Date Posted: December 9, 2020

REQUEST FOR QUALIFICATIONS (RFQ)

Develop Standard Operating Procedures for the Collection, Storage, and Extraction of Aqueous Samples for IVB screening (4828)

RFQ Due Date: 1/21/2021, 4:00pm MT
Maximum Funding: $245,000

WRF Project Contact: Erin Partlan, epartlan@waterrf.org

Purpose

The purpose of this RFQ is to identify a research team to assist The Water Research Foundation (WRF) in developing standard operating procedures (SOPs) for the collection, storage, preservation, extraction, and concentration of aqueous samples for subsequent CEC screening using *in vitro* bioanalytical tools (IVBs). This project is part of a larger initiative with WRF's partners (Southern California Coastal Water Research Project "SCCWRP", and California State Water Resource Control Board "SWB") to facilitate the implementation of bioanalytical tools among water quality managers. The goal of this project is to offer robust sample processing procedures applicable for various IVBs and water matrices. The specific IVBs will be identified by SCCWRP's research team prior to the start of this project (see Appendix A). The SOPs will go on to inform an assessment of the feasibility of standardized IVBs for use in water quality monitoring.

Background and Project Rationale

It is not practical to use conventional chemical monitoring for the full range of known and unknown chemicals, including transformation products, present in ambient and recycled water. Moreover, monitoring on a chemical-by-chemical basis does little to address the potential effects of complex mixtures on organisms. *In vitro*, or cell-based, bioanalytical tools (IVBs) are genetically modified cell lines that respond to chemicals by initiating a molecular event (e.g. expression of a gene) that may be indicative of an adverse outcome. Because their specificity is pre-engineered, IVBs can be used to screen for the bioactivity of targeted groups of chemicals and chemical mixtures (e.g. endocrine disrupting chemicals) extracted from water samples. A benefit of IVBs is the ability to provide an integrated measure of biological activity for chemicals that exhibit the same mode of action (e.g. estrogens). This identification of the effects of the "unknown unknowns" can supplement traditional chemical analysis in

monitoring frameworks by providing a more comprehensive, as well as a more directed evaluation of water quality.

Hundreds of IVBs have been developed to screen chemicals for various modes of bioactivity, however relatively few have been applied to or adapted for water quality monitoring and assessment. Of those endpoints that have been applied to screen water quality, the vast majority have not yet been adapted, optimized, standardized and fully vetted for widespread use by the water quality community (Appendix A). There is a need to understand how bioanalytical tools can be used in diverse water quality applications, which points to the rationale for this project to develop sample collection, storage, and processing SOPs for a range of aqueous matrixes. The findings will help to ensure bioanalytical measurements are relevant, robust and comparable among studies.

Summary of Project

Task 1: Literature Review

Considering at least the following water matrices: advanced treated water (e.g. by reverse osmosis, microfiltration or advanced oxidation processes), primary or secondary treated wastewater, seawater, and stormwater:

1. Perform a literature search on the performance of collection, preservation/storage, and extraction/concentration techniques for water sample analyses by conventional chemical analyses (e.g. LC-MS/MS and GC-MS/MS).
2. Perform a literature search on the performance of collection, preservation/storage, and extraction/concentration techniques for water samples in bioanalytical tools, focusing on the pre-selected IVBs.

Task 2: Procedure Identification

Considering the four selected water matrices and the pre-selected IVBs from Appendix A:

1. Identify the components of a baseline sample collection and processing sequence (e.g. solid phase extraction).
2. Identify alternative processing techniques (e.g. liquid-liquid extraction, extract purification) to address specific matrix interferences (e.g., high salinity, suspended solids, tannins, color) or variable that would affect the IVB assay (e.g., pH)
    a. Consider an approach that minimizes variabilities between procedures, such as choice of elution solvents (note that extract shall be in a solvent compatible with solvent exchange procedures) .
    b. If sample is filtered, consider how and whether an extraction is also done on the filter.
3. Identify quality assurance/quality control measures, including
    a. surrogate parameters by which to assess and compare extraction efficiency and retention of IVB response
    b. a negative control matrix (i.e. neutral pH, low conductivity)

Task 3: Bench-Scale Testing

Perform bench scale evaluation (as needed, based on outcomes of Task 1 and Task 2) to characterize and recommend SOPs for the three pre-selected IVBs in the four selected water matrices. Propose a protocol for determining if and what type of bench-scale testing will be needed. Consider evaluating the following:

1. Efficiency of baseline and alternative extraction procedures
2. Loss of target constituents and/or IVB response during collection, preservation/storage, and/or extraction/concentration, including pre- and post-extraction concentration steps.
    a. Identify and evaluate alternative techniques should losses for any step be deemed unacceptable
3. Optimal sample loading in baseline procedure to minimize target constituent losses;
4. The effects of physical, chemical and biological characteristics of the selected aqueous matrices of interest.
    a. Consider the volume required for extraction to achieve optimal performance based on known matrix interferences and method sensitivity.
    b. Consider matrix effects (e.g. pH, TOC/DOC, salinity, cytotoxicity, and microbial activity) on extraction efficiency and IVB response.
5. Maximum holding times and optimal storage conditions prior to extraction, considering effects on the analysis of extracts.

