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Focus on the GC-HRMS based analytical development for characterization of human internal exposure to pesticides, in a multiplex inter-laboratory approach

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Focus on the GC-HRMS based analytical development for characterization of human internal exposure to pesticides, in a multiplex inter-laboratory approach

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Introduction

Pesticides exposure assessment

External exposure

Internal exposure

Questionnaire

Targeted Screening

Suspect Screening

Unknown Screening

Indirect

Estimation

Quantitative

Focused

Semi-Qualitative

Medium Scale

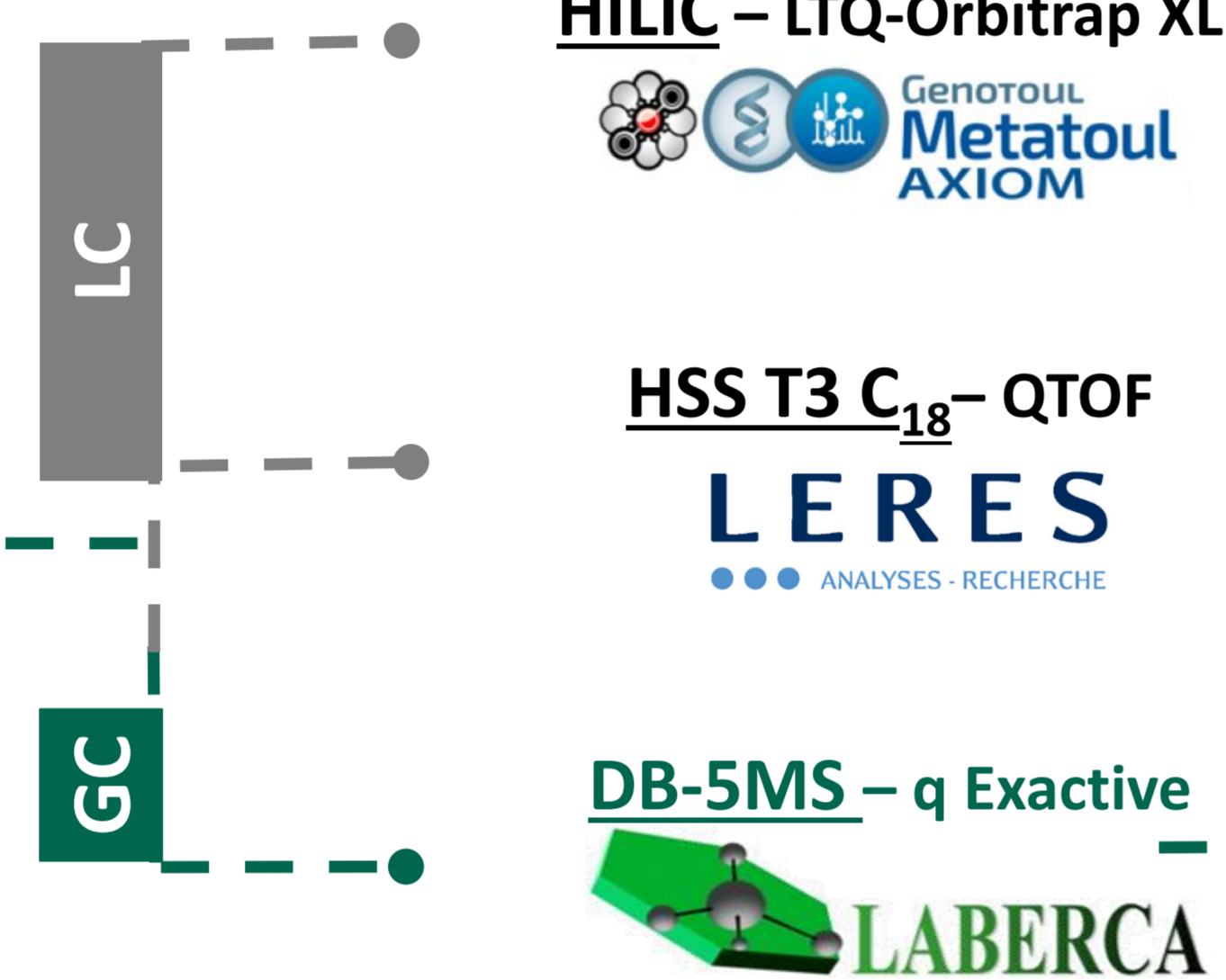
Qualitative

Large scale

The Screenpest Project

Providing a methodology for broad assessment of human internal exposure to pesticides, via suspect screening, based on urine samples.

