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The SCREENPEST project: Development and implementation of an innovative large-scale screening approach for extended characterisation of human exposure to pesticides

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HAL Authorization

The SCREENPEST project:

Development and implementation of an innovative large-scale screening approach for extended characterisation of human exposure to pesticides

Margaux HEURTÉ¹, Fatima-Zahra Alem¹, Tarek Moufawad², Elodie Mirmont³, Jean-Philippe Antignac², Julia Baudry⁴, Emmanuelle Bichon², Nathalie Bonvallot¹, Cécile Chevrier¹, Ingrid Guiffard², Emilien Jamin³, Emmanuelle Kesse-Guyot⁴, Arthur David¹, Laurent Debrauwer³

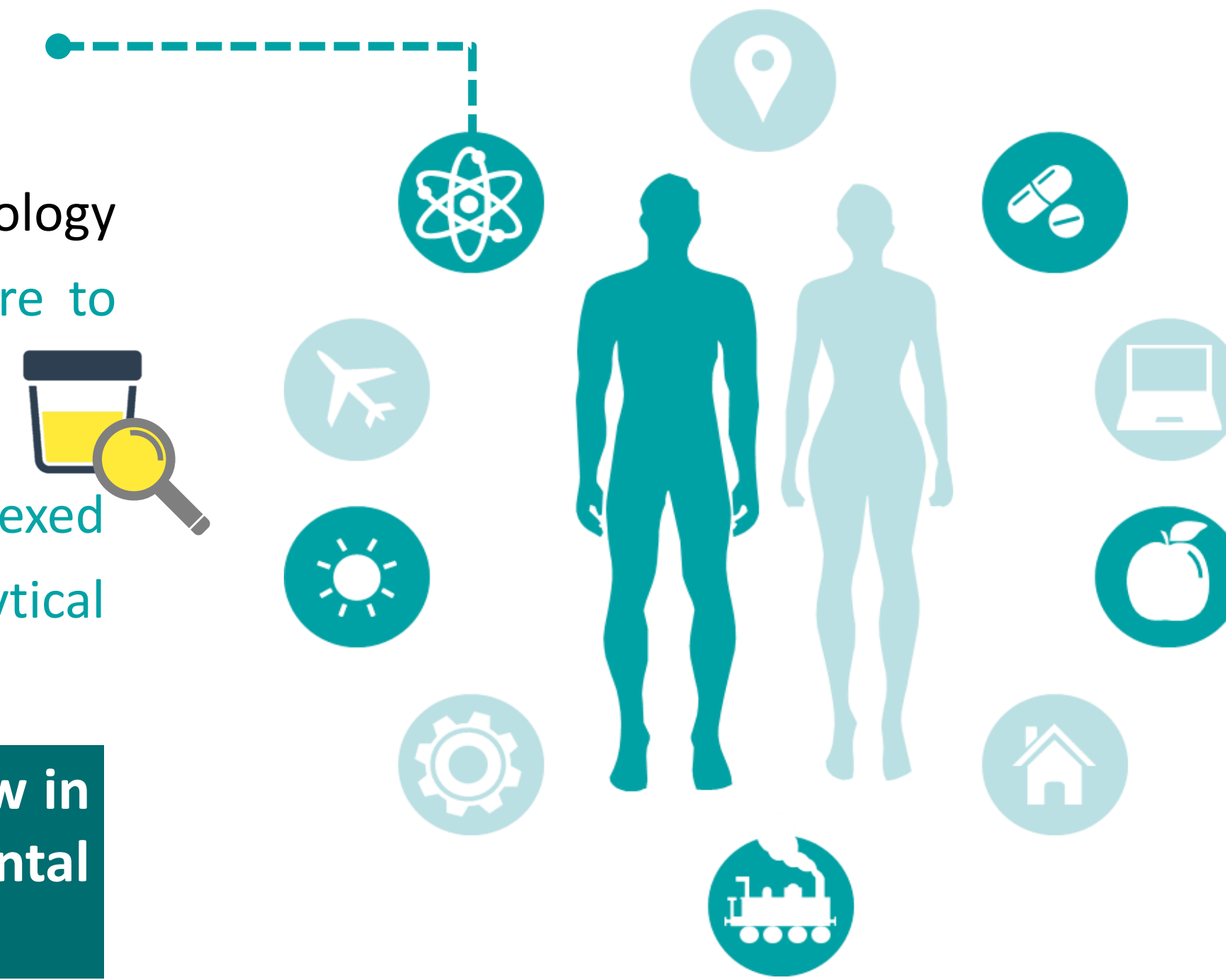
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Pesticides exposure assessment

