 10 pesticides applied depending on the scheme. Lethal and non-lethal effects were assessed and compared to a control group with no pesticide application. Despite low calculated toxic units, significant lethal and non-lethal effects were observed. Notably, L. rubellus showed 100% reproduction inhibition in four out of five scenarios, while L. terrestris experienced significant mortality in one scenario. The scenarios with the most pesticides had the highest toxic effects. These findings highlight the importance of considering cumulative pesticide risks in environmental assessments to better protect soil ecosystems.

2.3 Speaker 3

2.3.1 Name: Eoin Gunnigle

2.3.2 Organisation name: University College Cork

2.3.3 Type of organisation: Academic institute

2.3.4 Title of the presentation: From gut to brain: Behavorial effects of pesticide-induced microbiome changes

2.3.5 Summary of the presentation (max 200 words):

There are an increasing number of studies that highlight the key role gut microbial communities play in maintaining host health. Indeed, exposure to various pesticides has been shown to induce changes in the gut microbial profile in insects, rodents and marine animals. This is a worry for humans, with some studies extending the risk of pesticide exposure to harming brain function as seen in the higher occurrence of Parkinson's disease, autism spectrum disorder and dementia. The mechanisms and processes for these adverse effects of pesticide exposures are yet to be clearly understood. Here, we investigated the effects of administration of selected pesticides at relevant human exposure doses on behaviours including anxiety, social behaviour, cognitive performance, stress and depressive-like behaviour. Furthermore, we investigated the impact pesticide exposure on the gut microbiome through molecular approaches e.g., shotgun sequencing. We tested Glyphosate (ADI, ADIx10, ADIx100) in male and female mice. Tebuconazole (ADI, ADIx10, ADIx100) in male mice. Acetamiprid (ADI, ADIx10, ADIx100) in male mice. We also undertook a faecal microbiome transplant study using mice exposed to

Glyphosate and naïve mice to determine if behavioural phenotype could be transferred, hence understanding if responses driven by alterations to microbiome.

2.4 Speaker 4

2.4.1 Name: Nelson Abrantes

2.4.2 Organisation name: University of Aveiro

2.4.3 Type of organisation: Academic institute

2.4.4 Title of the presentation: Assessing the multifaceted impacts of realistic pesticide mixtures on aquatic ecosystems

2.4.5 Summary of the presentation (max 200 words):

Aquatic organisms from different trophic levels were exposed to realistic pesticide mixtures, demonstrating significant impacts, from growth inhibition to lethal effects. The study also assessed bioaccumulation and trophic transfer, highlighting the high toxicity of the mixtures compared to individual compounds. These findings underscore the substantial risk posed by pesticide mixtures to aquatic ecosystems.

2.5 Speaker 5

2.5.1 Name: Benjamin Vervaet

2.5.2 Organisation name: University of Antwerp

2.5.3 Type of organisation: Academic institute

2.5.4 Title of the presentation: Assessing health effects of pesticide mixtures: a rodent study.

2.5.5 Summary of the presentation (max 200 words):

Assessing health effects of pesticide mixtures in a translatable way is challenging. Many studies compile a pesticide cocktail based on average pesticide use or a chosen combinations of pesticide classes. Although important aspects are covered, these studies often reflect an arbitrary situation. Therefore, we aim to experimentally mimic a real-life low-dose exposure situation in rodents, based on a pesticide mixture measured during the SPRINT project in an actual human meal, replicating both its composition and dose. Analyses involve a broad spectrum of health parameters, including but not limiting to kidney, liver, heart, brain and gut function and structure. Preliminary data (upon availability) will be presented during the talk.