Development of a unique protocol for analysis of a single urine sample by 3 complementary analytical platforms providing extensive picture of the internal exposure to pesticides, including both parent compounds and metabolites.

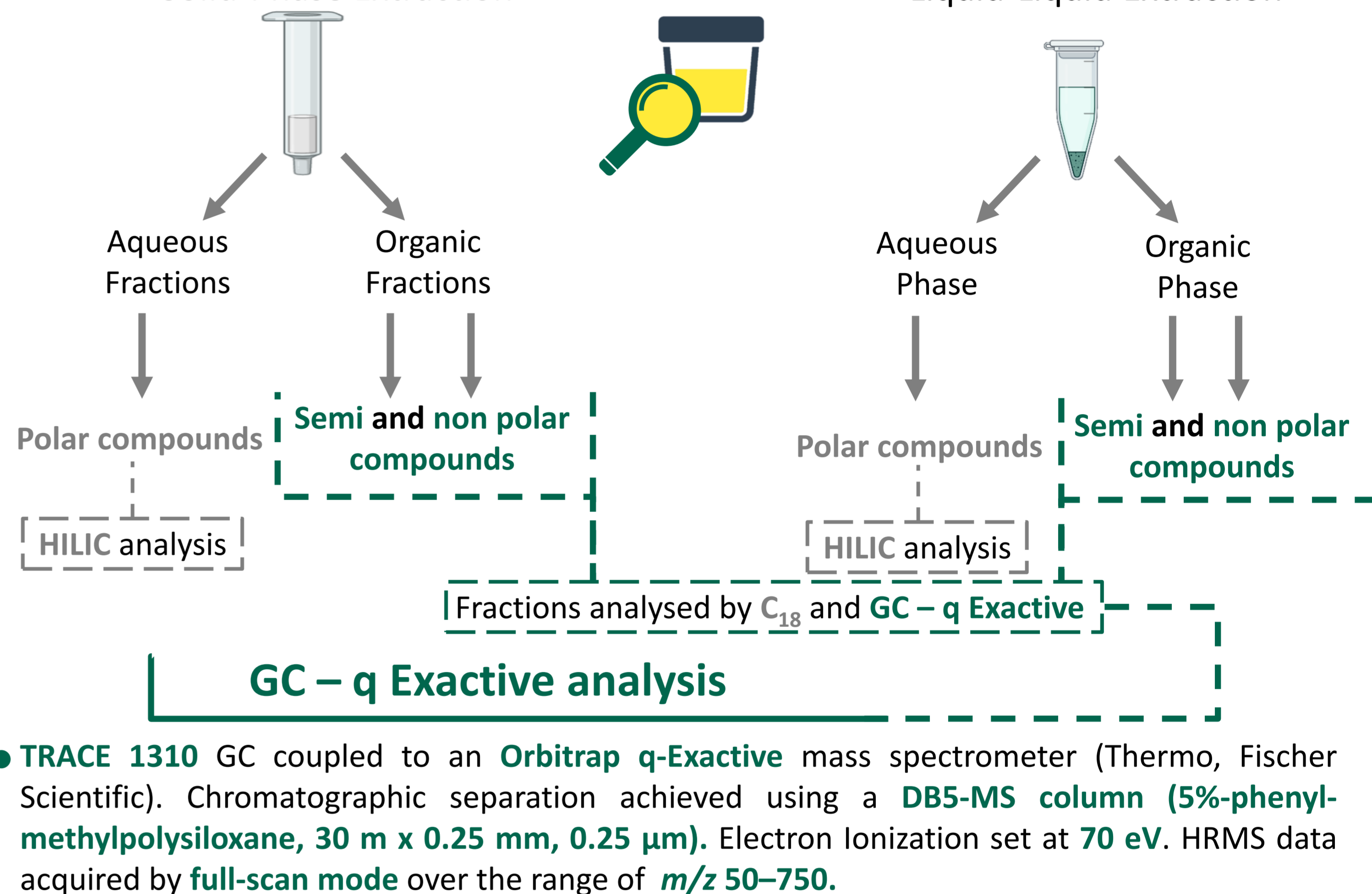


Experimental

Extraction Techniques

Solid-Phase Extraction

Liquid-Liquid Extraction



Results and Discussion

Suspects List

Pesticides **suspect list** elaborated based on commercially available compounds, known