

Proposals for NORMAN Joint Programme of Activities 2023

Title	NORMAN WG Prioritisation activities
Type of activity	Working Group activities
Leader	INERIS in collaboration with EI and UBA in collaboration with Ecotoxcentre
Topic / activities	<p>Background / Justification for the proposed activity:</p> <p>Better chemical management in line with the goals of the EU Chemicals Strategy and Zero Pollution Action Plan strongly relies on identification and control of pressures through efficient monitoring and knowledge of the properties and use patterns of chemicals. Given the high number of chemicals present in our environment, prioritisation of chemical contaminants is highly demanded by regulators and decision-makers in order to identify and justify the most urgent actions necessary to achieve these goals.</p> <p>The tasks of WG-1 are aimed to:</p> <ul style="list-style-type: none"> - Ensuring that all relevant information for assessment of chemical risks is maintained and regularly updated in a timely manner - Integrating and exploiting all this information for identification of lists of chemicals in need of priority actions (each priority list corresponds to an action). <p>In 2021, the new version of the NORMAN prioritisation framework, combining target and suspect-screening data, has been proposed, and subsequently been tested on a large-scale case study on wastewater in 2022. In this context, a number of tools: e.g. IP score, semi-quantified data approach, EMPODAT-Suspect Database, have especially been created and tested to support the new workflow and enable its integration in the NORMAN Database System (NDS). Further development in the implementation of the new workflow and upgrading of the on-line prioritisation tool are postponed to 2022/2023 (Task 6, 7 and 8), taking in mind considerations of the EU PARC project - Task 4.2 (mechanism for identification of priority actions for environmental monitoring, and EDC and PFAS monitoring campaign) and Task 8.2 (European Early Warning System), as well as the EEA indicators for Zero Pollution Action Plan and Green Deal research projects.</p> <p>The NDS Ecotoxicity Database module has been improved, with now almost 90,000 substances covered by predicted PNECs and more than 5,000 compounds for which experimental toxicity studies are available. The Ecotoxicity module has also gained in performance, thanks to the implementation of new functionalities. However, most of the data are related to the water compartment and it is now necessary to put more effort to extend the scope to new compartments and also to cover new prioritisation objectives in 2023. For example, it was proposed to derive protection values for reuse of reclaimed water in agriculture and prioritise the compounds which need to be controlled in the water resource before use in agriculture (collaboration with WG 5 on water re-use, see Task 2 and Task 3, JPA 2022).</p> <p>In 2022, the EcotoxCentre adapted their national database to enable direct export of PNECs and raw data to the NORMAN ECOTOX Database using the newly harmonised DCTs. The workflow applied to the whole database in 2022, and the exported PNEC files from EcotoxCentre are currently being verified and will be uploaded to the revised ECOTOX database module by the end of 2022. This initiative will be pursued in 2023.</p> <p>Another important step for improvement of the prioritisation activities will be the systematic collection and classification of information about the <i>uses of compounds</i> and the development of approaches to group the compounds based on these use(s), on functional groups or modes of action, etc. (see Task 5).</p> <p>We need also to consider mixture toxicity and to identify the compounds which – even if they are not exceeding threshold values individually – contribute to mixture risks (see Task 4).</p> <p>Description of the proposed activity and expected outcomes for 2023 (and beyond):</p> <p>Task 1: Support the prioritisation work of the Commission services at European level and provide comment on relevant consultation documents (PARC, EWS, where relevant) (ALL)</p> <p>NORMAN participates as a stakeholder in the WG Chemicals of DG ENV and intends to further contribute to the activities related with the review of the list of WFD Priority Substances and the Watch List. In 2022, NORMAN provided proposals for the 4th review of the Watch List.</p> <p>In 2023 NORMAN WG-1 will be able to contribute to the PARC partnership on the following prioritisation-related topics:</p> <ul style="list-style-type: none"> ▪ Collaboration in the <i>development of the mechanism for priority setting in environmental and multi-source monitoring – MonitoringFrame project</i> (PARC T4.2.1). The NORMAN scheme could be proposed as a starting point for the design of the prioritisation mechanism in PARC. Thereby, the action categories approach was already recognised as an efficient and pragmatic way to address regulatory questions while addressing existing data gaps. Next steps will be to extend the scope of

the NORMAN approach: the prioritisation should cover multi-compartments and should address human and environmental health. Overall, the ambition is to define a cross-regulation and cross-compartment prioritization mechanism, where the selection of chemicals/matrices/endpoints (effects) would be based on multiple lines of evidence.