2.6 Speaker 6

2.6.1 Name: Nina Wieland

2.6.2 Organisation name: Radboud University

2.6.3 Type of organisation: Academic institute

2.6.4 Title of the presentation: Consumer exposure to pesticide residues from food – an exploratory study of duplicate food portions (DFP) intake and urinary metabolite excretion

2.6.5 Summary of the presentation (max 200 words):

Food safety in the EU is maintained through restrictions on pesticide residues in food, both from the internal market and imported products. The European Food Safety Agency (EFSA) publishes food residue data, which can be used to estimate dietary pesticide uptake through models like EFSA's PRIMo, though experimental verification is needed. In the European Sustainable Plant Protection Transition (SPRINT) study, dietary pesticide uptake was examined in human volunteers. Forty-three participants collected duplicate portions of all food and beverages (DFP) consumed over 24 hours, along with 36-hour urine samples. These were analyzed for pesticide residues and exposure biomarkers (mainly metabolites) using LC-MS/MS and GC-MS/MS, with glyphosate and AMPA analyzed separately. Out of 183 pesticides, 86 were detected in DFPs. The most frequently detected were metalaxyl (100%), pirimiphos-methyl (77%), and tebuconazole (70%), with piperonyl-butoxide found in nearly all samples. Common urinary biomarkers included 3-PBA (81%), DCCA (63%), TCPy (84%), and DEAMPY (74%). Glyphosate and AMPA were found in 42% and 30% of urine samples, respectively. The highest concentrations detected were 136 µg/L for M605F002 (pyrimethanil metabolite), 18 µg/L for hydroxy-tebuconazole, and 14 µg/L for DEAMPY. This study highlights the value of DFP collection and analysis for understanding pesticide intake in consumers.

2.7 Speaker 7

2.7.1 Name: Peter Fantke

2.7.2 Organisation name: Technical University of Denmak

2.7.3 Type of organisation: Academic institute

2.7.4 Title of the presentation: Global distribution of pesticide use 2016-2020

2.7.5 Summary of the presentation (max 200 words):

Evaluating and mitigating global pesticide-related impacts on humans and the environment, data on actual pesticide use are essential. We propose a global dataset on pesticide use at the level of active ingredient, crop, and country, considering crop growth, application method and spatial crop distribution. We highlight pesticide use hotspots, enabling targeted reduction and substitution efforts in support of a transition toward sustainable crop protection.

2.8 Speaker 8

2.8.1 Name: Maaike Gerritse

2.8.2 Organisation name: Wageningen University and Reserach

2.8.3 Type of organisation: Academic institute

2.8.4 Title of the presentation: Gut microbiome and organoids as new indicators for pesticide toxicity

2.8.5 Summary of the presentation (max 200 words):

Farmers rely on pesticides to maximize yields, but the potential long-term health impacts of chemicals on humans and the environment are concerning. Pesticides, especially in mixtures, can disrupt the gut microbiome and compromise the intestinal epithelium's barrier function. As part of the SPRINT project, we examine the effects of Plant Protection Products (PPPs) on human health by integrating metagenomic data from approximately 700 individuals with PPP usage data and residue levels in biological samples. Notably, metagenomic analysis of faecal samples from the human biomonitoring study revealed that higher concentrations of glyphosate lead to significant alterations in the gut microbiome. In a next step: Human-derived intestinal and airway organoids are used to assess changes in gene expression, protein expression, and cellular functions. This research provides novel insights into the cumulative and long-term effects of pesticide exposure, using gut microbiome profiles and organoid models as indicators of toxicity. this study investigates the toxicological effects of pesticides on porcine gut organoids, focusing on gene expression changes. Using RNA-Seq data, we explore the impact of individual pesticides and mixtures, aiming to understand whether their combined effects exceed those of individual components. This bioinformatics project employs differential gene expression analysis (EdgeR, DESeq2) and multivariate techniques (PCA, RDA) to identify key biological processes affected by pesticide exposure.