pesticide usage in France, epidemiological expertise and extensive database elaborated from the HMB4EU project.

Novel multiplexed approach allowing to cover a wide structural diversity.



HRMS spectral libraries

1-For Suspect Screening

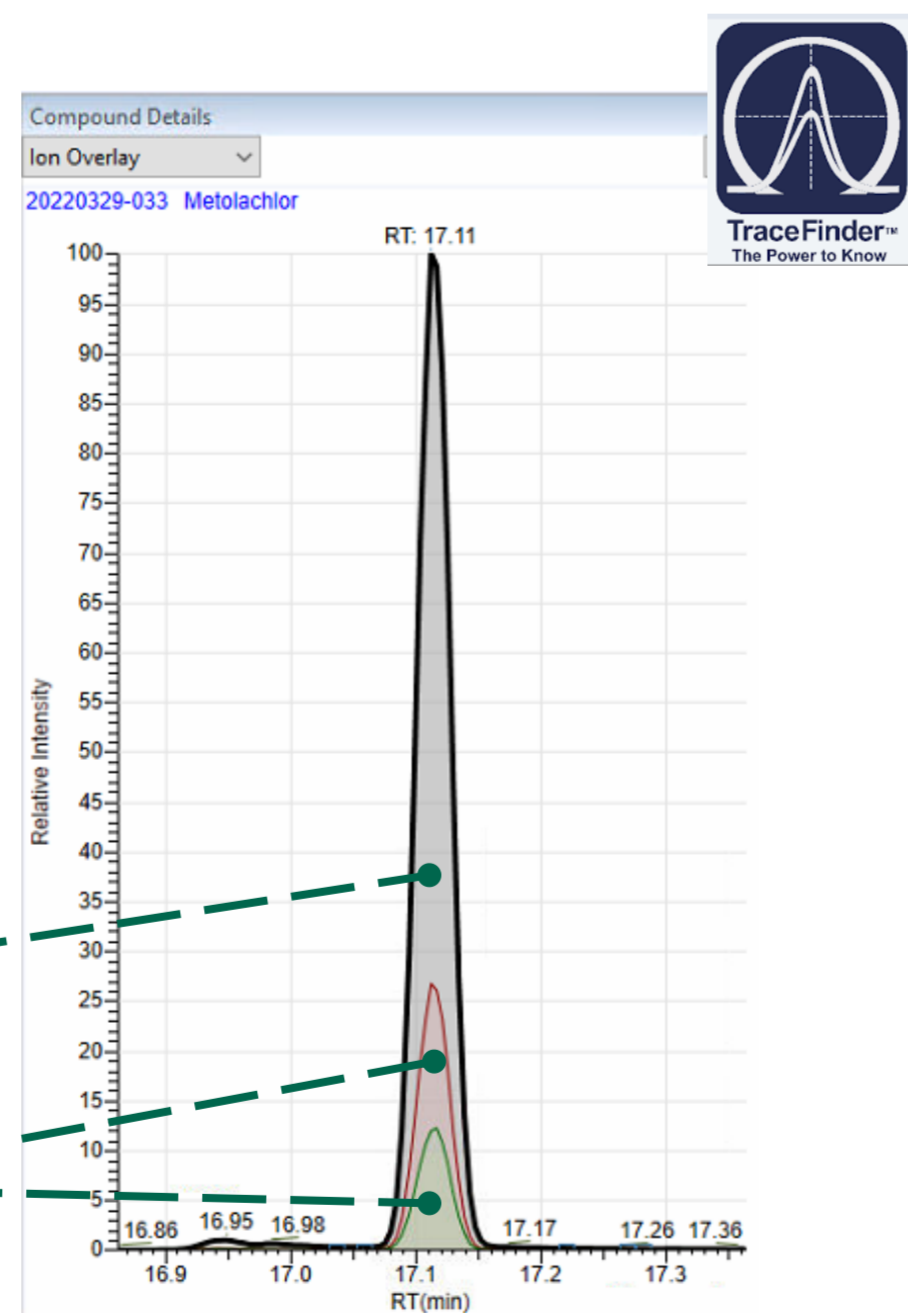
A first **experimental spectral library** was built using TraceFinder (ThermoFisher), allowing the **annotation** of the detected **exposure markers** with a **high confidence level**, using the following criteria:

