Technical/Regulatory Guidance

Contaminants of Emerging Concern Framework

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December 2023

Prepared By

The Interstate Technology & Regulatory Council

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Contaminants of Emerging Concern (CEC) require a clear technical approach on how to identify and evaluate them while acknowledging uncertainties in their environmental fate and transport, receptor exposure, and/or toxicity. Such an approach can be conducive to improved allocation of regulatory response resources and provide a foundation for communicating potential risk to stakeholders.

The ITRC CEC framework is comprised of a white paper and four associated fact sheets. In the white paper, CEC are defined as: **"substances and microorganisms including physical, chemical, biological, or radiological materials known or anticipated in the environment, that may pose newly identified risks to human health or the environment."** The framework is meant to help environmental regulatory agencies and other stakeholders identify examples of CEC monitoring programs; evaluate potential hazard by systematically applying key CEC characteristics; communicate real and perceived risk from CEC to the public; and understand how laboratory analytical methods can be used in the identification process.

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About ITRC

The Interstate Technology and Regulatory Council (ITRC) is a state-led coalition working to reduce barriers to the use of innovative environmental technologies and approaches so that compliance costs are reduced and cleanup efficacy is maximized. ITRC produces documents and training that broaden and deepen technical knowledge and expedite quality regulatory decision making while protecting human health and the environment. With private and public sector members from all 50 states and the District of Columbia, ITRC truly provides a national perspective. More information on ITRC is available at www.itrcweb.org.

ITRC is a program of the Environmental Research Institute of the States (ERIS), a 501(c)(3) organization incorporated in the District of Columbia and managed by the Environmental Council of the States (ECOS). ECOS is the national, nonprofit, nonpartisan association representing the state and territorial environmental commissioners. Its mission is to serve as a champion for states; to provide a clearinghouse of information for state environmental commissioners; to promote coordination in environmental management; and to articulate state positions on environmental issues to Congress, federal agencies, and the public.

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CEC White Paper

This White Paper has been organized into the following subsections:

1. Introduction

The United States Environmental Protection Agency (USEPA) and state environmental or health regulatory agencies (collectively referred to as states) are tasked with protecting human health and the environment. As part of this mandate, both USEPA and states regularly develop guidance and/or regulations that serve to limit public exposure to contaminants in the environment. USEPA water quality programs that may serve as good resources can be found at the following link: Contaminants of Emerging Concern including Pharmaceuticals and Personal Care Products | USEPA. States may also develop programs to monitor and identify potentially harmful substances that could be present in the environment. These substances could include contaminants with known occurrence but limited exposure and toxicity information, contaminants with limited to no data on potential presence in the environment or potential toxicity, or known or existing contaminants with new exposure or toxicity information. Understanding the potential exposure, toxicity, and fate and transport of these contaminants is critical to assessing risk and, in turn, risk management options for protecting human health and the environment. This document is intended to provide guidance on how to identify and evaluate contaminant(s) of emerging concern (CEC).

This White Paper and the four associated CEC Fact Sheets provide a framework that may help states make decisions when undertaking or developing a program to identify, evaluate, and monitor potentially harmful substances in the environment. This framework can be used whether or not a state has a formal CEC program. A state's interest in taking action may be driven by the potential risk posed by a CEC. Ideally, the goal of any CEC monitoring program should be to shorten the time from the identification of a CEC to risk mitigation, thereby minimizing the potential risk to human health and the environment.

Protecting public health and the environment may include identifying and evaluating CEC present in environmental media (e.g., soil, groundwater, surface water, air, biota), even when only minimal information is available. Patterns of use and disposal may cause CEC to end up in one or more environmental media. States can more easily track concentrations of contaminants in the environment with a CEC program. In some cases, CEC monitoring programs may allow corrective actions and regulatory responses to be implemented before potential exposures and adverse human health or ecological effects occur (NSTC, IWG-EC 2022) (IWG-EC, January 2022). Developing a CEC program may also provide opportunities for states to address environmental justice issues such as improving water quality in disproportionally impacted communities.

This White Paper addresses three broad topics:

1. factors that can influence a state's ability to address CEC
2. current CEC programs and approaches
3. a new framework for identifying and monitoring CEC

For the purposes of this White Paper and four associated Fact Sheets, CEC are defined as **substances and microorganisms, including physical, chemical, biological, or radiological materials known or anticipated to be in the environment, that may pose newly identified risks to human health or the environment**. This definition aligns with the language provided in the USEPA Memorandum, "Implementation of the Clean Water and Drinking Water State Revolving Fund Provisions of the Bipartisan Infrastructure Law [BIL]" dated March 8, 2022. Per the definition provided in the USEPA Memorandum, CEC "can include many different types of natural or manufactured chemicals and substances — such as those in some compounds of personal care products, pharmaceuticals, industrial chemicals, pesticides, and microplastics." The definition incorporates many substances listed on the Contaminant Candidate List that can be addressed with drinking water state revolving funds. The USEPA memorandum provides guidance for obtaining funding to address CEC (Fox 2022), and more information can be found in the Bipartisan Infrastructure Law SRF Memorandum | USEPA. States that identify CEC in a manner consistent with the USEPA's definition and meet various other requirements may use funds from the BIL to develop programs and projects that address a wide variety of local water quality and public health challenges. These can include addressing CEC in drinking water and wastewater discharges, investing in ecological challenges, or addressing public health challenges experienced by disadvantaged communities.

A chemical may no longer be considered a CEC when one or more of the following criteria have been met: (1) the chemical can be analyzed using validated analytical methods, (2) the chemical's toxicity has been evaluated/identified, or (3) the chemical has regulatory screening levels. The specific decision on when a chemical is no longer considered a CEC will be up to each individual state to determine.

The approaches and discussion provided in this White Paper are further detailed in four Fact Sheets, which are discussed in Section 1.4. This White Paper and the associated Fact Sheets provide a framework for states to consider when developing a strategy for additional data collection and monitoring (CEC Monitoring Programs Fact Sheet), evaluating and prioritizing exposure and potential to cause toxicity (Identification of Key CEC Variables Fact Sheet and Adoption of Analytical Methods for CEC Fact Sheet), and communicating information to the public and other stakeholders in a timely fashion (Risk Perception and Communication Fact Sheet).

The definition of CEC covers a wide range of substances, including biological and radiological materials, but this White Paper and the CEC Monitoring Programs Fact Sheet, Identification of Key CEC Variables Fact Sheet, and Risk Perception and Communication Fact Sheet focus more on chemical CEC as a starting point to address the issue. Nevertheless, the concepts presented in this document also apply to other types of CEC (e.g., biological), and the Adoption of Analytical Methods for CEC Fact Sheet, which provides a summary of CEC analytical methods, addresses a wider range of CEC.

2. Factors that May Influence a State's Ability to Address CEC

The Interstate Technology and Regulatory Council (ITRC) CEC Team developed and distributed a 21-question survey when the team was formed. The survey was designed to gather information that would help the team understand the variety of efforts and resources that state agencies are currently directing toward CEC programs and what additional information is needed. Thirty states and five federal agencies responded. Respondents identified the following key issues:

- Several states do not have or use databases to track or assess specific CEC but would find such tools useful.
- Funding, staff resources, guidance, and agency/legislative support are critical to launching a formal CEC program.
- Several states do not have their own process to identify and evaluate characteristics of CEC for prioritization.

The information obtained from the state survey was used as a general guide for the discussion below and discussions presented in the Fact Sheets. Other factors identified in the state survey that could limit development of a CEC program, such as state-specific bureaucracy, legislative support, and other regulatory issues, are not addressed further in this White Paper or associated Fact Sheets.

2.1 Available Information About a Potential CEC

Gathering information on CEC can be a challenging and time-consuming process that may require staffing and expertise that

are not currently available within many state organizations. The options available for establishing regulations or guidance for a CEC are heavily dependent on data sufficiency and sharing. For some states it may be possible to conduct comprehensive literature reviews, prepare research articles and reports, and review regulatory databases to identify substances that have recently gained attention as potential CEC.

In particular, when CEC have been identified through monitoring, information on distribution and/or toxicity may be very limited[1]. Moreover, in many cases, there is not enough information to evaluate risk using standard regulatory approaches, as most CEC have not been sufficiently studied to fully assess their toxicity. The chemical may still be considered a CEC if it may pose a potential risk pending further investigation. Even when *some* toxicity information is available, that information may not be adequate to permit the calculation of a toxicity value (e.g., reference dose, cancer slope factor, or ecological effects threshold) that is scientifically supportable using standard risk assessment methods, and it may be necessary to use a surrogate or other modeling approaches (See the Identification of Key CEC Variables Fact Sheet).

The Risk Perception and Communication Fact Sheet provides some guidance on addressing situations with little data and high potential consequences.

2.2 Communication, Public Concern, and Coordination

Stakeholders play an important role in the process of identifying and addressing CEC, but communicating information about CEC with internal and external stakeholders can be challenging. More details on strategies for communicating with stakeholders are provided in the Risk Perception and Communication Fact Sheet. Below is a brief discussion of the variety of communication challenges that may develop.

2.2.1 Importance of Effective Communication and Outreach

The local community and public are often alerted to a new CEC via news or social media, which may give the impression of a long-ignored problem or may paint the issue in alarmist terms. This may generate fear and distrust. Regulatory agencies and responsible parties should engage with the local community early and establish information to be shared with the public and open lines of communication as soon as a new CEC has been identified using a CEC identification framework or process such as one presented in the Identification of Key CEC Variables Fact Sheet. Technical and health experts should be made available to address public concerns. These experts, together with a risk communicator or health educator, need to have a plan for communicating the risk associated with the CEC, including uncertainties such as data sources, unknowns, assumptions, etc. (see the Risk Perception and Communication Fact Sheet). Use of social media and well-publicized websites for frequent information sharing, combined with prompt and effective responsiveness to questions, are essential in the early stages when there may be a high fear factor. Engaging with local community organizations is also helpful. Finally, it may be advisable to regularly hold meetings with the community based on the phase of the CEC or the level of public concern.

In a world with instant information sharing, the public fear factor is easily raised and can be challenging to address. A useful way to address fear and public outcry is by listening to and accepting public concerns and developing prompt responses that reflect knowledge and awareness and are presented in clear terms and straightforward language. Effective dialogue is not achieved through one meeting or media release; fear and outcry can only be reduced through frequent communications. If the specific fears and concerns of the public are known early in the process, it may be possible to effectively address the public's concerns if the high-profile individual is willing to learn more about the issues. Otherwise, further public interaction is necessary. Refer to the Risk Perception and Communication Fact Sheet for a more detailed discussion about communication with the public.

2.2.2 Coordination with Other States, the Federal Government, and Academia

A state advisory council that includes representatives from the applicable scientific disciplines and state and federal government agencies should be formed to facilitate information sharing and development of a road map to guide scientific and legislative processes. Including representatives from the health care system, such as state and local health departments, hospitals, and physicians, as well as environmental departments and similar organizations, should also be considered. These agencies and sectors, which are often viewed as a trusted source, could provide critical help when disseminating information about CEC to the public. The elements of the road map will identify the types of information required and facilitate sharing of ideas between agencies and experts. The process of investigating and addressing CEC is a complex multi-year effort. It is important to communicate consistently in clear, plain language. Communications should be provided in English and in other languages as appropriate based on the limited English proficiency data for the impacted community. Communications should also be accessible to those with hearing or sight disabilities. Because states may have different risk concerns, it is important to recognize and consider local expertise, including the lived experiences of

community members. States should have at least one identified CEC point of contact and a mechanism for information transfer among agencies.

2.3 Funding

Funding for state CEC programs, monitoring, and investigative activities can include two major sources: state and federal funds. State funding for CEC is dependent on the priorities and policies of the state. Funding for CEC can come from state laws that give state agencies the authority and funding to establish a CEC program or otherwise monitor and characterize CEC. State CEC programs are often established gradually, with an assortment of federal and state funding sources; therefore, acquiring appropriate funding may be a challenge when a program is first established.

The second major source of funding is federal laws that provide funding for specific programs. Federal funding is typically assigned a steward such as USEPA or the United States Centers for Disease Control and Prevention (CDC), which has the financial processes and resources to control the distribution of the funding. Grant managers should be familiar with federal and state accounting regulations.

The BIL is an example of federal funding that can be used for CEC. BIL funding includes $5 billion in principal forgiveness loans and/or grants for drinking water and clean water state revolving funds. USEPA oversees both the Drinking Water and Clean Water State Revolving Funds, and each of the 50 states and Puerto Rico operates its own Drinking Water and Clean Water State Revolving Fund program. The specific procedures and uses of BIL funding are captured in detailed guidance provided by USEPA to state funding authorities.

Another example of federal funding that could be used for CEC is the CDC's State Biomonitoring Grant Program. The CDC's Division of Laboratory Sciences administers the National Biomonitoring Program, which assesses the exposure of U.S. populations to environmental chemicals and toxic substances (https://www.cdc.gov/biomonitoring/index.html) (CDC 2022). This program can be used by the states to set up laboratories and to fund the collection of samples that would enhance understanding of human exposure to and the fate and transport of chemicals in the environment.

USEPA and other federal agencies are working to address environmental and public health challenges affecting historically underserved communities. These include communities adversely impacted by persistent poverty, inequality, and lack of funding/resources (Fox 2022). One mechanism for addressing these challenges is the environmental justice program, under which several grant programs have been established to help states and other entities better serve these communities (OEJECR USEPA 2020). Other federal and state funding is available for addressing CEC, but a comprehensive list of funding opportunities is beyond the scope of this document.

2.4 Other Factors to Consider

Despite these challenges, states may still seek to proactively address CEC or develop a CEC program based on external influences/considerations. In the face of limited scientific and regulatory information, state environmental and human health experts may leverage their participation in national networks like ITRC, the Environmental Council of the States, and other organizations to amplify technical understanding of CEC, identify policy options to address CEC, and direct resources available to fund responses to CEC. High-profile events may also have the potential to redirect public resources and political will toward addressing CEC and improving the capability for appropriate responses to future CEC detections.

3. Current CEC Programs and Approaches

When determining whether to set up a CEC program or evaluating CEC data, states may wish to consider existing programs and review approaches developed by other federal and state agencies. States can learn how these existing programs or approaches have tackled the factors discussed in the previous section. The Association of State and Territorial Solid Waste Management Officials developed additional guidance related to developing a CEC monitoring program that may be worth considering (2023-01_State_CEC_Program_Guide.pdf (astswmo.org)). Several existing programs that have considered these factors are briefly summarized in the following sections.

3.1 State Programs

In general, state environmental agencies have the mission to protect the environment and public health. States use a variety of approaches, which depend on priorities and resources, to monitor, address, or regulate CEC. These approaches range from basic identification of specific CEC as a potential concern based on properties of persistence and bioaccumulation to development of a weight of evidence approach that considers a wider range of variables. A few states

also have programs (e.g., California) that focus on preventing the upstream use of chemicals in manufacturing, consumer products, or other processes that have the potential to release chemicals to the environment. Discussion of these types of programs are beyond the scope of this project. Additional details on state CEC programs can be found in the CEC Monitoring Programs Fact Sheet.

The following established state programs focused on CEC are provided to serve as useful examples. This section is not meant to be exhaustive; a more complete list of state programs can be found in the CEC Monitoring Programs Fact Sheet.

California has a CEC Program that is a joint effort of the California State Water Resources Control Board and the Regional Water Quality Control Boards. The California CEC Program is developing a statewide plan that applies a data-driven process and a risk-based framework to prioritize CEC for assessment, monitoring, and management. This approach has been used to support recommendations for monitoring CEC in aquatic ecosystems and potable recycled water. The CEC Program is working to support useful data collection and data transparency through development of statewide CEC data management and quality assurance program plans. The CEC Program is also working with interagency partners to leverage resources and develop collaborative solutions to address CEC using an approach that considers the impacts of chemical management from product sourcing, manufacturing, transportation, use, and disposal.

Minnesota has been monitoring CEC in its water resources and has had a dedicated program to develop health-based guidance for CEC in drinking water since 2009. The Minnesota Pollution Control Agency (MPCA) monitors for CEC in groundwater annually and in its rivers and lakes every five years in connection with the National Aquatic Resource Surveys conducted by USEPA. The MPCA established a process for developing Aquatic Toxicity Profiles (https://www.pca.state.mn.us/water/contaminants-emerging-concern) (MPCA 2023) that provides a review of information about a CEC and then ranks it using a weighting formula for comparison with other CEC. In addition, the Minnesota Department of Health (MDH) uses a quantitative scoring system to establish priorities for emerging contaminants identified in surface and groundwater and generates health-based guidance for identified CEC (https://www.health.state.mn.us/communities/environment/risk/guidance/devprocess.html) (MDH 2022). For CEC with limited information, MDH describes the hazard posed by the CEC instead of generating a health-based guidance.

Michigan Department of Environment, Great Lakes, and Energy (MI EGLE) regulations require owners and operators of contaminated properties to consider CEC when taking actions to eliminate unacceptable exposures from contamination (MI EGLE-RRD Due Care Guide) (EGLE 2019). If a CEC has no established cleanup criteria, owners and operators are required to evaluate the detected chemical against a state cleanup standard. The state cleanup standard is developed by (1) using USEPA screening levels or risk-based criteria developed by MI EGLE and (2) determining availability of an analytical method.

3.2 U.S. Environmental Protection Agency Approaches

USEPA has processes for addressing chemicals that are not currently regulated. These processes can serve as sources of information for identification and evaluation of CEC. Key programs that USEPA uses to monitor and/or evaluate CEC are associated with the Safe Drinking Water Act (SDWA) and the Toxic Substances Control Act (TSCA). Under each of these statutes, USEPA has developed regulations and guidance to address CEC. Additionally, USEPA has instituted voluntary programs for phasing out or reporting CEC.

First, under the SDWA, USEPA's Office of Water is required to develop a Contaminant Candidate List (CCL) that identifies priority contaminants for regulatory decision-making and information collection (OW USEPA 2014). The CCL is a list of drinking water contaminants that are known or anticipated to occur in public water systems but are not currently subject to USEPA drinking water regulations. The SDWA directs USEPA, when developing the CCL, to consider the health effects and occurrence information to identify the contaminants that present the greatest public health concern related to exposure from drinking water. The USEPA must decide whether to regulate five or more contaminants on the CCL list, a process known as regulatory determination (https://www.epa.gov/ccl) (OW USEPA 2014). In addition, USEPA uses the CCL to prioritize drinking water research and guide decisions about which contaminants to monitor for under the Unregulated Contaminant Monitoring Rule (UCMR) (https://www.epa.gov/dwucmr) (OW USEPA 2015). The UCMR requires that every five years, large public water systems, small public water systems between 3,300 and 10,000 people (subject to the availability of USEPA appropriations and sufficient laboratory capacity), and a nationally representative sample of small public water systems serving less than 3,300 people monitor for up to 30 unregulated contaminants. This monitoring is used by USEPA to understand the frequency and level of occurrence to support future regulatory decisions to protect public health.

Second, under TSCA, USEPA has developed a Chemical Prioritization Process for Risk Evaluation (OCSPP USEPA 2023). TSCA requires that when identifying candidates for the prioritization process, 50% of all high-priority designations be drawn from

the 2014 Update of the TSCA Work Plan (OCSPP USEPA 2014) and that USEPA give preference to Work Plan chemicals with the following characteristics:

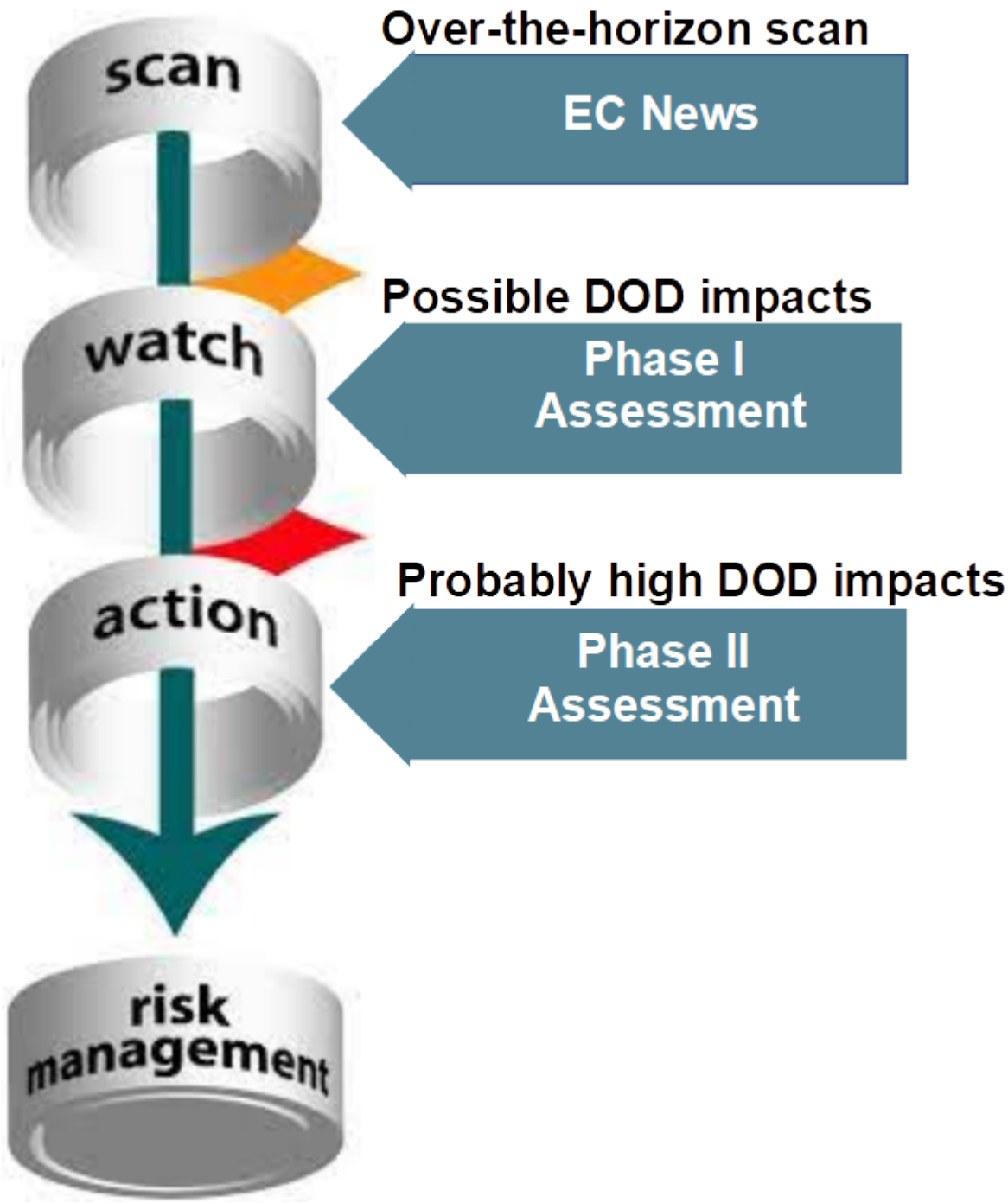
- high persistence and bioaccumulation
- known human carcinogens
- acute or chronic toxicity at low doses

Aside from these statutory preferences and requirements, USEPA has discretion to determine which of the thousands of active chemicals to prioritize for risk management.