The aim of the SCREENPEST project is to provide a methodology for large-scale characterisation of human internal exposure to pesticides, via a "suspect profiling" approach, using urine.

To gain access to this variety of compounds a novel multiplexed approach by profiling a single sample using different analytical platforms is needed.

Development of a harmonised analytical workflow in terms of sample preparation, instrumental measurement and data processing.



Cohort studies

PELAGIE

- Mother-child cohort (France, 2002-2006)
- Association between the exposure to pesticides of pregnant women and biometric data at birth
- Access to 200 samples

NutriNet-Health

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

Methodology & Sample Preparation

Elaboration of a large list of suspects, around 200 pesticides and phase I/II metabolites, covering a wide range of physicochemical properties for methodological developments. (logKow:[-4.71;8.38], MM/g.mol⁻¹: [72;720])

Commercial availability, bibliography, pesticide used in France in 2019, epidemiologists expertise and available data from the HMB4EU project.

10.1021/acs.analchem.2c00061

Optimisation of the 3 HRMS techniques to get the best separation and detection of the suspects (selected for development) by LC and GC.

Characterisation of the suspects by HRMS.

Optimisation of sample preparation: methodological developments at various concentration levels (20, 50 and 100 ng.mL⁻¹) in pooled urine in 5 replicates.

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

Solid-Phase Extraction

Liquid-Liquid Extraction

Aqueous Fractions

Organic Fractions

Aqueous Phase

Organic Phase

Polar compounds

Semi and non polar compounds

Polar compounds

Semi and non polar compounds

Extracts from one unique sample

Analysis of polar compounds

Analysis of semi and non polar compounds

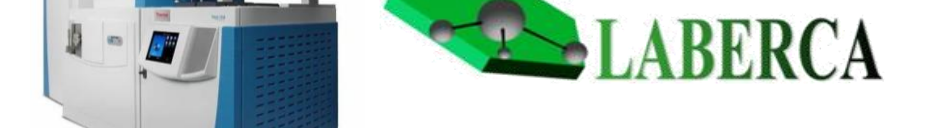
HILIC – LTQ-Orbitrap XL
Acquity UPLC® BEH Amide
(1.7µm, 1.0x100mm)
ESI+ and ESI-



C₁₈ polymeric phase – QTOF
ACQUITY UPLC® HSS T3
(1.8µm, 1.0x150mm)
ESI+ and ESI-



GC – Q Exactive Orbitrap
DB-5MS
(0.25µm, 0.250mmx30m)



HRMS Analysis



GC - Orbitrap

Reversed Phase (C18) LC - QToF

HILIC – LTQ-Orbitrap XL

Analytical challenges to cover a wide range of compounds with:

- Different physicochemical properties from a unique sample
- Poorly characterised biotransformation products
- Low levels concentration

Data treatment - Bioinformatic tools

Extending the HR spectral library of reference pesticides and their metabolites.

Complementing bioinformatic tools in non-targeted and suspect screening approaches using in house developed softwares (Galaxy, Scannotation).

