Solicited Research RFP

Critical Evaluation and Assessment of Health and Environmental Risks from Antibiotic Resistance in Reuse and Wastewater Applications (RFP No. WRF 4813 LINK 17-10)

Project Goal

The goal of this project is to examine approaches to quantify the public health and environmental risks related to antibiotic resistance in reuse and wastewater applications.

Budget

Proposals may request WRF funds in the range of $120,000 - $140,000. WRF funds requested and total project value will be considered in the proposal selection process.

Background

The World Health Organization (WHO) has recognized antibiotic resistance (AR) as “one of the three greatest threats” to human health, and has highlighted the need to develop standards addressing AR occurrence in the environment, specifically in reuse water and wastewater (WHO, 20151).

Several key collaborators, utilities, and financial partners, including the Global Water Research Coalition (GWRC), launched the project Occurrence, Proliferation, and Persistence of Antibiotics and Antibiotic Resistance during Wastewater Treatment (WERF1C15 published), addressing questions related to biological wastewater treatment, to advance the science toward the broader goal of fully characterizing the implications of antibiotic resistance (AR) in water. This research project, along with similar studies, expands the AR knowledge base and defines putative risks associated with AR. This is the first step in establishing frameworks for quantifying public and environmental health risks related to antibiotic resistance.

The 2014 advent of Ebola in the U.S. heightened awareness of the potential risks water resource recovery facilities face regarding bio-contaminated wastewater. While Ebola virus is quite rare, other infectious diseases, including those caused by antibiotic resistant bacteria and viruses, are of concern. Numerous reports have suggested that antibiotic resistant genes and bacteria resistant to multiple antibiotics can be abundant in municipal wastewater that can serve as environmental reservoirs for antibiotic resistance and for horizontal gene transfer (Michael et al. 2013). Therefore, water resource recovery facilities (WRRFs) can be challenging environments that can contribute to antibiotic resistant bacteria (ARB), antibiotic resistant genes (ARGs), and the dispersal of ARB and ARGs into environments such as groundwater. However, WRRFs using advanced treatment processes are important because they can also control the concentration of ARB and the spread of ARGs into environmental systems, such as groundwater and rivers. As understanding of infectious disease risks faced by wastewater and sewer works evolves, identifying effective ways to define and frame these risks may play a prominent role in achieving the cultural change needed within the water quality community.

There is growing interest and demand in quantifying AR associated risk by utilities and regulators for discharges and both nonpotable and potable reuse. The identification of this risk, followed by establishing dose response curves for ARB, the fate and transport of ARGs and ARB in the treatment process environments, and exposure assessment, is needed to fully characterize and estimate risk of infection for drinking water, recreational water, other challenging water matrices, and occupational exposure. It is expected that the results of this project will provide a roadmap that can be used by policymakers to determine the level of risk and the level of mitigation needed (if any) for antibiotic resistant bacteria, including multiple drug resistant (MDR) bacteria, and antibiotic resistant genes. The intention of this project is to apply the most current information available to inform stakeholders on the risks associated with ARB and ARGs in wastewater and reuse waters, as well as to provide a framework for assessing risk in these waters going forward.

The GWRC works on a global matrix structure where data for a quantitative health risk assessment can be gathered. This matrix consists of the classical steps of a quantitative microbial risk assessment (QMRA) (i.e., hazard characterization, type of hazard, type of water, sources of contamination), exposure (i.e., ingestion, inhalation, tissue contact, and recreation), and health risks (i.e., calculated risks/illness or measured risks/illness). In collaboration with GWRC, the Foundation for Applied Water Research (STOWA) currently has a dynamic and working draft AR risk matrix organized by world zones and scenarios that would serve as a resource and guidance tool in quantifying the risks related to AR in reuse and wastewater applications.

This matrix is set up to compile an overview of the current state of knowledge on antibiotic resistance and antibiotic resistant genes, identify knowledge gaps, use existing knowledge to assess actual risk, avoid duplication in work, and obtain an understanding of the robustness and/or variability of data available worldwide. A well populated matrix with data from studies worldwide can be used to calculate certain scenarios, such as reuse scenarios.

The data used in this study will be a part of this matrix. An expert meeting will be held to further populate the matrix, define research gaps, and discuss scenarios (e.g., hot spots like wastewater discharge) to evaluate the global risk matrix.

This project will benefit WRF subscribers and stakeholders by:

1. Informing stakeholders of the current state of ARB/ARG risk assessment in wastewater and reuse water.
2. Outlining current research gaps and challenges with reference to ARB/ARG risk assessment.
3. Providing a framework outlining how ARB/ARG risk assessment in wastewater and reuse water can be achieved.
4. Providing a condensed summary (i.e., FAQ sheet, video clip, infographic) that communicates the major findings to WRF subscribers and stakeholders in an easy to understand and straightforward manner.