- Retention time
- Base peak (most abundant fragment ion)
- 2 additional fragment ions
- 2 m/z abundance ratios between the base peak ion and the 2 additional fragment ions

Highest annotation/ Identification confidence level of - Level 1/2 (based on Shymanski scale)
doi.org/10.1021/es5002105

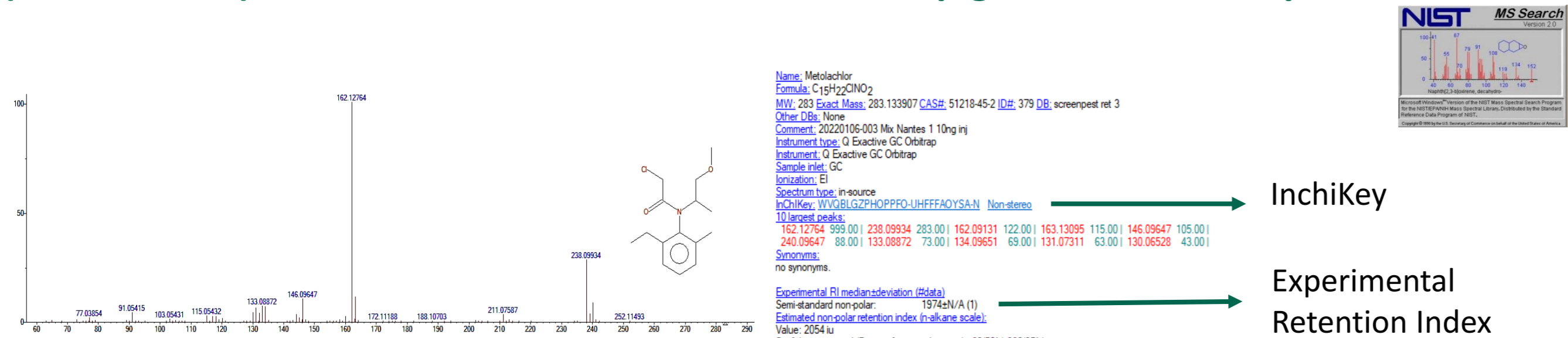
Base peak used for detection and quantification

Additional fragments used for the confirmation of the detected analytes, with an acceptable ion ratios



