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Contact: Sophie LARDY-FONTAN
sophie.lardy-fontan@lne.fr



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CONTEXT

- **Endocrine disrupting chemicals (EDC):** exogenous substances or mixtures which **alter** function(s) of the endocrine system and consequently **cause** adverse health effects in an intact organism, or its progeny, or (sub) populations.
- **Estrogens:** group of chemicals of similar structure mainly responsible for female sexual development and reproduction.
- **Pseudo-ubiquitous** and occur at **ultra-trace level** ($< \text{ng L}^{-1}$)

Substance	EQS (ng L^{-1}) (inland waters)
17-alpha-ethinylestradiol	0.035
17-beta-estradiol	0.4
Estrone	0.4



... level at which they can have effects in natural species \Rightarrow threat to **biodiversity**

Included in the first Watch List

- **No EN or ISO standard for MS-based methods** currently available or in progress
- (Accredited) testing laboratories **develop and validate in-house methods** according to internal criteria
- Most of (accredited) testing laboratories **failed to achieve the very low LOQ** to enable **monitoring of estrogens at EQS level**
- **Metrological endpoints** have been highlighted of particular importance if effect-based method (EBM) results are to be used in a regulatory context
- **Lack/absence of reference materials and proficiency tests**

Insufficient quality of measurements / data generated at EU level to support WFD process (risk assessment + prioritisation)

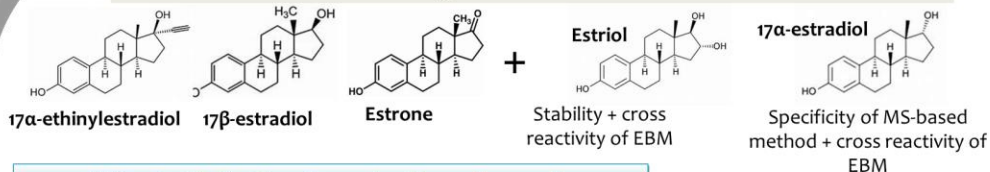
AIMS:

- ❖ **Address the standardisation lack for harmonised measurement methods for key EDC in whole water**
- ❖ **Ensure that measurements of EDC are traceable, well defined, meet the requirements of the WFD, and thus comparable across Europe**
- Collaboration between National Metrology Institutes and advanced research institutes from 6 European countries
- **A Balance of expertise:** development and certification of RM, proficiency tests / interlaboratory comparison design, method development and validation, standardisation
- **A 3 years project:** September 2019- August 2022
- Strong engagement with stakeholders (Advisory Group)

THE PROJECT



Targeted substances



Matrix

- Inland freshwaters: surface water and ground water
- Representative of European inland waters panel



WP1: Optimisation & evaluation of sample preparation methods

- **Stabilisation** of substances between sampling and analysis
- Optimisation of complementary extraction methods (LLE, SPE on-line/off-line, SPE-Disk)
- Evaluation of the ability of optimised sample preparation method to address **whole water**

DEVELOPMENT

WP2: Optimisation & evaluation of detection methods

- **Purity assessment** of calibrants/analytical standards
- Optimisation of complementary MS-based methods (GC- or LC- hyphenated to MS² or HRMS)
- Optimisation of selected EBM in vitro bioassays (ER-Calux[®], A-YES, L-YES, ERA)
- Comparison of optimised detection methods

Comparison

Evaluation

WP3: Evaluation & Demonstration of fitness for purpose of the methods

- Feasibility and preparation of a synthetic **real-matrix reference material(s)** for selected estrogens
- **Interlaboratory comparison**
- Demonstration of **methods' validity** and **equivalency of measurements**

Comparison

Evaluation

Focus on key metrological endpoints

➤ Fully validated MS-based reference methods:

- Validated MS-based reference methods in whole water samples at EQS levels with:
 - ❖ 30% EQS ≤ LOQ ≤ EQS
 - ❖ **U ≤ 50% at EQS**
- Specified capability of developed methods to address the different fractions of matrix

➤ Comprehensive study on the partitioning of estrogens in water:

- Knowledge of interaction and partitioning between water and suspended particulate matter

➤ Well characterised effect-based methods and measurements:

- ❖ **Definition of measurand**
- ❖ 30% EQS ≤ LOQ ≤ EQS or eq.
- ❖ **U ≤ 50% at EQS**

➤ Traceability to SI