3.3 Department of Defense Approach

In 2006, the Office of the Deputy Under Secretary of Defense for Installations and Environment initiated a program to proactively minimize adverse impacts from emerging chemicals (ECs) to human health, the environment, and vital Department of Defense (DOD) mission areas. ECs are defined by DOD as “chemicals relevant to the DOD that are characterized by a perceived or real threat to human health or the environment and that have new or changing toxicity values or new or changing human health or environmental regulatory standards” (DOD 2019, 15).

The Chemical and Material Risk Management (CMRM) Program implements a three-step process to identify and mitigate EC risks (Figure 1) (CMRM 2022). The data-driven process leverages current science and subject matter expertise from regulatory agencies, industry, academia, and private organizations. Additionally, DOD is required to integrate Environmental, Safety, and Occupational Health (ESOH) risk management into their overall systems engineering process for all developmental and sustaining engineering activities under DOD Instruction 5000.02 (DOD 2022). Managers must eliminate ESOH hazards where possible and manage ESOH risks where they cannot be eliminated.



Adapted from DoDI 4715.18, 2019

Scan evolving science literature and regulatory actions for chemicals or risk assessment actions that may impact the DOD, human health, or the environment.

Conduct qualitative Phase I assessments to estimate possible impact of screened chemicals to five DOD functional areas: (1) Environment, Safety, and Health; (2) Training and Readiness; (3) Acquisition/ Research, Development, Testing, and Evaluation; (4) Production, Operations, Maintenance, and Disposal of Assets; and (5) Environmental Cleanup. If assessment determines no high risk of impact, chemical is managed on the EC Watch List. If assessment, and subsequent verification, determines high risk of impact, chemical is moved to the EC Action List. The EC Watch and Action Lists are managed through routine monitoring of new and changing toxicity values and/or regulatory standards.

Conduct quantitative Phase II assessments to identify Risk Management Options (RMOs). A Phase II Impact Assessment evaluates likely impacts and costs to the DOD and identifies RMOs, ranging from developing substitute materials to implementing new pollution prevention measures or technologies.

Propose RMOs to DOD's Emerging Chemicals Governance Council (ECGC) for endorsement. Endorsed RMOs are designated as Risk Management Actions (RMAs). If the ECGC does not endorse an RMO, the CMPM Program will either dismiss the RMO, develop a new RMO, or refine the existing RMO based upon the ECGC recommendations. The CMPM Program monitors the implementation of the RMAs by the appropriate DOD components and periodically reports on the status.

Figure 1. Emerging chemicals "Scan-Watch-Action" process for assessing and managing risks.

Source: Adapted from Cunniff, S. 2009. Identifying Emerging Contaminants. The Military Engineer, January–February 2009. (Cunniff 2009)

4. A New Framework for Identifying and Monitoring CEC

This White Paper summarizes and provides context for the four associated Fact Sheets developed by the ITRC CEC Team to aid state agencies in the development and implementation of a CEC program. The four Fact Sheets were developed from key concepts that the CEC Team identified as vital to the structure of a CEC program. A brief overview of each of the Fact Sheets is provided below and summarized in Figure 2. The Fact Sheets are not intended to be used as a flow chart or linear process. The Fact Sheets provide different information that can be used as part of a CEC program and should be used as needed and not in any particular order.

CEC Monitoring Programs Fact Sheet: This Fact Sheet provides a detailed table of current federal, state, local, and international CEC programs that monitor and/or compile data on CEC. Although most of these current programs are focused on monitoring activities related to per- and polyfluoroalkyl substances (PFAS), the information provides a starting point for addressing other CEC. At this time, only a few states have the funding and capacity to establish research programs to evaluate contaminants to determine whether they are CEC. The information in this Fact Sheet can be used as a resource by states that do not currently have the resources or capacity to monitor CEC in the environment. The purpose of the table is to provide information on existing programs in a variety of media that states and other stakeholders can explore and use when formulating their own CEC monitoring programs. States may also consider establishing processes for addressing known CEC such as data sharing across state environmental programs, data mining, expanded monitoring, source identification, and treatment.

Identification of Key CEC Variables Fact Sheet: This Fact Sheet outlines a strategic process for evaluating and prioritizing candidate CEC using the following criteria: occurrence, human health and/or ecological toxicity, and physical-chemical properties. The Fact Sheet provides an initial screening approach to discern whether a CEC is a low, medium, or high priority. A detailed flow chart and supporting tables provide more criteria-related information and data sources. The Identification of Key CEC Variables Fact Sheet also presents a case study outlining the process applied to a hypothetical substance.

Risk Perception and Communication Fact Sheet: This Fact Sheet discusses risk communication for CEC, including the benefits and challenges of communicating risk to internal and external stakeholders. It also provides guidance on appropriate communication and some pitfalls to avoid. A library of risk communication and community engagement materials is included. The Risk Perception and Communication Fact Sheet also presents links to the ITRC CEC Case Study, which provides examples of risk communication strategies and challenges.

Adoption of Analytical Methods for Identifying CEC Fact Sheet: This Fact Sheet summarizes the types of analytical methods that can be used to identify and potentially quantify most CEC, including chemical and chemical classes, biological contaminants, and particulates. The Fact Sheet provides analytical options that can be selected based on how much data, if any, are available for a CEC, including nontargeted and targeted analyses when information on specific chemicals that may be present is not known.

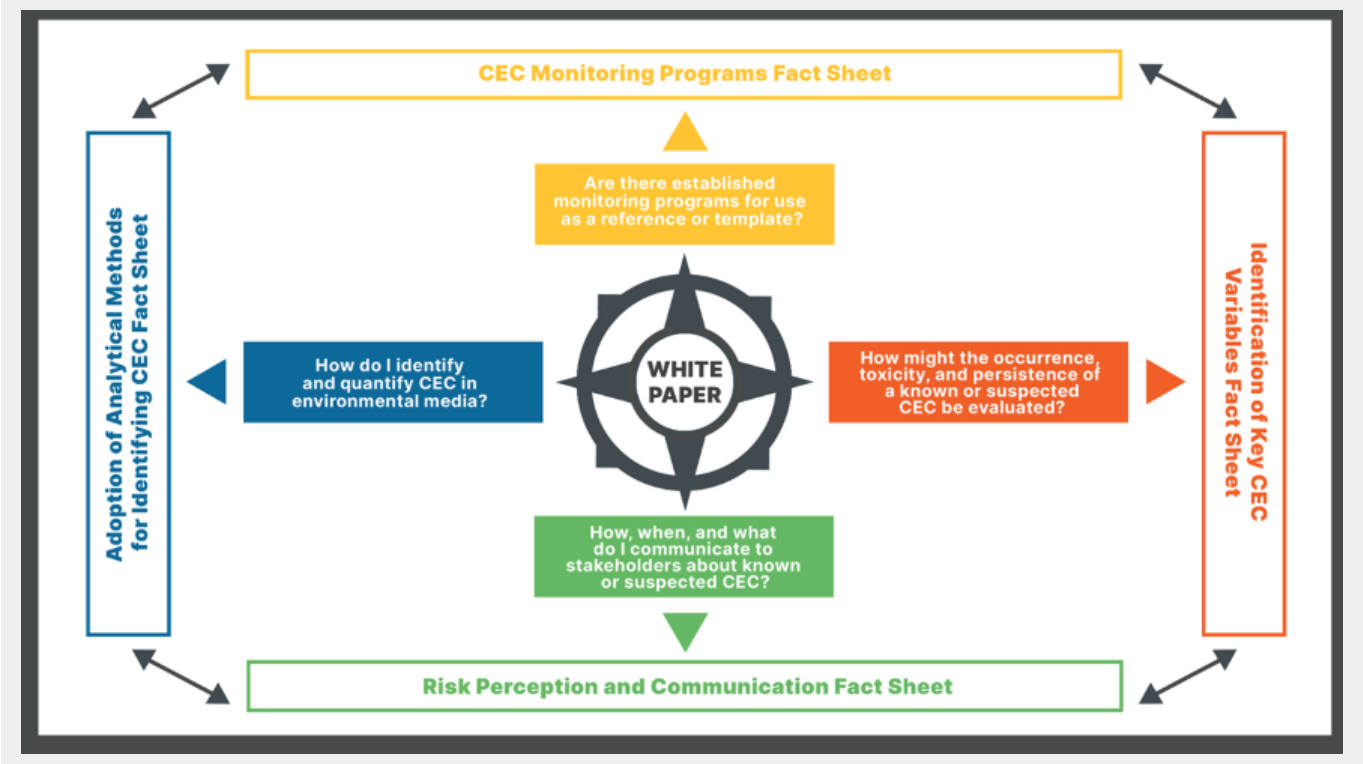


Figure 2. CEC Framework.

Click on an outer rectangle to be moved to that fact sheet.

Source: ITRC CEC Team.

5. Closing

Protecting public health and the environment includes identifying and evaluating CEC present in environmental media even when minimal information is available. By doing so, state agencies can evaluate potential risks posed by CEC, prioritize CEC based on exposure and potential toxicity, and communicate critical information to the public and other stakeholders. Developing such a program not only helps agencies manage risk but also presents an opportunity to address other issues such as those related to environmental justice. In most cases, understanding and managing CEC is a complex process that requires careful planning and consideration of many factors, as indicated above. To support this process, this White Paper and the associated fact sheets provide a framework that state environmental or health agencies can use to develop a CEC program. This framework is intended to be useful whether or not a state has a CEC program. Overall, understanding and monitoring CEC can provide the information necessary to allow states to take corrective and regulatory action and, ultimately, safeguard public health and the environment.

[1] The Risk Perception and Communication Fact Sheet provides some guidance on addressing situations with little data and high potential consequences.

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Identification of Key CEC Variables Fact Sheet

This Fact Sheet has been organized into the following subsections:

1. INTRODUCTION

This Identification of Key CEC Variables Fact Sheet presents the key variables that may be used as criteria to prioritize actions to address a contaminant of emerging concern (CEC). In addition, this Fact Sheet contains suggested resources that can be used to determine the best available scientific information for these variables. The lack of scientific information on any one variable or multiple variables (e.g., exposure, toxicity, fate, and transport) poses a need for further research or data gathering to reduce the uncertainty and increase the accuracy when evaluating the risk posed by a CEC.

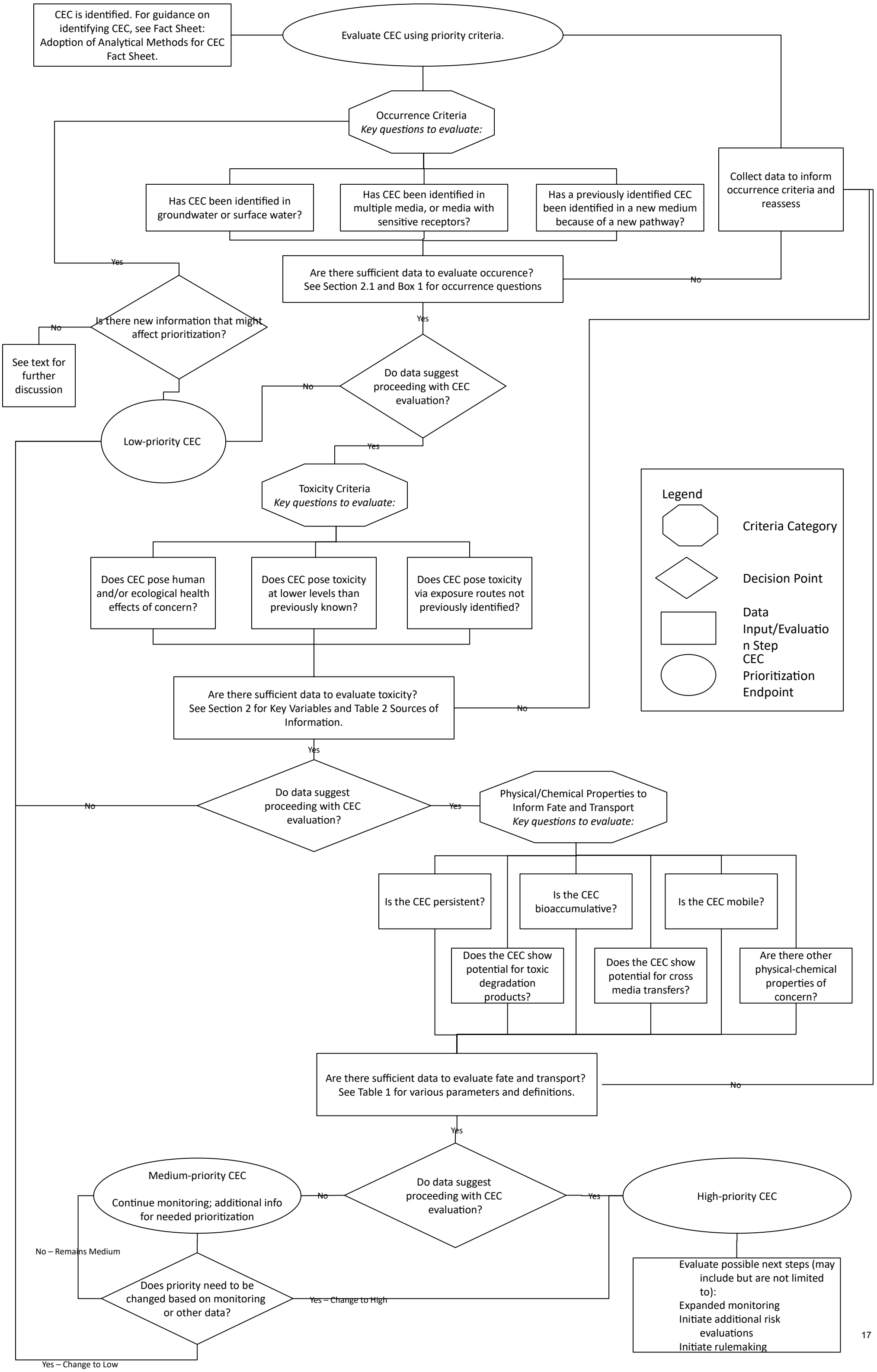
Section 2 provides a process flowchart on how to approach the evaluation of CEC, the specific types of information about the CEC that need to be considered as part of prioritization, and the order in which the information should be considered. Section 3 summarizes key variables that are important for newly identified risks stemming from the exposure and toxicity domains and includes sources where both empirical and estimated (calculated) variable information can be found. Section 4 summarizes available schemes and tools for prioritizing and/or interpreting CEC data.

Concerns about contaminants emerge because human activities relating to substances (e.g., the built environment, production, use, and disposal) release contaminants into the environment and/or lead to exposures that then may become public and environmental health concerns. These contaminants become recognized through detection and identification in environmental media locally, regionally, or globally. The term "**CEC**" **refers to substances and microorganisms, including physical, chemical, biological, or radiological materials known or anticipated to be present in the environment, that may pose newly identified risks to human health or the environment.** Thousands of chemicals are released into and identified in the environment, and communities, regulators, and policy makers need to know how to determine which of these CEC should be prioritized.

The flowchart presented in Figure 1 was newly developed by the Interstate Technology and Regulatory Council (ITRC) CEC Team to identify a logical process for evaluating CEC other than pathogens and radiologicals. The process uses prioritization criteria and assumes the CEC (which has presumably been identified as the result of an event, a concern from the media or public, or a discovery of new information) can be measured in the environment (see the Adoption of Analytical Methods for CEC Fact Sheet). The process flowchart is intended primarily for chemical contaminants. Due to the unique characteristics of biological (microbials) and radiological materials and the lack of expert resources within the ITRC CEC Team, process flowcharts for those CEC are not currently available but may be considered in future efforts. Additionally, this Fact Sheet addresses CEC with direct effects to human and ecological endpoints and does not consider those that may have indirect effects, such as chemicals, for example, that may impact climate change or deplete ozone in the upper atmosphere.

2. PROCESS FOR PRIORITIZING CEC

Figure 1. Process Flowchart for prioritizing CEC



Ultimately, the intent of this process is to designate a CEC as low, medium, or high priority to inform the next evaluation steps and decision-making options (Table 1). The designations are based on occurrence, risk/toxicity, potential for exposure to receptors, and physical-chemical characteristics that inform mobility, bioaccumulation potential, and/or environmental degradation. These designations involve a certain degree of professional judgment that must be applied when weighing different factors and evidence.

Table 1. CEC prioritization

	LOW-PRIORITY CEC	**MEDIUM-PRIORITY CEC**	**HIGH-PRIORITY CEC**
Summary of Current Data	No significant concern	Additional information needed for further prioritization	Widespread or significant concern
Monitoring Follow-Up	No monitoring at this time	Continued monitoring	Expanded monitoring
Additional Steps	Watch for new information	Seek out new information that may inform a need for risk characterization	Additional risk characterization and potential rulemaking

Table 1 summarizes the CEC prioritization scheme in terms of level of concern, monitoring follow-up, and potential additional steps. Each category is expanded on below:

- Low-priority CEC: A CEC that is present in the environment, but current data suggest it does not pose a significant threat and does not require further monitoring at this time, either due to infrequent occurrence, low risk/toxicity, minimal potential for exposure to receptors or absence of receptors, or physical-chemical characteristics that may suggest poor mobility, low bioaccumulation potential, or high environmental degradation rate. Watching for new information is important for potential reprioritization. Additionally, the possibility of toxic breakdown products should be considered.

- Medium priority CEC: A CEC that is present in the environment for which additional information is needed and should be sought out. Continued monitoring is recommended. New information (e.g., lower toxicity endpoint, sensitive health effect, new impacted medium (vapor/air), or new fate and transport characteristic) may require additional risk characterization to determine whether the medium-priority CEC is downgraded to a low priority, remains a medium priority, or is elevated to a high-priority CEC.

- High-priority CEC: A CEC that, based on its physical-chemical characteristics and occurrence, risk/toxicity, potential exposure pathways, and/or presence of receptors, is recommended for expanded monitoring, additional risk characterization, and potential rulemaking.

The science and information on CEC are evolving. Per- and polyfluoroalkyl substances (PFAS) are a notable example. Compound classes and mixtures may also emerge as CEC. *CEC can be shifted between priority levels at any time.* For example, a low-priority CEC can be reintroduced into the evaluation process at any time based on new data (e.g., new information on toxicity, exposure pathways or impacted media) and can result in reconsideration of its CEC status. As such, reevaluation, or reassessment of any given CEC should periodically occur depending on the latest information. As shown in the flowchart, additional data could result in the reclassification of a CEC's priority.

To differentiate among the low, medium, and high priorities, the CEC flowchart considers three categories of criteria for prioritizing CEC. These are, in sequence: occurrence, toxicity, and physical-chemical properties that inform fate and transport and chemical behavior. Following the risk assessment paradigm, occurrence and toxicity are considered first—the consideration of occurrence before toxicity was selected for practical purposes. These are discussed in the following sections.

2.1 Occurrence

Box 1 – Example Data Sufficiency Questions

- Is the analytical method adequate for the need (i.e., is the detection and/or reporting level sufficiently sensitive)?
- Are there data of sufficient quantity/quality to evaluate?
- Are results reproducible?
- What media are data available for?
- Are there sufficient quality assurance/quality control (QA/QC) samples to validate the data?
- Were data collected using/following proper standards and guidelines?
- Were enough samples collected to indicate the presence of the substance in the environment?

The identification of a CEC in groundwater or surface water used for drinking water purposes is often a priority compared to other environmental media because of direct exposures to humans through drinking water and other household uses of water. For this reason, groundwater or surface water is often the first exposure source assessed and is highlighted in the flowchart. Depending on the situation, concerns over other exposure sources may predominate. For example, the occurrence of a CEC in soil may lead to a higher priority assignment depending on several factors, including land use (e.g., residential, day care, or school) or presence of sensitive subpopulations (e.g., children). Another example could be consumption of recreationally caught fish where a bioaccumulative CEC may be present at levels of concern even when it is nondetectable in surface water. CEC may also be identified in consumer products, which could lead to various exposure sources and pathways (e.g., dermal exposure, ingestion of contaminated food, inhalation of contaminated house dust, etc.). Overall, detection in multiple media adds to the concern due to the combined exposures to these multiple media (e.g., water, wastewater, air, soil, and biota) and likely multiple exposure routes (e.g., ingestion, dermal contact, inhalation) and higher potential for cross-media transfer. Importantly, an already regulated, well-established contaminant may be identified as a potential CEC. This could be due to new information that indicates potential for toxicity at lower exposure levels, its identification in a new media (e.g., air), or awareness of migration along a new exposure pathway (e.g., vapor intrusion).

Proximity of the CEC to sensitive receptors, and the exposure sources (e.g., drinking water, bathing, ingestion, recreation) and exposure routes (e.g., ingestion, inhalation, and dermal absorption) for those receptors, are also critical inputs to the occurrence evaluation. For drinking water, the source type (private well, public water system, groundwater- vs. surface water–based system, etc.) would also need to be evaluated. Agencies may also consider analyzing wastewater samples from treatment plants to detect and quantify the presence of the CEC, which can provide valuable information on its occurrence and distribution, as CEC often enter the environment through wastewater effluent.

An analogous process can be applied to ecological exposures. For example, occurrence in aquatic ecosystems (surface water and sediment) is often the first exposure question to evaluate if there is enhanced mobility and biological transfer potential within complex food webs. Occurrence in soil can lead to higher prioritization based on the presence of sensitive receptors (such as endangered species or valued keystone species), or the CEC may be susceptible to uptake by herbivorous or carnivorous animals via vegetation or soil biota. The priority assignment may also consider whether occurrence can affect the diversity and abundance of ecological communities.