2.9 Speaker 9

2.9.1 Name: Philipp Maeder

2.9.2 Organisation name: University of Hohenheim

2.9.3 Type of organisation: Academic institute

2.9.4 Title of the presentation: Effects of multiple pesticides on soil microorganisms and glyphosate degradation

2.9.5 Summary of the presentation (max 200 words):

Modern agriculture relies on pesticide mixtures to meet the growing demand for food quality and quantity, leading to diverse residues in soils. These pesticides and their metabolites can affect non-target organisms like soil microorganisms. While pesticides are usually tested for their individual effects, studies on their interactive effects are limited. This study aimed to determine the impact of up to three simultaneously applied pesticides on the microbial community and their role in pesticide degradation. Agricultural soil, previously untreated with pesticides, was exposed to different mixtures of the herbicides glyphosate (GLP), MCPA (2-methyl-4-chlorophenoxyacetic acid), and the fungicide difenoconazole (DFC) for up to 56 days. Isotopic and molecular methods were used to assess the effects on the microbial community and to track GLP mineralization. The presence of MCPA increased the metabolic quotient by up to 35%, indicating stress on the microbial community. Additionally, the presence of multiple pesticides reduced gram-positive bacteria by 13% and decreased the abundance of microorganisms capable of degrading GLP via AMPA. Interestingly, a 40% increase in GLP mineralization was observed alongside reduced carbon use efficiency (CUE). These results emphasize the need to study not just individual pesticides but also their mixtures and interactions, as they can significantly alter microbial community behavior.

2.10 Speaker 10

2.10.1 Name: Daniel Figueiredo

2.10.2 Organisation name: Utrecht University

2.10.3 Type of organisation: Academic institute

2.10.4 Title of the presentation: Dietary and non-dietary external exposure versus aggregated internal exposure: what does it mean for risk?

2.10.5 Summary of the presentation (max 200 words):

Individuals are frequently exposed to pesticides via different routes, which can have an impact on human health, hence there is a growing need for aggregated (dietary and non-dietary) pesticide exposure estimates and consequent risk assessment. Combined estimated and measured (via wristbands) external exposure was compared with aggregated internal exposure through measurement of urinary biomarkers. Risk was calculated by comparing probable aggregated exposure estimates with Acute Reference Doses (ARfD). For 6 out of 14 pesticides, we observed that dietary exposure was a statistically significant predictor for variability in urinary excretion concentrations of (metabolites of) chlorpyrifos-methyl, boscalid, glyphosate, AMPA and tebuconazole. Wristband concentrations (proxy for environmental route) also turned out to be significant predictors for chlorpyrifos-methyl, tebuconazole, 2,4D and MCPA. Realistic "worst-case" exposures (i.e. high exposure from both diet and environment) can lead to appreciable risk. For several pesticides the environmental exposure route should be considered in aggregate exposure and risk assessment. Currently, health-related acute and long-term limit values fail to include the contribution of the environmental route, which can be the tipping point.

3 Content

3.1 Session Abstract (max. 500 words)

The SPRINT projects (sprint-h2020.eu) addresses the urgent need to develop a pesticide health risk assessment based on large monitoring programs related to actual presence of pesticide residues in terrestrial and aquatic ecosystems, indoor dust and human matrices. SPRINT introduces innovative ecosystem and human health indicators and addresses the impact of residue mixtures on ecosystem and human health based on data from a large-scale field campaign conducted in 2021 across Europe and in Argentina. We took about 600 samples across environmental matrices - soil, plant, surface water, sediment, air and indoor dust and blood, urine and faeces samples from around 700 persons.

Based on field results we tested the single residue and mixtures' impact on the aquatic and terrestrial ecosystem conducting innovative ecotoxicological tests with sensitive indicators. We tested the effects of pesticide mixtures on the soil microbiome composition and enzymes and on native earthworms to assess effects on soil health as important indicators of ecosystem health. For the aquatic ecosystem, innovative indicators were used to address the health effect of pesticide mixtures.

Furthermore, we assessed human health effects of single pesticides and their mixtures on innovative indicators: 1) conducting in vitro tests with colon ileum organoids, 2) assessing effects on the gut microbiome composition, 3) conducting behavioural studies with mice as model organisms, 4) testing effects of high number residue mixtures on innovative indicators using rats as a model.

Solution oriented, we highlight pesticide use hotspots based on a global data set, enabling targeted reduction and substitution efforts in support of a transition toward sustainable crop protection. The SPRINT session provides highly important knowledge needed to solve the urgent questions on how to assess health risk related to real-world pesticide residue occurrence, the actual health effects based on innovative indicators and show the urgent need for a transition to sustainable agriculture. We provide data and a new risk indicator that can be included in new regulations.

3.2 Project Objectives

List the key objectives your session or project aimed to achieve.

3.2.1 Objective 1 (max 50 words)

To develop a comprehensive pesticide health risk assessment approach that incorporates real-world monitoring data from the terrestrial and aquatic ecosystem and human matrices, focusing on both individual and cumulative effects of pesticide residues.