Statistical analysis and data interpretation

Workflow



Elaboration of a list of suspects

Optimisation of the analytical methods

Generation of a HR spectral library

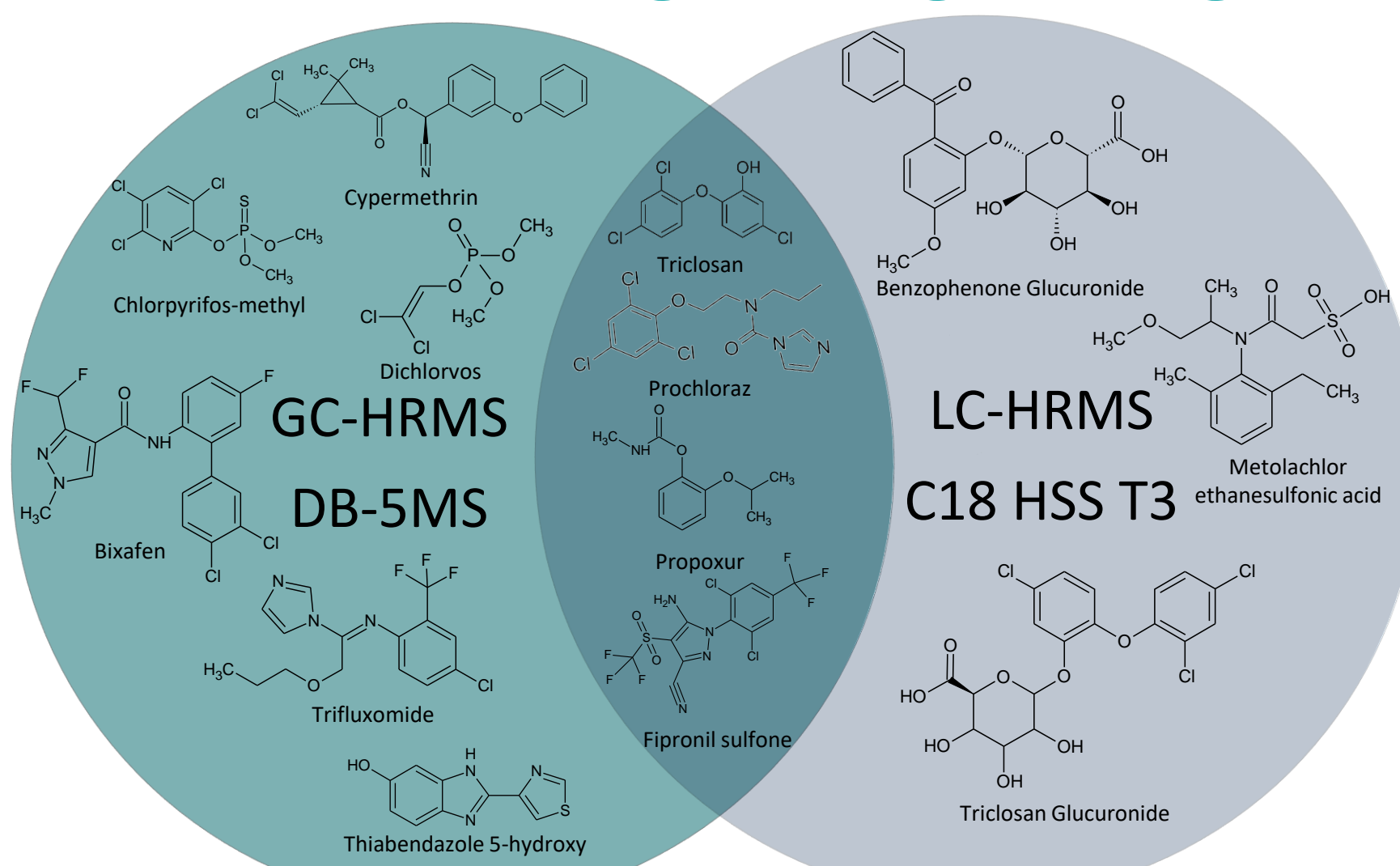
Development of non discriminating extraction techniques

Application on urine samples from PELAGIE and NutriNet-Health cohorts.