When evaluating the occurrence criteria, agencies will want to consider analytical data sufficiency factors such as those identified in Box 1. Adequate characterization can be taken into account when making a decision about whether a CEC needs further evaluation or should be prioritized as a CEC. When data are not sufficient to make a judgment, the flowchart recommends additional data collection and reassessment. If sufficient data are found to be available, the reviewer determines whether (1) the CEC is a low priority (in which case, it would not be evaluated further in the flowchart) or (2) evaluation should proceed to a risk/toxicity assessment to determine next steps (e.g., monitoring/surveillance).

2.2 Toxicity

A toxicity value provides a concentration or dose above which exposure per unit of time may result in unacceptable health risks (for expmle, milligrams per kilogram body weight pre day [mg/kg bw/day])

The toxicities posed by a CEC are evaluated in relation to human health–based and/or ecological health effects. Many CEC may have information available on chemical characteristics but no available information on toxicity. For other CEC, toxicity information may be available but information about new exposure routes or exposure media may be lacking. In many cases, toxicity data may be limited and may not include the types of studies typically used to evaluate health effects in federal and/or state risk assessments. Toxicity data should be vetted to determine whether it can provide an adequate assessment of human health or ecological risks. Other potential considerations for evaluating CEC include the identification of toxicities at lower levels than previously known or identification of toxicities for one or more additional exposure routes. Toxicity evaluations (whether for human health or ecological receptors) will inform the degree to which a CEC poses a risk. This evaluation should also potentially include sensitive subpopulations that would be specific to a given site and CEC. Details

regarding specific toxicity information are discussed in Section 3: Sources of Key Variables to Consider When Evaluating Potential Toxicity and Exposure.

For a toxicity assessment to be meaningful, the extent and quality of information is a consideration. When incomplete toxicity data impede the development of numerical toxicity values, other tools may be used to develop or estimate toxicity values (see Section 3.3, Table 2: Sources of key variables information). For all estimates, an explanation of uncertainties, data sources, and assumptions should be provided to allow for clarity and transparency (see the Risk Perception and Communication Fact Sheet).

After reviewing toxicity information, three questions are considered:

- Does the CEC pose human and/or ecological health effects of concern?
- Does the CEC pose toxicity at lower levels than previously known?
- Does the CEC pose toxicity via exposure routes not previously identified?

Pathways to consider should include the potential for toxicity by uptake via the food chain (e.g., via feed, animal products, or edible plants). If data are insufficient to assess these factors, additional data should be collected for reassessment (see Section 3: Sources of Key Variables to Consider When Evaluating Potential Toxicity and Exposure). If data are available, an assessment can be made as to whether a specific CEC should be prioritized. For ecological toxicity, it is important to note that a variety of endpoints may need to be considered in addition to acute mortality, such as behavioral changes, reproductive damage, sex changes, etc. If the assessment indicates sufficient toxicity data, the next step is to consider the physical-chemical property criterion.

Box 2 – Potential Additional Questions Regarding Physical-Chemical Mobi8lity and Transport

- Was free product encountered in groundwater or siil?
- Were degaradation products identified in the analyzed media?
- Does the CEC have uniue characteristics (e.g., foam, amphiphilic) which affect transport?
- Can the CEC migrate along preferential pathways such as utility corridors or backfill?
- Is the CEC moving or behaving defferently than other substances detected in the area

2.3 Physical-chemical Properties That Inform Fate and Transport and Chemical Behavior

Physical-chemical properties influence how long a CEC remains in the environment and the environmental media in which it is present. They inform how the CEC's potential for exposure could increase, through its persistence in the environment, bioaccumulation, mobility, toxic degradation products, cross-media transfer, or other factors. This is the final step for determining whether a CEC should be considered a high-priority CEC. See Table 3 in Section 3.3 for a brief description of various properties used to determine persistence, bioaccumulation, and mobility.

These attributes reflect the potential for CEC to remain in the environment and cause exposure to human and ecological receptors. Physical-chemical properties may be empirical or estimated. Consideration may be given to the circumstances that dictate collection of site-specific data. Published data may be used when available. Data used to establish these properties also need to be of sufficient quality. Box 2 identifies additional considerations relative to physical-chemical mobility and transport.

3. SOURCES OF KEY VARIABLES TO CONSIDER WHEN EVALUATING POTENTIAL TOXICITY AND EXPOSURE

Assessments of CEC require some information on the CEC's toxicity as well as information on potential exposures. When considering toxicity, regulatory agencies usually consider chronic (cancer or noncancer), subchronic (noncancer, reproductive, or developmental), and acute (noncancer) health effects. Federal and state environmental and health agencies establish toxicity values, but the values generated can vary due to several factors. These can include the scientific information available at the time the value was developed, the consideration of a sensitive health effect or endpoint, and the choice of uncertainty factors (for noncancer endpoints). When no federal or state-developed toxicity value is available, or when toxicologists need to consider new information, the state may need to conduct its own toxicological assessment to develop a value that is defensible based on best available information. Many states prefer to use existing toxicity values developed by authoritative agencies or do not have the resources to develop their own values, while other states develop

their own toxicity values when necessary. Some states may choose to develop their own values if they do not agree with the scientific basis of available values; some states may be required to make different assumptions (e.g., regarding risk); and some states may also decide the available values are not applicable to or representative of conditions and situations present in their respective state (e.g., exposure of specific populations, water quality differences for aquatic life values, etc.). To facilitate a valid process for deciding which toxicity values should be applied in any given risk evaluation, the United States Environmental Protection Agency (USEPA) and many states use a hierarchy of sources (ECOS 2007; ITRC 2005; 2008; OSWER USEPA 2013, 3; 2009; ORD USEPA 2023d; 2015a). Table 2 presents a summary of sources relevant to the toxicity of a CEC.

There is less consensus on standard toxicity values and source hierarchies for ecological risk than for human health values. This is due to the wide variety of potential plant and animal receptors and differences in responses from exposure to environmental CEC. Defensible values require careful attention to study validity, endpoints, and uncertainty factors. Information on CEC of interest may be available in various databases curated by state agencies, federal sources (e.g., National Oceanic and Atmospheric Administration (NOAA), USEPA, the Department of Defense, and the Department of Energy), or national and international organizations.

When considering exposure pathways, physical-chemical criteria influence how long a chemical remains in the environment and the environmental media in which it is present and could increase the CEC's potential for exposure (persistence, degradation products), influence how it is taken up and processed in biota, and affect how it behaves in the food chain (e.g., bioaccumulation, cross-media transfer). Table 3 presents a brief description of key variables used to help prioritize CEC in relation to persistence, bioaccumulation, and mobility.

When standard approaches are not immediately applicable for use in evaluating CEC, the resources presented here can help states with decision-making regarding CEC. Table 2 summarizes sources of key variables and is explained in Sections 3.1 and 3.2.

Table 3 summarizes properties that inform fate and transport and is explained in Section 3.3.

3.1 Human Health Risk

Suitable criteria for considering risk to human health (i.e., toxicity values) may be available in multiple sources of widely varying quality and applicability. The sources are discussed below in three groupings without ranking relative importance. Table 2 provides a summary of each.

3.1.1 Group 1: U.S. Federal Values—IRIS, OW, ATSDR, PPRTV, and OPP

This group includes U.S. federal sources of human health toxicity values. For chemical exposures, the Integrated Risk Information System (IRIS) (ORD USEPA 2023d) is typically the preferred source for toxicity values because they are based on high-quality assessments that include internal and external reviews. IRIS includes cancer slope factors and inhalation risk values. The IRIS database may not include a value for the contaminant of interest, or the IRIS assessment may not have considered newly available information. Values may be available from other USEPA offices such as the Office of Water (OW) Health Advisories (OW USEPA 2023h) or the Office of Ground Water and Drinking Water (OW USEPA 2023i). These OW values are toxicity values developed by USEPA OW for use in drinking water health advisories or ambient water quality criteria. Another widely accepted source is the Agency for Toxic Substances and Disease Registry's (ATSDR) (ATSDR 2023) toxicity assessments for acute, intermediate, and chronic noncancer effects. ATSDR uses these to calculate peer-reviewed minimal risk levels for contaminants. The Provisional Peer Reviewed Toxicity Values (PPRTVs) (ORD USEPA 2023e) are developed to support the USEPA Superfund program for chemicals that do not have IRIS values or those with identified subchronic or acute health effects (which are not evaluated in IRIS). PPRTVs undergo both internal and external peer review but are considered a second-tier source by USEPA. The USEPA Office of Pesticide Programs (OPP) (OCSPP USEPA 2023c) generates health effects assessment for pesticides.

3.1.2 Group 2: State Values, ECHA, OECD, Other International Values, PubChem

Most states have their own processes for determining human health toxicity values. Generally, states use the Group 1 sources to initially identify their toxicity values; however, many states conduct their own toxicological assessments even when an IRIS value is available. Examples of these states are California (OEHHA 2016), New Jersey (NJDEP 2020), and Minnesota (MDH 2022). Toxicity values from the European Chemicals Agency's (ECHA) Guidance on Information Requirements and Chemical Safety Assessment (ECHA 2023d) and REACH (ECHA 2023h) and other countries (e.g., Canada and its provinces (Health Canada 2007) and Australia (Australian Government 2022)) may be considered when selecting

values. Selection of values from these sources when available will need to consider the toxicity assessment process, including evaluating principal studies (preferably peer reviewed and published/publicly available) and evaluating whether the risk assessment guidance used by other countries differs from USEPA's guidance. The value should be appropriate and sufficiently protective for the exposure scenario of interest. The Organisation for Economic Cooperation and Development (OECD) Echem Portal (OECD 2023a) and the National Library of Medicine's PubChem (PubChem 2023a) are excellent toxicity data resources but do not offer human health toxicity values that are used in human health risk assessment.

3.1.3 Group 3: Other Sources of Toxicity Data That Provide Supporting Evidence to Health Effects

If the level of concern for the CEC is potentially high based on other factors, and limited toxicity data are available, it may be advisable for the state to conduct a toxicological assessment. One resource that may provide additional weight of evidence to the assessment is the USEPA Toxicity Forecaster (ToxCast), which provides experimental and predictive data (ORD USEPA 2023g). ToxCast predictive capabilities are also available through the USEPA CompTox Dashboard (USEPA 2023a). A suite of models and tools are available for considering chemicals regulated under the Toxic Substances Control Act (OCSPP USEPA 2022b). Other estimation and modeling resources include the Toxicity Estimation Software Tool (TEST) (ORD USEPA 2023f), OPERA (NTP 2023), EpiSuite (OCSPP USEPA 2023a), Derex Nexus (Labcorp 2023), OncoLogic (OCSPP USEPA 2023b), and ToxTree (Jeliazkova et al. 2018).

3.2 Ecological Risks

Identification of suitable criteria for considering risk to the environment, wildlife, and water quality may be available from multiple sources of widely varying quality and applicability.

3.2.1 Group 1: Established CEC Frameworks

Many potential CEC may have already been evaluated as part of permitting requirements or other chemical management purposes using established CEC frameworks. A good starting point is the ECHA dossiers for new chemicals (ECHA 2023h), which assemble available information, including ecological and environmental toxicological data, as part of the European chemical classification process. As an example, for aquatic and terrestrial (soil) organisms, hazards may be represented under ECHA by the predicted no effect concentration values. The Chemicals Management Plan in Canada is a similar compilation of data (Government of Canada 2006).

3.1.2 Group 2: Established Media Concentrations or Screening Values Deemed Protective of Various Ecological Endpoints

Established media concentrations or screening values deemed protective of different ecological endpoints may have been established by various agencies. Unfortunately, they are typically established for well-known contaminants and may not be available for CEC. One source is the USEPA National Recommended Water Quality Criteria (OW USEPA 2022a) for surface water. Many states (e.g., Texas (TCEQ 2023), New Jersey (NJDEP 2010), and Oregon (Oregon DEQ 2023)) maintain surface water, sediment, and soil screening values for extensive lists of chemicals. Other sources include the USEPA regional office compilations for media concentrations (e.g., Region 3 (ORD USEPA 2015c), Region 4, (ORD USEPA 2015b), and Region 5 (USEPA 2023b)); the NOAA SquiRTs (NOAA 2023) screening value compilations for sediment, soil, and surface water; the Department of Energy (DOE) Oak Ridge National Laboratory Ecological Benchmark Tool for Chemicals (RAIS 2022a) as part of the Risk Assessment Information System (RAIS 2022b); and Los Alamos National Laboratory ECORISK Database (Kieling 2017). Many other countries also maintain similar databases. These values are generally, but not always, compilations developed from primary or secondary sources, can be based on widely different methodologies, and can be of varying quality and applicability. They are also generally limited to more common contaminants. Nevertheless, they are some of the primary sources to consider when evaluating a CEC.

3.2.3 Group 3: Compilations of Measured Toxicity Criteria and Bioaccumulation Potential from Exposures to CEC

These sources typically present a review of toxicity or bioaccumulation testing results available in the research literature and may or may not include the prioritization and selection of a preferred toxicity reference value (TRV). In the first group are databases of research results such as USEPA ECOTOX (Olker et al. 2022), which presents details of toxicity evaluations for a great many chemicals and species of aquatic and terrestrial biota. ECOTOX also now has several data summary tools that allow the user to summarize and manage data outcomes. A similar database for bioaccumulation and tissue residue studies in aquatic environments is the United States Army Corps of Engineers Environmental Residue Effects Database (USACE ERED) (USACE 2023). These sources present a wealth of information but require the user to have toxicological knowledge to determine the quality and applicability to the specific site and concern at hand. The scientific literature can be referenced for

additional information.

3.2.4 Group 4: Surrogates and Models

Potential CEC may be lacking in published empirical evaluations of potential toxicity and hazard to the environment. It may therefore be useful to consider modeling approaches for such chemicals. Among these are the USEPA Ecological Structure Activity Relationships (ECOSAR) (OCSPP USEPA 2022a) Predictive Model, a quantitative structure activity relationships (QSAR) model to estimate aquatic toxicity for organic chemicals. QSAR models can be accessed through the OECD QSAR Toolbox (OECD 2023b) and VEGA (VEGA HUB 2023). In the absence of useful data on the chemical of interest, it may also be possible to consider similar chemicals as surrogates for the chemical of interest. This is a common approach for chemicals that exist as very similar congeners or isomers that can be extrapolated across the chemical class. Resources identified in the prior human health toxicity section "Group 3: State Toxicological Assessment Using Available Information" may also provide values that can be considered for evaluation of potential impacts on ecological receptors (see ,for example, James and colleagues (2023), where high-throughput laboratory in vitro cell-line bioassay exposure-response data are being used as a surrogate for ecological risk thresholds).

3.2.5 Other Sources

In the absence of useful information in complied data sources for either human health or ecological toxicity, it may also be necessary to search and evaluate the primary research literature for information not already reflected in many of these sources. Some manufactured chemicals are proprietary, and existing human health and/or ecological toxicological information may not be publicly available. Values based on published scientific research are generally preferred to modeled data.

It is important to consider not only the exposure medium of concern, but also the biological organism level (individual, population, community, ecosystem) these data sources apply to. Toxicity data may be expressed in terms of toxicity (e.g., reference doses or effect concentrations) to an individual or populations of receptors or as values describing an effect at the community level (i.e., measures of diversity and abundance).

3.3 Properties That Inform Fate and Transport

Table 3 presents some indicators of persistence, bioaccumulation, and environmental partitioning. Persistence or bioaccumulation potential may be the result of direct empirical measurement or may be estimated from chemical-specific properties.

Some common sources for primary data (measured and/or estimated) used in the evaluation of environmental presence and exposure include the following:

- US EPA CompTox Dashboard (USEPA 2023a): The source presents chemistry, toxicity, and exposure information for more than 900,000 chemicals. Data and models presented in the dashboard can help with efforts to identify chemicals most in need of further testing.
- ATSDR Toxicological Profiles (ATSDR 2023): Peer-reviewed information reflecting a comprehensive and extensive evaluation, summary, and interpretation based on available toxicological, epidemiological, and fate and transport information.
- PubChem (PubChem 2023a): Comprehensive listing of chemicals and their physical-chemical, biological effect, and other attributes, including citations to original empirical data.
- EPISuite (OCSPP USEPA 2023a): A compendium of empirical and estimated physical, chemical, degradation, and bioaccumulation parameters, searchable by CAS number, SMILES structure, or name. This database focuses on attributes useful for estimating whether a chemical should be identified as a CEC.
- CRC Handbook of Chemistry and Physics (Rumble 2022): A classical source of comprehensive physical and chemical data for many chemicals.
- National Institutes of Standards and Technology (NIST) Chemistry WebBook (NIST 2023) Includes collected information on chemical and physical property data curated by the NIST Standard Reference Data Program and others.
- COSMO*therm* (COLaN 2023): Computational chemistry software program to predict thermodynamic properties.

Other countries also maintain compendia containing physical-chemical properties for thousands of chemicals. Some states specifically call out preferred sources for values to be used in a CEC evaluation. In addition, international and domestic

specialized databases for bioaccumulation and bioconcentration data, biodegradability constants, and environmental degradation rates are available (e.g., USACE ERED, USEPA Envirofate) (USACE 2023; USEPA 2023c).

Careful review and assessment of the data quality and applicability of the information from a data source, including any cited primary data, are essential to a comprehensive evaluation of the fate and transport characteristics of a chemical undergoing a CEC evaluation. Large ranges of empirical and measured values between sources may be present and could be problematic for the evaluation.

Table 2. Sources of key variables information

Source (hyperlinked)	Categories of Variables Available	Responsible Agency	Summary
Human Health Toxicity Group 1: U.S. Federal Values			
IRIS (ORD USEPA 2023d)	Human health toxicity values: reference dose (RfD), reference concentration (RfC) inhalation unit risk (IUR) oral slope factor (OSF) weight of evidence for carcinogenicity	USEPA	The program characterizes and identifies the health hazards of chemicals found in the environment. It provides toxicity values for health effects resulting from chronic exposure to chemicals through the assessment of Hazard Identification and Dose-Response Assessment.
Office of Water (OW) (OA USEPA 2013) and Office of Ground Water and Drinking Water (OW USEPA 2023i)	Provides RfDs, OSFs, weight of evidence for carcinogenicity, Health Advisories (OW USEPA 2018), maximum contaminant levels, maximum contaminant level goals, and recommended human health-based water quality criteria for many different contaminants	USEPA	Information on toxicity criteria for and management of contaminants in surface waters and drinking water sources, for implementation of the Clean Water Act and Safe Drinking Water Act.
ATSDR ToxGuides (ATSDR 2021a) ATSDR Tox Profiles (ATSDR 2023)	Human health toxicity values: minimal risk levels noncancer toxicity factors for acute, intermediate (subchronic), and/or chronic exposure durations	CDC/ATSDR	The ATSDR program provides information on chemical and physical properties, sources of exposure, routes of exposure, minimal risk levels based on varying length of exposure, children's health, and health effects (ToxGuides™) (ATSDR 2021a) and a compilation of toxicological information on a given hazardous substance (ToxProfile) (ATSDR 2023). Established minimal risk levels can be found here. The Toxicological Profiles reflect a comprehensive and extensive evaluation, summary, and interpretation of available toxicological and epidemiological information on a substance. The program also offers additional toxicological resources (e.g., chemical classifications, health effects of exposure to toxic substances, etc.) and a database on a wide range of substances (Toxic substances Portal) (ATSDR 2021b).

PPRTVs (ORD USEPA 2023e)	Human health toxicity values: RfD, RfC, IUR, OSF, and weight of evidence for carcinogenicity	USEPA	The PPRTV (ORD USEPA 2023e) program provides toxicity information and values for chemicals of concern to the Superfund Program, focusing on those not addressed by IRIS.
OPP (OCSPP USEPA 2023c)	Ecological and human health toxicity values	USEPA	OPP provides ecological and human health risk assessment information for existing and new pesticides.
Human Health Toxicity Group 2: State Values, ECHA, OECD, Other International Values, PubChem (Selected Examples of State Resources)			
CA OEHHA (OEHHA 2016)	Noncancer reference exposure levels and cancer potency factors for toxic air contaminants; health protective exposure levels for contaminants in air, water, and soil; listing of cancer and reproductive toxicants under Proposition 65; and fish advisories. Toxicity factors for noncancer and cancer effects by the oral exposure route are also provided.	California	Chemical toxicity levels provided by the state of California.
NJDEP (NJDEP 2020) NJDEP (NJDEP 2023)	URF, Reference Concentrations Toxicity factors (RfDs, RfCs, CSFs, IURs) used for New Jersey drinking water, groundwater, surface water, and soil remediation standards	New Jersey	Air toxic criteria provided by the state of New Jersey. NJDEP Standards Compendium
MDH (MDH 2022)	Health-based values, health risk limits	Minnesota	Risk information on drinking water contaminants from the state of Minnesota.
Texas Commission on Environmental Quality (TCEQ)	Texas Risk Reduction Program (TRRP), e.g., Tiered Protective Concentration Levels for soil and groundwater; TRRP human health surface water risk-based evaluation levels (RBELs)	Texas	The TRRP program presents extensive guidance on identifying and developing toxicity criteria and physical-chemical characteristics for contaminants in soil, groundwater, surface water, and sediment.

Health Canada and Environment Canada (Health Canada 2007)	Toxicological reference values (TRVs) and guidance on Federal Contaminated Site Risk Assessment in Canada: Toxicological Reference Values (TRVs), Version 3.0, is a companion to Federal Contaminated Site Risk Assessment in Canada: Guidance on Human Health Preliminary Quantitative Risk Assessment (PQRA), Version 3.0, and to Federal Contaminated Site Risk Assessment in Canada, Part V: Guidance on Human Health Detailed Quantitative Risk Assessment for Chemicals (DQRAchem).	Health Canada	Provides guidance and advice on human health risk assessment and public involvement to other federal departments by reviewing human health risk assessment and integration of health issues in environmental assessments conducted under the Canadian Environmental Assessment Act. Risk assessment guidelines and approaches used by Health Canada to develop toxicity values may differ in some ways from those used by USEPA and states. Most Canadian provinces have their own requirements for carrying out risk assessments for contaminated sites (e.g., Ontario has requirements established under the Ontario Environmental Protection Act.
Australia Department of Climate Change, Energy, the Environment and Water (A); Department of Health and Aged Care (B) (Australian Government 2022)	A. Management plans for selected contaminants (e.g., PFAS) but no information on toxicity assessment or human toxicity values. B. Health-based guidance values expressed as tolerable daily intakes used for assessing potential exposure to contaminants through food, drinking water, and recreational water during site investigations.	Australia	A. Provides risk assessments to determine how chemicals will impact the environment at various stages of the chemical life cycle and manages the environmental risks from industrial chemicals through Industrial Chemicals and Environmental Management Standard (IChEMS). B. Collaborate with other Australian government agencies on policies and programs that aim to improve and maintain health-supporting environments including environmental and human health risk assessments.
Guidance on Information Requirements and Chemical Safety Assessment and REACH (ECHA 2023d; 2023h)	Under the Public Activities Coordination tool (PACT) Data generation and assessment (dossier evaluation (ECHA 2023c), substance evaluation, informal hazard assessment (PBTs (persistent, bioaccumulative, and toxic), and very persistent and very bioaccumulative (ECHA 2023g) Assessment of regulatory needs (ARN) Regulatory risk management	ECHA	Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) (ECHA 2023h) is a regulation of the European Union adopted to improve the protection of human health and the environment from the risks that can be posed by chemicals. ECHA provides information on substances that were assessed under REACH. The information provided includes a brief profile, REACH registered substance fact sheet, C&L Inventory (ECHA 2023b), biocidal active substance fact sheet (ECHA 2023e), the PACT (ECHA 2023f), and regulatory obligations.