- Contribution to the *selection / prioritisation of EDCs for the PARC pilot monitoring study*: Suspect screening of the list of candidate EDCs in the samples of the DSFP to have an overview of the estimated frequency of occurrence of these compounds and estimations of semi-quantified concentration levels.
- *Early Warning System for Europe (EWS)*

Task 2: Collection and compilation of compound-specific information in support of prioritisation (UBA / EI / NKUA / DERAC)

In 2022, efforts focused on harmonisation of the current PNEC collection templates to meet the revised NORMAN Ecotoxicology Database metadata requirements. The DCT template was upgraded and the respective transformation tables from the source files were revised, e.g. harmonisation of PNEC type, quality / robustness of the PNEC, associated matrix and protection asset (to ensure a harmonised ontology). At the end of 2022, the curated and harmonised PNEC data were re-uploaded into the database to fit the new layout.

Further to the finalisation of the above-mentioned harmonised DCTs, it will be possible to start the extraction and **compilation of additional experimental ecotoxicity data from other existing ecotox databases** in 2023, i.e. the REACH portal and the UBA ETOX database, which was still pending from JPA 2020. **Regulatory quality targets for reused matrices** were collected and compiled under WG-5 2022 activities and will be uploaded in the Ecotoxicity database. This activity **will continue in 2023** (see Task 3 of the WG-5 JPA 2023 proposal).

*In order to enable the conversion of $PNEC_{C_{tw}}$ for application to other matrices, the **compilation of experimental data for physico-chemical properties, like the BCF and Koc**, is crucial and will therefore be pursued in 2023. Moreover, data on **other hazardous properties (ED, CMR, PBT, PMT)** will be retrieved from **CLP dossiers** and integrated in the Substance Factsheets to support the hazard score in the prioritisation module. One example regards the evaluation of the PBT and PMT criteria, where a P score is now assigned to 65,000 compounds in the SusDat list, thanks to the fruitful cooperation with UBA and the implementation of the JANUS model for prediction of PBT criteria in the NDS. It is planned to **extend the model predictions to the remaining compounds in SUSDAT**.*

Task 3: PNEC derivation module (UBA / EcotoxCentre / DERAC / EI)

For 2023, it is proposed to **continue with the predictions of acute toxicity values for species** of at least three trophic levels to **derive P-PNECs for the compounds that have recently been added to SUSDAT**.

Moreover, it is proposed to **extend the existing QSAR models to cover additional species (3 additional fish species and 2 insects) and additional species sensitivities and MOAs**. The final aim is to enable a more robust statistical approach for the derivation of freshwater P-PNECs and their subsequent conversion for application to other matrices.

The upload of existing PNEC and the derivation of new PNECs will be revised in 2023 to **include MAC-EQS values as well as values for the marine environment** (delayed from JPA 2022). This will allow the evaluation of marine monitoring data, as well as peak exposure concentrations, such as those resulting from the German small water body monitoring project. **Moreover, new compartments, such as soil or sediments should be added in 2023** to extend the scope of the current prioritisation scheme, to allow consideration of multiple lines of evidence from different compartments.

In order to assess the internal concentrations in biota samples (i.e. LifeApex) with regard to potential effects in top predators, it is proposed to **compile a set of about 10,000 experimental rat toxicity endpoints**, as commonly available from HH risk assessments, **to derive a new ecotox threshold** for the protection of birds and mammals, in line with the principles of the risk assessment of PPPs. This should **enable prioritisation of chemicals that have potential detrimental effects if accumulated in birds and mammals**. To cover also compounds without experimental data, a respective **QSAR model it is planned to be developed based on the experimental datasets** mentioned above.

WG-1 will continue to promote and coordinate the participation of Ecotoxicity Experts to derive and approve (i.e. vote for) new or revised Lowest PNEC values for substances of the SusDat list, with a specific focus on substances that were highly prioritised in EU projects using the NORMAN Prioritisation Framework. The aim is to progressively replace predicted PNEC values for substances prioritised in Cat 3 and 5, by experimentally-based PNEC values, with a special focus on comprehensive datasets, including new data.