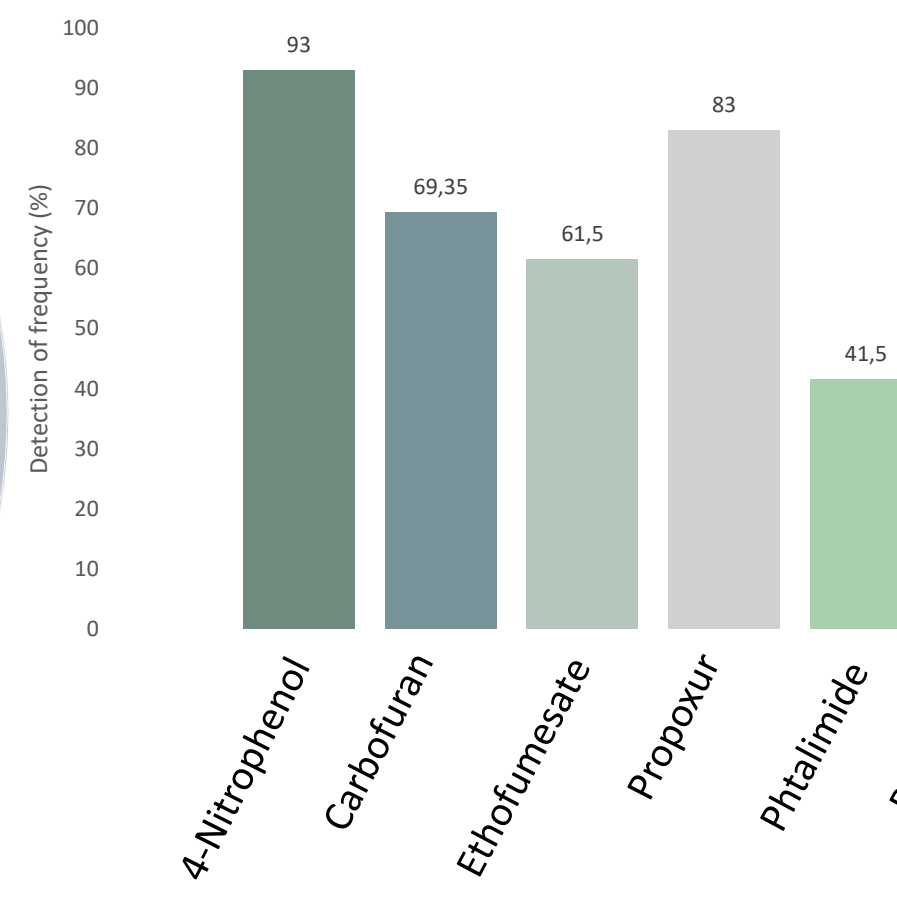
Study of QA/QC for NTA/SS (2 levels of concentration 20-100 ng.mL⁻¹)

