

Proposals for NORMAN Joint Programme of Activities 2022

Title	Optimal in vitro genotoxicity bioassay testing strategy
Type of activity	Research
Leader	KWR
Topic / activities	<p>Background / Justification for the proposed activity:</p> <p>Bioassays can be applied for assessment of relevant hazards of individual substances, but also for complex environmental mixtures. Multiple (standardized) in vitro genotoxicity bioassays that cover different modes of action have been developed for (drinking) water quality assessment or adopted from genotoxicity assays that are applied in a regulatory context (for registration of chemicals, pharmaceuticals and food and feed ingredients), but a testing strategy for hazard and risk assessment is currently lacking. Due to the different modes of action in genotoxicity, more than one bioassay is needed for thorough hazard and risk assessment. Moreover, there are non-standardized assays available that may be of added value.</p> <p>In 2018, the performance of seven standardized and non-standardized in vitro genotoxicity bioassays has been investigated in a NORMAN collaborative trial. Twenty-four laboratories blindly tested five samples, including chemical mixtures dissolved in dimethyl sulfoxide and wastewater treatment plant effluent. This joint effort was a starting point for analysis of the performance of different bioassays. The large variations in responses observed within and between different bioassays emphasized the need of using harmonized protocols for (drinking) water quality assessment. A scientific publication on this research is currently in preparation (draft manuscript is available).</p> <p>In addition to experimental research, the performance of in vitro genotoxicity bioassays for (drinking) water quality assessment can also be investigated by data analysis of existing data of individual substances. For bioassays that are frequently used, such as the Ames fluctuation test and umu-test, quite a bit of data is available from literature. The performance of different bioassays on the same individual substances can be compared between different bioassays and with available in vivo genotoxicity data or human carcinogenicity data. This exercise will result in a proposal for an optimal (tiered) testing strategy supported by data science. Depending on the outcome of this project, follow-up research on optimisation and standardization could be prioritized.</p> <p>Description of the proposed activity and expected outcomes for 2022:</p> <p>Databases on the Ames fluctuation test, umu-test and p53-CALUX have already been build up as part of ongoing projects at KWR. Further expansion on databases will increase the robustness of the proposed testing battery. Feasibility of adding data of the micronucleus and comet assay will also be investigated (large differences in experimental procedures are expected for these bioassays).</p> <p>Based on available data on individual substances, an optimal (tiered) in vitro testing strategy for genotoxicity in (drinking) water quality assessment will be proposed. The goal is to develop a cost-effective testing strategy by using a minimal number of assays without losing accuracy on the prediction of potential genotoxicity. This approach is in line with in vitro genotoxicity testing batteries that are applied for regulatory purposes, but a testing strategy specific for (drinking) water quality assessment may include different (non-standardized) bioassays. The proposed testing strategy will guide stakeholders of the water cycle, in particular drinking water utilities, water boards and public health authorities, in hazard and risk assessment and herewith safeguard human health.</p> <p>Added value / Link with other NORMAN activities and / or other projects</p> <p>This project links to research and discussions in NORMAN working group WG-2 (Bioassays and biomarkers in water quality monitoring) by designing an optimal (tiered) in vitro testing strategy for genotoxicity in (drinking) water quality assessment. There is a link with the NORMAN collaborative trial on bioassays for genotoxicity testing (link to final report) for which a scientific publication is currently in preparation. In addition, there is a link with the further development of the bioactivity database based on the blueprint presented in 2020 (link to final report). This includes work on properties of a prototype and inclusion of case study data (e.g. data 100 compounds study UFZ), with respondents of the questionnaire for contributing data.</p>
Participants	<p>KWR Water Research Institute (the Netherlands)</p> <p>Astrid Reus, MSc.</p> <p>Dr. Renske Hoondert</p> <p>Contribution of laboratories that were involved in the NORMAN collaborative trial on genotoxicity testing is preferred.</p>
Proposed contribution	<p>KWR will use the databases on the Ames fluctuation test, umu-test and p53-CALUX that have already been build up as part of ongoing projects at KWR.</p> <p>NORMAN members will be asked to share their (qualitative) in-house data on individual substances on genotoxicity bioassays to further expand the database.</p>



Contribution needed from NORMAN Association¹	<p>Activity 1: Enquiry to NORMAN members for participation in this project</p> <p>Activity 2: Expansion of the database with data received from laboratories and quality check of the dataset</p> <p>Activity 3: Data analysis using R</p> <ul style="list-style-type: none">- Selection of substances for which data is available from multiple bioassays- Calculation of possible outcomes when using single or multiple bioassays in a testing battery- Selection of a minimal number of bioassays without losing accuracy on the prediction of potential genotoxicity <p>Activity 4: Brief project outcome report in which the proposed testing strategy on genotoxicity will be described.</p> <p>Total: 10,000 EUR</p>
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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.)