Task 4: Integration of a Mixture Risk Indicator (UBA / INERIS / EI)

This activity was started end of 2021. The aim is to identify and prioritise compounds for which there is no or limited evidence of exceedance of the toxicity thresholds, but there is a chance that they contribute to

mixture risks at the local scale, because they are frequently present just below their quality thresholds (i.e. RQ comprised between 0.1 and 1). The new Mixture Risk Indicator (MRI) should enable the identification and prioritisation of these compounds. This new indicator is complementary to the existing Frequency of Exceedance (FoE) and Extent of Exceedance (EoE) of the Lowest PNEC that so far only considered single compounds exceedances. In this way, compounds in Cat. 6 could be better distinguished and ranked to ensure that compounds are not overlooked.

In 2022 the MRI was tested on different datasets from Germany and from France. Some preliminary results from the application on the French data (NAIADE, national database for the freshwater compartment) were presented at the WG-1 meeting. As a follow-up in 2023, it is planned to organise some consultation meetings with WG-1 experts and PARC to reach consensus on how to integrate this new indicator in the NORMAN/PARC prioritisation scheme and the associated online prioritisation tool. It is also planned to draft a paper on this topic.

Task 5: Compilation of data / information regarding 'Use categories' and 'Chemical Functional Use' for all SusDat compounds (LCSB / UBA / INERIS / EI)

The following has already been proposed at the WG-1 meeting in June 2022 and has subsequently been discussed among some experts, but the operational implementation of the task is postponed for 2023. With the ever-growing number of NORMAN SusDat substances, it becomes inevitable to group them by 'Use category' and 'Chemical groups category'. The NORMAN Substance Factsheets already contain information retrieved from the US EPA Dashboard, but at present this is not sufficient to allow searching in the NDS by e.g., all pesticides, all herbicides; all pharmaceuticals, all antibiotics; or by, e.g. all PFAS, pyrethroids, PAHs, ionic surfactants. The classification of the compounds is not trivial, since each substance has often multiple uses and associated sub-classes. The different approaches applied for categorisation of the uses (e.g. by REACH, US EPA Dashboard, PubChem) are not fully harmonised. In the same context, categorisation of transformation products and their linkage to single / multiple parents is another challenge that NORMAN wants to address.

The collection of this information is crucial to the prioritisation work (e.g. identification of contamination sources for which actions are required, exploitation of lists of substances).

To achieve this objective, we propose to organise a strategy within WG-1 in line with the on-going collaboration between NORMAN and PubChem addressing the following sub-tasks:

- a) Finalise and approve the DCT template (as agreed on in the last WG1 meeting). This will require controlled vocabulary and a common understanding about "use categories" and "functional uses". We should aim at a harmonised classification for NORMAN as well as for PARC.
- b) The DCT should be uploaded into a newly developed sub-module and should be used as an interface for experts to be able to interact online (to upload the information and amendments where needed). All changes made by the experts should be traceable (as it is done in the Ecotox module). All the information (use and functional categories) will be directly linked and searchable from the Substances factsheets / SusDat and the prioritisation system.
- c) Discuss in consultation with the WG what the best platform is to create a group repository for NORMAN to exchange expert views and establish harmonised "use" terms (e.g. Gitlab, Github page for the NORMAN network similar to MassBank consortium). Should the platform be open to NORMAN members only? We propose it should also be open to external experts like the PARC consortium? (LCSB^o)
- d) The DCT is meant to be a living tool. The experts in WG-1 are invited to regularly review and upgrade the categories (e.g. add the mode of action) and harmonise the drop-down entries. Volunteers in WG1 will be appointed to be in charge of complex groups of compounds (e.g. all REACH or PFAS compounds) to suggest their categorisation.
- e) Extraction of "Use" information from the various SLE lists (already available) and export of this information into PubChem (LSCB & PubChem Team, part of SLE activities) and into the DCT (citing SLE as the reference source). WG-1 members will help to prioritize the most relevant lists.
- f) Pilot efforts to retrieve "Use" information from PubChem and other sources (e.g. Wikipedia, Wikidata, USEPA Dashboard, ChemSpider etc.) and integrate them into the Use category module. Translation tables will be created for each source to ensure harmonised entries compatible with the NORMAN Use category module. (EI, LCSB, UBA to be discussed)
- g) Programming the workflow resulting from the pilot efforts (cf. e) for the transfer of the information retrieved from PubChem and other sources into the Use category module (EI)