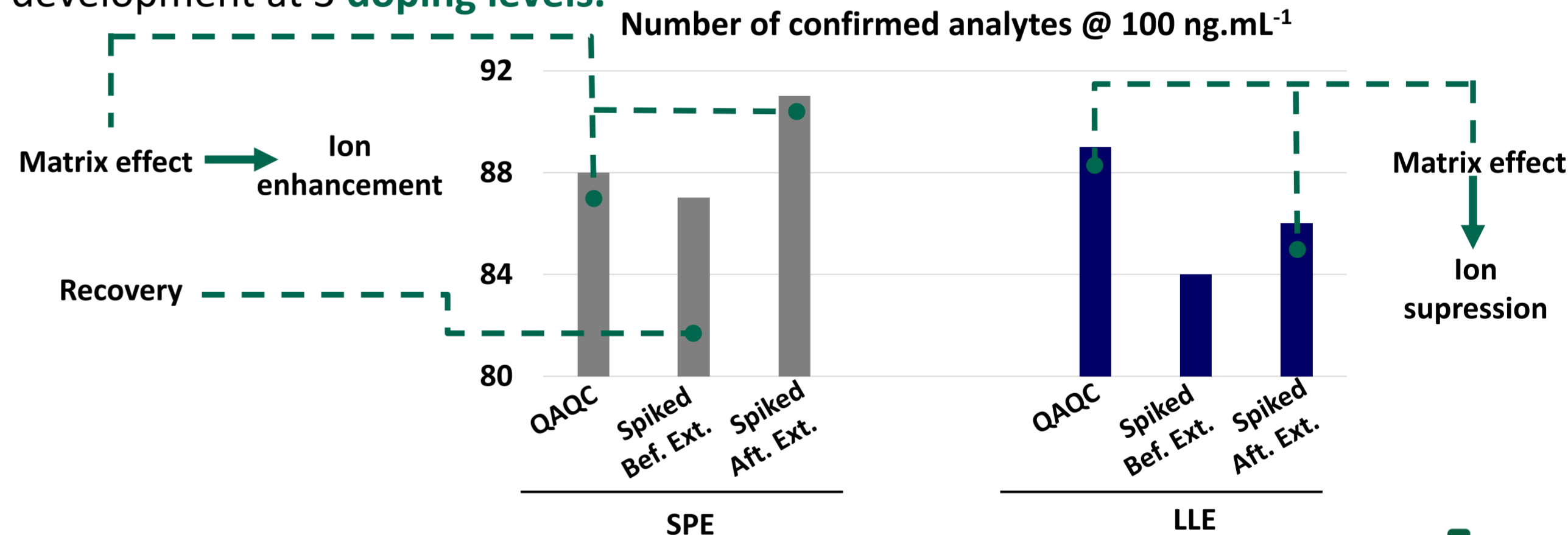
2-For Unknown Screening

A second **experimental spectral library** was built using **MS search NIST software**. The use of the NIST database gives access to a **well documented, interchangeable and universal HRMS library**, which can be **integrated** into in house annotation softwares (Peakforest...) or **enrich online libraries** with Orbitrap generated mass spectra.



Method development

103 compounds were used as **QA/QC markers** as **positive control (pooled urine samples)** for GC method development at **3 doping levels**.



GC-MS performance maintenance

- Boosting GC performances :** → Using Focus Inert Liner, pure cyclohexane & septa 100% PTFE without siloxane
- Handling and Monitoring** the q-Exactive system, focused on the **Ion source** : → Repeller and the different lens voltage, throughout cleaning and adjustment.
- QA/QC** → On cue system **pre-check & control chart** from QC all along the batch

Exposure markers detection

11 pesticides were successfully detected and confirmed in **real human pooled urine** → **Confirmation of the applicability** of the developed technique for **suspect and unknown screening approaches**

Conclusion & Perspectives

- Elaboration of a **suspect list** covering **200 substances** with a **wide range of physicochemical properties**
- Elaboration of an **experimental extended HRMS spectral library** of reference pesticides and their metabolites
- Evaluation of **different extraction techniques** for pesticides extraction from urine samples
- Development of a **GC-HRMS based workflow** for characterising **human internal pesticides exposure**
- Detection and confirmation of **11 pesticides related exposure markers** in **real pooled human urines**
- Application of a multiplexed approach on real urine samples from (PELAGIE / NutriNet-Health cohorts) → Linking **pesticides exposure** with possible **adverse health effects**
- Increase the knowledge of the **human exposome to pesticides**
- Early warning on **emerging substances** & Weighing in the **decision making**