Research Approach

This project is not experimental in nature; investigators should focus on developing a proposal that addresses the topic of ARB/ARG risk assessment using information and resources that are currently available. Successful proposals will describe a comprehensive approach to assessing the risks associated with ARB and ARGs in wastewater and reuse waters using the most up-to-date information available. Qualifying proposals should include plans to address the following tasks, as well as other ideas pertinent to ARB/ARG risk assessment:

1. A summary of current literature concerning ARB/ARG risk assessment in reuse water and wastewater. Suggested topics include:
   b. An evaluation of the current situation with respect to antibiotic resistance risk assessment in water.
   c. An estimation or measurement of ARB and ARGs in surface waters, reuse, and wastewater applications.
   d. An assessment of health and environmental risks from antibiotic resistance outlining recent and novel strategies for linking environmental antibiotic resistance with human health outcomes.
   e. A characterization of potential waterborne sources of ARB/ARG, including sources prior to wastewater treatment (e.g., excretion by individuals, agriculture, hospitals, etc.), as well as post-treatment (i.e., distribution pipe biofilm), along with the magnitude that each has with respect to the risks associated with antibiotic resistance in wastewater and reuse waters.
   f. An assessment of ARB/ARG occurrence, exposure routes, and pathways that lead to acquisition or loss of antibiotic resistance, such as horizontal gene transfer, mutation, transposition or recombination, co-resistance, and cross-resistance.
   g. A description of selective pressures related to antibiotic resistance in reuse water and wastewater, including pressures from other materials in the matrix.
   h. An assessment of the removal of ARB and ARGs by current wastewater treatment processes, along with a comparison to concentrations of fecal indicator organisms (bacteria, viruses, etc.) in the associated waters.
   i. A research inventory of field data related to antibiotic resistant bacteria and antibiotic resistant genes in water reuse and wastewater, providing an AR catalog, including study metadata, in a “Tidy Data” machine readable format. The research inventory should include both qualitative (presence/absence) and quantitative studies of antibiotic
resistant associated with water reuse and wastewater, and serve as a resource for future risk assessment efforts.

j. Identification of goals that will lead to an effective assessment of ARG/ARB risk in reuse and wastewater, along with an estimated timeline associated with each goal.
   i. Identify processes needed to establish a framework for quantifying risk related to antibiotic resistance in reuse applications including occurrence, dose response, and ingestion rates.
   ii. Provide a current evaluation on the progress made to date for each goal.
   iii. Identify and prioritize current research gaps associated with each goal.
   iv. Successful proposals should also include an approach to address the research gaps identified above.
   v. The end product should provide a framework for review, synthesis, and systematic testing of theories by the scientific community.

k. Identification of organizational and logistical challenges to achieving effective ARB/ARG risk assessment in reuse and wastewater, along with recommendations for overcoming these challenges. Examples of potential challenges include, but are not limited to:
   i. How to identify and address the needs of utilities and public health and regulatory agencies with reference to ARB/ARG risk assessment.
   ii. How to connect researchers, utilities, funding, and other resources to more efficiently achieve the goals stated above.
   iii. How to effectively disseminate risk assessment knowledge among researchers, utilities, public health officials, regulatory agencies, and other stakeholders in a timely and effective manner.

l. A critical evaluation of risk addressing and summarizing the current understanding of the issue at local, national, and international scales, incorporating data and case studies from a global perspective.

2. An assessment of the risk associated with ARB/ARGs in various wastewaters and reuse waters. The assessment should:
   a. Identify types of bacteria and ARGs that are important to assessing risk associated with antibiotic resistance in wastewater and reuse waters.
   b. Explain how public health risks compare in various scenarios. Include relevant issues such as:
      i. Type of wastewater to be treated, such as domestic and industrial.
      ii. Type of treatment processes (conventional vs advanced).
      iii. Type of reuse applications (potable, agricultural, recreational).
      iv. A list of both broad and specific research gaps that need to be answered to better inform future risk models in field data collection, technical and engineering solutions, and human dimensions needed.
   c. Describe the potential for pathogens to acquire ARGs in different post-treatment and reuse waters.
   d. Compare the risks associated with multidrug resistant bacteria to those associated with single drug resistance in the relevant water types.
   e. Produce a framework describing what is needed to achieve effective risk assessment of ARB/ARGs in reuse water and wastewater.

3. Fate and transport pathways should be articulated, and integrated with knowledge on exposures to identify likely “hot spots” and critical control points.

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Deliverables

Final deliverables for this project should include:

1. A literature review (peer reviewed literature preferred)
2. A research inventory
3. A risk evaluation (published in a peer reviewed journal) including:
   a. A summary infographic or alternative communications geared towards the public
   b. A list of top research questions, potentially published in a peer reviewed journal
4. A technical report including
   a. An executive summary
   b. A roadmap with a prioritized list of research gaps
   c. Recommendations for research integration
   d. A communications plan
   e. A guide to deliverables
5. An expert meeting/evaluation of the global risk matrix for integrating worldwide research for local identification of hot spots.

