

ENKORE Cluster Deliverable

SCIENTIFIC STRATEGY OF THE CLUSTER

Lead project	Cluster Coordination Team 2024: MERLON & ENDOMIX)
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1. Introduction

The Scientific Strategy of the ENKORE cluster aims to provide a clear and structured overview of the main strategic steps the projects will undertake to promote cross-project scientific collaborations to achieve their desired outcomes. This approach also aims to ensure maximum scientific impact from the five projects.

The ENKORE Cluster is comprised of five projects: MERLON, NEMESIS, EDC-MASLD, ENDOMIX and HYPIEND, funded under the EU call HORIZON-HLTH-2023-ENVHLTH-02-03 (Health impacts of endocrine-disrupting chemicals: bridging science-policy gaps by addressing persistent scientific uncertainties). The cluster will be active from 1 January 2024 until 31 December 2028 and will include several working groups.

Focusing on the health impacts of endocrine-disrupting chemicals (EDCs), the ENKORE cluster aims to bridge science-to-policy gaps and address persistent scientific uncertainties. The Scientific Strategy is designed to amplify the scientific output of individual projects by improving outreach to scientific communities, policymakers, and citizens. Additionally, the strategy emphasises identifying overlaps and complementarities in research focus to foster synergies between projects, thereby democratising important scientific skills and resources within the cluster and creating opportunities for high-impact outcomes.

This Scientific Strategy outlines the scientific objectives, methodologies, and collaborative efforts to be undertaken by the cluster during its operational period from January 2024 to December 2028.

This Scientific Strategy of the ENKORE Cluster is a living document, subject to revisions and updates throughout the duration of the ENKORE Cluster's activities.

2. Objectives of the Scientific Strategy

The ENKORE Scientific Strategy focuses on five key research priorities to address pressing health challenges related to EDCs and is tailored to facilitate the objectives of the ENKORE cluster's Scientific Policy objectives. The five research priorities for the cluster are:

1. Further characterise key life-stages, in humans, that are particularly sensitive to endocrine disruption.
2. Improve mechanistic understanding of causal pathways linking initial chemical stressor events with adverse health outcomes in humans.
3. Provide robust scientific evidence for the human health impacts of EDCs.
4. Develop New Approach Methodologies that are fit for purpose in identifying, testing and regulation of EDCs.
5. Facilitate interdisciplinary and cross-sectorial collaborations between the five projects and beyond.



ENDOMIX

HYPIEND



3. Methodologies

The Scientific Strategy of the ENKORE cluster focuses on leveraging the added value of cross-project collaborations and aligning with external initiatives and projects relevant to improving the identification and testing of endocrine-disrupting chemicals (EDCs) within the EU. Accordingly, the scientific strategies of the five individual projects are not detailed here. Instead, this strategy emphasises methodologies for facilitating collaboration across projects and initiatives and enhancing research outcomes for stakeholders. Key approaches include sharing common data where appropriate, organising joint workshops to promote the exchange of knowledge and skills, and establishing working groups to provide forums for ongoing collaboration.

Research and Data Sharing:

The ENKORE cluster projects have adopted a multifaceted approach to address the health effects of EDCs. Central to this effort is compiling comprehensive data information and knowledge base as described below that shed light on the many ways EDCs can impact human health. By consolidating findings from diverse studies within the cluster, researchers across the five projects (and within) aim to create a robust knowledge base that supports risk assessment and regulatory decision-making. A key strategy is, therefore, sharing data among projects where appropriate, to avoid duplication and foster synergistic efforts.

A central pillar of ENKORE, as an EU-funded research cluster, is the promotion of open science principles, specifically through the adoption of FAIR (Findable, Accessible, Interoperable, Reusable) data practices. These practices will be adopted by the Scientific Strategy to ensure that data generated within the five projects are not only accessible to researchers but also usable across diverse scientific disciplines, fostering collaboration and innovation as described in the deliverable “Cluster Common Data Management Plan”.

Advanced analytical techniques are employed for precise data collection and analysis, to achieve high-quality insights. These state-of-the-art methodologies enable the identification of subtle effects of EDCs, the characterisation of exposure levels, and the unravelling of complex interactions between EDCs and biological systems. The ENKORE Scientific Strategy will, through for instance joint research workshops (see below), aim to facilitate systems approaches across projects to account for multi-organ, multi-temporal effects in the identification of complex effect outcomes in humans at various life stages.

With the support of the European Commission’s Joint Research Centre (JRC), the five ENKORE projects will facilitate the sharing of chemical monitoring data through IPCHEM (the Information Platform for Chemical Monitoring). This is also described in the deliverable “Cluster Common Data Management Plan”.

This collaboration ensures that critical chemical monitoring data are readily available to support policymaking and enhance public health protection.