Echem Portal (OECD 2023a)	Toxicity, exposure, use information, risk assessment data	OECD	OECD eChemPortal provides links to chemical hazard and risk information prepared for government chemical programs. It also provides toxicity, exposure, and use information on chemicals and access to any risk assessment data. Databases participating in eChemPortal include USEPA databases, ECHA, Canada, Japan, and Nordic countries).
PubChem (PubChem 2023a)	Toxicity and pharmacology information including links to chemical toxicity assessments, carcinogenicity classification, target organs, and human and nonhuman effects if available.	National Library of Medicine, National Institute of Health	PubChem, an open chemistry database that includes ToxNet (PubChem 2023b) data from Chemical Carcinogenesis Research Information System (CCRIS), ChemIDplus, Genetic Toxicology Data Bank (Gene-Tox), and Hazardous Substances Data Bank (HSDB) (HSDB 2023).
Human Health Toxicity Group 3: Other Sources of Toxicity Data That Provide Supporting Evidence to Health Effects			
ToxCast (ORD USEPA 2023g)	High-throughput screening assays endpoints—identify the potential of chemicals for toxic effects including endocrine disruption and neuro-developmental effects; includes predictive capabilities access through the ComTox Dashboard (USEPA 2023a).	USEPA	USEPA's Toxicity Forecaster (ToxCast) generates data and predictive models on thousands of chemicals using high-throughput screening methods and computational toxicology approaches to rank and prioritize chemicals.
The Toxicity Estimation Software Tool (TEST) (ORD USEPA 2023f)	A calculation tool that may be used to predict acute and developmental toxicity in the absence of appropriate animal toxicity or epidemiological studies. The modeled toxicity estimates provide another weight of evidence to the toxicological assessment of a chemical.	USEPA	Estimates the toxicity values and physical properties of organic chemicals based on an entered molecular structure using QSAR methods.
EpiSuite (OCSPP USEPA 2023a)	Physical-chemical properties Environmental fate properties	USEPA	Estimates physical-chemical and environmental fate properties.
OECD QSAR Toolbox	A software application intended to be used by governments, the chemical industry, and other stakeholders in filling gaps in (eco)toxicity data needed for assessing the hazards of chemicals.	OECD/ECHA	Identifies relevant structural characteristics and potential mechanism or mode of action of a target chemical based on other chemicals that have the same structural characteristics and/or mechanism or mode of action and uses existing experimental data to fill data gap(s).
OncoLogic (OCSPP USEPA 2023b)	Estimated carcinogenicity	USEPA / OECD	The OncoLogic™ model estimates carcinogenicity from chemical and use information based on a set of knowledge rules.

Derek Nexus (Labcorp 2023)	Skin sensitization	Lhasa Limited	Derek Nexus can predict a number of toxicological endpoints. It is expert, knowledge-based toxicology software that gives predictions for a variety of endpoints.
ToxTree (Jeliazkova et al. 2018)	Hazard estimation	Ideaconsult Ltd	ToxTree uses a decision-tree approach to estimate hazards.
Ecological Toxicity Group 1: Established Evaluation Frameworks			
ECHA REACH Dossiers (ECHA 2023i)	Hazard classification; use	ECHA	(See REACH above)
Chemicals Management Plan (Government of Canada 2006)	Risk assessment and risk management information	Health Canada	Assessment and management of risks to human health and the environment posed by chemical substances that can be found in food and food products, consumer products, cosmetics, drugs, drinking water, and industrial releases.
OPP (OCSPP USEPA 2023c)	Ecological and human health toxicity	USEPA	OPP provides ecological and human health risk assessment information for existing and new pesticides.
Ecological Toxicity Group 2: Established Media Concentrations or Screening Values Deemed Protective of Various Ecological Endpoints			
US EPA National Recommended Water Quality Criteria (OW USEPA 2022a)	Water quality criteria	USEPA	Summary tables of recommended water quality criteria for the protection of aquatic life and human health in surface water for approximately 150 pollutants.
State-level compilations available in most states (e.g., Texas (TCEQ 2023), New Jersey (NJDEP 2010), Oregon (Oregon DEQ 2023))	Ecological screening criteria	Various	States provide ecological screening and risk assessment criteria and information.
Regional Screening (Region 3 (ORD USEPA 2015c), Region 4 (ORD USEPA 2015b), and Region 5 (USEPA 2023b, 5))	Biological Technical Assistance Group (BTAG) Screening Values, Regional Ecological Risk Assessment (ERA) Guidance	USEPA	USEPA regions provide specific guidance to states, tribes, and local governments.
SquiRTs (NOAA 2023)	Sediment, soil, and surface water screening values	NOAA	Screening Quick Reference Tables (SquiRTs) provide information to evaluate potential risks from contaminated water, sediment, or soil.

Ecological Benchmark Tool for Chemicals (RAIS 2022a)	Ecological screening levels	DOE Oak Ridge National Laboratory	Contains ecological screening benchmarks for surface water, sediment, surface soil, and biota applicable to a range of aquatic organisms, soil invertebrates, mammals, and terrestrial plants.
ECORISK Database (Kieling 2017)	Ecological screening levels	DOE Los Alamos National Laboratory	Compilation of ecological screening levels to inform ecological risk assessments.
Ecological Toxicity Group 3: Compilations of Measured Toxicity Criteria and Bioaccumulation Potential from Exposures to CEC			
ECOTOX (Olker et al. 2022)	Toxicological endpoints	USEPA	The ECOTOXicology Knowledgebase contains single chemical toxicity data for aquatic life, terrestrial plants, and wildlife.
ERED (USACE 2023)	Residue-effects data	U.S. Army Corp of Engineers	The ERED contains residue-effects data, useful for understanding potential bioaccumulation from exposure to dredged sediment.
Ecological Toxicity Group 4: Surrogated and Models			
ECOSAR (OCSPP USEPA 2022a)	Acute and chronic toxicity	USEPA	ECOSAR is used to estimate toxicity to aquatic organisms, such as fish, aquatic invertebrates, and aquatic plants, by using computerized Structure Activity Relationships.
OECD QSAR Toolbox (OECD 2023b)	Ecotoxicity endpoints	OECD	Developed in collaboration with ECHA, fills ecotoxicity data for assessing the chemical hazards.
VEGA (VEGA HUB 2023)	Ecotoxicity endpoints	Istituto di Ricerche Farmacologiche Mario Negri	Provides a platform to access QSAR models.

Table 3. Properties that inform potential fate and transport

	Property	Symbol	Description

Some Indicators of Persistence			**Measures estimating persistence of chemicals in environmental compartments. Environmental persistence is a fundamental component of the classification process related to persistence, bioaccumulation, and toxicity (PBT).**
	Half-life	t ½	Measures of environmental persistence are defined as the time required for the concentration of a substance in an environmental medium to diminish by one-half. Persistence criteria under several PBT classification schemes (e.g., the REACH Annex XIII PBT or very persistent and very bioaccumulative (vPvB) criteria) are defined on the basis of persistence half-lives in water and sediment. Analogous half-lives can be derived for volatilization from water to air, biotransformation, and other processes and are a common tool in evaluating fate and transport of substances.
	Biodegradability		The capacity for microbial degradation of organic chemicals to base substances. Degradability is a key measure of persistence of chemicals and is usually tested by standard degradation tests. “Ready” degradability are chemicals that quickly and extensively degrade. “Inherent” biodegradability is the ability of a chemical to degrade to base products over a longer period of time. Definitions of “persistence” in several PBT classification schemes are defined from measures of biodegradability. Multiple experimental methods exist.
	Photodegradation and atmospheric oxidation potential		Measures of chemical propensity to transformation under influence of sunlight and atmospheric oxidation processes. Note that photodegradation products may be of concern in their own right.

Some Indicators of Bioaccumulation			**Measured or estimated properties that estimate uptake and bioaccumulation to biota from environmental media. Can be based on standard tests or biokinetic models. Bioaccumulation is a fundamental component of the PBT classification process.**
	Bioaccumulation and bioconcentration factors	BAF/BCF	Measures describing the degree to which substances are taken up or accumulated into tissues, typically but not exclusively aquatic organisms, from the surrounding medium. The BAF describes the total ratio (at equilibrium) of the concentration in the tissue to the concentration in the medium. Definitions on bioaccumulation in PBT schemes are often based on BAF or BCF ranges. BAF and BCFs are derived from standardized bioaccumulation tests. A related concept, trophic biomagnification factors, considers the ability of some substances to bioaccumulate across ecological trophic levels (i.e., from consumers to primary predators to secondary predators).
	Biota-sediment accumulation factors	BSAF	A special case of bioaccumulation factors often applied in sediment, where the units are based on organic carbon normalized values in sediment and lipid content values in tissue.
	Biota and trophic transfer factors	BTF/TTF	Measures describing the transfer of substances between different levels of biota or between different organ systems in biota. These factors help describe the ability of a substance to biomagnify (i.e., increase in concentration in higher trophic levels). Also describe a propensity to particularly concentrate in milk, meat, or particular food items.
	Bioavailability and bioaccessibility	BA	Measures of how much a substance in the environment may enter living organisms. Many factors such as chemical forms, adsorption to environmental media, exposure route to the organism, and physiological characteristics of the organism affect this measure. Understanding bioavailability is essential to predict the biological effects of environmental contaminants. Bioavailability is usually measured as relative (where bioavailability is compared relative to a standard bioavailability) or absolute (where bioavailability directly measures the relationship between the environmental concentration and the effective dose in the organism). Bioaccessibility describes the physical ability of a substance to come into direct contact with a living organism in a form that may be bioavailable.

Some Indicators of Environmental Partitioning and Fate			**Measured or estimated properties that estimate the partitioning of chemicals between environmental media and between biota and environmental media.**
	Octanol-water partitioning coefficient	K_{ow}	A measure of the partitioning coefficient of a chemical in a two-phase system of n-octanol and water. The octanol is considered a surrogate for organism lipids. The K_{ow} describes the propensity of nonpolar organic chemicals to accumulate in organism lipids and is therefore used as a surrogate for bioaccumulation. Most PBT classification schemes use K_{ow} to classify chemicals as bioaccumulative. K_{ow} may not be an appropriate indicator of bioaccumulative potential for polar or charged contaminants.
	Organic carbon-sediment partitioning coefficient	K_{oc}	A measure of the partitioning coefficient of a chemical between organic carbon (in soil, sediment, or particulates) and surrounding water. The K_{oc} describes the propensity of nonpolar organics to exist as a freely dissolved form enhancing migration potential and bioavailability. The K_{oc} is an important measure to estimate bioavailability and migration potential and thereby the potential to bioaccumulate or exert toxic effects. (While databases often include K_{oc} values for polar and charged chemicals, it may not be appropriate in certain contexts; e.g., other soil components can influence adsorption for polar/charged compounds).
	Soil/sediment to water partitioning coefficient	K_d	A measured value describing the amount of chemical adsorbed onto soil (or sediment) per amount of water. It is related to K_{ow} and K_{oc} but is an empirical measure considering the totality of factors affecting the partitioning.
	Octanol air partitioning coefficient	K_{oa}	Analogous measure to the K_{ow} but estimates the partitioning between volatile chemicals in air and biological tissue lipids, represented by n-octanol. It is used to predict partitioning among air, soil, vegetation, and aerosols.
	Fugacity	F	Fugacity describes the propensity of a substance to move among multiple environmental compartments (air, soil, sediment, and water) under given conditions, based on fugacity model outputs. These models use default parameters such as temperature and substance K_{ow} to distribute a substance among compartments and are useful in evaluating transport and persistence.
	Particulate sorption	phi (φ)	Measure of the fraction of a substance adsorbed to atmospheric particulates

Other Physical-Chemical Factors Informing Evaluations			**Basic empirical or estimated physical-chemical properties that can provide insight into fate, transport, persistence, and bioaccumulation of chemicals**
	Henry's Law constant	H' or K_H	A chemical-specific property predicting the volatility of a chemical. This measure is frequently used to classify chemicals as volatile or nonvolatile and affects persistence.
	Vapor pressure	P	A chemical-specific property that estimates the partitioning of a substance between liquid and air phase. It is related to H'. This measure is frequently used to classify chemicals as volatile or nonvolatile and affects persistence.
	Solubility	Wsol	Key indicator property predicting availability and migration potential of chemicals in aqueous environments via dissolution in water. Very insoluble substances have limited partitioning to the aqueous phase and high retardation factors and thereby have limited transport potential in aqueous systems.
	Boiling and melting points	BP, MP	Boiling and melting points are useful to understand environmental occurrence and transport potential of a substance.

4. SCHEMES FOR INTERPRETING INFORMATION ON VARIABLES

A number of published prioritization schemes/approaches for a range of environmental media and contaminant groups are available. Table 4 summarizes select schemes and frameworks used to prioritize emerging contaminants/chemicals and is intended to represent a broad spectrum of national, international, and state frameworks. Table 4 serves as a resource for the states to explore alternative prioritization approaches (in addition to the one presented in this Fact Sheet) to facilitate development of their own programs to monitor, identify, and evaluate CEC.

Table 4. Schemes for interpreting information on variables

Prioritization Approach/ Reference	Year Developed/ Updated	Environmental Media	Contaminant Group	Brief Summary of Approach / Links for Additional Information
USEPA Screening Risk of Emerging Contaminants (SIREN) (Guiseppi-Elie, Pollard, and Zambrana 2022)	2023	All	All	USEPA is developing a technical framework that may eventually be adaptable to states to support the agency's response to potential CEC. SIREN will consider factors such as potential hazards, exposure, persistence, bioaccumulation, and cross-media impacts.

USEPA Contaminant Candidate List (CCL) (OW USEPA 2022b)	2022	Drinking Water	All emerging contaminant groups	The CCL is prepared every five years based on nominations from the public and comments received from the public and Science Advisory Board. The following three criteria are used to determine (prioritize) whether the contaminant on the CCL may require regulation: (1) the contaminant may have an adverse effect on the health of persons; (2) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in PWSs with a frequency and at levels of public health concern; and (3) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems. Contaminant Candidate List 5 – CCL 5 ("Drinking Water Contaminant Candidate List 5-Final" 2022)
USEPA Unregulated Contaminant Monitoring Rule (UCMR)	2021	Drinking Water	All emerging contaminant groups	The USEPA UCMR requires that every five years all large public water systems and a subset of small public water systems monitor for a list of 30 contaminants that are not currently regulated. The goal of the UCMR program is to help the agency determine whether it should regulate a specific contaminant.
Watch List for European Union–Wide Surface Water Monitoring (Gomez Cortes et al. 2022)	2022	Surface Water	All emerging contaminant groups	Three pillars of information are used to select candidate substances for the Watch List. The first pillar is the outcome of the last review of substances for the third Watch List, the second is information from Member States and stakeholders, and the third is literature search and/or other information (Gomez Cortes et al. 2022). The three criteria used to prioritize substances for inclusion in the Watch List are (1) the need for more monitoring data to perform a risk assessment, (2) the existence of reliable information on the toxicity of the substances that points to a possible risk, and (3) sufficiently sensitive analytical methods exist for the substances. Selection of substances for the 4th Watch List under the Water Framework Directive (Gomez Cortes et al. 2022)
Association of State Drinking Water Administrators (ASDWA) (ASDWA 2020)	2020	Drinking Water	All emerging contaminant groups	Supports agencies' programs addressing potential risks from CEC in drinking water, including management and treatment options.

Voluntary Groundwater Watch List – European Union (Kozel and Wolter 2018)	2018	Groundwater	All emerging contaminant groups	Watch list of pollutants is developed based on (1) the occurrence of substances in groundwater (based on monitoring data) and (2) the theoretical leaching potential of substances (based on the substance properties). The combined outcome of these two assessments ("Combined groundwater leaching potential score") is linked with the hazard potential of these substances to form a ranked list, the "Integrated groundwater score." Voluntary Groundwater Watch List (Kozel and Wolter 2018), Voluntary Groundwater Watch List Concept & Methodology (Kozel and Wolter 2018)
NORMAN Prioritization Framework (Dulio and von der Ohe 2013)	2013	Aquatic environment (water, sediment, suspended particulate matter and biota)	All emerging contaminant groups	The overall prioritization procedure is carried out in two successive stages. In the first stage, the NORMAN prioritization methodology uses a decision tree that classifies chemicals into six categories, based on identified ("categories" of) knowledge gaps and actions to be taken by the research community and public authorities to fill them. The second stage entails the prioritization of the substances within each (action) category on the basis of the criteria / indicators identified for each category (Dulio and von der Ohe 2013). NORMAN Prioritization framework for emerging substances (Dulio and von der Ohe 2013)
U.S. Department of Defense (DOD) Instruction 4715.18 (DOD 2019)	2019	All	All emerging contaminant groups	This DOD Instruction (DOD 2019) establishes an enterprise-wide program to identify emerging chemicals (ECs); assess the likelihood and severity of impacts associated with ECs to people, the environment, and DOD mission; and take management actions to reduce these impacts. To be considered an EC, a chemical must (1) be relevant to the DOD, (2) have a perceived or real threat to human health or the environment, and (3) have new or changing toxicity values or regulatory standards as a result of new science, detection capabilities, or exposure pathways (DOD 2019).

Michigan	2019	All	All new or emerging chemical contaminants	The Natural Resources and Environmental Protection Act, 1994 PA 451, as amended, Parts 201 (remediation) and 213 (LUSTs), regulates facilities of environmental contamination. “New” contaminants detected in soil and groundwater are substances that are not listed in the Part 201 Cleanup Criteria Rules and therefore do not have cleanup criteria that can be used to determine whether a property is a “facility.” The Part 201 regulations require “facility” determination for any property with detected contaminants to ensure due care is met. The owners and operators of property that is contaminated are required to take actions to ensure that the contamination does not cause unacceptable exposures and assure the safe use of the property. (Due Care Obligations (michigan.gov) (EGLE 2019).
Minnesota				MDH collaborates with partners and the public to identify contaminants of interest; investigates the health and exposure potential of CEC in water; and informs partners and the public of appropriate actions for pollution prevention and reducing exposures to contaminants that might be unhealthy.
REACH	2022	All	All new or emerging chemical contaminants	REACH seeks to identify substances of very high concern based on carcinogenic, mutagenic, or toxic for reproduction categorization and PBT/vPVB properties. Substances of Very High Concern Identification (ECHA 2023a)

Toxicity Forecaster (ToxCast™)	2022	All	All new or emerging chemical contaminants	The Toxicity Forecaster (ToxCast) database contains the results from automated screening assays for thousands of chemicals and can be accessed using the CompTox Chemicals Dashboard (CompTox Chemicals Dashboard) (USEPA 2023a). These assays, termed high-throughput screening assays, expose living cells or isolated proteins to contaminants one at a time; following exposure, the cells and proteins are screened for changes in biologic activity that suggest biologic and potentially toxic effects. This *in silico* data provides information to assess the toxicity of specific contaminants, but it is not equivalent to traditional toxicity tests. Scientists are using this tool and related techniques in field studies to assist in the identification of CEC that may be impacting aquatic life and the prioritization of CEC for further research and identification. (Ankley et al. 2021; Blackwell et al. 2019) (ORD USEPA 2017a) ToxCast Owner's Manual – Guidance for Exploring Data, ToxCast Data: Example Use Cases and Scenarios for Exploring Data (ORD USEPA 2017b)
Toxic Substances Control Act (TSCA)	2019–2020	All	Chemical contaminants	The TSCA, as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act, requires USEPA to evaluate the safety of existing chemicals. The first step in USEPA's process for evaluating the safety of existing chemicals is prioritization (OCSPP USEPA 2017), which is a risk-based screening process for designating chemical substances as either High-Priority Substances for risk evaluation or Low-Priority Substances. Preferences are given to prioritizing chemicals on the 2014 TSCA Work Plan (OCSPP USEPA 2014) and to considering certain criteria, such as hazard/exposure, persistence, and bioaccumulation.
California State Water Resources Control Board Constituents of Emerging Concern	2023	Water	Emerging chemicals and substances	The California Water Resources Control Board's Constituents of Emerging Concern program supports source control issues for emerging contaminants that are "hardest to treat, not regulated and/or routinely monitored, and have not been adequately tested for human or ecological toxicity." The webpage contains information and recommendations for strategic prioritization and characterization as well as potential rulemaking for constituents that impact California waters.

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CEC Risk Perception and Communication Fact Sheet

This Fact Sheet has been organized into the following subsections:

1. Introduction

This Fact Sheet provides guidance on what, how, when, and to whom to communicate, as well as the pitfalls to avoid when communicating about contaminants of emerging concern (CEC). It is intended to support state-level programs and project managers with specific information about communicating CEC to stakeholders. It is neither a "how-to" guide nor a project-specific tool for risk communication. The ITRC Risk Communication Toolkit contains much more detail, including guidance on communications plans, message maps, and audience identification, among other tools. A list of additional resources about risk communication is included in Section 5.

2. Risk Communication Basics

There are many different definitions of risk communication. For this Fact Sheet, we will use the United States Environmental Protection Agency (USEPA's) definition: "Communication intended to provide a general or specific audience with the information they need to make informed, independent judgments about risks to their health, safety, and the environment" (OA USEPA 2021).

Likewise, there are multiple definitions of "risk." The definition often used by risk assessment professionals is that risk is the potential for realization of unwanted, adverse consequences to human life, health, property, or the environment. Estimation of risk is usually based on the expected value of the conditional probability of the event occurring multiplied by the consequence of the event, given that it has occurred (ITRC 2020).

