

A project to deliver reliable measurements of estrogens for better monitoring surveys and risk assessments

L. Steinhäuser, S. Lardy-Fontan, C. Piechotta, E. Heath, N. Perkola, S. Balzamo, M. Cotman, T. Gökçen, C. Gardia-Parège, H. Budzinski, B. Lalère

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**

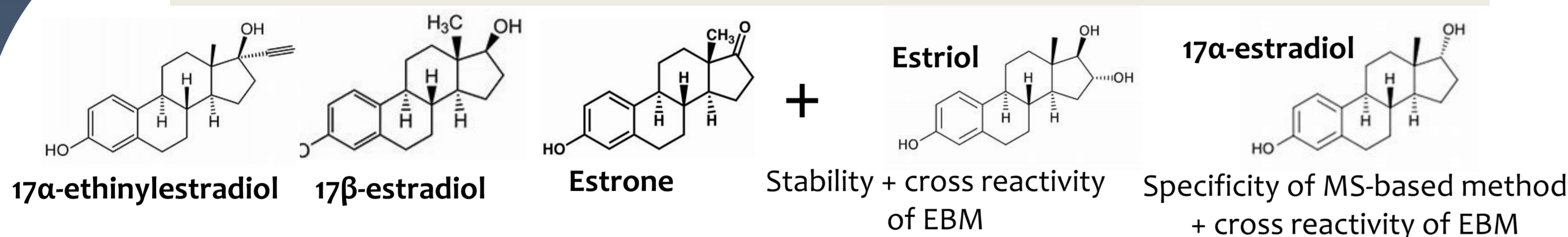
- Collaboration between National Metrology Institutes and advanced research institutes from 6 European countries
- **A Balance of expertise:** development and certification of RM, proficiency tests / interlaboratory comparison design, method development and validation, standardisation
- **A 3 years project:** September 2019- August 2022
- Strong engagement with stakeholders (Advisory Group)

THE PROJECT



SCIENTIFIC & TECHNICAL PROGRAMME \Rightarrow OBJECTIVES

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:
 - ❖ $30\% \text{ EQS} \leq \text{LOQ} \leq \text{EQS}$
 - ❖ **$U \leq 50\%$ 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**
 - ❖ $30\% \text{ EQS} \leq \text{LOQ} \leq \text{EQS}$ or eq.
 - ❖ **$U \leq 50\%$ at EQS**
- **Traceability to SI**

IMPACT TO:

- **STANDARDISATION-CEN TC/230 and ISO TC/147:** recommendations, technical report(s), technical specification(s)
- **TESTING LABORATORIES:** quick uptake of the methods, support for accreditation, improved capabilities
- **SCIENTIFIC COMMUNITY:** knowledge gain in metrology
- **REGULATORY BODIES AT NATIONAL AND EUROPEAN LEVELS:** fit for purpose methods, improved level of confidence, scientific support to the revision of WFD

KNOWLEDGE TRANSFER / CAPABILITIES BUILDING

- ❖ Trainings (**Winter 2021**)
- ❖ Interlaboratory comparison (**Spring 2022**)
- ❖ Open final meeting (**August 2022**)
- ❖ Briefs for stakeholders
- ❖ Engagements with main stakeholders

✓ If you want to collaborate, participate to our programme of activities or

✓ for more information

Follow us on our website
<http://projects.lne.eu/jrp-edc-wfd/>

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



This project 18NMR01 has received funding from the EMPIR programme co-financed by the Participating States and from the European Union's Horizon 2020 research and innovation programme.