Task 6: Prioritisation framework: follow-up activities to apply the new workflow beyond the freshwater compartment and across compartments and for specific chemical groups (ALL)

In 2022, the NORMAN workflow for prioritisation of chemicals, integrating both target and suspect screening data, underwent a detailed consolidation phase involving as main steps:

- the refinement, validation (using data from 4 different labs and different types of instruments) of the IP score, which is now part of a paper by Alygizakis et al. (paper in review).
- the exploitation of the results of the WW effluents case study (wastewater effluents from SOLUTIONS (12 WWTPs), JDS4 (11 WWTPs), UFZ JPA 2019, Germany (34 WWTPs) and other European countries).

All this represents a significant progress. The work was presented at the SETAC NonTarget2022 conference. However, the drafting of a publication proposed by INERIS on the new methodology was

delayed due to high workload and hence will be postponed to 2023.

The focus of 2023 will be on:

- a) **Development of the IT infrastructure (EI and ALL):** the development of the appropriate infrastructure to support this new prioritisation workflow. The final goal is to implement the online prioritisation tool linking the compounds' data in SUSDAT, target monitoring data (EMPODAT), suspect screening data (EMPODAT-SUSPECT under construction) and PNEC values in the ECOTOXICOLOGY database. The design of a prototype is already under way (see NDS factsheet). It is planned that the features of such a prioritisation tool (interface, type of queries, parameters, etc.) will be defined in consultation with the experts in WG-1 (meetings to be organised in 2023) and PARC (Collaboration in Task 4.2.1) before the programming phase (low fidelity >> high fidelity prototype).
- b) Initiate the **design of a multi-compartment, integrated prioritisation framework (ALL)**, starting from the results of the three case studies listed below and literature review (i.e. proposal of a global score, integrated visualisation of the action categories / ranking from the different matrices):
 - Danube River Basin Specific Pollutants based on wide-scope target and suspect screening using JDS4 data
 - Black Sea Specific Pollutants based on wide-scope target and suspect screening using EMBLAS project data
 - Prioritisation of contaminants in top predators and their prey using LIFE APEX project data.
- c) As regards the substances, NORMAN WG-1 will focus on **EDCs, PFAS and PMT compounds** in support of PARC and Green Deal projects (**WG-1 and PARC**).
- d) **Prioritisation of contaminants in soil (WG-1 and WG-7):** WG-1 will contribute in the project "Non-target screening in soils – towards harmonized methods and a priority list" (proposed by UBA) (duration: 3 years). One of the main aims of this project is to obtain a list of priority chemicals in soils. The work of WG-1 together with WG-7 will focus on the application and upgrading of the NORMAN prioritisation workflow (NTS & target data) to the specificities of the soil compartment. A series of meetings will be devoted to discuss the approach.
- e) **Prioritisation of contaminants in reused matrices (WG-1 and WG-5):** in 2022, WG-5 updated six EMPODAT DCTs (i.e. WWTP, surface water, groundwater, sediment, soil, biota) to collect and compile occurrence data on reused matrices. Regulatory quality targets on reused matrices were also collected for upload in the Ecotoxicology database and overall contribute to the WG-1 prioritisation framework. In 2023, the support from WG-5 will focus on the application and upgrading of the NORMAN prioritisation workflow to the specificities of the reused matrices.
- f) Identification of list of ranked SusDat chemicals relevant for **acquisition of their chemical standards or MS(MS) information** allowing for target screening (**UFZ, Eawag, LCSB**). This task has already stated in 2022. A list of candidate compounds for acquisition of mass spectra in MassBank was prepared by EI and INERIS in 2022, using the results of the WW case study (NTS prioritisation scheme applied on the list of 65,690 SUSDAT compounds suspect screened in 84 WW effluents from 19 countries (LC-HRMS in ESI+/-). The final selection of a list of the "most wanted" spectra by UFZ will take into account the information available in NORMAN SLE, PubChem and CompTox, and check which compounds are not in MassBank or other open spectral libraries already. Once purchased and measured, the data should become available on the NORMAN database system (e.g. MassBank, NORMAN-SLE).