Effectively communicating risk requires understanding both the professional's viewpoint and that of the public. The public's understanding of risk often differs significantly from the professional's assessment. It may be based more on a sense that something is harmless or unacceptably dangerous rather than objective data. This perspective may focus on things not easily measured, such as fear, anger, mistrust, or unfairness (Covello and Allen 1988). This view of risk is often referred to as "outrage" or "subjective risk" (Sandman 2012; Telg 2010). Effectively communicating risk requires understanding both the professional's viewpoint and that of nonexperts, such as the public or other stakeholders.

Risk communication is intended to educate people so they can make informed decisions about risk. This can be accomplished in multiple ways, depending on the audience and situation, but most communication products about CEC will use one of two approaches:

- Encourage stakeholders to take action to reduce risk, also known as “precaution advocacy” (Sandman 2007)
- Reduce stakeholder perception of a disproportionate level of risk, also called “outrage management” (Sandman 2007)

Note that while stakeholders are often the general public or affected communities, they can just as easily be internal leaders or decision-makers. In many cases, these internal stakeholders are not experts in the subject matter or in risk communication. It may be just as important to encourage them to take action or to reduce their anxieties as it is with the general public. Risk communicators (which for our purposes may include internal subject matter experts) may find themselves attempting to get additional resources for monitoring or research for a CEC or divert resources to an area more important to public or environmental health.

Examples of precaution advocacy can include risk avoidance actions like smoking cessation, programs that promote radon testing in the home, or simply participating in listening sessions. Outrage management is used when stakeholders have a high level of concern about an issue, but the available data does not support such concern. In this situation, communication efforts should seek to calm stakeholder concerns while simultaneously being empathetic. Typical examples are attempts to reduce community concern around potential pollution sources that appear to have a limited effect on the surrounding area. Additional guidance on effective communication using message mapping tools can be found in ITRC’s risk communication guidance (ITRC 2020).

Whether you succeed at inspiring people to take action or calming their concerns depends on the level of trust you develop with the audience. A community’s trust in the risk communicator is challenging to build, but easily broken. It is imperative to communicate in a way that connects with the audience; and is honest, transparent, and empathetic. This can be summarized as “know your audience.”

Most of this Fact Sheet focuses on educating and communicating with the general public. Your internal stakeholders may be making final decisions about agency priorities, so educating your internal stakeholders about the risks associated with CEC is as essential—or even more so, in some cases—as educating the public. These skills are also useful to subject matter experts who may not normally be the face of the organization when public interest is high. While the communication professionals typically write the press releases and deliver the message to mass audiences, it is often the subject matter experts who are answering individual phone and email inquiries from the public.

3. Risk Communication: Considerations and Challenges with CEC

3.1 Communicating Uncertainty

The Key Variables Fact Sheet includes a flowchart for the recommended process of evaluating and prioritizing potential CEC. It identifies a logical process for assessing whether substances are low, medium, or high priority based on occurrence, toxicity, and physical-chemical criteria. A potential CEC can be shifted between priorities at any time. In short, uncertainty is a major factor when communicating with the public and other stakeholders. It is essential to acknowledge information gaps when developing communications products.

While we recognize that people prefer certainty , your credibility may be damaged if you present information as definite when it is not. The early days of the COVID-19 pandemic exemplify how credibility can be damaged if the uncertainty surrounding a situation is inadequately acknowledged (Sandman 2021).

It is often assumed that communicating uncertainty will decrease trust in the messenger; however, more recent experience shows that people can understand uncertainty when it is communicated (Lyshol and Rolfheim-Bye 2021; van der Bles et al. 2020). Most importantly, when uncertainty is pointed out from the beginning, they do not appear to lose trust in the source. In some cases, their trust in the data may be reduced (van der Bles et al. 2020). This should not be a surprise, given high levels of uncertainty. Still, they will not stop trusting the messenger (you) so long as you are honest about the limitations of the data (Sandman 2021). Increased trust may even lead to higher receptiveness to the message (Lyshol and Rolfheim-Bye 2021).

3.2 Precaution Advocacy

Depending on the situation, the CEC’s properties, and its priority (determined using the method described in the Identification of Key CEC Variables Fact Sheet), the risk communicator’s strategy will vary (Committee on Decision Making Under Uncertainty, Board on Population Health and Public Health Practice, and Institute of Medicine 2013). It may range from

educating internal or external stakeholders to providing guidance on how the public may protect themselves from potential harm. For low-priority CEC, the subject matter experts may be in the best position to take the lead. For high-priority CEC, more experienced risk communication professionals may need to be involved.

There may be limited goals or data for low-priority CEC, but as priorities increase, more information should be available to allow subject matter experts to determine potential harms and recommendations to avoid them. Although data will be limited, the risk communicator should focus on the data that are available, particularly data that indicate a potential for harm.

A useful tool is the Precaution Adoption Process Model (PAPM) (Figure 1). The PAPM describes a series of stages that people go through when deciding whether to take action of some sort and how that decision gets put into action (Meyer et al. 2023; Weinstein, Sandman, and Blalock 2020). These stages range from being unaware of the issue to action. Knowing where your audience is in the model's stages will help you tailor the message.

It is probably easier to move an audience in stage 1 (unaware) or 2 (unengaged) in the desired direction by providing them with basic education than someone who has already made a decision (stage 4 or 5). If someone has already decided to act, your work may be somewhat easier. Stages 5 or 6 may need only guidance, reminders, or other assistance (Weinstein, Sandman, and Blalock 2020).

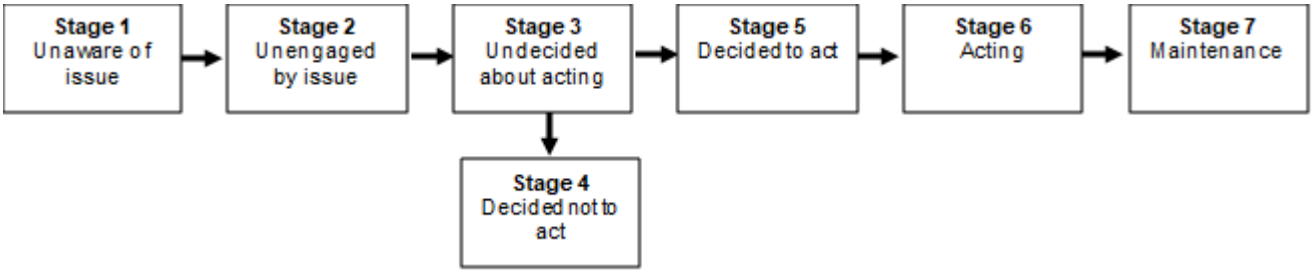

Figure 1. Stages of the Precaution Adoption Process Model

Source: Adapted and redrawn from Weinstein and colleagues (2008)

3.3 Outrage Management

Depending on the overall situation, the CEC properties, and CEC priority, your strategy will vary. One major difficulty for the risk communication professional is the simple fact that if you feel the need to lower the level of outrage, your audience is probably past stages 1 or 2 of the PAPM. People who are already angry, concerned, or stressed have difficulty processing information (Covello, Minamyer, and Clayton 2007; Christine and Petersen 2007). They also tend toward distrust and worst-case thinking (Christine and Petersen 2007).

In a low-trust situation where the public is more inclined to trust bad news ("We're all going to die!") than good news ("You're unlikely to get sick."), the best advice is to recognize and acknowledge the bad news from the beginning (Covello, Minamyer, and Clayton 2007; Sandman 2012). While you may wish to bring your audience around to your view, it is vital to start where they are and not where you would like them to be. In addition, as pointed out above, uncertainty is a constant when communicating about CEC, and admitting that you do not have all the answers is key to maintaining credibility (e.g., Lyshol and Rolfheim-Bye 2021; Sandman 2021; van der Bles et al. 2020).

4. Some Best Practices in Risk Communication

The past several years have given us examples of chemical and biological contaminants that have come upon us seemingly out of nowhere. Public health and government risk communicators have had to discuss these CEC with little time to prepare or with minimal information upon which to base decisions. They have often been criticized for over-emphasis (Sandman 2021) and under-emphasis of potential risk (Ducatman et al. 2022).

Discussing a situation with little data and high potential consequences is a challenging situation. Four practices that should be kept in mind are discussed below.

4.1 Avoid One-Size-Fits-All Risk Communication

Your intended message should be tailored to your audience and your specific goal (e.g., Ricci 2012; University of Pittsburgh

2023). This includes the level of detail of the information being presented and matching the specifics about how the message is delivered with how the audience is prepared to receive it. The stage of the CEC life cycle will also inform how the message should be constructed to achieve your goal.

The tools and methods best suited to achieve the goal of educating the public to allow for more educated decisions when limited information is available will be very different from those needed to inspire the public to take immediate action to prevent illness (Zoller 2005). In turn, those tools will differ from those required to calm the public's fears when they are disproportionate to the risk (Sandman 2012).

4.2 Keep Your Audience Informed

When dealing with CEC, it is vital to update the audience as frequently as possible. By their very nature, CEC are likely to have rapidly changing information. The main goal of most risk communication is to get accurate and timely information to the public (LaFraniere and Weiland 2022). Failure to keep abreast of rapidly changing information can lead to a loss of trust in public institutions (Ducatman et al. 2022).

4.3 Avoid Overconfidence

Navigating between communicating frequent changes and trying to provide a consistent and understandable message can be difficult. It is important to project competence and trustworthiness in your communications (Gallo 2019), and there is a legitimate concern that frequent changes in the message make speakers look indecisive and incompetent. On the other hand, repeated confident assertions of fact that later turn out to be wrong can do tremendous damage to your credibility (Sandman 2021).

In most cases, the uncertainty about the risks of CEC is likely to be high. A confident and matter-of-fact tone when proclaiming the current (and very likely future) uncertainty will help with maintaining your credibility with the public (Sandman 2021; van der Bles et al. 2020).

4.4 Be Honest

In some situations, the decisions the public will make based on the information being presented will be vital. It can be tempting to omit information, overstate your case, or outright lie to influence your audience to make what you view to be the "correct" decision. Our recommendation is not to give in to the temptation.

When trust in an institution is high, that institution may be tempted to stretch the truth, or worse. They may do so by intentionally lying, but it is more commonly done by providing incomplete or biased information to lead (or mislead) the audience to their preferred conclusion. Aside from being unethical (Ulmer and Sellnow 1997), these "noble lies" can damage or destroy your credibility (Parasidis and Fairchild 2022). If you have misread your audience, a single piece of evidence that you are not entirely truthful can convince them that your organization is incapable of telling the truth (Haidt 2012). And trust, once lost, is very difficult to regain.

5. Conclusion

There are several challenges to consider when communicating risk associated with CEC. Recall that the purpose of risk communication is to help people make informed choices. In situations with CEC, however, people may be experiencing emotions ranging from apathy to fear, which affect their decision-making processes. Be thoughtful, proactive, and intentional when communicating. Consider not only the CEC priority level but also lessons learned and things to avoid when communicating. If you are not careful from the initial communication, it will become increasingly challenging to gain and/or regain trust—which may be to the community's detriment.

6. Available Resources

More in-depth information and training on risk communication is provided in the following resources, which may be helpful.

United States Agency for Toxic Substances and Disease Registry (ATSDR) Communication Toolkit

Provides tools to optimize communication efforts with local communities.
https://www.atsdr.cdc.gov/communications-toolkit/index.html (ATSDR 2018)

ATSDR Primer on Health Risk Communication

Provides a framework of approaches for communication to diverse audiences with a focus on health communications by government agencies. https://www.atsdr.cdc.gov/risk/riskprimer/index.html (ATSDR 1994)

USEPA Risk Communication Tools Website

Videos and case studies demonstrating the essential elements of risk communication. https://www.epa.gov/risk-communication/ (OA USEPA 2023)

ITRC Risk Communication Toolkit

This is the flagship risk communication guidance from the ITRC. https://rct-1.itrcweb.org/ (ITRC 2020)

Peter M. Sandman Risk Communication Website

Dr. Sandman is one of the pioneers of risk communication. Most of his knowledge and material can be found here, written and delivered in his unique down-to-earth style. http://www.psandman.com/ (Sandman 2023)

World Health Organization Risk Communication Training

A short but comprehensive course in risk communication with a focus on emergencies and disease outbreaks. https://openwho.org/courses/risk-communication (WHO 2023)

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Adoption of Analytical Methods for Identifying CEC Fact Sheet

This Fact Sheet has been organized into the following subsections:

1. Introduction

Reliable analysis of a contaminant in environmental media requires a high degree of confidence in its identity and its quantitation. This is normally achieved using reference materials such as analytical standards for chemicals and genomic sequence libraries for pathogens. In lieu of such reference materials, as is often the case for contaminants of emerging concern (CEC), identification and, subsequently, quantitation in environmental samples are uncertain. CEC are typically compounds or substances that one is previously unaware of (i.e., either in identity or in effect), but may (known-unknown) or may not (unknown-unknown) understand through similar compounds or substances (Figure 1). For example, true unknown-unknowns in the environment can include substances such as a transformation product of a known synthetic chemical (Tian et al. 2020) or a new strain of an existing pathogen, both of which are unlikely to have reference materials for identity confirmation and quantitation.

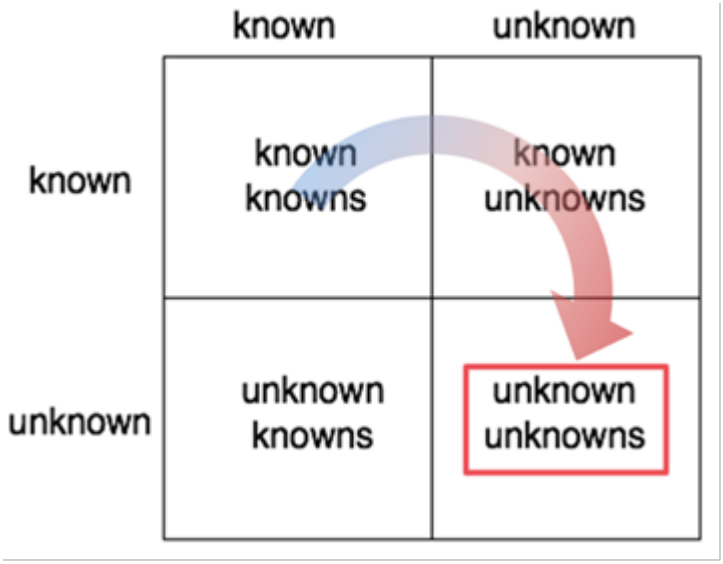


Figure 1. Knowns and unknowns. The matrix of knowns and unknowns (a.k.a. the "Rumsfeld Matrix") can be used to map uncertainty in the identification and quantitation of CEC. CEC are typically compounds or substances that one is previously unaware of but may (known-unknown) or may not (unknown-unknown) understand through similar compounds or substances. The analysis of a CEC, when first encountered, follows a process of elimination whereby a full suite of targeted methods is exhausted to rule out known-knowns. CEC analysis then falls into the right two quadrants of the matrix where identification and is attempted under a higher degree of uncertainty. Note that unlike in other fields, there is no clear meaning of "unknown knowns" (bottom left quadrant) in CEC analysis.

Source: Adapted from Stein (2012)

Characterizing and communicating risk associated with CEC generally requires an adaptive management approach (Aven and Bouder 2020) that reduces uncertainty with additional data collection over time (i.e., moving from the unknown-unknown quadrant to the known-known quadrant in Figure 1), but analyzing CEC in the environment generally takes the opposite path. First, existing targeted analysis methods are attempted to ensure that the substance is not already known (e.g., a manufactured substance that was previously undetected in the environment). Then, "suspect lists" may be developed using additional lines of evidence to assess whether the CEC is similar to an existing substance. Finally, as a last resort, non-target analysis (NTA) methods might be employed to localize the identity of the CEC.

This Fact Sheet is intended primarily for a technical audience (analytical chemists, biotechnologists, etc.) who might be involved in the development of programs for the analysis of previously unidentified CEC. It is accompanied by a glossary of technical terms and a case study that focuses on the identification of a previously unknown CEC. The overview of recent advances in analytical methods adoption and development covered in this Fact Sheet is presented for four categories of CEC: individual chemical compounds, chemical classes, biological contaminants, and particulates. Challenges to the development of analytical methods for these categories range widely from the absence of reference materials for identification and quantitation (e.g., individual chemicals and biological contaminants) to the lack of specificity (e.g., chemical class analysis and biological contaminant molecular primers) and unique categorization and characterization procedures (e.g., particulates and subclasses within chemical classes). Analytical approaches that address these challenges are described in the sections that follow.

2. Individual Chemical Compound Analysis

2.1 Individual Compound Identification

Investigation of high-priority CEC has grown in recent years due to advances in analytical methods, instrumentation, and data processing that make it possible to detect lower concentrations of more compounds in complex environmental samples. Common instruments used to analyze CEC include separation by liquid chromatography (LC) or gas chromatography (GC), and detection by tandem mass spectrometry (MS/MS) or high-resolution mass spectrometry (HRMS).

There are three approaches to detecting CEC in environmental samples (Figure 2 and Table 1): targeted analysis, suspect screening, and NTA.

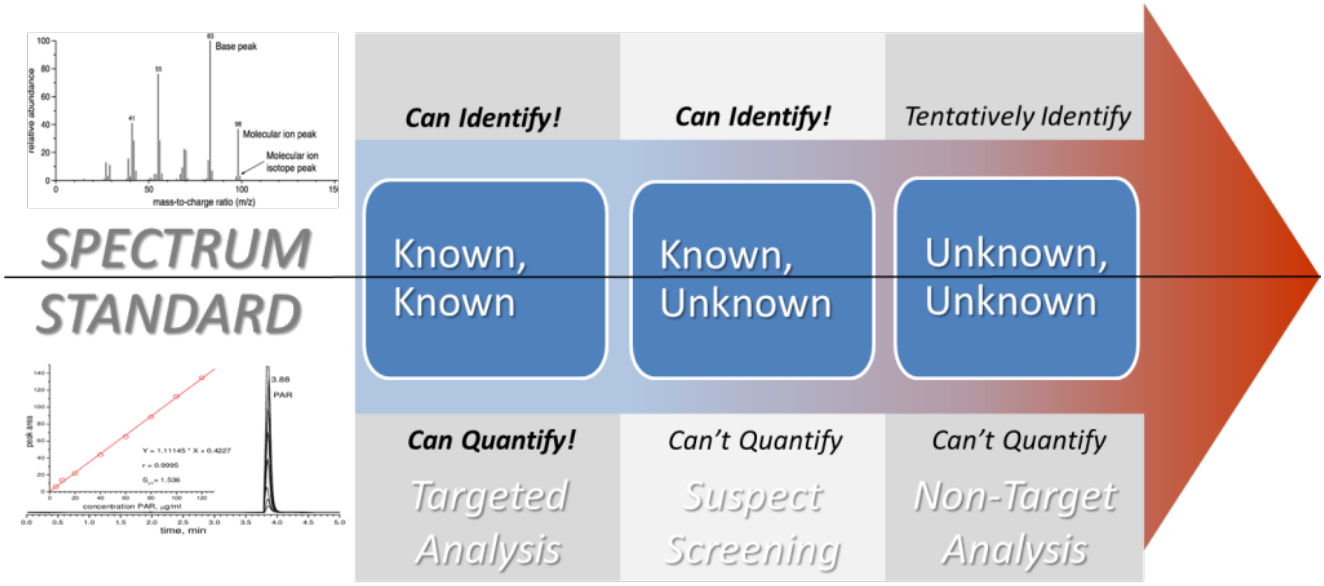


Figure 2. Targeted screening to non-target analysis. CEC that are known-knowns are compounds that are on target analyte lists and have established methods for detection and quantitation (targeted analysis). CEC that are known-unknowns are compounds included in a suspect list and can be identified but not quantified because a reference analytical standard is not available. CEC that are unknown-unknowns are compounds that were not included in a suspect list and cannot be quantified; experimental data must be used to elucidate a tentative chemical structure. Both known-unknowns (suspect screening) and unknown-unknowns (NTA) require HRMS for structural identification and confirmation.

Source: ITRC CEC Team.

Table 1. Targeted, suspect screening, and non-target analysis

Source: ITRC CEC Team.

	Targeted Analysis	**Suspect Screening Analysis**	**Non-Target Analysis**
Description	"Known-Knowns"	"Known-Unknowns"	"Unknown-Unknowns"
Question	*Is Compound X in the sample? At what concentration?*	*Which compounds from the list are in the sample?*	*Which compounds are in the sample?*
Uses	Quantify known CEC	Identify likely compounds without standards	Identify any compounds without standards
Scale of Use	Widely used "Gold Standard"	Moderate, primarily in research labs Minimal in commercial labs	Moderate, primarily in research labs Minimal in commercial labs
Instrument	Tandem MS (MS/MS)	HRMS	HRMS
Before You Start	Analytical standards List of compounds prior to analysis Compound-specific methods	No standards required Suspect list after analysis Spectra library General method	See Suspect Screening Analysis Peak picking algorithms *in silico* spectral library
Resources	USEPA Environmental Sampling and Analytical Methods (ESAM) Program (ORD USEPA 2022) ISO methods (ISO 2023)	NORMAN Suspect Exchange USEPA Chemical Dashboard Confidence level identification BP4NTA	See Suspect Screening Analysis Highly skilled analyst

Benefits:	Quantitative Standardized QA/QC Well defined scope Established analytical methods Highly selective and sensitive High analytical accuracy and precision Matrix-specific reference material available	Broad scope Defined list of compounds No standards required General method Data can be reanalyzed later	See Suspect Screening Analysis Undefined scope
Uncertainty/ Challenges	Multiple methods required Narrow scope Expensive standards Method development for each compound Cannot reprocess data	Qualitative (presence or absence) Limited by database and spectral library Defining confidence level Limited QA/QC available Expensive instrumentation Less sensitivity than targeted methods	See Suspect Screening Analysis Communicating uncertainty in identification
Resources	SW-846 Style Guide (USEPA 2012) ISO 17025 (ISO 2017) ASTM International D3975-93 (ASTM International 2023)	Chemical database Spectral library BP4NTA Schymanski confidence scale (Schymanski et al. 2014)	See Suspect Screening Analysis
When to Use This	Monitoring Program for Specific CEC Example: 1,4-dioxane in drinking water Approach: Use 1,4-dioxane method	Suspect CEC occurrence Example: known AFFF release Approach: use of comprehensive PFAS suspect list to match data to named compounds from list.	Unknown CEC occurrence Example: industrial release of unknown compound Approach: find features and identify using databases, *in silico* spectral libraries, homologous series, and characteristic fragments and evaluate importance using known or surrogate toxicity data.