Pre-Annotation of exposure biomarkers with open source software

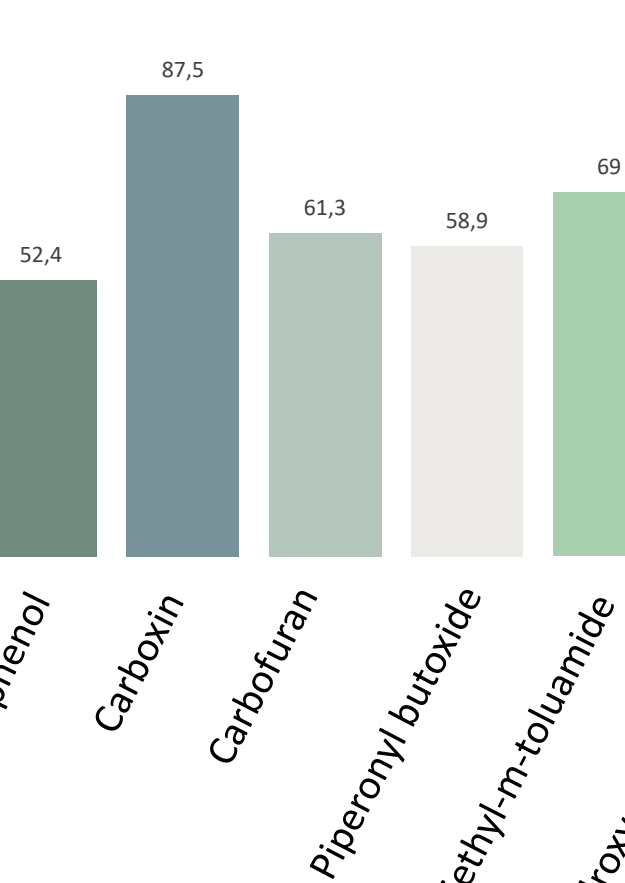
PRE-ANNOTATION BIOMARKERS EXPOSITION*



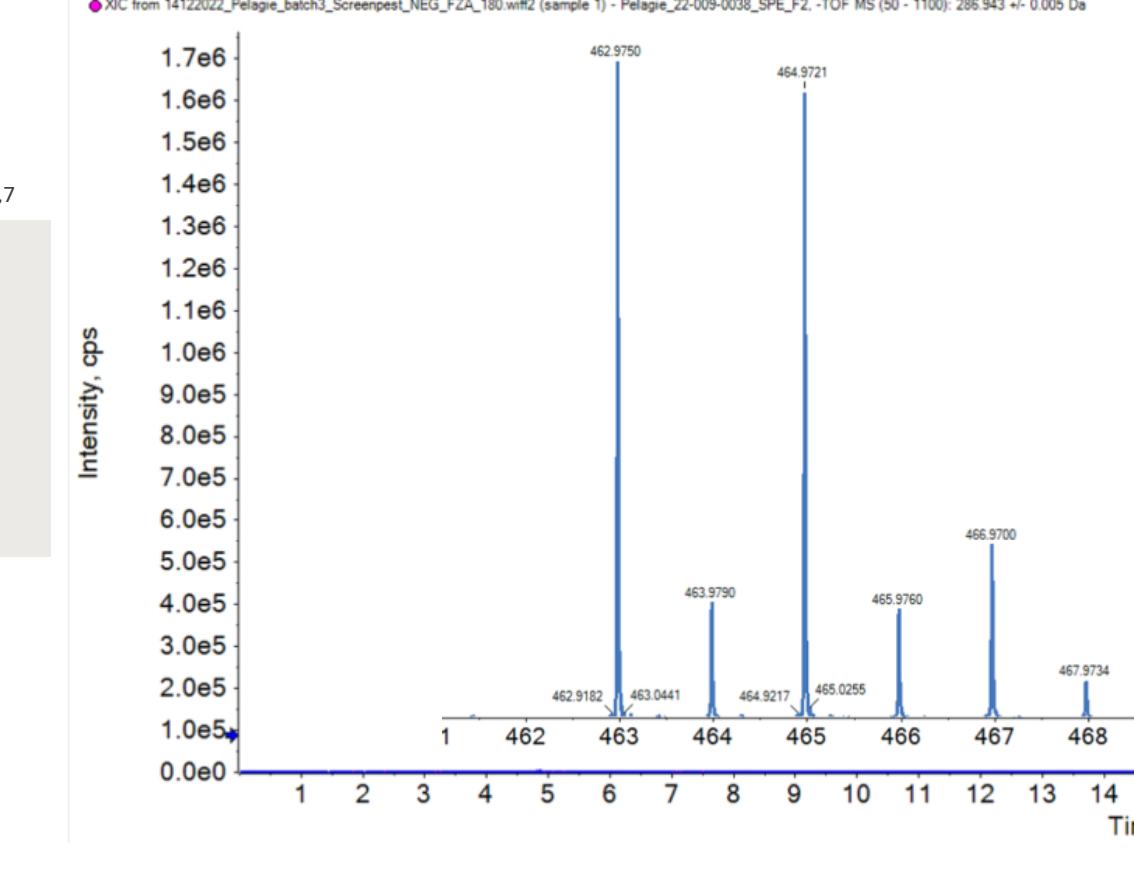
GC-HRMS Annotation (Cohort NutriNet)



GC-HRMS Annotation (Cohort Pelagie)



GC-HRMS Annotation (Cohort Pelagie)



Scannotation
AUTOMATED PRE-ANNOTATION

*The annotation are currently being validated through the study of MSMS results (annotation level 1 to 5) for LC-HRMS.

Conclusion: This multi-complementary project has demonstrated the complementarity of analytical methods for describing the large-scale chemical exposome using a single optimized analytical workflow. Multiple SS analysis highlights the presence of pesticides in their parent or metabolized form in LC-HRMS.