

## Proposal for NORMAN Joint Programme of Activities 2025

<b>Title</b>	<b>Comparison of non-target screening (NTS) workflows across laboratories in chemical exposome studies</b>
<b>Type of activity</b>	Interlaboratory Study (ILS)
<b>Leader</b>	Prof. Nikolaos S. Thomaidis (National and Kapodistrian University of Athens -NKUA-) in collaboration with Prof. Pablo Gago-Ferrero (Spanish National Research Council -CSIC-) and Prof. Jonathan Martin (Stockholm University -SU-)
<b>Topic / activities</b>	<p><b>Background / Justification for the proposed activity:</b></p> <p>The extensive production and use of anthropogenic chemicals across the society has led to significant emissions in the environment and widespread human exposure. The assessment of human exposure levels to anthropogenic chemicals can be assessed indirectly through the analysis of samples from the ambient environment (water, soil, air) or directly by analyzing human biospecimens [biofluids (e.g. blood, urine) or tissue (e.g. hair placenta)]. The systematic and comprehensive monitoring of xenobiotics using human biospecimens and their linkage with metabolomic alterations and adverse health effects can provide critical information to support stakeholders in improving chemical management practices across Europe.</p> <p>Human biomonitoring studies typically focus on the detection and quantification of specific classes of potentially hazardous chemicals and common metabolites using triple quadrupole mass spectrometers, known for their high sensitivity and wide dynamic range. In contrast, high resolution mass spectrometry (HRMS) allows for a more comprehensive screening of the <u>chemical fingerprints</u> of anthropogenic chemicals in biological samples through wide-scope target, suspect and non-target screening approaches. The <u>harmonization of chemical regulations in Europe</u> has driven the need for common strategies in monitoring xenobiotics. The establishment of dedicated NTS approaches in exposome studies is essential for the prioritization of hazardous chemicals and, thus, protecting the human health.</p> <p><b>Description of the proposed activity and expected outcomes for 2025 (and beyond):</b></p> <p>The proposed JPA seeks to <u>address existing knowledge gaps in the harmonization of non-target screening (NTS) workflows</u> currently used in studies focusing on chemical exposure. Current methods show variability across laboratories, leading to inconsistencies in data quality and interpretation. This JPA aims to identify differences in the currently applied analytical methodologies across laboratories and, thus, enhance the understanding of xenobiotics present in human biological samples.</p> <p>For this purpose, a diverse set of samples, including (i) serum extracts and (ii) "blind" serum extracts (spiked with numerous xenobiotics at different concentration levels) and (iii) the respective serum samples, will be distributed to participating laboratories. For quality control purposes, the sample set will also include reference standards and procedural blanks. Each participating laboratory will conduct independent analyses using their chromatographic and HRMS conditions, as well as their in-house NTS workflows and optional extraction using their in-house sample preparation protocols.</p> <p>The primary objectives of this interlaboratory study are the evaluation and comparison of:</p> <ul style="list-style-type: none"> <li>• <u>Analytical techniques</u>: Assessment of the applied instrumental methods employed by different laboratories, focusing on their efficacy in separating and identifying a broad range of xenobiotics.</li> <li>• <u>Post-acquisition data processing workflows</u>: Assessment of the applied workflows used in data processing, including <i>in-silico</i> tools and algorithms for peak picking, prioritization, feature alignment, and annotation of unknown features using a specific suspect list (e.g. PubChemLite for Exposomics).</li> <li>• <u>Semi-quantification approaches</u>: Assessment of the semi quantification strategies currently applied to estimate the reported concentrations.</li> </ul> <p>By systematically evaluating these objectives, the JPA aims to highlight consistent HRMS based NTS approaches to foster a <u>comprehensive monitoring of xenobiotics and their metabolites in exposome studies</u>.</p> <p><b>Timeframe and expected outcomes:</b></p> <ul style="list-style-type: none"> <li>• March 2025: Distribution of a detailed questionnaire to all participating laboratories to gather information on current NTS workflows and methodologies.</li> <li>• April 2025: Shipment of sample extracts, including (i) serum extracts and (ii) "blind" serum extracts, (iii) serum samples to each participating laboratory for analysis.</li> <li>• August 2025: Submission of DCTs from all participants, summarizing the analytical methods, data processing steps, and findings.</li> <li>• November 2025: Accomplishment of statistical analysis; conceptualization of conclusions based on interlaboratory comparisons.</li> <li>• January 2026: Publication of a comprehensive report summarizing the findings of the proposed ILS.</li> </ul> <p><b>Added value / Link with other NORMAN activities and / or other projects:</b></p> <p>The proposed activities of the present JPA link with the activities of Cross-Working Group Non-target Screening (NTS).</p>



	Other potential collaborations include links to The European Partnership for the Assessment of Risks from Chemicals (PARC).
<b>Participants</b>	Potential participants are all NORMAN network working group members.
<b>Proposed in-kind contribution</b>	The findings from the proposed JPA, along with recommendations, will be submitted for publication in a high-impact, peer-reviewed journal.
<b>Contribution needed from NORMAN Association<sup>1</sup></b>	sample preparation, shipment related costs, publication fees Total requested: <b>€ 12,000.00</b>

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<sup>1</sup> Please, provide here a transparent justification of the requested resources and of the in-kind contribution, thereby distinguishing between the costs associated with “person-months” for the organisation, the “travelling costs” for invited speakers and the costs for the logistics (e.g. meals, room rental etc.)