Task 4: Develop SOPs

1. Synthesize a single SOP, if possible, for water collection/storage/extraction & concentration that would be suitable for multiple in vitro bioassays and include QAQC and key performance metrics.
2. If variations on the SOP are required for IVBs and/or matrices, a statement detailing the benefits of developing additional or separate procedures (e.g. decreased bioassay performance) should be provided.
    a. Specify assay-specific collection, preservation/storage and extraction/concentration methods.
    b. Specify whether multiple extraction and/or concentration steps are required.
    c. Specify whether additional lines of evidence (e.g. TOC, field analysis, or other metrics) for evaluating the performance of baseline and alternative SOPs in recovering target constituents/surrogates and/or preserving IVB response are useful
3. Provide recommendations for dissemination of SOPs in a manner that ensures both broad applicability to users and maximizes the robustness of measurements.

Task 5: Participate in an Interlaboratory Comparison (led by SCCWRP research team)

1. Provide prepared SOP(s) to interlaboratory comparison participants. In addition, prepare a set of aqueous sample extracts (spiked and unspiked) and a set of unextracted/unfiltered water samples. Note: The SCCWRP team will handle distribution of samples to participating laboratories for IVB analysis.

2. Perform chemical analysis to verify concentrations of target analytes. Targeted chemicals to measure will be selected in collaboration with SCCWRP's research based on the outcome of Tasks 3 and 4.
3. Review results of the interlaboratory comparison exercise and propose revisions to the SOPs.

Expected Deliverables

- Standard Operating Procedures for at least three pre-selected IVBs in at least four selected water matrices that include:
    - Water collection
    - Preservation/storage
    - Sample preparation, including extraction and concentration
    - QA/QC with key performance criteria acceptance ranges when available
- Final report describing how the SOPS were selected and optimized

Research Team Qualification Requirements

The following is a list of the minimum requirements that the research team must demonstrate to be considered for selection. If one of these items is not included or missing from the submittal, the submittal will be rejected:

- Research Team Lab has the equipment, personnel, and availability to implement the scope of work according to the schedule outlined in this RFQ, including equipment for conventional analytical methods (LC/GC-MS) and sample processing (SPE/LLE).
- Research Team has demonstrated experience in the successful and timely completion of development and/or optimization of chemistry SOPs
- Research Team Lab has a quality assurance plan for the overall operation of the lab

Additional qualifications are not required, but describe a preferred candidate:

- Research Team has access to a cell biology lab for bioscreening (collaboration with SCCWRP Research Team is also expected for bioscreening)
- Research Team has extensive and demonstrated knowledge in the areas of chemical bioactivity and toxicity potential
- Research Team has experience working with CECs such as phthalates, glucocorticoids and other pharmaceuticals (see Appendix A), which are most likely to be selected.

Project Duration

The anticipated period of performance for this project is 24 months from the contract start date, with the SOP due at the end of 18 months to accommodate the development of the guidance document in that last 6 months.

Project start date is anticipated 6-8 weeks after qualifications deadline.

References and Resources

The following list includes examples of research reports, tools, and other resources that may be helpful to proposers. It is not intended to be comprehensive, nor is it a required list for consideration.

- Bioanalytical Tools for Detection and Quantification of Estrogenic and Dioxin-Like Chemicals in Water Recycling and Reuse: Guidance Document for Developing a Standard Operating Procedure. (Jan 2020) NWRI. https://watereuse.org/wp-content/uploads/2020/01/NWRI.WRCA_.BIAG_.Final_.Report.pdf
- Development of Bio-analytical Techniques to Assess the Potential Human Health Impacts of Recycled Water - WRRF 10-07/ WRF 1677. (2014) https://www.waterrf.org/research/projects/bio-analytical-techniques-assess-potential-human-health-impacts-reclaimed-water

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RFQ Submittal

Statement of Qualifications must be received via email by **4:00pm MT on Thursday, January 21, 2021. Please send RFQ submittals to Erin Partlan, Email:** requestforqualifications@WaterRF.org Phone: (571) 384-2095.