The ENKORE projects emphasize the development and dissemination of strategies for identifying EDCs and their mixtures. Examples includes roadmap to improve current regulatory systems by proposing amendments and enhancements and informing general public on strategies to minimise exposure to EDCs. These strategies will not only help pinpoint individual chemicals of concern but also elucidate the combined effects of chemical mixtures, the impacts of which are often more pronounced.

By deepening the understanding of how EDCs influence human health, these efforts pave the way for more effective interventions and regulatory measures. The ENKORE Scientific Strategy will strive toward



cross-project sharing of data and knowledge related to, for instance, human cohorts to establish more holistic and realistic picture of real-life human exposure to EDCs and potential health effects.

Interdisciplinary Workshops and Trainings:

Thematic workshops and training sessions will be pivotal to effectuate the ENKORE Scientific Strategy, address shared challenges and advance collective expertise in critical areas such as data management, science-policy linkages, and methodological advancements. By bringing together researchers, policymakers, and other stakeholders, these sessions will foster a collaborative environment in which innovative ideas and best practices can be shared. It will also serve as a checkpoint to capture activities running in the projects and other initiatives external to ENKORE, such as PARC, to avoid duplication of work and facilitate synergistic activities.

The ENKORE workshops will also be complemented by efforts to facilitate knowledge exchange and strengthen capacity among participants. Examples of such workshops could be to;

- Organise a teaching session/workshop on building AOP (by MERLON).
- Organise a workshop on analytical strategies to identify and characterize the EDCs (by EDC-MASLD).

Participants from all ENKORE projects could be invited and the workshop should be organised by the coordinating team. By providing platforms for dialogue and collaboration, these activities empower researchers and stakeholders with the skills and resources needed to tackle complex scientific and regulatory issues. The ultimate goal is to build a more interconnected and capable scientific community equipped to address pressing societal challenges.

The ENKORE cluster will organize 4 workshops throughout the lifetime of the project. The first workshop will be held in M24 (AOP Workshop), followed by three workshops on M36, M48 and M54 (see also Section 5, Workshop Plan).

The ENKORE cluster projects will also attend or participate in meeting sessions such as the Annual Forum on Endocrine Disruptors arranged by the EC.



Working Groups:

The Scientific Strategy for the ENKORE cluster foresees the expansion beyond the three existing working groups by emphasising the importance of fostering new working groups that address specific, critical scientific research questions. Such new working groups will be discussed at the ENKORE cluster meetings and at the annual meetings of ENKORE. With this, the strategy's objective is to encourage the development of collaborative research areas that can tackle specific challenges and enhance the depth and scope of the cluster's scientific exploration. A SharePoint platform was developed in ENKORE where an overview of the participants in the working groups and contact information is shared. At the ENKORE cluster homepage the WGs are described and contact point mentioned: <https://enkore-cluster.eu/about/working-groups/>

The following working groups 1-3 were already agreed upon at the coordinator's meeting on 12th of December 2023 and included in the document MODALITIES FOR IMPLEMENTING THE 'ENKORE' CLUSTER ON ENDOCRINE DISRUPTING CHEMICALS AND KNOWLEDGE ON HEALTH-RELATED EFFECTS. Please find below the 3 WGs and their Leads and co-leads.

WG1: Science translation for policy and practice (lead by MERLON, co-lead by NEMESIS and HYPIEND)

WG2: Data analysis/management and protection (lead by EDC-MASLD, co-lead by HYPIEND)

WG3: Communication and Dissemination (lead by ENDOMIX). For the last 12 months of the cluster activities, the leadership of WG3 will need to be shifted to another project since ENDOMIX will be finished.

New working groups will be established on key topics to ensure comprehensive and impactful research, as described in more detail below. These should support scientific synergies within ENKORE. The working groups will, for instance, include activities related to adverse outcome pathways (AOPs), which can provide mechanistic knowledge of adverse health outcomes and thereby facilitate EDC identification and provide a platform for targeting NAMs development and/or their implementation for regulatory use. Suggestions for new Working Groups (4 and 5) are:

WG4. Adverse Outcome Pathways: Advance the development of adverse outcome pathways to couple mechanistic data with adverse health outcomes, which is crucial for EDC identification and regulation. This working group will be co-led by MERLON and EDC-MASLD.

WG5. Innovative technologies: considering validation and regulatory applications: This group focuses on the alignment of the cluster research activities with the leading chemical regulatory frameworks and the aspects regarding validation and regulatory application of innovative technologies developed within the ENKORE projects. This working group will be co-led by NEMESIS and ENDOMIX.

The working groups will promote active participation and collaboration across projects, especially when scientific objectives overlap or shared methodologies could be leveraged to strengthen chemical testing strategies, including developing and implementing NAMs or identifying human-relevant effect biomarkers. This collaborative approach will foster cross-project communication, leading to more integrated research efforts and the potential for more robust and reproducible findings.