What will Success Look like?

Successful completion of the tasks specified in this RFP will result in a report yielding a current and comprehensive assessment of the risks associated with ARB and ARGs in wastewater and reuse waters. Additionally, the report should also provide a roadmap focusing on what is needed for effective risk assessment with respect to ARB/ARGs going forward.

Proposal Preparation Instructions

Proposals submitted in response to this RFP must be prepared in accordance with The Water Research Foundation’s document Guidelines for Focus Area Program Proposals. These Guidelines are applied to the Solicited program as well. The most current version of these guidelines is available at: http://www.waterrf.org/funding/ProposalDocuments/GuidelinesForFocusAreaProgramProposals.pdf. The guidelines contain instructions for the technical aspects, financial statements, and administrative requirements that the applicant must follow when preparing a proposal.

Eligibility to Submit Proposals

This RFP solicits proposals from all technically qualified applicants, including educational institutions, research organizations, federal or state agencies, municipalities, and consultants or other for-profit entities.

WRF’s Board of Directors has established a Timeliness Policy that addresses researcher adherence to the project schedule. The policy can be reviewed at http://www.waterrf.org/funding/Pages/policies.aspx. Researchers who are late on any ongoing WRF-sponsored studies without an approved no-cost extension are not eligible to be a named participant in any proposal. If you have any questions about your eligibility for WRF projects, please contact the WRF research staff listed at the bottom of this RFP.
Administrative, Cost, and Audit Standards

WRF’s Solicited Research Program standards for administrative, cost, and audit compliance are based upon, and comply with, Office of Management and Budget Uniform Grants Guidance, 2 CFR Part 200 Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards, and 48 CFR 31.2 Contracts with Commercial Organizations. These standards are referenced in the WRF’s Guidelines for Focus Area Program Proposals, and include specific guidelines outlining the requirements for indirect cost negotiation agreements; financial statements; and the Statement of Direct Labor, Fringe Benefits and General Overhead. Inclusion of indirect costs must be substantiated by a negotiated agreement or appropriate Statement of Direct Labor, Fringe Benefits and General Overhead. Well in advance of preparing the proposal, your financial staff should review the detailed instructions included in WRF’s annually released Guidelines for Focus Area Program Proposals.

Budget and Funding Information

The funding available from WRF for this project is in the range of $120,000 - $140,000. A minimum of 25 percent of the total project value must be contributed by the applicant (i.e., the applicant’s minimum contribution must equal one-third of WRF funds requested). Acceptable forms of applicant contribution include cost-share, applicant in-kind, or third-party in-kind that comply with 2 CFR Part 200.306 cost sharing or matching. The applicant may elect to contribute more than 25 percent to the project, but the maximum WRF funding available remains fixed at $140,000. Proposals that do not meet the minimum match of 25 percent of the total project value will not be accepted.

Period of Performance

The proposed project schedule should be realistic, allowing ample time for the preparation of final reports and for review of project results. It is WRF’s policy to negotiate a reasonable schedule for each research project. Once this schedule is established, WRF and its sub-recipients have a contractual obligation to adhere to the agreed-upon schedule. Under WRF’s No-Cost Extension Policy, a project schedule cannot be extended more than nine months beyond the original contracted schedule, regardless of the number of extensions granted. The policy can be reviewed at http://www.waterrf.org/funding/Pages/policies.aspx.

Utility and Organization Participation

WRF is especially interested in receiving proposals that include both participation and contribution of resources from water utilities and organizations in the research effort. Information on utilities and/or organizations that have indicated an interest in participating in this research project are listed on the last page of this RFP. While WRF makes utility and organization participation volunteers known to applicants, it is the applicant’s responsibility to negotiate utility and organization participation in their particular proposal, and the utilities and/or organizations are under no obligation to participate.

Application Procedure and Deadline

Proposals are now being accepted exclusively online in PDF format. Proposals must be submitted before 5:00 PM Mountain Time (7:00 pm Eastern Time), Wednesday, October 10, 2018. All the forms and components of the proposal are available online in the “Proposal Component Packet” zip file. A
login is required to download this packet and use the proposal website. This information is available at https://proposals.waterrf.org/Pages/RFPs.aspx.

The online proposal system allows submission of your documents until the date and time stated in the RFP. To avoid the risk of the system closing before you press the submit button, do not wait until the last minute to complete your submission.

Questions to clarify the intent of this Request for Proposals and WRF’s administrative, cost, and financial requirements may be addressed to the WRF staff contact, Lola Olabode, at (571) 384-2109 or by e-mail at lolabode@waterrf.org.
UTILITY AND ORGANIZATION PARTICIPANTS

To date, no utilities have indicated an interest in participating in this research. As utilities express interest, their information will be added below within 24 business hours of receipt of a volunteer form, and this RFP will be re-posted with the new information. (Depending upon your settings, you may need to click refresh on your browser to load the latest file.)

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