3.2.2 Objective 2 (max 50 words)

To introduce and validate innovative ecotoxicological and human health indicators for assessing the impact of pesticide mixtures, facilitating a better understanding of the risks of pesticide use and residues associated with current agricultural practices.

3.2.3 Objective 3 (max 50 words)

To provide evidence-based recommendations for transitioning towards sustainable agricultural practices that minimize health and environmental risks while ensuring food security.

3.3 Key Themes

- One Health
- Food systems
- Environment and Climate

4 Planned Impacts of the science and innovation presented in you session

4.1 Contribution to the SDGs

The SDGs provide a comprehensive framework for addressing the world's most pressing challenges and promoting sustainable development globally. Select the Goal/s that your project contributes to (max 3 SDGs)

3. **Good Health and Well-Being**: Ensuring healthy lives by assessing and mitigating the health risks posed by pesticide exposure.

12. **Responsible Consumption and Production**: Promoting sustainable agricultural practices that minimize the use of harmful pesticides and ensure safer food production.

15. **Life on Land**: Protecting terrestrial ecosystems by assessing the impact of pesticides on soil health and biodiversity and advocating for practices that reduce these risks.

5 Contribution to the UN Summit of the Future

5.1 Main challenges (max 200 words)

The main challenges and difficulties experienced in implementing SPRINT to contribute to the Sustainable Development Goals is the ongoing controversial discussion on food security - the provision of cheap food to avoid poverty - and sustainable food production - avoiding harmful effects to environmental and human health. SDG 1 (No poverty) and 2 (Zero hunger) require the production of affordable food, whereas SDG 3 (Good Health and Well-Being), 12 (Responsible Consumption and Production) and 15 (Life on Land) require sustainable food production which may increase the food prices for consumers. The challenge is to establish a global approach to calculate real costs for non- sustainable food production assessing the indirect costs for the harm on ecosystem and human health. Introducing this approach globally can support the transition to a global sustainable food production system providing safe food for all.

5.2 Additional goals (max 200 words)

Additional goals, beyond the Goals, which are considered priorities

<u>Enhance public awareness</u> of the risks associated with pesticide use and the benefits of transitioning to more sustainable practices.

<u>Foster international collaboration</u> in pesticide risk assessment and sustainable agriculture, ensuring knowledge and technology transfer to developing countries.

<u>Contribute to policy development</u> by providing evidence-based recommendations that can inform regulations and standards for pesticide use, promoting global health and environmental sustainability.

5.3 Integration: economic, social and environmental (max 500 words)

SPRINT provides a global health approach to assess the risk of pesticide use on ecosystem and human health and providing recommendations to sustainable transition. Working on a European scale we develop a transition strategy being social, economic and environmentally sustainable. This is conducted by high stakeholder involvement across Europe on regional, national and international level. The SPRINT approach can be used as an example for further sustainable transitions in other regions.

5.4 Impact on the 2030 Agenda (max 1000 words)

SPRINT is committed to the principle of respecting human rights, which is central to the 2030 agenda of the UN. By focusing on the health risks associated with pesticide exposure, the project aims to protect the fundamental right to health. Improving access to clean and safe environments aligns with **SDG 3** (Good health and well-being) and contributes to protecting the human right to a healthy life. SPRINT also integrates another SDG, namely **SDG 5** (Gender Equality) by actively promoting the involvement of women in all aspects of its research and outreach. The project ensures that not only gender balance in the researchers involved but also in the human volunteer studies and the lab based studies. Next, in social outreach we try to target an equal amount of male and female thereby fostering empowerment and equal opportunities.

Environmental sustainability is a core objective of the 2030 Agenda, particularly as it relates to combating climate change and preserving natural ecosystems. SPRINT's focus on reducing pesticide-related pollution and protecting biodiversity supports **SDG 15** (Life on Land) and **SDG 13** (Climate Action). Moreover, the project addresses environmental justice by ensuring that its research contributes to reducing environmental harms that disproportionately affect low-income and rural communities.

The SPRINT project mostly aligns with the transition focusing on **(6) Climate change, biodiversity loss, and pollution**. This transition is key in addressing the environmental challenges that directly affect the health of ecosystems and, subsequently, human well-being. The project's work on assessing the impact of pesticide residues on terrestrial and aquatic ecosystems ties closely with efforts to combat biodiversity loss and reduce pollution - a key component of this transition.

