**Effect-directed Monitoring (EDM) Tools as a Toxicological Fingerprint for Ecological and Human Risk Assessment of Water Bodies**

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**Introduction**

Because of widespread human activities, water pollution is a global issue, potentially threatening human and environmental health due to exposure to complex mixtures of chemicals. Nowadays, regulatory risk assessment in the EU is mainly based on an analytical approach, which measures the concentrations of known individual chemicals in water samples. This approach suffers from several shortcomings. Preferably, next-generation risk assessment tools, such as those using effect-directed analytical methods, should be employed. These tools aim to detect a broad panel of (bio)active compounds that may impact human health, risk assessment, and the environment. EDM, which is a promising new approach, can be used to identify new chemicals and modes of action. EDM involves the systematic identification of chemicals and modes of action contributing to biological responses in (bio)assays applied in water and aquatic environments. This list should highlight specific adverse outcomes, or modes of action, which need to be assessed by the set of bioassays. This list is not complete and might be updated in the future.

**List of chemicals**

Table 1 shows an overview of 12 literature sources that were used to compile a total of 317 concerning and prioritized chemicals occurring in different water bodies (wells, surface and drinking water). Figure 1 shows the percentages of the different categories of the 317 chemicals. The majority of chemicals are pesticides (40%), followed by functional industrial compounds (29%) and pharmaceuticals (22%). This distribution also reflects the causative anthropic activities (agriculture, chemical industry, pharmaceutical industry). Interestingly, 17% of the chemicals appears not to be approved by the EU of the pesticides, 49% is not approved by the EU.

**Bioassays**

A literature review was performed in order to produce an overview of different bioassays, which have already been applied in the context of water quality assessment. For each endpoint, bioassays were selected based on criteria such as sensitivity, availability of standard protocols, and specificity. Here we propose a preliminary set of 14 bioassays covering the different relevant endpoints for human health. The list is shown in Table 1. For 7 endpoints, none or very few bioassays are available, and pre-selected bioassays were proposed. Work in progress will attempt to define specific bioassays to cover these less available endpoints in context of water quality assessment as well.

**Neurotoxicity endpoint**

Because the majority of the chemicals is neuroactive (Figure 2), special focus is put on the neurotoxicity endpoint. The pre-selected endpoints in Table 2 are defined as new neurotoxicants for which a strong neurotoxic effect—Acetylcholine (AChE) inhibition. 

**Table 1:** Classification of the 12 references used to select 317 chemicals detected in waste water, water cycle, surface water and drinking water.

**Table 2:** List of different endpoints which should be assessed for human health risk and associated with different bioassays currently used in water quality assessment. From this list, 14 bioassays have been pre-selected for such endpoints.

**Table 3:** List of different mechanisms of action of the 30 neurotoxicants in the list of chemicals.

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**Figure 1:** Different categories of the 317 chemicals in the list.

**Figure 2:** Percentage of the aquatic modes of action (MoAs) in the database.

**Figure 4:** Range of NOAELs of the 30 neurotoxicants from the list of chemicals.

**Figure 3:** Different molecular initiating events (MIE) leading to an alteration of the neuronal excitability which could be assessed by multiregulatory array (MRA). The MRA comprises 12 different bioassays (EHC, ER, AhR, AhR agonists, AChE, AChE agonists, LHR, LHRagonists, NAA, NAA antagonists, GABA, GABA receptor antagonists) distributed over 3 different endpoints (cytotoxicity, mutagenicity, mutagenicity) and one endpoint (endothelial cell proliferation). One endpoint, NOAEL, was calculated for each MIE. This figure is the first to show the NOAEL distribution in a complex chemical mixture.