



Proposals for NORMAN Joint Programme of Activities 2024

Title	Bringing together NTS and toxicity – Cooperation between DSFP and MlinvitroTox, MS2Tox and other tools
Type of activity	Research and database development
Leader	Eawag and Environmental Institute (EI)
Topic / activities	<p>Background / Justification for the proposed activity: Analytical laboratories routinely conduct daily measurements employing high-resolution mass spectrometry (HRMS). Despite advancements in target and suspect screening workflows, a significant proportion of signals detected in samples remain unidentified, posing a challenge to comprehensive chemical analysis. This challenge prompted NORMAN laboratories to organize and share the HRMS data with the scientific community, a task facilitated by the Digital Sample Freezing Platform (DSFP). DSFP processes the data through an optimized and standardized workflow generating component lists that retain all useful analytical information from the mzML files, including the HRMS/MS spectra of isolated precursor ions. Within these spectra lies valuable information about unidentified chemicals. Recent demonstrations have highlighted the use of fragmentation information in conjunction with machine learning models to predict toxic effects. This means that a combination of fragments can drive specific effects. Employing this approach seeks to enhance the understanding of chemical effects, a task that remains challenging even for well-known endpoints when considering only target compounds. This strategy aids in the prioritization of unknown substances and also holds the potential to increase the percentage of explained effects, contributing to a more comprehensive understanding of chemical impacts.</p> <p>Description of the proposed activity and expected outcomes for 2024: The proposed activity serves as an early-warning system for chemicals and their potential impact. Leveraging HRMS data obtained from the Joint Danube Survey 4 (JDS4), known for its comprehensive characterization, we aim to employ a two-pronged approach. First, we will aggregate existing target and suspect screening chemical occurrence data and evaluate their contribution to measured effects. Subsequently, employing HRMS data stored in DSFP, we will analyze spectra of unknown compounds, allowing us to predict individual contributions to the overall effects and discern the drivers of specific endpoints within complex mixtures. Our strategy is expected to increase the percentage of explained effects and highlight the contributions from unknown components. This activity, functioning as an early-warning system, holds the potential to identify specific signals indicative of chemical hazards. If a limited number of signals prove relevant, we can proceed with a full identification workflow. Our overarching goal is to utilize advanced hazard tools and tap into the wealth of component lists harmoniously stored in DSFP. This comprehensive approach, if applied at large scale, ensures not only effective monitoring but also the potential for early intervention and risk mitigation in the realm of chemical impact assessment.</p> <p>Added value / Link with other NORMAN activities and / or other projects -Deployment and use of hazard assessment tools in DSFP -Provide input to the new prioritization scheme (NORMAN WG1) -Tentative identification of drivers for well-known endpoints (connection with NORMAN WG2) -Making a step to bring non-target screening closer to regulation (NORMAN NTS CWG) -Enrichment of the bioactivity database, which hosts known structures and their effects -Early-warning system for chemicals (Connection with PARC T8.2) -Preparation of a new tool for further testing in the upcoming JDS5</p>
Participants	NKUA, UBA, SU, UFZ and any other interested NTS laboratory.
Proposed in-kind contribution	Testing the integration of hazard assessment and NTS tools. Writing a scientific publication based on the outcomes of the activity.
Contribution needed from NORMAN Association¹	Building database infrastructure and technical support to make the tools readily available to the research community (9,000 €)

¹ 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.)