A Statement of Qualifications must be submitted as one PDF file and include the following items and detail how the respondent(s) meets the evaluation criteria:

- Research team qualifications as outlined above (maximum 5 pages).
- Resumes or CVs outlining the research team's experience and experience of key team members. (2 pages/ each resume/CV)
- Scope of Work (SOW) including research approach, budget narrative, and schedule (max 6 pages). Anticipated value with respect to proposed efforts and budget will be a selection consideration. The SOW must include:
    - Research approach including the sourcing of samples, matrix of parameters for evaluation, statistical approach, and presentation of the data.
    - Estimate of budget (line items for labor, transport and shipping, indirect costs)
    - Estimate of schedule of deliverables
- Part of a successful response to this RFQ will be the ability of the research team to contract quickly with WRF. In your response to this RFQ, please indicate that you are able to accept the following terms:
    - This project will be contract for hire.
    - WRF will own the intellectual property of the final results.
    - Liability insurance of $1 million US dollars.
    - Applicable law and venue is Colorado.
    - Please become familiar with the WRF budget form (see Research Priority Program, Forms).

- Must comply with all US laws and regulations, including 2 CFR 200, GAAP, and guidelines found in WRF proposal guidelines.

Evaluation Criteria

1. Research approach, budget narrative, schedule, deliverables, and applicability (30%)
2. Qualifications, capabilities, and management (70%). Competitive candidates will demonstrate strong experience and qualifications in the following areas:
    a. Relevant Project Experience (30%)
    b. Research Team and Participating Lab Qualifications (20%)
    c. Qualifications of Personnel (20%)

RFQ Evaluation and Award

WRF will evaluate RFQs and may elect to interview a short-list of candidates. Award notification is anticipated by mid-February, 2021.

Submittal and Acceptance of Required Contract Elements

The maximum funding for this project is $245,000. This project is funded by WRF and will be administered by WRF. After selection and award, the research team will develop, at their own expense, a refined and final SOW, budget narrative, and budget form addressing comments from WRF'S project advisory committee (PAC), and present it to WRF and the PAC for discussion and approval. Please visit the WRF website for instructions on budget preparation, the required budget narrative, and the required budget form.

Attachment A: Forms

Form 1: Checklist for Minimum Research Team Qualifications

Minimum Qualifications	Does Lab Satisfy the Criteria (Yes/No)?
[Required] Research Team Lab has the equipment, personnel, and availability to implement the scope of work according to the schedule outlined in this RFQ, including equipment for conventional analytical methods (LC/GC-MS) and sample processing (SPE/LLE).	
[Required] Research Team has demonstrated experience in the successful and timely completion of development and/or optimization of chemistry SOPs	
[Required] Research Team Lab has a quality assurance plan for the overall operation of the lab	
[Preferred] Research Team has access to a cell biology lab for bioscreening (collaboration with SCCWRP Research Team is also expected for bioscreening)	
[Preferred] Research Team has extensive and demonstrated knowledge in the areas of chemical bioactivity and toxicity potential	
[Preferred] Research Team has experience working with CECs such as phthalates, glucocorticoids and other pharmaceuticals (see Appendix A), which are most likely to be selected.	

Print Name:
Title:
Signature:
Date:

Appendix A

Candidate *in vitro* bioanalytical tools (IVBs) for optimization. Three endpoints will be selected by SCCWRP's research team prior to the start of the project. Those highlighted are strong candidates. under consideration.

Endpoint Activity	Relevant CECs	Adverse effect	Development Stage[a]
I. Endocrine disrupting chemicals (EDCs)			
Anti-androgen receptor (AR-)	Musks, phthalates, pesticides	Androgen insensitivity, impaired reproduction, cancer	2
Glucocorticoid receptor (GR)	Anti-inflammatory steroids	Development, immune diseases, diabetes	3
Progesterone receptor (PR)	Progestins	Cancer, hormone resistance syndrome, impaired reproduction	2
II. Carcinogenic chemicals			
Tumor suppressor protein Response Element (p53RE)	Dioxin-like chemicals, PAH metabolites	Oxidative stress, tissue and DNA damage, cancer	1
III. Immunosuppressants, neurotoxins and other chemicals of concern			
Thyroid receptor (TR)	Pesticides, bisphenol A	Impaired metabolism, auto-immune diseases	1
Peroxisome proliferator activated receptor (PPAR)	Pharmaceuticals, phthalates	Metabolic disorders, impaired immune function, cancer	1

Stage 1 - Exploratory: is endpoint amenable to WQ screening?
Stage 2 - Optimization: is performance consistent with monitoring goals?
Stage 3 - Standardization: can SOPs and thresholds be developed?
Stage 4 - Pilot evaluation: does it provide value in practice?
Stage 5 - Implementation: can it be run by commercial labs and certified as a method by the California Environmental Laboratory Accreditation Program?