Task 7: Prepare input to the Early Warning System for Europe (WG-1 and T8.2 PARC) (to be pursued in 2023)

Task 8: Lessons learnt from the case studies: improving the features of the prioritisation tool (consultation and programming activities) (ALL) (this task planned in JPA 2022 was not started and will be postponed to 2023)

An expert consultation within WG-1 will be organised to upgrade the interface and the features of the current on-line prioritisation tool.

At the moment, there is a set of parameters that can be defined before running the prioritisation (e.g. substance, country, year). There are also parameters that are integrated in the queries (e.g. choice of the dilution factor when we perform the prioritisation on wastewater effluent datasets).

Further additional features could be discussed. Some examples are given:

- Since we now want to extend the application of the prioritisation framework to other compartments and matrices (soil, terrestrial ecosystems, marine environment, etc.), it is useful to design the interface to automatically select the proper PNEC, depending on the matrix and the prioritisation objective. For example, if we want to prioritise contaminants in reclaimed water for reuse in irrigation, we might need to select the wastewater effluent datasets labelled as "reclaimed water / reuse irrigation" and match the concentration data with the corresponding PNEC_crop, specific for protection of human health.
- We can also discuss the possibility of improving the "proxy pressures" metadata field in the current Data Collection Templates for the monitoring sites. This field is already included in the DCTs but it is not mandatory and it has rarely been filled in by the data suppliers. This metadata and the associated drop-down list could be revised by the experts based on the lessons learnt. This information is in fact very valuable for interpretation of the prioritisation results and for the selection of sub-datasets. It might also help to verify certain high concentrations.
- Integration of the Mixture Risk Indicator (MRI) in the results of the prioritisation module. This is

	<p>connected with a previous task (see Task 4), where we will define the integration of this new indicator in the overall scoring system of the prioritisation framework.</p> <ul style="list-style-type: none"> - Options for the spatial visualisation of the prioritisation results. <p>This task will be organised in two steps:</p> <ol style="list-style-type: none"> 1) Meetings (virtual, if possible 1 physical meeting) for consultation of the WG-1 experts and PARC: proposals / desk work to revise the features of the prioritisation tool 2) Programming work: the programming work is expected to start in the second part of the year 2023 after agreement with the WG-1 experts, based on dedicated instructions derived by a smaller team of experts (resources: an envelope will be set aside for possible expenditure in 2023, in line with the outcomes of the consultation within WG-1). <p>Task 9: State of the environment in Europe (this task planned in JPA 2022 was not started and will be postponed to 2023) (EI and ALL)</p> <p>We would like to integrate the results of single substances risks at certain sites into a total effect, by mapping the concurrent occurrence of chemical contaminants in Europe, across compartments: e.g. “how many compounds exceed the lowest PNEC at each site”?, or “what is the total mixture risk at each site”? These might become new chemical indicators to measure progress in the quality of the environment e.g. as a result of remediation measures and inform policy decisions (cf. pesticides indicator of the EEA) about the trends. This would allow NORMAN to e.g. support the Zero pollution monitoring report of the EEA. Moreover, analysis of datasets regarding the minimum (most toxic compounds) compared to the total effect (mixture risk) might allow to derive an indication of a retrospective mixture allocation factor (MAF) in support of the COM EGD initiative.</p> <p>Added value / Link with other NORMAN activities and / or other projects</p> <ul style="list-style-type: none"> - Support the preparation of the programme of activities of the PARC partnership, with particular focus on inventory of existing data and common knowledge on chemicals in order to identify gaps in data and anticipate future trends. - Support the implementation of an Early Warning System for Europe (DG ENV) - Support to DG ENV / JRC for the review of the list of WFD Priority Substances, the Watch List for surface water and the Watch List for groundwater. - Support other MS or RB if requested. - Support prioritisation of CECs as Sea Specific Contaminants in the marine environment (OSPAR, HELCOM, MED POL, Black Sea Commission). - Links with WG-5 for identification of priority contaminants in treated wastewater intended for reuse - Links with WG on Soil and the Terrestrial environment for prioritisation activities. - Link with NTS CWG, in particular as regards DSFP, SLE and the definition of a mechanism for updating the NORMAN List of emerging substances as top priority substances of SusDat. - NORMAN MassBank: prioritisation of relevant compounds whose mass spectra are not yet included in the online repository MassBank.
Participants	INERIS, EI, UBA, Ecotoxcentre, NKUA, LCSB, ISSeP (All WG-1 are welcome)
Proposed contribution in-kind	<p>Ecotoxcentre: Contribution of raw data collection for Swiss EQS Dossiers, Compilation of existing national EQS and validation of NORMAN PNEC proposals.</p> <p>UBA: Compiling of single substances dossiers and a list of pesticide RAC values.</p> <p>INERIS: Coordination of the WG, pursue the work for the review of the prioritisation methodology and testing of the “revised methodology” on five case studies. Proposals for improvement from lessons learnt (Task 1, 5, 6, 8)</p> <p>EI: Testing of the “revised methodology”. Contribution to Tasks 1, 6, 7, 9.</p> <p>LCSB: Extensive efforts associated with the NORMAN-SLE and related collaborations</p> <p>DERAC: contribution to Task 2, 3 and 6 for the application and upgrading of the NORMAN prioritisation workflow to the specificities of the reused matrices.</p>
Contribution needed from Association¹	<p>Total net budget under JPA 2023: 15,000 € (plus budget not spent in 2022 and postponed to 2023). See details below.</p> <p>Task 1: Support the prioritisation work of the Commission services at European level and comment on relevant documents and queries (PARC, EWS, where relevant). (in kind)</p> <p>Task 2: Collection and compilation of compound-specific information in support of prioritisation</p>