Finally, this strategy aims to establish standardised and common analytical tools, procedures, and databases to maximise data sharing and facilitate comprehensive utilisation of resources across



ENKORE

projects. By adopting uniform standards, the ENKORE cluster can ensure that data is seamlessly shared and effectively used, boosting the efficiency of collective research efforts and contributing to more meaningful scientific advancements.

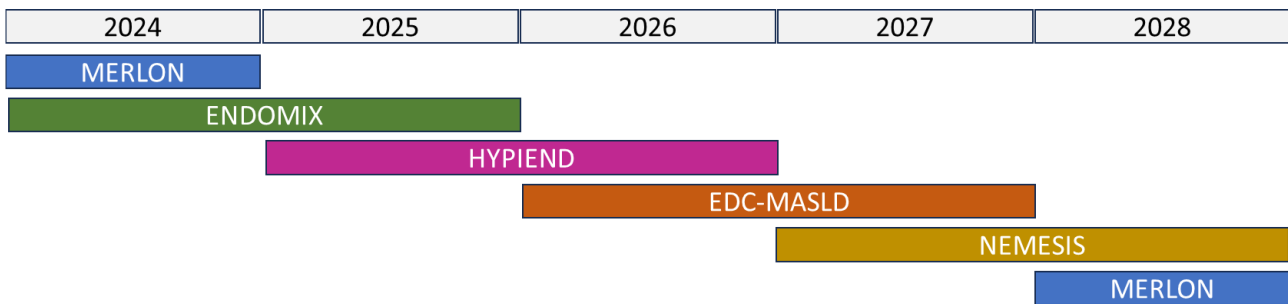


4. Governance

1. Cluster Coordination Team

The implementation of the ENKORE Scientific Strategy will be overseen by the five project coordinators and their deputies, who will assume rotating leadership roles on an annual basis. This dynamic structure ensures continuous oversight and seamless execution of strategy activities. To maintain consistent progress, two projects will be assigned joint responsibility for overseeing the operational execution of the Scientific Strategy at any given time. These joint leadership pairs, as depicted in Figure 1, will collaborate closely to coordinate efforts, monitor progress, and address any challenges that arise during implementation. This model fosters adaptability, shared expertise, and accountability among the project teams, contributing to the strategy's sustained success.

Figure 1: Structure of rotating stewardship of the five projects in the ENKORE cluster.



2. Risk Management

Number	Risk	Mitigation Strategy
1	Lack of engagement from project partners (likelihood: low, impact: high)	Coordinators holding stewardship will engage with coordinators of the remaining three projects. Likewise, project coordinators will engage and encourage active participation by their respective project partners.
2	Unexpected budget constraints (likelihood: low, impact: medium)	All partners have budgeted significant contributions to cluster activities (approx. 2% of total grant allocations), including cluster-wide workshops and working groups. Hosting meetings, workshops, and other events online rather than in person can reduce costs.
3	Failure to establish working groups (likelihood: low, impact: medium)	Coordinator teams must establish working groups across all five projects in the absence of active participating project partners. The establishment of additional working groups (WGs) can be considered during the lifetime of the ENKORE projects and should be discussed at online coordinators' meetings held several times a year. Regularly discussing this at each coordination meeting will help ensure the successful establishment of new WGs.

5. Scientific Strategy Activities and Actions

Opportunities for Scientific Synergies:

- Leverage the five projects' complementary expertise and research focus (EDC-MASLD, ENDOMIX, NEMESIS, MERLON, HYPIEND) to enhance the overall impact.
- Identify overlapping research areas to foster collaborative studies and data sharing.
- Engage with projects and initiatives external to the ENKORE project. Especially, all five projects will engage with PARC via the SYNnet programme.

New Working Groups (WGs):

The Scientific Strategy will be updated if new working groups are initiated.

Workshop Plan:

The ENKORE cluster coordination team, represented by all five projects, will organise four thematic workshops to address topics of common interest across the ENKORE cluster. These will be scheduled for M24, M36, M48, and M54. These workshops will be designed to foster collaboration, share knowledge, and align efforts across the cluster's projects.

The first workshop was planned and held in M5 (by ENDOMIX); this was not an ENKORE Cluster workshop, but all interested sister projects were invited to participate. This workshop focused on chemical mixtures, with a particular emphasis on exposure assessments and mixture risk assessment. This theme reflects the cluster's priority on tackling complex toxicology and risk evaluation challenges.

The themes of the remaining four workshops will be determined in alignment with the scientific strategy of the cluster, ensuring relevance to emerging research priorities and goals. Updates on these themes will be documented in the modalities of implementation for the cluster, maintaining a flexible and responsive framework for ongoing scientific engagement.

To maximise the impact of these workshops, they will be designed to be interactive and inclusive, involving active participation from all cluster projects as well as external experts and participants. This approach will promote a multidisciplinary exchange of ideas and strengthen the cluster's capacity to address shared scientific objectives.