Notes: AFFF = aqueous film–forming foams, BP4NTA = Benchmarking and Publications for Non-targeted Analysis, HRMS = high-resolution mass spectrometry, ISO = International Organization for Standardization, MS = mass spectrometry, NORMAN = network of reference laboratories, research centers, and related organizations for monitoring of emerging environmental substances, PFAS = perfluoroalkyl and polyfluoroalkyl substances, QA/QC = quality assurance / quality control, USEPA = United States Environmental Protection Agency.

2.1.1 Targeted Analysis: “Known-Knowns”

Is compound X in the sample and at what concentration?

Targeted analysis is used when (1) a CEC is identified prior to analysis, (2) there is an established analytical method and (3) analytical standards are available. Targeted analysis uses MS/MS to identify and quantify target compounds. It is the current “gold standard” of CEC detection and quantitation. It is highly selective and sensitive, has high analytical accuracy and precision, and includes a well-defined scope. Best practices for developing targeted methods can be found in many sources including, but not limited to, peer-reviewed journal articles, the SW-846 Method Style Guide (SW-846 Style Guide, 2012) (USEPA 2012), International Organization for Standardization (ISO) 17025 (ISO 17025) (ISO 2017), or the ASTM International D3975-93 (ASTM International 2023).

Targeted analysis relies on available reference material, analytical standards, and established analytical methods. If the CEC is not known or a standard is not currently available, targeted screening cannot be performed. Targeted methods are specific to a select set of compounds. For a complete CEC characterization, a full suite of targeted methods may be performed to capture the widest range of possible chemistries of the potential CEC.

2.1.2 Suspect Screening: "Known-Unknowns"

Which compounds from the list are in the sample?

Suspect screening is a qualitative analysis. It is an evolving analytical technique that aims to identify compounds that are expected to be present in the sample (e.g., based on a user-generated list of past chemical uses and releases at a site) without using reference or analytical standards. Suspect screening requires HRMS and the use of chemical databases, prioritization lists, and spectral libraries (when available) or *in silico* structural prediction algorithms to identify compounds and determine the confidence and uncertainty in the match. Suspect screening lists are user defined and may be tailored to a specific site (e.g., wastewater treatment plant), situation (e.g., chemical spill), or concern (e.g., forensic analysis of illicit drugs). The user-defined list must contain analytes that are relevant to the analytical instrument chosen for analysis. For example, nonvolatile compounds such as pharmaceuticals, personal care products, or PFAS are more amenable to liquid chromatography–mass spectrometry (LC-MS) analysis whereas volatile compounds, such as solvents, some pesticides, and flame retardants are more amenable to gas chromatography–mass spectrometry (GC-MS) analysis and may be captured as tentatively identified compounds (TICs) when high-quality mass spectra are available. The user-defined lists will require updates as needed.

Spectral libraries, when available, provide an additional layer of confidence to the identification of an unknown molecular feature (i.e., a peak with a specified mass to charge ratio (*m/z*), retention time, and area). Volatile compound analysis employs GC-MS with high-energy electron impact (EI) ionization at 70 eV (electron volts) as the standard approach. EI produces highly reproducible fragments, or "fingerprints," which are comparable across different laboratories and instrument manufacturer platforms. Therefore, experimental fragments can be screened against a curated spectral library of authentic chemical standards. If an authentic chemical standard is not available, the feature may be assigned a similarity or "match" score based on another structurally similar compound. Database or spectral libraries that are commercially available are curated, maintained, and updated on a regular basis. A spectral library may contain anywhere from 10,000 to more than 750,000 compounds collected by GC-EI-MS and may be used for spectral interpretation.

Analysis of nonvolatile or semi-volatile compounds by LC-MS is not standardized because a compound class may require optimization of the ionization mode, polarity, ionization energy, or collision energies. MS method conditions or fragments can be specific to the laboratory or instrument manufacturer platform. Many LC-MS spectral libraries are open-source repositories that allow public sharing of reference mass spectra and provide the MS conditions so that results can be replicated. These spectral libraries may be user generated, uncurated, poorly annotated, or still under development. For these reasons, many LC-MS users prefer to create and use their own spectral libraries and perform manually or *in silico* MS fragment interpretation when reference spectra are not available. Resources are identified in Table 1. Suspect screening may provide a more comprehensive result of which compounds are in the sample; however, it is not quantitative, and the scope may be undefined.

2.1.3 Non-Target Analysis: "Unknown-Unknowns"

What is in the sample?

Non-target analysis (NTA) is another qualitative analysis. It is an evolving analytical technique that uses many of the same tools as suspect screening (see above for information regarding suspect lists and spectral libraries) but aims to identify as many compounds as possible in a sample. NTA relies on algorithms to select important features in the data, compare them to available databases and spectral libraries, and prioritize those features in the data by occurrence or available toxicity data (experimental or predicted) to make conclusions about the results.

At the time of writing, there are no standardized methods for suspect screening and NTA, but advances in study design (Hollender et al. 2017), quality assurance/quality control (QA/QC) metrics (Peter et al. 2021), and Open and FAIR (Findability, Accessibility, Interoperability, Reusability) databases (Mohammed Taha et al. 2022) are developing rapidly (Schymanski and Bolton 2021). Two main challenges with suspect screening and NTA include standardizing QA/QC metrics and developing common language around identification confidence.

Benchmarking and Publications for Non-Targeted Analysis (BP4NTA) has developed a rigorous QA/QC framework to evaluate performance criteria such as study design, data acquisition, data processing and analysis, data outputs, and QA/QC metrics (Peter et al. 2021). The Study Reporting Tool (SRT) is an open-source guide for reporting NTA data. It provides a framework for NTA design, data communication, and reporting performance metrics to ensure gathering and interpreting high quality data.

The other main challenge to NTA is communicating the level of confidence and, conversely, uncertainty in the compound identification. The confidence levels developed by Schymanski and colleagues in 2014 for characterizing uncertainty in structural identification (Schymanski et al. 2014) are widely used to assess the evidence gathered by HRMS analysis (Figure 3). For example, if an authentic chemical standard is used to verify the CEC, then it would have Level 1 Identification Confidence. If an authentic standard is not available, but a chemical database and spectral libraries can provide supporting evidence for molecular formula and molecular structure, then it would have Level 2 Identification Confidence. A Level 3 identification would include a CEC with descriptive spectral information that could be used to assign a tentative structure to the CEC. Level 4 identification would only include a chemical formula with no structural information, and a Level 5 identification would only contain an exact mass with no chemical formula or structural information. Charbonnet and colleagues modified the Schymanski scale for PFAS (Charbonnet et al. 2022) by including the presence of homologues and characteristic fragments when additional information, like a spectral library match, is not available.

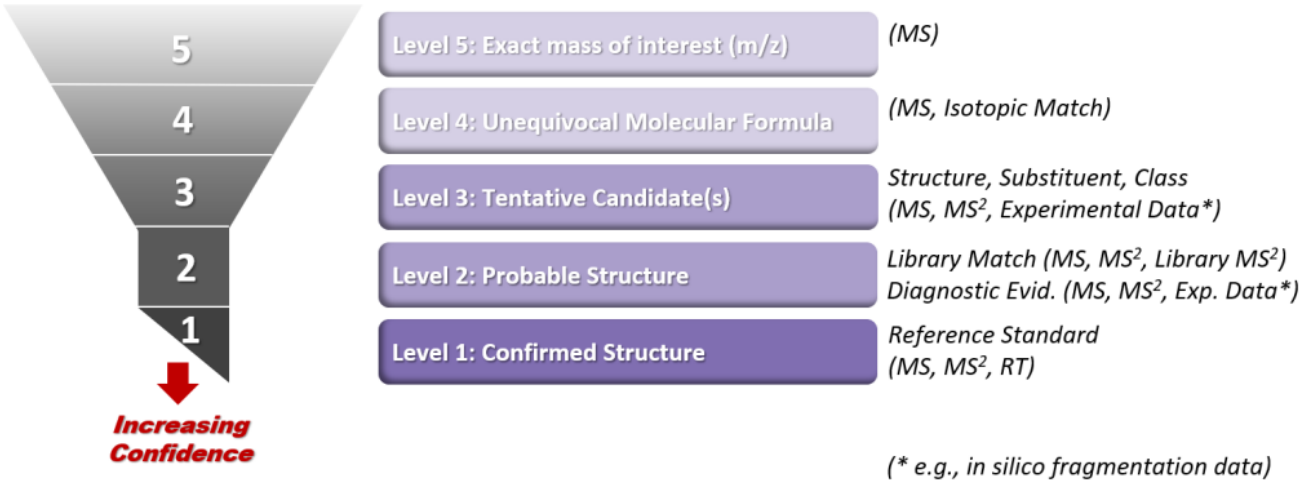


Figure 3. Schymanski scale. The Schymanski Confidence Levels are used for categorizing uncertainty in the identification of small chemical molecules using HRMS. Levels 5 and 4 rely primarily on the HRMS molecular ion peak (MS). Levels 3 and 2 use MS fragmentation data (MS^2) and experimental information as well. Level 1 identification relies on all of the prior information and a confirmation (retention time and spectra) using a reference standard.

Source: Adapted from Schymanski and colleagues (2014).

These approaches can be used in parallel to assess risk, characterize CEC, and make more informed decisions. At the time of writing, NTA is mainly performed in academic and government research laboratories and research and development specialty projects because the analysis requires specialized equipment, highly trained analysts, and time-intensive data processing. Developments in databases and libraries, data processing, information sharing, and communication have created an opportunity for NTA methods for detecting CEC to become more widespread.

2.2 Resources

The lists below provide examples of where to find information on methods, lists, and spectral data.

- Where to find methods?
  - United States Environmental Protection Agency (USEPA) Selected Analytical Methods (SAM) for Environmental Remediation and Recovery, 2022, Appendix A, https://www.epa.gov/esam/selected-analytical-methods-environmental-remediation-and-recovery-sam-2022 (ORD USEPA 2022)
  - ISO (ISO 2023)
  - National Institute for Occupational Safety and Health (NIOSH 2003)
  - Occupational Safety and Health Administration (OSHA) (DOL 2023)
  - National Environmental Monitoring Index (NEMI): https://www.nemi.gov/home/ (USGS 2023)

- Where to find lists?
    - CompTox Chemicals Dashboard: https://comptox.epa.gov/dashboard/chemical-lists (ORD USEPA 2023)
    - NORMAN Network: https://www.norman-network.com/?q=suspect-list-exchange (Mohammed Taha et al. 2022)
    - PFAS Suspect Lists: NIST https://github.com/usnistgov/NISTPFAS (Place 2023)
    - ChemSpider: http://www.chemspider.com/ (Royal Society of Chemistry 2023)
    - PubChem: https://pubchem.ncbi.nlm.nih.gov/ (PubChem 2023)
    - TSCA: https://www.epa.gov/tsca-inventory (OCSPP USEPA 2014)
    - NIST Chemistry WebBook: https://webbook.nist.gov/chemistry/ (DOC 2023)

- Where to find spectral data?
    - Experimental data:
        - MassBank: https://massbank.eu (MassBank-Consortium 2021)
        - MoNA: https://massbank.us (MoNA 2023)
        - mzCloud: https://www.mzcloud.org (mzCloud 2023)
        - NIST Tandem Mass Spectral Library: https://www.nist.gov/programs-projects/tandem-mass-spectral-library (NIST 2012)

    - *in silico* spectral data
        - SIRIUS+CSI:FingerID: https://bio.informatik.uni-jena.de/ (Lehrstuhl Bioinformatik Jena 2023)
        - BioTransformer: http://biotransformer.ca/ (Djoumbou-Feunang et al. 2019)
        - MetFrag: https://msbi.ipb-halle.de/MetFragBeta/ (Ruttkies et al. 2016)

3. Analytical Methods For Chemical Classes

3.1 Why Chemical Class Analysis?

A contaminant chemical class can be defined structurally, as in the case of PFAS (ITRC 2018), leading to a theoretical possibility of thousands of compounds (OECD 2018). Correspondingly, a chemical class can also be defined operationally as in the case of disinfection byproducts (DBPs), where any organic or inorganic compound formed during disinfection is a DBP, thereby leading to near infinite structural possibilities of its members (Dong, Cuthbertson, and Richardson 2020) (Dong et al. 2020). For such chemical classes, targeted analysis is limited to the few compounds for which reference analytical standards are commercially available, leaving the threat posed by the remining fraction unknown. Consequently, chemical class analysis is needed to assess the full scope of the problem, especially when toxicity is perceived to be similar across the chemical class.

The main characteristics of chemical class analysis include the following: (1) the class consists of a considerable number of members; (2) the specific identities of the majority of its members are unknown; and (3) a key property of the chemical class can be exploited to develop a class- or subclass-wide analytical method. A major challenge in the development and use of chemical class methods is the exclusion of interfering compounds outside the chemical class. This specificity problem is prevalent in chemical class methods, especially since the identities of the vast majority of its members are unknown. To illustrate the challenges associated with chemical class analysis, we present the case of total organofluorine and total PFAS analysis below.

3.2 Example of Chemical Class Analysis: Organofluorines and PFAS

In recent years, there has been heightened interest in organofluorine analysis because of the persistence of PFAS in environmental media and their widespread use in commercial products (Robel et al. 2017). PFAS rarely occur in the environment as isolated individual compounds and occur more commonly as mixtures (Bălan et al. 2021). According to the

latest estimates, somewhere between 4,730 (2018)(OECD 2018) and 6,330 (Bălan et al. 2021) different PFAS compounds have been commercially produced to date. Broadly speaking, PFAS can be divided into four different categories: perfluoroalkyl acids (PFAAs), PFAA precursors, perfluoropolyethers (PFPEs), and fluoropolymers (Buck et al. 2011). Although PFAS consist of a wide universe of functionally different substances, there is a dynamic nature to PFAS mixtures in the environment because many PFAS (other than PFAAs) act as precursors and transform to PFAA terminal products over time (Bălan et al. 2021).

To date, targeted analytical methods have focused on a limited number of PFAS, with a hard limit of less than 100 commercially available analytical reference standards for the identification and quantitation of these compounds (ITRC 2023a; McDonough, Guelfo, and Higgins 2019). This leaves the vast majority of PFAS in environmental media as an unknown fraction that cannot be evaluated further without methods that target PFAS and organofluorines more generally as a chemical class. A variety of methods ranging from total fluorine analysis to PFAS organofluorine analysis have been attempted to characterize the unknown fraction. The relationships among the most common total and PFAS organofluorine methods are depicted in Figure 4 and summarized in Table 2. The reader is directed to the Interstate Technology and Regulatory Council (ITRC) PFAS Committee product Section 11 (Sampling and Analysis Methods) for further details on most of these methods (ITRC 2023a). Section 11 details published chemical class and targeted analysis methods for PFAS.

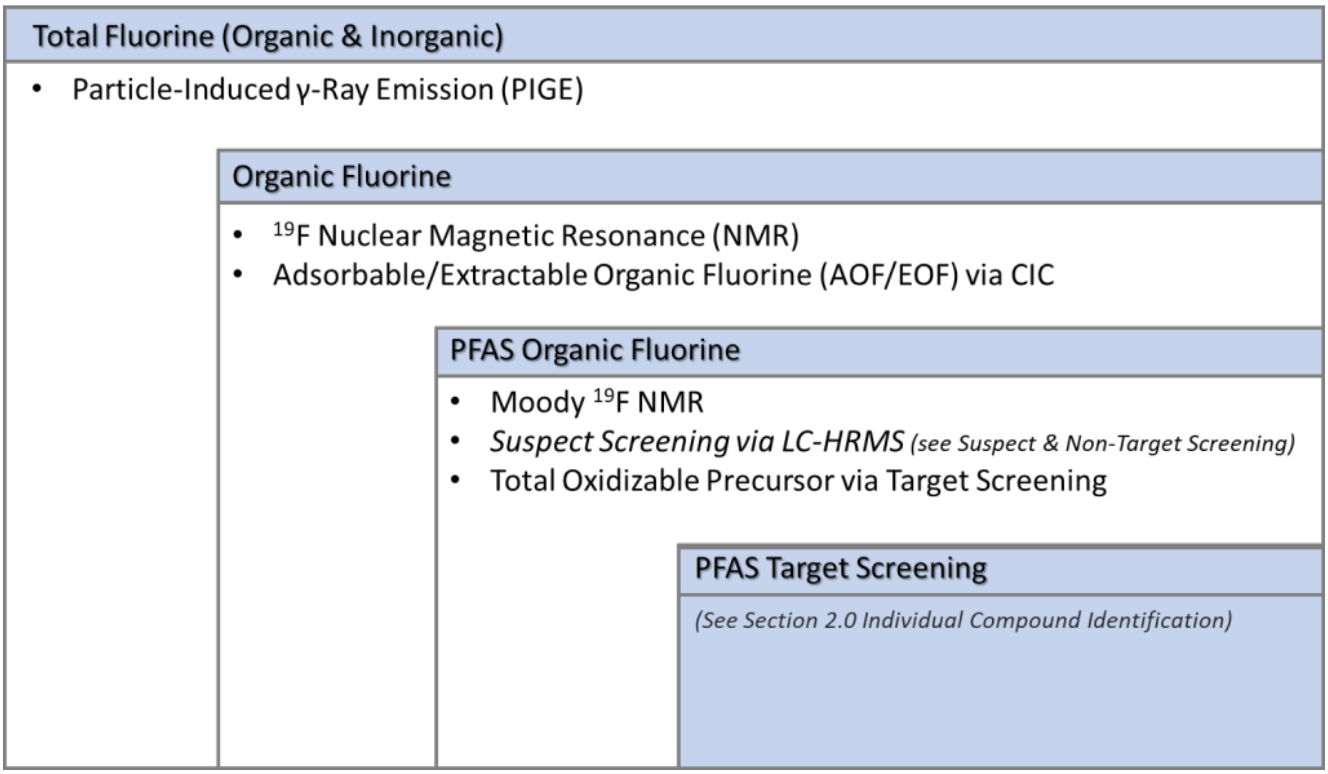


Figure 4. The relationships among total fluorine, organofluorine, PFAS organofluorine, and targeted PFAS methods.

Source: ITRC CEC Team.

Table 2. Summary of major methods used for the analysis of total fluorine, organofluorine, and PFAS organofluorine

Method	Chemical Class/ Subclass Targeted	Principle	Destructive/ Nondestructive to Sample	Environmental Matrices Analyzed	Sensitivity	Limitations	Key References

Particle-Induced Gamma Ray Emission (PIGE)	Total fluorine (organic + inorganic)	An accelerated beam of protons strikes the surface of the sample of interest, exciting ^{19}F nuclei. γ-rays emitted upon de-excitation provide a unique signature proportional to the number of fluorine atoms on the surface. Technique has been applied to textile-based standards.	Nondestructive	Consumer products	13–45 nmol-F/cm^2 (~ 0.1 µg-F/L)	Surface-based technique with limited penetration depth (˂0.22 mm). Includes inorganic fluoride.	(Ritter et al. 2017)
Adsorbable/ Extractable Organic Fluorine (AOF/EOF) via Combustion Ion Chromatography (CIC)	Organic fluorine	AOF uses a polystyrene divinylbenzene-based solid phase while EOF uses a customizable ion-pairing solid phase extraction of samples. The extract is then eluted and analyzed via combustion ion chromatography (CIC).	Destructive	AOF: natural waters; wastewater. EOF: biological materials; sediments, soils, and sludge; natural waters; wastewater	≤ 1 µg-F/L	Influenced by choice of sample preparation approach for isolation of the organofluorine-containing fraction. Can include non-PFAS compounds such as fluorinated pharmaceuticals and pesticides. EOF has yet to be standardized.	AOF: (Wagner et al. 2013; OW USEPA 2022; Willach, Brauch, and Lange 2016) EOF: (Miyake et al. 2007; Kärrman et al. 2021)
Moody ^{19}F Nuclear Magnetic Resonance	PFAS organic fluorine	Monitors chemical shift associated with the terminal CF_3 peak, thereby selecting mainly for fluorinated surfactants and eliminating most interferences from common classes of organofluorine pesticides or pharmaceuticals, as well as inorganic fluoride.	Nondestructive	Natural waters, wastewater	≥ 1 µg-F/L (this technique selects for fluorinated PFAS surfactants)	Relatively high detection limits in aqueous samples.	(Moody et al. 2001)
Total Oxidizable Precursor (TOP)	PFAS organic fluorine	Oxidizes “precursor” molecules using an excess of hydroxyl radicals. The resulting predominantly PFAA fraction is then target screened using LC-MS/MS.	Destructive	Consumer products; sediments, soils, and sludge; natural waters; wastewater	0.1–0.5 ng/L for individual PFAS	Oxidation products analyzed via targeted analysis for PFAAs and, therefore, limited by the available reference standards for PFAAs. PFAS that are not PFAA precursors are not measured by this assay.	(Houtz et al. 2013; Houtz and Sedlak 2012)

Notes: LC-MS/MS = liquid chromatography–tandem mass spectrometry, µg-F/L = microgram fluorine per liter, mm = millimeters, ng/L = nanogram per liter, nmol-F/cm^2 = nanomole fluorine per square centimeter, PFAA = perfluoroalkyl acids, PFAS = perfluoroalkyl and polyfluoroalkyl substances

3.3 Online Resources

Sample online resources are listed below:

- ITRC PFAS Section 11.2, Analytical Methods and Techniques, https://pfas-1.itrcweb.org/11-sampling-and-analytical-methods/ (ITRC 2023a)
- USEPA Draft Method 1621, Screening Method for the Determination of AOF in Aqueous Matrices by CIC,

https://www.epa.gov/system/files/documents/2022-04/draft-method-1621-for-screening-aof-in-aqueous-matrices-by-cic_0.pdf, (OW USEPA 2022)

- USEPA, Frequent Questions about PFAS Methods for National Pollutant Discharge Elimination System Permits (NPDES), https://www.epa.gov/cwa-methods/frequent-questions-about-pfas-methods-npdes-permits (OW USEPA 2020)

4. METHODS FOR BIOLOGICAL CONTAMINANTS

4.1 Survey of Microbial Pathogens That Are Established or Emerging

There are established lists of known microbial pathogens that are reliably detected by a variety of molecular biological, culture-based, or analytical methods. These lists are published by the Food and Drug Administration (FDA), Centers for Disease Control (CDC), and other regulatory agencies globally. Some examples are listed below:

- In food: https://www.fda.gov/media/83271/download (FDA 2012) and https://www.fsis.usda.gov/food-safety/foodborne-illness-and-disease/illnesses-and-pathogens (USDA 2020)
- Various sources: https://wwwnc.cdc.gov/eid/ (CDC 2022) and https://www.cdc.gov/ncezid/index.html (CDC 2023b)
- MicrobNet: https://www.cdc.gov/amd/what-we-do/emerging-threats.html (CDC 2019) and https://microbenet.cdc.gov/ (CDC 2023a); new pathogens are added to this database monthly, and it can be searched by organism name, or for unknowns, search by 16S sequence results (biochemical test results), phenotypic results, or from matrix assisted laser desorption or ionization–time of flight (MALDI-TOF) data
- EMERGE: Efficient response to highly dangerous and emerging pathogens at the European Union level, https://www.emerge.rki.eu/Emerge (Robert Koch Institute 2023); 40 diagnostic laboratories focused on risk group 3 bacteria and risk group 3 and 4 viruses
- GWPP: Global Water Pathogen Network, https://www.waterpathogens.org/ (GWPP 2015); pathogens impacting sanitation and safe water

Emerging concerns include reliably identifying previously unknown organisms that present public health impacts before they become a public health concern.