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.)

(UBA/EI: 4,000 €)

- Extraction and compilation (automated retrieval using script) of experimental ecotoxicity data from existing ecotox databases
- Compilation and uploading of regulatory PNECs for marine compartment, biota, soil and sediments, including the respective MAC-EQS values
- Compilation of experimental data for physico-chemical properties, like BCF and Koc from ECHA dossiers and scientific papers
- Retrieval of other hazardous properties (ED, CMR, PBT, PMT) from CLP dossiers
- Application of the JANUS model for prediction of PBT criteria to the new entries in SUSDAT

Task 3: PNEC derivation module (UBA: 6,000 €)

- predictions of acute toxicity values for species from at least three trophic levels to derive P-PNECs for the compounds that have recently been added to SUSDAT
- extend the existing QSAR models to cover additional species (3 additional fish species and 2 insects) and additional species sensitivities and MOAs
- derivation of a new ecotox threshold for the protection of birds and mammals based on data from experimental rat toxicity endpoints
- development of a QSAR model to predict oral rat toxicity for derivation of P-PNECs for birds and mammals

Task 4: Integration of a Mixture Risk Indicator (MRI)

- see below Task 8 (EI: already included in the NDS Factsheet)

Task 5: Compilation of data / information regarding 'Use categories' and 'Chemical Functional Use' for all SusDat compounds

- Organisation and harmonisation / Collection and compilation of data / information available on 'Use categories' and 'Chemical Functional Use'. (LCBS: 3,000€ not spent in 2022)
- Programming the workflow resulting from the pilot efforts for the transfer of the information retrieved from PubChem and other sources into the Use Category module. (EI: 3,600 € not spent in 2022)

Task 6: Prioritisation framework: follow-up activities to apply the new workflow across compartments and specific chemical groups

- Follow-up of work done in 2022 (EI /UBA / INERIS: 5,000 €)

Task 7: Prepare input to the Early Warning System for Europe (EWS) (to be pursued in 2022)

Task 8: Lessons learnt from the case studies: improving the features of the prioritisation tool (consultation and programming activities)

- Update/programming of the prioritisation module bringing together target and suspect screening data.
- Interface to automatically select the proper matrix- and prioritisation objective-related PNEC; integration of the MRI in the NORMAN/PARC prioritisation scheme; design and update of the interface for spatial visualisation of the prioritisation results. (EI: 5,000€ envelope for possible expenditure postponed from 2022, to be used in line with the outcomes of the consultation within WG-1)

Task 9: State of the environment in Europe

- Programming of the module and visualisation of the results (EI / UBA / INERIS: 4,000 not spent in 2022)