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For more reliable measurements of pharmaceuticals in the environment: Overall measurement uncertainty estimation, QA/QC implementation and metrological considerations. A case study on the Seine River

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ABSTRACT

Credibility of environmental monitoring data became compulsory, especially with the implementation of the Water Framework Directive. The key principles for quality of measurements are to demonstrate their traceability and their accuracy with well-defined uncertainty. Although significant efforts have been made in designing procedures for analytical measurements, very little attention has been paid to the sampling stage.

To sustain the need of more reliable measurements, this study, applied to pharmaceuticals monitoring in the Seine River, evaluates the following points:

- comparability of measurements between laboratory,
- overall measurement uncertainty,
- sampling uncertainty main contribution at the station.

This work demonstrates the consequence of methodological and metrological laboratory choices on the measurements. Therefore, it should be highly recommended to laboratories to specify their practices and to incorporate them in their budgets to allow a better comparability of measurements. Moreover, it highlights that sampling uncertainty (method and natural variability) is a significant contributor of measurement uncertainty.

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1. Introduction

The Water Framework directive and Daughter directives (WFD) are some of the most important and ambitious environmental regulations to ever be implemented. Their objectives are to improve, protect and prevent further deterioration of water quality across UE Member States. Being an ongoing process, the WFD includes a set of water quality elements: physicochemical properties, micropollutants and biological parameters as well as hydromorphological criteria for groundwater and surface water. Within its scope, the need for effective chemical water monitoring is evident as the overall management and decision making system is strongly dependent on monitoring data. In fact, without accurate and comparable measurements, it cannot deliver a sound basis for proper decisions. Moreover, in the Blueprint to Safeguard Europe's Water Resources [1], the need to "display of robust monitoring and methods for a comprehensive assessment of the status of water bodies are essential elements for sound water management" has been reinforced. Accordingly, in addition to accuracy, it implies uncertainty, which is one of the most significant parameters to describe the quality of a given measurement.

Although significant efforts have been made in designing procedures for analytical measurements, very little attention has been paid to the sampling stage. The main difficulties in sampling are to ensure representativity and preserve integrity. Interestingly, many people still consider that the measurement starts when the sample arrives in the laboratory, and undergoes the uncertainty estimation.

Field sampling should be the first stage where Quality Assurance is required but uncertainties associated with this stage are often ignored. A badly designed sampling plan would reach the wrong conclusions. In environmental survey and especially within WFD, it could lead to (i) misunderstanding of natural phenomena, (ii) application of wrong statutory (bad/good chemical status) and (iii) poor protection/prevention of water bodies. Moreover, it could induce controversy, unnecessary loss of confidence and penalties [2].

Because the laboratory provides the results, it always tends to get the blame. In most cases, the measurement procedure encompasses sampling. Thus, it is necessary to include the uncertainty relating to the sampling procedure in the uncertainty-budget. Otherwise, the measurement uncertainty could be underestimated and could, in turn, have financial, health and environmental consequences. Accordingly, measurement uncertainty should be defined as the sum of two components, i.e.:

- uncertainty related to the analytical procedure and
- uncertainty related to the sampling procedure.

The estimation of the global measurement uncertainty should include as many sources of contributing errors as possible.

Historically, a strong attention has been paid to the estimation of laboratory uncertainties: guidance, ISO standards are available (e.g. [3]). Moreover, the ability to provide a measurement uncertainty is a requirement of the standard ISO 17025, mandatory for the WFD.

As highlighted in the CIRCA guidance n°19 [2], the quality of assessments is based on the quality of measurements. It depends on the quality of the sampling and also the understanding of the variability of the water body. Moreover, it relies on the implementation of QA/QC procedures: selection of samples, pre-treatment, subsampling, preservation, storage and transport. Sampling and analysis are both essential for the quality of measurements.This is also of particular concern considering that separate organisations, simultaneously or successively, may be involved in monitoring programs.

Research activities concerning sampling procedures focused, to the greatest extent, on the issue of reaching the most representative data, focusing on temporal variability. To support this statement, numerous research works on the development and calibration of passive sampling approach have emerged over the last ten years [4–6]. It is noteworthy that discussion on sampling, especially methodological perspectives in aquatic media by classical approach (e.g. spot sampling), is very sparse in the literature [7–9], as demonstrated by Ort [10]. The authors showed that less than 5% of all peer-reviewed studies declared to be following "established" guidelines or methods. Moreover, depending on the study, an avoidable sampling artefact ranging from "not significant" to "100% or more" was observed. Accordingly, the variability introduced by the sampling of aquatic media is not or cannot be evaluated yet.

To sustain the need of more reliable measurements, this study was conducted by two laboratories: LNE and Eau de Paris. They focussed on the following points:

1 Evaluation of the comparability of measurements between laboratories,
2 Estimation of overall measurement uncertainty,
3 Understanding of the sampling uncertainty's main contribution at the station.

The two laboratories focussed on pharmaceutical residues. Concerns towards pharmaceuticals in the environment, especially through the water cycle, were brought up in the late 90s [11] and are now laid down in the Article 8c of the WFD (Directive 2013/39/EU). The lingering question of whether the relative low environmental concentration levels of pharmaceuticals would cause adverse effects in humans or wildlife remains unsolved. In France, monitoring programs have clearly emphasised the ubiquity of the contamination by pharmaceuticals from various therapeutic classes: veterinary and human, prescribed and non-prescribed, licit and illicit, and in a wide range of concentrations [12–18]. This monitoring of tens to thousands of molecules at ultra-trace levels in complex matrix was enabled by the important innovation and speeded-up transfer of instrumentation especially hybrid mass spectrometry, e.g. generalization of LC/MS, associated to more efficient sample preparation techniques (e.g. SPE with wide range of sorbents) ([4,19]).

The sampling strategy was designed following the recommendation of the Eurachem Sampling Uncertainty Working Group [20]. Each laboratory implemented its own analytical methodology with various performances (Limit of quantification, precision. . .) on common samples. This led to the understanding of the main source contributions to measurement uncertainty.

2. Material and methods

2.1. Selected pharmaceuticals

Target compounds analyzed in this study belong to different medical classes and were selected taking into account different