4.2 Microorganism Detection and Quantification Methods in Environmental Media

Detection and enumeration of emerging pathogens in water, wastewater, and/or environmental matrices (e.g., indoor or outdoor air, soil, surfaces) can be done by multiple different molecular biology–based or culture-based techniques. Many of these techniques were originally developed for applications in medicine, industry, agriculture, or defense. A prior ITRC group, Environmental Molecular Diagnostics (EMD) (ITRC 2013c), discussed a myriad of methods for detection and quantitation of microorganisms of importance for environmental remediation applications. Many of the methods described in the EMD guidance document could be and have been modified for the detection of emerging pathogens. For example, the gold standard method for detecting SARS-CoV-2 shed by individuals ill with COVID-19 in wastewater is quantitative polymerase chain reaction (qPCR). The detailed description of qPCR and other molecular biology–based methods are described in the EMD guidance. These methods are described briefly in Table 3 below with links to the pertinent information on the ITRC website. Additional techniques available for emerging pathogen detection (e.g., new “omics”-based techniques) are also presented in Table 3. Many of these “omics” techniques, such as metagenomics, metatranscriptomics, metabolomics, and proteomics, are described further in the table below and are defined in the glossary.

Table 3. Detection methods for emerging pathogens

Source: CEC Team.

Method	Brief Description	Advantages for Detecting Emerging Pathogens	Disadvantages for Detecting Emerging Pathogens	Example Use for Emerging Pathogen Detection

Polymerase Chain Reaction (PCR) (ITRC 2013b)	Detects pathogenic microorganism nucleic acids (ITRC 2013b) or genes in sample. Provides a direct line of evidence of the presence of a pathogen.	• More rapid than methods requiring cultivation • Can detect a pathogen among mixed microbial communities with great sensitivity • Many commercial laboratories available	• Not quantitative • Detects both viable and nonviable pathogens, potentially overestimating disease risk • Needs primers and probes specific to the pathogen, requiring other methods to first identify the pathogen or target gene	Detection of polio and monkeypox in wastewater
Real-Time Quantitative Polymerase Chain Reaction (qPCR) (ITRC 2013a) or Reverse Transcriptase qPCR (RT-qPCR) for RNA	Quantifies the abundance and/or activity of a target pathogenic microorganism through detection of nucleic acids or genes (ITRC 2013b) in a sample. This provides a direct line of evidence of the presence of a pathogen.	• More rapid than methods requiring cultivation • Allows detection of non-cultivable organisms • Can detect a pathogen among mixed microbial communities with great sensitivity • TaqMan-based plate assays and microfluidics allow for detection of variants in a high-throughput manner • Many commercial laboratories available	• Detects both viable and nonviable pathogens, which can overestimate disease risk • Needs primers and probes specific to the pathogen, requiring other methods to first identify the pathogen or target gene • False positive and negative detections possible	Detection of SARS-CoV-2, polio, and monkeypox in wastewater Clinical gastroenteritis and antimicrobial-resistant qPCR array cards commercially available such as those from GenPix and Biomerieux
Genomics or Metagenomics	Analysis of genome of multiple organisms by next-generation sequencing (NGS) methods (N. Li et al. 2021; Loman et al. 2013) or complete analysis of the genome of a single pathogen.	• Allows for unbiased and comprehensive detection and taxonomic characterization of pathogens in mixed microbial community samples • Prior knowledge of primers and probes not needed • Commercial laboratories available	• Bioinformatic expertise is needed to understand the data • Need to collect samples from primary site of infection in humans (e.g., sputum or cerebrospinal fluid) for sequencing • Specificity limited by available data in bioinformatic databases on emerging pathogens	Investigate outbreaks of *Escherichia coli* strain O104:H4 in food supply (Loman et al. 2013)

Meta-transcriptomics	Analysis of the active genes in a pathogen or mixed sample of microorganisms (i.e., a virulence gene of *E. coli)* by NGS methods.	• Single assay can identify vector (mosquito), pathogens (eukaryote, bacteria, or viral), and the animal hosts (blood in vector) • Prior knowledge of primers and probes not needed • Commercial laboratories available	• Not as sensitive as RT-qPCR • Specificity limited by available data in bioinformatic databases on emerging pathogens	Identification of vector-(i.e., mosquito) borne viruses (Batson et al. 2021)
Metabolomics	Mass spectroscopy technique to identify the suite of metabolites that are generated by microorganisms or pathogens.	• Links pathogen presence to disease markers • Can directly measure the small molecules associated with disease diagnosis, microbial toxins, and allergens, regardless of organism identity (i.e., aflatoxins from various *Aspergillus* species)	• Few commercial laboratories available • Discrimination of pathogens limited to small molecules available in metabolomics databases • Few commercial laboratories available	Nasopharyngeal swab samples identify acute respiratory illness caused by influenza (Hogan et al. 2021) Used for food safety monitoring (S. Li et al. 2021; Jadhav et al. 2018)
Proteomics	Mass spectrometry to identify the protein expression of pathogens.	• Rapid method compared to culture-based identification • Sensitive method capable of identifying pathogens to the species level	• Discrimination of pathogens limited to proteins identified in proteomics databases (i.e., MALDI-TOF MS spectral databases) • Few commercial laboratories available	Species-level detection of foodborne pathogens (e.g., *Listeria*, *Salmonella,* and *E. coli*) (Syu, Dunn, and Zhu 2020)
Microarrays	Massively parallel detection of functional pathogen proteins or nucleic acids of pathogens.	• Multiple arrays commercially available and scalable to hundreds to thousands of pathogen targets • Many clinical and commercial laboratories available for routinely utilized pathogen microarrays	• Needs primers and probes specific to the pathogen, requiring other methods to first identify the pathogen or target gene • May be limited commercial laboratories if using a nonstandard microarray	Functional protein arrays for zika and dengue fever (Savidis et al. 2016)

Flow Cytometry	A type of automated fluorescence detection technique allowing for detection of cells in complex matrices.	• Sensitive and suitable for detecting low numbers of pathogens in fluids • Results available in hours	• Relatively few commercial laboratories available • Not capable of subspecies identification if pathogen subpopulations have similar responses (i.e., marker expressions)	Viral pathogen detection in treated wastewater for potable reuse (Rockey et al. 2019)
Culture-Based Methods	Growth of organisms in selective media specific to pathogen. Isolation of the pathogen may be required.	• Many commercial laboratories available	• May require extensive culturing in the laboratory and confirmation testing via other methods to confirm pathogen species and pathogenicity	FDA methods (FDA 2023) for detection of pathogens in food

Metagenomics is the analysis of the genome (complete DNA or RNA sequence) of one or more organisms. In environmental surveillance for emerging pathogens, metagenomics can be used to identify the genome of new organisms within a community of interest (e.g., sputum or serum from ill individuals or environmental samples suspected of harboring human pathogen) (N. Li et al. 2021). This method allows for identification of suspected pathogens from among the complex microbial communities. Additional methods will be required to conclusively link any suspected genome identified in a sample to a particular morbidity or disease. Bioinformatics is then leveraged to identify pathogens from among the mixed community sequences. Therefore, if a novel pathogen is sequenced for which there are few similar sequences in the databases used for bioinformatic comparison, it will be difficult to impossible to determine which organism may be responsible for the disease.

Metatranscriptomics is similar to metagenomics in the way it depends on sequencing of nucleic acids and bioinformatics. The methods differ in that metatranscriptomics is targeted to sequencing genes that are currently being expressed in an organism—either a pathogen or a host organism (e.g., human). For example, genes associated with immune responses to respiratory viruses (e.g., interferon response genes and chemokines) can be sequenced from the host and compared to databases of known metabolic genes in humans (Rajagopala et al. 2021), such as those compiled in the Kyoto Encyclopedia of Genes and Genomes (KEGG) (Kanehisa et al. 2023).

Metabolomics harnesses the investigation of the organic compounds in samples (i.e., water or biological samples) that arise from metabolic activity of pathogens that are present in a sample or that are infecting a living organism. Some of the organic compounds metabolized by living organisms are volatile and can be detected by mass spectroscopy. Specifically, volatile organic compounds (VOCs) can be detected from pathogen isolates, expired human breath, sputum, feces, saliva, throat swabs, and vaginal discharge. Detection of these VOCs or biomarkers are an indicator of active infection and/or the presence of the pathogen in a sample. While routine microbiology surveillance for a known pathogen is time-consuming, the response in humans to a particular disease state may be a suitable and rapid marker of the presence of a pathogen (i.e., detection of VOCs in the breath of individuals with cystic fibrosis infected with *Pseudomonas aeruginosa*) (Gilligan 2021). Other examples of the use of metabolomics include the detection of *Salmonella* in milk via testing of exogenous VOCs (Bahroun et al. 2018).

Protein function is representative of the entirety of active biological processes in a cell, tissue, or bodily fluid. While metatranscriptomics measures the RNA that serves as intermediates between the genome and the protein, RNA is only an approximation of the levels of a protein that are in an infected host or a pathogen. The term proteome refers to the entire complement of proteins that can be made by a genome, while proteomics refers to the analysis of those proteins. By analyzing proteins in a microbial community or in an infected host, it is possible to identify groups of pathogens. However,

additional tools are needed to conclusively determine the identity of novel pathogens (Bostanci et al. 2021). Biotyping of bacteria by proteomics is used in clinical laboratories, but is not typically applied for viruses (Grossegesse et al. 2020).

4.3 New Pathogen Detection Method Validation Approaches

Once an emerging pathogen has been identified as a causative agent of a disease, robust, rapid, reproducible, and ideally inexpensive detection methods are required. Robustness of the method here refers to the ability to detect the pathogen among many inhibitory compounds and/or confounding microorganisms or signals. Ideally, the analytical method would be rapid, and results would be obtained in near real time or within minutes of sample collection. Reproducibility of the method would occur if many different laboratories and/or analysts could obtain the same results within an acceptable margin of error on identical samples. The ideal method would be inexpensive as potentially tens, hundreds, or thousands of samples would need to be processed during a suspected public health outbreak or investigation of a site.

Analytical methods for pathogens would ideally have the following characteristics, in decreasing order of importance:

1. quantitation (preferred) of viable and infectious pathogens (i.e., counts of cells)
2. detection of markers (less preferred) of the pathogen (e.g., proteins or nucleic acids such as DNA)
3. rapid quantitation or detection of pathogen (i.e., real-time results or within minutes of sample collection)
4. sensitive detection of the pathogen in mixed matrices and from among mixtures of microorganisms
5. reproducible method among many laboratories
6. conducted with readily available and common equipment or test kits

Various guidance documents are available from federal agencies that recommend validation approaches for analytical methods. These references include, among others, the following:

- FDA guidance for validation of analytical methods for microbial pathogens in food and feed, https://www.fda.gov/media/83812/download (FDA 2019)
- MIQE (minimum information for publication of qPCR experiments) https://pubmed.ncbi.nlm.nih.gov/19246619/ (Bustin et al. 2009)
- USEPA QA/QC for labs running qPCR, https://projects.itrcweb.org/emd-2/Content/Resources/EPA-815-B-04-001.pdf (USEPA 2004)
- USEPA method validation and peer-review guidelines: Microbiological Methods of Analysis https://www.epa.gov/measurements-modeling/method-validation-and-peer-review-policies-and-guidelines (USEPA 2016)

A summary of the advantages and drawbacks to various methods of pathogen identification and detection has been presented previously and should also be referenced when considering methods for identification of emerging pathogens (Rajapaksha et al. 2019).

5. Analysis of Particulates

5.1 Microplastics

The ITRC Microplastics Team Materials (ITRC 2023b) details sampling and analysis techniques for microplastics (MPs).

5.1.1 Sampling

Techniques and best practices for sample collection and analysis of MPs and fibers are still evolving. In 2020, ASTM

International adopted a standard for water sample collection, which covers low, medium, and high ranges of suspended solids (ASTM International 2020).

Publications on appropriate study data quality objectives (DQOs) for monitoring programs exist (OCSPP USEPA 2023) and could include the following:

- identification and determination of mass of MP
- identification of particle number, size, and shape of MP
- characterization of specific properties of individual MP
- polymer type

For general monitoring, the size of the MP should be defined by the program, with the understanding that the smaller sizes are more difficult (i.e., more costly) to sample, extract, and identify.

5.1.2 Analysis

Chemical identification/compositional analysis of the particles is critical for accurate quantification of MPs in environmental samples and is challenging because MPs can mimic naturally occurring materials and vice-versa. Visual microscopic methods are generally less than 70% accurate (Lenz et al. 2015) for larger fractions of MPs but far less effective for smaller MP fragments. Instrumentation allows not only for the identification of specific polymers of MPs, but also for the identification of other contaminants and adsorbates associated with the MPs. Detection approaches can be divided into the following categories:

1. **Visual Methods:** Visual examination of a sample with or without magnification.

2. **Spectroscopic Methods:** Capture and assign the characteristics of specific chemical structure of polymers using reference spectra (e.g., Fourier Transform Infrared (FTIR) microscopy and Raman Spectroscopy).

3. **Thermoanalytical/Chemical Methods:** Pyrolyze the sample under inert conditions and detect specific decomposition products of the individual polymers (e.g., Pyrolysis GC-MS and Thermal Desorption GC-MS).

Applicable standards that discuss analysis include Raman and FTIR microscopy methods for MP identification in drinking water. This standard was adopted by the California State Water Board (Wong 2021).

Instrumentation methods are well summarized in the draft ITRC guide on MPs and are reproduced here in Table 4 (ITRC 2023b). The general workflow for selecting analysis and measurement methods based on the target and type of analysis is presented in Figure 5.

Table 4. Summary of microplastics characterization techniques

Source: ITRC 2022b.

Description	Analysis Time/ Sample	Size Detection Limit	Measurement Preparation	Identifies Polymer Types	Detects Additives/ Surface Chemicals	Detects Particles or Mass
Visual Methods						
NE Naked Eye	Hours	1 mm	None	No	No	Particle
SM Stereo Microscopy	Hours	100 µm	On filter	No	No	Particles

FM Fluorescence Microscopy	Hours	50 µm (possibly smaller based on objective lens used)	On filter	No	No	Particles
SEM Scanning Electron Microscopy	Hours	0.001 µm	On filter	Yes	No	Particles
Spectroscopic Methods						
FPA-FTIR Focal Plane Array-Fourier Transform Infrared Spectroscopy (in Transmission Mode)	Hours	20 µm	On special filter	Yes	No	Particles
FTIR Fourier Transform Infrared Spectroscopy (in Transmission Mode)	Days	20 µm	On special filter	Yes	No	Particles
LDIR Laser Direct Infrared Spectroscopy	Minutes particles/ hour	20 µm	Special microscope slide	Yes	No	Particles
NIR, vizNIR Near Infrared Spectroscopy, Visible-Near Infrared Spectroscopy	Hours	Unspecified	On filter	Yes	Surface chemicals only	Particles
Raman Spectroscopy	Days	1 µm (theoretically but challenging to achieve)	Extraction and placed on filter	All polymers	Yes	Particles
Thermoanalytical/Chemical Methods						
DSC+TGA Differential Scanning Calorimetry+ Thermal gravimetric Analysis	Hours	Unspecified	Filtrate	Yes, only PE, PP	No	Mass
Py-GC/MS Pyrolysis–Gas Chromatography–Mass Spectrometry	Hours	<1–0.5 µg	Isolated particles	Yes	Yes	Mass

Notes: µg = microgram, µm = micrometer, mm = millimeter, PE = polyethylene, PP = polypropylene

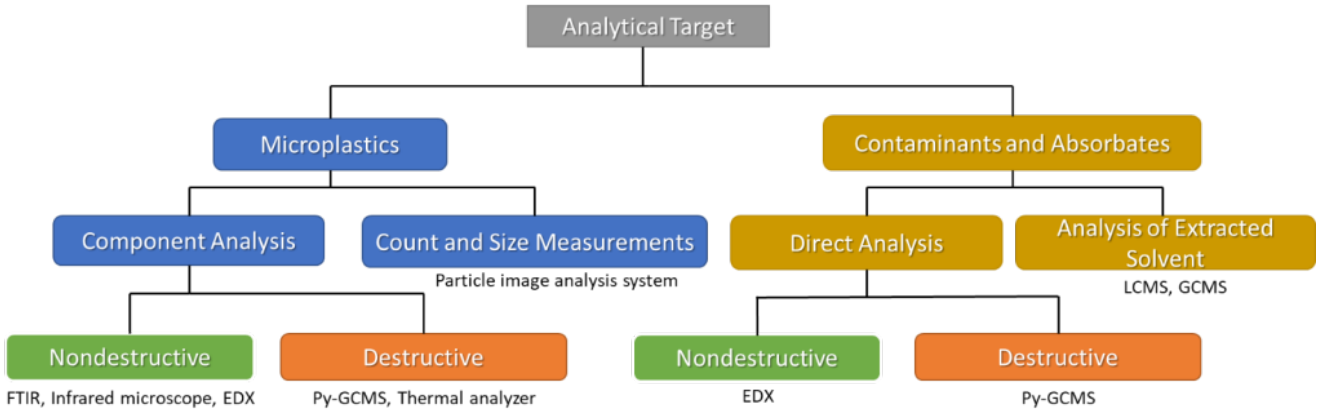


Figure 5. Workflow for selecting an analysis and measurement method for microplastics.

Source: Adapted from Shimadzu (2020).

5.2 Engineered Nanoparticles

As technology evolves toward the nanoscale, the long-term effects on human health and ecosystem impacts are yet to be seen. This aspect of nanotechnology is a growing concern. The release of engineered nanomaterials (ENMs) and engineered nanoparticles (ENPs) into the environment is inevitable, but information on their long-term effects on plant life, human health, and the ecosystem is in short supply and often conflicting.

Accurate detection of ENPs in the environment is imperative to assess the risk posed to the environment and to human health. Establishing discharge levels from point/nonpoint sources of ENPs will not be possible unless there are reliable methods for identifying, characterizing, and measuring ENPs in environmental media. Traditional analytical technologies and systems need improvement in both sensitivity and specificity to various types of ENPs in a wide concentration range. Due to the nature and composition of ENPs, the sensitivity of traditional analytical methods is often not adequate to produce findings below the detection limit (false negatives).

ENPs vary in properties such as size, morphology, elemental composition, crystalline structure, etc.; therefore, it is essential to devise methods that detect nanoparticles in the environment by focusing on these properties. Small variations in these properties influence the bulk properties of nanoparticles, which in turn can have negative implications once end products are discharged into the environment. Therefore, multiple measurement and analytical techniques used to detect, quantify, and analyze nanoparticles have been developed. The methods have been grouped into different categories, as represented in Figure 6, based on their ability to determine and analyze distinct characterizing properties.

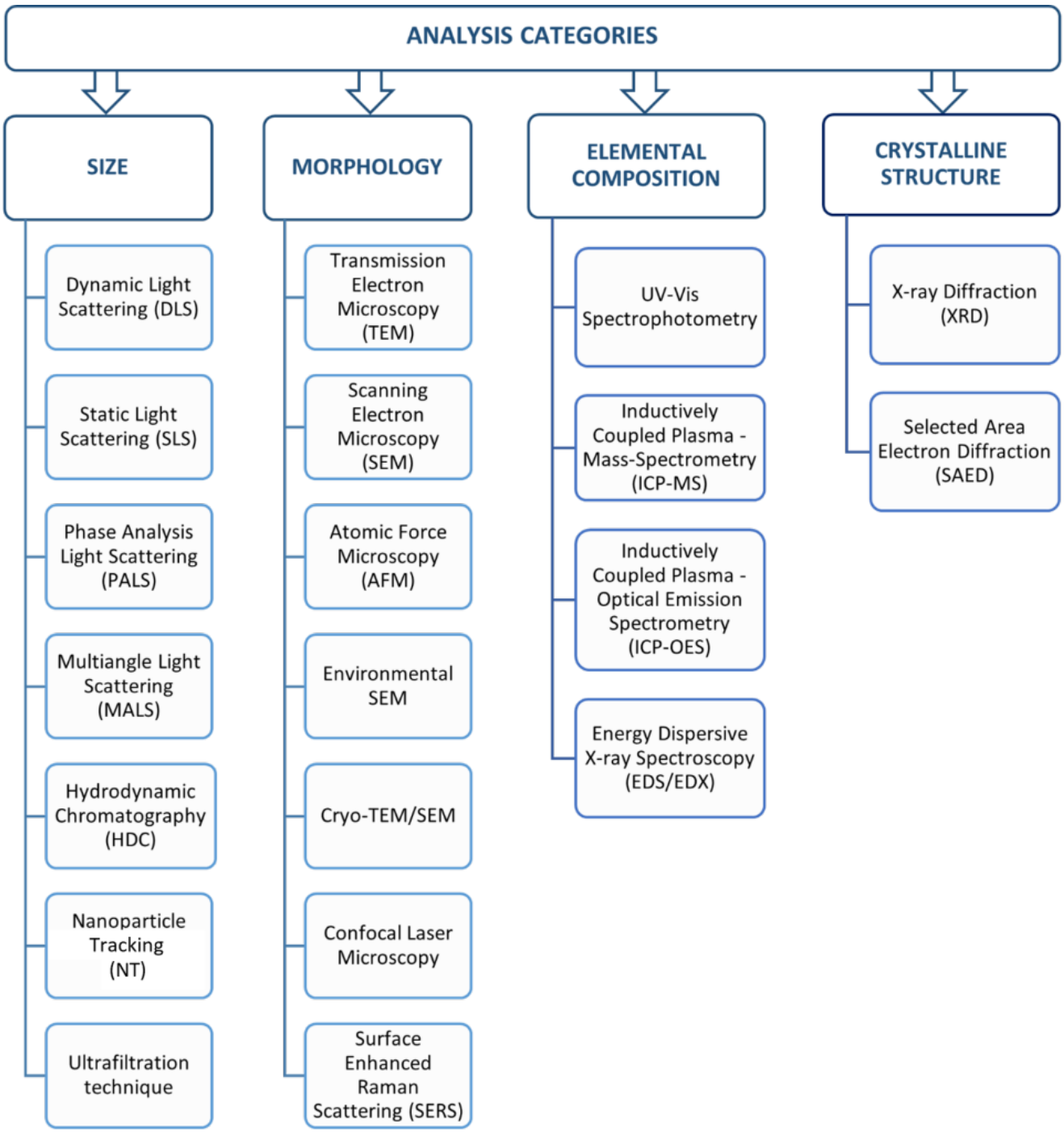


Figure 6. Analytical methods for characterizing engineered nanoparticles based on characterization property. See supplementary information table.

