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### ► To cite this version:

Elodie Mirmont, Tarek Moufawad, Fatima-Zahra Alem, Cécile Chevrier, Nathalie Bonvallot, et al.. Widening exposome exploration by means of complementary HRMS analytical platforms: use case on pesticide exposure. 39ème édition des Journées Françaises de Spectrométrie de Masse, Sep 2023, Marseille, France. hal-04357806

**HAL Id: hal-04357806**

**<https://hal.science/hal-04357806v1>**

Submitted on 21 Dec 2023

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# Widening exposome exploration by means of complementary HRMS analytical platforms: use case on pesticide exposure

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## Introduction

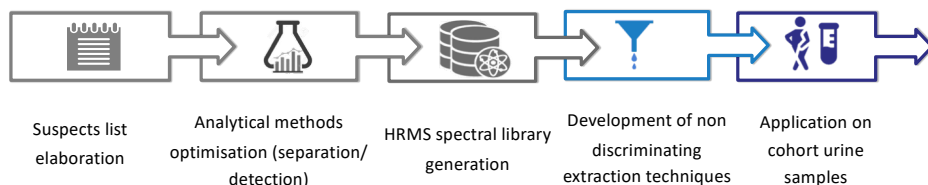
Human exposure to food and environmental contaminants (such as pesticides) is generally estimated by indirect methods. Targeted bio-monitoring is a way to assess the internal exposure on a limited number of substances, needing large sample amounts for analyses as rigorous and sensitive as possible. Thus, the human health risks associated with multi-exposure to complex mixtures currently remain under-explored. In this context, the SCREENPEST project aims at providing a unified methodology for large-scale characterisation of human internal exposure to pesticides, via a "suspect profiling" approach, using urine.



## Objectives

- Develop and set-up an harmonised analytical workflow including sample preparation, instrumental measurement and data processing.
- Increase the coverage on human exposure to pesticides by a non-targeted multiplexed approach.
- Test the method developed through urine samples from cohorts to study possible links between exposure and adverse health effects.
- Provide extended information capabilities for early warning on emerging substances and help for decision making.

## Developed workflow



### PÉLAGIE

- Mother-child cohort (France, 2002-2006)
- Association between the exposure to pesticides of pregnant women and biometric data at birth
- Access to 168 samples



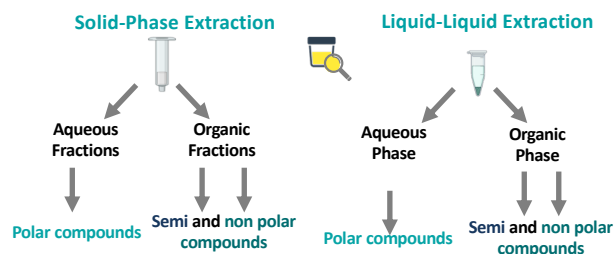
### NutriNet-Santé

- General population (France, since 2009)
- Association between the exposure to pesticides and the onset of type 2 diabetes
- Access to 200 samples

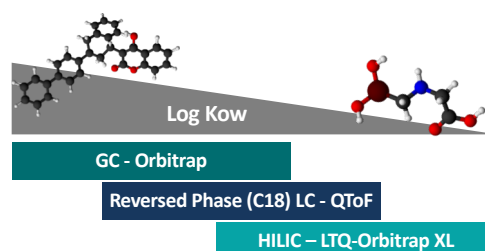
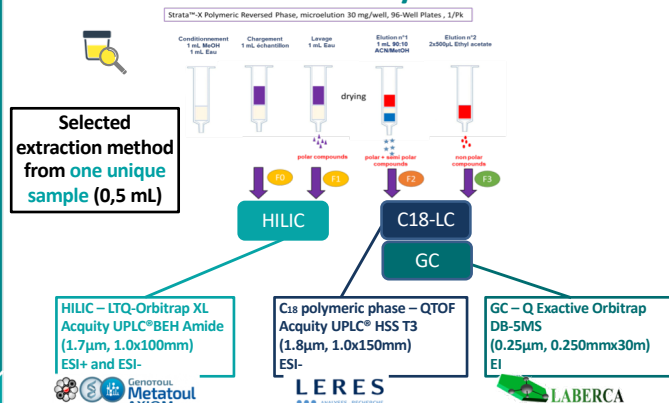
## Method development

- Large list of standards** (ca. 200 pesticides and phase I/II metabolites), covering a wide range of physicochemical properties (logKow: [-4.71;8.38], MM/g.mol<sup>-1</sup>: [72;720]) for analytical developments. Standard selection: commercial availability, bibliography, pesticide use in France (2019), epidemiologists expertise and available data from the HMB4EU project (10.1021/acs.analchem.2c00061)
- Optimisation of 3 HRMS techniques** to get the best separation and detection of the suspects by both LC and GC. Characterisation of the suspects by HRMS
- Optimisation of sample preparation**: various concentration levels (20, 50 and 100 ng mL<sup>-1</sup>) spiked in pooled urine (5 replicates).

Performance comparison of two non discriminating extraction techniques (recovery and matrix effect)



## Extraction and HRMS analysis



Analytical challenges to cover a wide range of compounds with:

- Different physicochemical properties :
  - Mol. weight [72;720]
  - Polarity / Log Kow [-4.71;8.38]
- Poorly characterised biotransformation products
- Low levels concentration

## Data treatment - Bioinformatic tools

- Extended HRMS spectral library of reference pesticides and metabolites.
- Complemented in house non-targeted and suspect screening chemo-informatics tools (XenoScreener / PeakForest / MetaboHUB W4M).
- Improved annotation and identification capacities on a large range of pesticides
- Statistical analysis and data interpretation (in progress)