Combating pollution: SPRINT's large-scale monitoring of pesticide residues in environmental matrices (eg. soil, water, air) and human matrices (eg. blood, urine) directly addresses pollution, particularly the contamination of natural resources. The findings provide data that can inform strategies to reduce pesticide use and limit environmental pollution. Secondly, by developing new risk assessment models that consider the cumulative effects of pesticide mixtures, SPRINT supports in creating a more accurate understanding of pollution's impact on both ecosystems and human health, leading to better regulatory frameworks.

Concerning biodiversity loss, SPRINT's research shows the significant adverse effects of pesticide mixtures on various ecosystems, including soil health and aquatic life. By studying these impacts, the project contributes to the broader goal of conserving biodiversity by identifying harmful practices and suggesting alternative, more sustainable agricultural practices. The project's focus on the effects of pesticides on non-target organisms, such as earthworms and soil microorganisms, is essential for maintaining ecosystem services that are critical to biodiversity.

Lastly the project supports the transition to sustainable agriculture, which is important for mitigating climate change. Reducing the reliance on chemical pesticides can lead to healthier soils, which act as carbon sinks, thereby contributing to climate change mitigation efforts.

SPRINT's efforts to map pesticide use globally highlight hotspots that require intervention, aligning with climate action plans that focus on reducing environmental footprints in agriculture.

While Transition 6 is the most relevant, the SPRINT project also touches on aspects of **Food Systems (Transition 1)** by striving towards safe food production and contributing to the sustainability of food systems maintaining food security. SPRINT directly contributes to safe food production by investigating the presence and impact of pesticide residues in food. Through monitoring and assessment, the project identifies the potential health risks posed by pesticide-contaminated food, which is a concern for public health. The project also supports the sustainability of food systems by advocating for agricultural practices that minimize environmental harm but maintaining agricultural productivity. SPRINT is providing data and recommendations that balance the need for high agricultural productivity yet protecting human health and the environment.

6 Forward-looking Statement

6.1 Financial aspects

In SPRINT, we identified that pesticide residues, particularly in indoor dust, result in chronic exposure to over 120 pesticide residues for humans. The health effects of ingesting or inhaling these residues remain unknown. A $1 million investment will enable us to excecute organoid and animal studies to investigate these health risks.

To reduce the increasing health and environmental impacts of pesticide use, we need $1 million to launch a global awareness campaign. This campaign will educate stakeholders across the value chain on the importance of sustainable food production practices, aiming to shift agricultural paradigms and protect global health and ecosystems.

6.2 To further advance your science project, you will need:

Please select an option and develop it further (50 words). Multiple selection is possible.

- **Access to funding** - It will allow us to scale up research activities, conduct more comprehensive studies, and implement innovative solutions at a larger scale. Increased funding will also support the development of new technologies and tools.
- **Dissemination and communication activities -** Effective dissemination and communication are vital for translating research findings into actionable changes. We need to enhance outreach efforts to educate stakeholders, policymakers, and the public about the risks of pesticide use and the benefits of sustainable practices. This will drive global awareness and adoption of safer agricultural methods.
- **Enhance the regulatory environment** – By enhancing regulations that supports research initiatives, we can ensure that innovative research is encouraged, adequately funded, and translated into impactful policies that promote sustainable development.

7 Conclusions (max. 300 words)

This session addresses the SDGs Good Health and Well-Being, Responsible Consumption and Production and Life on Land. By providing a global risk assessment tool and providing data on the actual health risk caused by cocktails of pesticide residues in ecosystems and human matrices we provide important tools to achieve the three SDG. Furthermore, we give recommendations for a sustainable transition of the food production systems.

SPRINT states that applying the precautionary principle related to ecosystem and human health, a transition of food production is urgently needed. Innovative technologies such as robotics and AI are available. Next steps are to implement the transition to innovative agriculture globally and to implement the innovative global health approach for risk assessment.

Support is needed to conduct efficient awareness raising campaigns for the transition of agriculture. Furthermore, we need adaptions in the pesticide regulation implementing the global health