Source: ITRC CEC Team.

One strategy to obtain concentrated particles without changing the intrinsic properties of the ENPs is enrichment-separation-detection (Zhang et al. 2019). An oversimplified model for detecting, monitoring, and controlling ENPs is shown in Figure 7. The outlook and challenges for ENP enrichment-separation-detection are not fully developed due to a lack of standardization of methods for broad-spectrum detection. Each step is its own isolated process, which can introduce error during measurement. This can be mitigated if a rapid, fully integrated device is developed, but such a device is currently absent in analytical technologies.

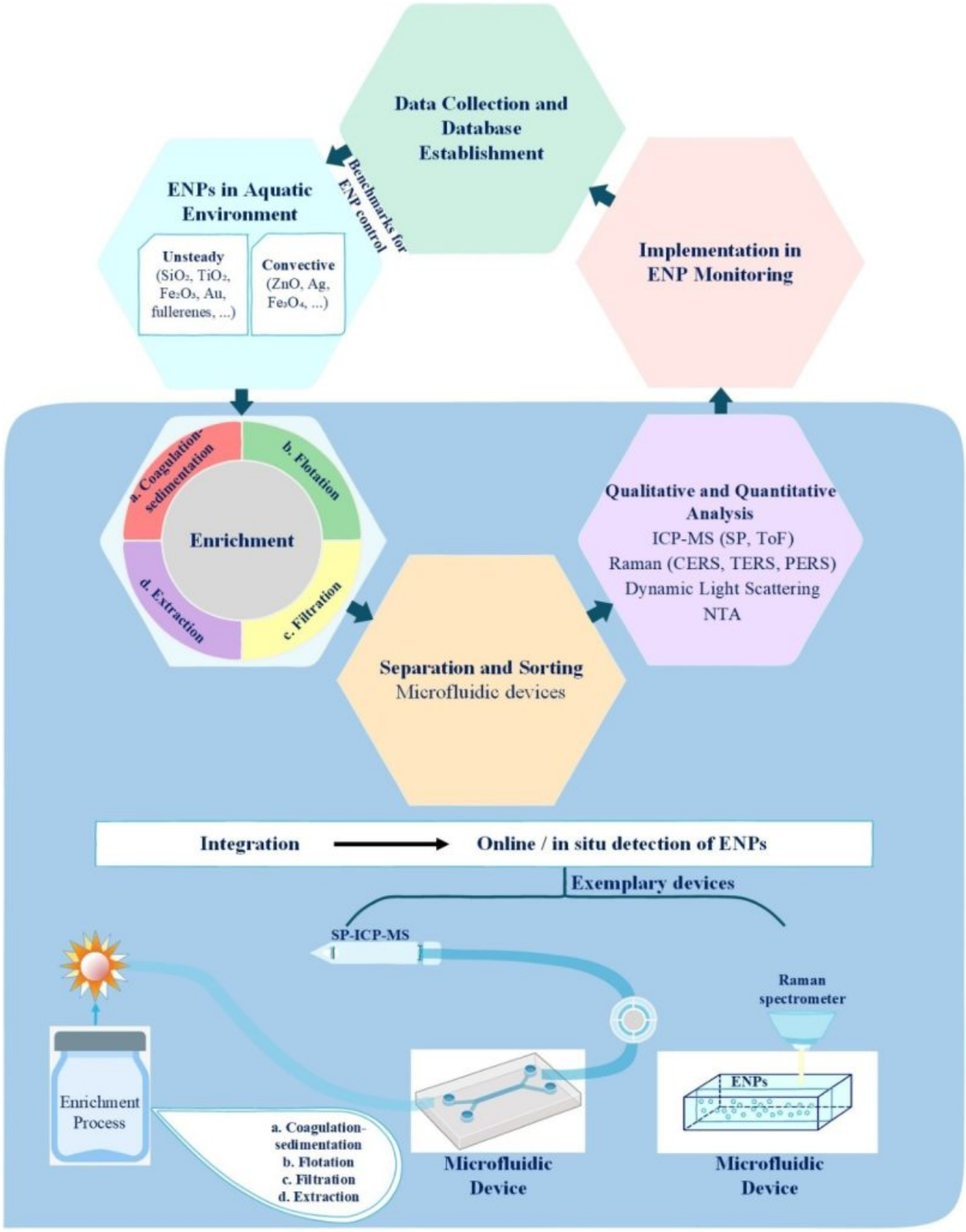


Figure 7. Overview of detecting, monitoring, and controlling ENPs in an aquatic environment.

Source:Adapted from Zhang and colleagues (2019).

Some of the more commonly used qualitative and quantitative analysis techniques for ENPs are summarized below:

5.2.1 Single Particle Inductively Coupled Plasma–Mass Spectrometry

Single particle inductively coupled plasma–mass spectrometry (SP ICP-MS) was developed to facilitate chemical

characterization of individual nanoparticles and to differentiate those particles from dissolved ions. In SP ICP-MS, a dilute suspension of particles is introduced into the ICP. In the ICP a dense ion cloud is produced, which is then transferred into the mass spectrometer, where it is guided through the ion optics and mass separation device as a transient pulse of ions with a typical temporal duration between 300 and 500 microseconds (µs). If enough ions from an ENP are passed through the MS instrument, then the ENP-produced transient pulse of ions is registered as a signal spike in the time-trace of the mass spectrometer. By counting these ENP spikes, particle number concentrations (PNCs) of analyte ENPs can be determined. The amount of ion signal in each ENP-produced signal spike can be related to the amount (i.e., mass) of an element in the ENP. In SP ICP-MS, the signal is monitored at a higher time resolution than standard ICP-MS. This allows the discrimination between the ion plumes caused by the particle and the background analyte. The intensity of the ion plume is related to the mass of metal in the ENP (Heithmar 2011). It is used for measuring inorganic ENPs at low number concentrations (10^2–10^6 particles/milliliter).

5.2.2 Raman Spectroscopy (Surface Enhanced Raman Spectroscopy [SERS], Tip Enhanced Raman Spectroscopy [TERS], Plasmon Enhanced Raman Spectroscopy [PERS])

For many nanomaterials, Raman spectroscopy has become one of the go-to characterization methods. The main reason is that Raman spectroscopy can not only determine the composition of each nanomaterial, allowing it to be identified, but it can often determine the structural arrangement that distinguishes two different forms of the same type of nanomaterial. One example of this is its ability to distinguish between single-walled carbon nanotubes and multi-walled carbon nanotubes.

5.2.3 Dynamic Light Scattering

Dynamic light scattering (DLS) uses scattered light to measure the rate of diffusion of ENPs. It provides information about size distribution in terms of hydrodynamic diameter. DLS uses a laser beam that passes through a liquid suspension containing the analyte particles. They scatter the incident laser at different scattering angles. The Brownian motion of the detected particles induces the shift in light frequency, which varies with different particle sizes (Langevin et al. 2018). DLS is a useful tool for determining the hydrodynamic diameter and particle size distribution in suspension and for investigating colloidal properties of nanoparticles. It is used for size characterization of lipid nano-capsules in food samples (Yegin and Lamprecht 2006).

5.2.4 Nanoparticle Tracking

Nanoparticle tracking (NT) involves the application of intense laser light to illuminate free-diffusing particles to track their Brownian motion with monochrome imaging (Bhattacharjee 2016). Unlike DLS, NT can measure particle-by-particle size. NT provides individual particle intensity as well as motion videos (Hou et al. 2018). NT is better relative to DLS in detecting smaller aggregates (Hou et al. 2018). Setup parameters need to be adjusted carefully to obtain high accuracy.

5.2.5 Electrochemical Methods

“Nano-impact”–based electrochemical methods have shown great promise in detecting ENPs at the single-entity level. The method is based on the direct impact of individual particles on the electrode surface, which leads to current spikes as a function of time that can correlate to various characteristics of an ENP’s property (Neves et al. 2020). Quantitative information for ENP characteristics such as size, concentration, aggregation, and catalytic reactivity can be generated (Cheng and Compton 2014).

Case Study: Effect-Directed Nontarget Analysis Identifies 6PPD-q as Cause of Urban Runoff Mortality Syndrome

1. Introduction

This case study describes an effect-directed nontargeted analysis (NTA) experimental study (Tian et al. 2021) to identify the contaminant of emerging concern (CEC) responsible for acute mortality in coho salmon (*Oncorhynchus kisutch*) observed during runoff events in the Pacific Northwest (a.k.a. “urban runoff mortality syndrome” [URMS]). URMS occurs among adult

coho salmon populations annually when they return to spawn in freshwater, especially to waters located in urbanized watersheds. Effect-directed analysis (EDA) is a strategy for environmental profiling of samples that combines sample fractionation schemes, toxic effect assays, and chemical analysis to identify toxic pollutants (Dong, Cuthbertson, and Richardson 2020). More recently, EDA has been paired with NTA using high-resolution mass spectrometry (HRMS) for chemical analysis to identify CEC in complex environmental samples (Dong, Cuthbertson, and Richardson 2020; Hollender et al. 2019). The case study begins with tire leachate (i.e., tread wear particle leachate [TWPL]) in the "known-unknowns" quadrant of the Rumsfeld matrix (see Figure 1, Analytical Methods Fact Sheet) after targeted analysis methods had been exhausted and after a chemical compositional similarity had been established among TWPL, roadway runoff, and URMS–associated waters (Peter et al. 2018).

2. Experimental Methodology and Results

The experimental design of the study relied upon three key tools for identifying the CEC:

1. A fractionation scheme to simplify the complex TWPL mixture
2. Acute exposure toxicity assays to screen TWPL fractions for their ability to induce mortality in juvenile coho salmon
3. Ultra-high-performance liquid chromatography–high-resolution mass spectrometry (UHPLC-HRMS) for structural determination (i.e., by molecular formula determination using accurate mass—see Figure 1)

Acute toxicity assays were performed on juvenile coho salmon as a proxy for adult coho (Chow et al. 2019). The CEC was eventually determined to be a quinone oxidation byproduct of the tire antioxidant N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine (6PPD), or 6PPD-quinone (6PPD-q). Note that only a cursory description of follow-up work beyond the molecular formula determination (i.e., to elucidate the chemical structure of the CEC) is provided within this case study writeup. The subsections that follow describe various stages of the study, which are also graphically summarized in Figure 2.

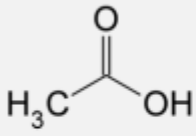
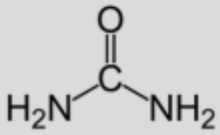
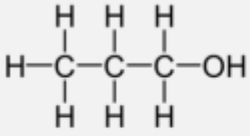
Compound		Nominal Mass[a]	Accurate Mass[b]
	Acetic Acid ($C_2H_4O_2$)	60	60.021128
	Urea (CH_4N_2O)	60	60.032362
	Propan-1-ol (C_3H_8O)	60	60.057514
	Ethylenediamine ($C_2H_8N_2$)	60	60.068748

Figure 1. Accurate mass from HRMS for determining molecular formula. HRMS yields ion mass at an accuracy of three to seven decimal places (i.e., 0.001 Dalton [Da] [or amu] or less), thereby deciphering its unique molecular formula. A conventional unit-resolution quadrupole mass spectrometer cannot distinguish the identity of a hypothetical 60 amu or Da (60 m/z) nominal mass molecular ion peak among four different compounds (i.e., acetic acid, urea, propan-1-ol, and ethylenediamine); however, a molecular ion peak of 60.0687 amu obtained using HRMS (e.g., by using a quadrupole-time-of-flight mass spectrometer) would clearly indicate the compound ethylenediamine.
Source: ITRC CEC Team

a. Nominal mass is at unit resolution and is expressed as an integer. For monoisotopic ions (i.e., ions made up of only the most abundant isotope of each of its constituent elements), nominal masses of elements in atomic mass units (amu) or Daltons are C=12, H=1, N=14, and O=16.

b. Accurate mass is obtained from a high-resolution instrument that gives a molecular mass at an accuracy of three to seven decimal places. For monoisotopic ions, accurate masses of elements in amu or Daltons are C=12.000000, H=1.007825, N=14.003074, and O=15.994914.

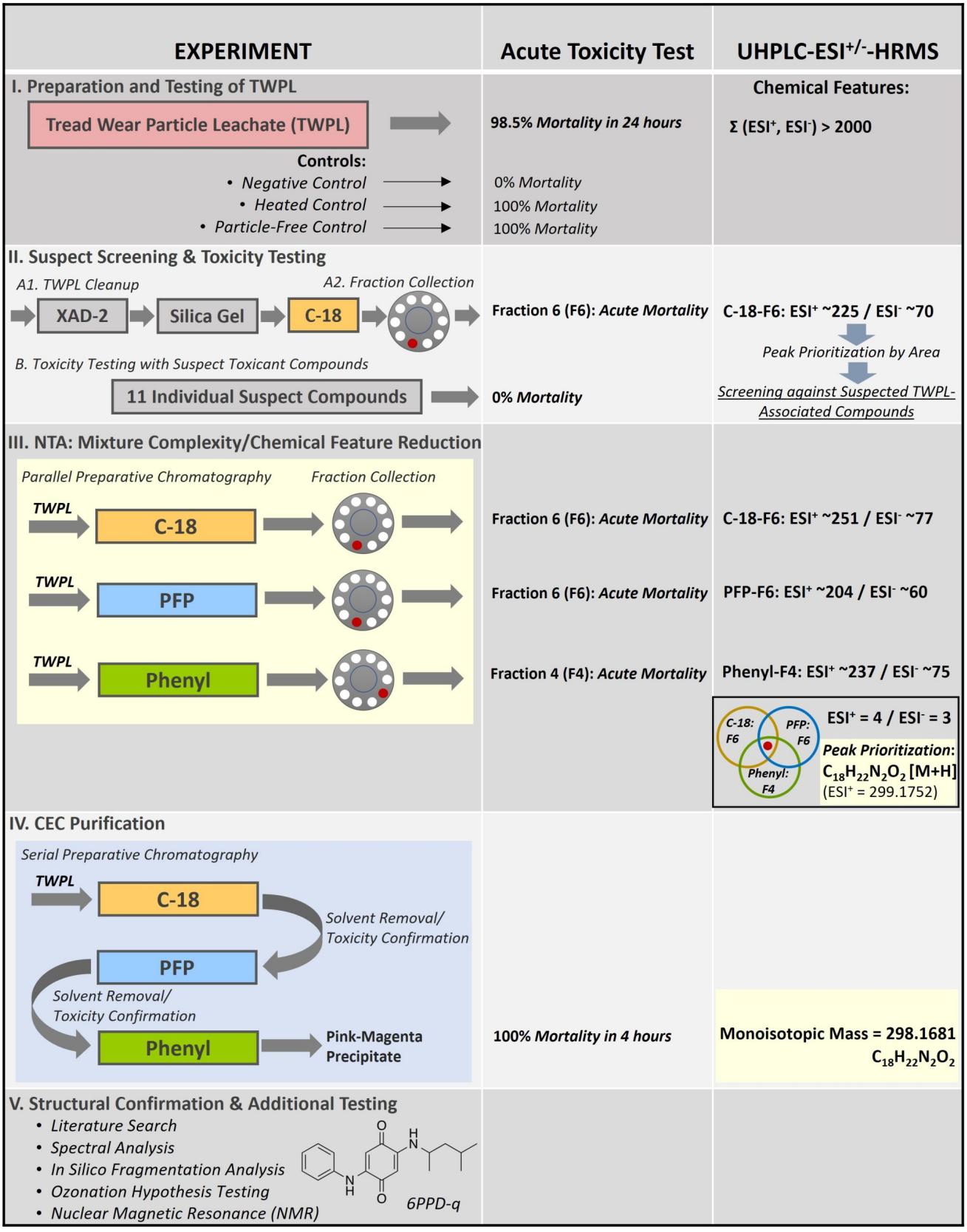


Figure 2. Overall schema for 6PPD-q effect-directed analysis (EDA) study
Source: Tian and colleagues (2021).

2.1 Stage I. Preparation and Testing of TWPL

An aqueous TWPL was prepared using tread particles from nine different used and new tires. The TWPL was found to be

lethal (98.5% mortality in <6 hours) to juvenile coho salmon in a 24-hour acute toxicity test. A negative control demonstrated no mortality while toxicity remained unabated in a heated control, indicating stability during handling, and in a particle-free control, indicating that the CEC was dissolved and not particle-associated. Toxicity also remained unchanged after the leachate was treated with ion exchange resins (cation and anion) and ethylenediaminetetraacetic acid (EDTA) indicating that the CEC was not ionized and was not a metal, respectively. UHPLC-HRMS of the TWPL in positive and negative electrospray ionization modes (i.e., ESI^+ and ESI^-, respectively) produced more than 2,000 combined chemical features with unique mass to charge ratio (*m/z*) and retention time, indicating the complexity of the TWPL mixture. This necessitated cleanup of the mixture in Stage 2 to generate a simplified yet toxic mixture more amenable to individual compound identification.

2.2 Stage II. Suspect Screening and Individual Compound Toxicity Testing

In Stage II, the TWPL underwent sequential cleanup using cation exchange, silica gel, and reversed-phase C-18 separation. Fractions were collected and were subjected to acute toxicity testing. Only one fraction (Fraction 6 or F6) produced acute mortality in coho salmon, indicating that it contained the suspected CEC. The fraction was analyzed using UHPLC-HRMS, which resulted in approximately 225 and 70 chemical features in ESI^+ and ESI^- ionization modes, respectively. This constituted a significant reduction in sample complexity because only 10% of the features found in the initial TWPL mixture remained in the active fraction. A suspect screening list was compiled using an in-house database of tire rubber compounds (n=258) and a larger database from the NORMAN (network of reference laboratories, research centers and related organizations for monitoring of emerging environmental substances) Suspect List Exchange Database of approximately 30,000 environmental pollutants. These lists were integrated into the data-dependent acquisition to prioritize tandem mass spectral (MS/MS) collection for suspected compounds. Eleven compounds, including plasticizers, antioxidants, emulsifiers, and their transformation products, were identified in the active fraction but none induced mortality in the test organisms. The negative results from the suspect screening stage led the authors to conclude that the ***CEC responsible for URMS was previously unreported in scientific literature and required an NTA approach for identification.***

2.3 Stage III. NTA: Mixture Complexity and Chemical Feature Reduction

A parallel preparative-level chromatography approach was employed to further reduce the mixture complexity and limit the number of chemical features. Columns with different stationary phases (C-18, pentafluorophenyl [PFP], and phenyl), together with fraction collection, were used to change the elution order of the CEC, as well as the mixture composition of each fraction. Only fractions C-18-F6, PFP-F6, and Phenyl-F4 induced acute mortality in test organisms. These toxic fractions were independently analyzed using UHPLC-HRMS and resulted in the ESI^+ chemical features of 251 for C-18-F6, 204 for PFP-F6, and 237 for Phenyl-F4. Similarly, ESI^- chemical features of 77 for C-18-F6, 60 for PFP-F6, and 75 for Phenyl-F4 were obtained. Common chemical features present in all three lethal fractions were identified, resulting in only four ESI^+ and three ESI^- chemical features.

Peaks for these common chemical features were prioritized by abundance, resulting in the identification of a dominant chemical feature (i.e., 10-fold higher intensity in both ESI^+ and ESI^-) that that had a measured mass of 298.1681 atomic mass units (amu) (or ESI^+ [M+H] protonated peaks of 299.1752–299.1777 amu). After subtracting the proton mass, this molecular ion peak corresponded to the monoisotopic ion (i.e., an ion composed of only the most abundant isotope of each element) with a molecular formula of $C_{18}H_{22}N_2O_2$. The structural information gleaned about the CEC at this stage would place it at Level 5 on the Schymanski Confidence Level Scale (see Figure 3, Analytical Methods Fact Sheet), where the exact mass of interest had been identified, but remained a high-priority CEC based on the toxicity results.

2.4 Stage IV. CEC Purification

The preparative chromatography setup in Stage III was converted from parallel to serial (i.e., C-18 → PFP → Phenyl) to recover a sufficient amount of material to facilitate chemical structure studies in Stage V. Solvent removal via centrifugal evaporation and toxicity confirmation between separations yielded a pink-magenta precipitate that was dominated by the $C_{18}H_{22}N_2O_2$ molecular ion peak via UHPLC-HRMS (chemical features: $ESI^+ = 4$ and $ESI^- = 3$). The material caused 100% mortality in juvenile coho salmon upon 4 hours of exposure.

2.5 Stage V. Structural Confirmation and Additional Testing

Various tools were employed to elucidate the structure of the CEC with a molecular formula of $C_{18}H_{22}N_2O_2$, including (a) an

extensive crumb rubber literature review, (b) manual structural elucidation from mass spectra of the CEC, and (c) *in silico* fragmentation algorithms of the molecular ion peak at different ionization energies in software tools such as MetFrag and CSI:FingerID with matching against PubChem and ChemSpider databases. None of these approaches provided structural information.

The breakthrough for the structural elucidation came when the literature search included slight variations in the molecular formula based on the assumption that the causative agent could be an abiotic oxidative transformation product of a substance already used in tire rubber. Literature searches identified 6PPD with a molecular formula of $C_{18}H_{22}N_2$ as a possible proto-toxicant. This hypothesis was tested when 6PPD was transformed using gas phase ozonation to a transformation product that was an exact match of the CEC isolated from the TWPL by UHPLC-HRMS and nuclear magnetic resonance (NMR) spectroscopy. The CEC was tentatively identified as 6PPD-q based on the parent compound and the structural information gleaned from the oxidation of 6PPD, which places the structural information about the CEC at Schymanski Confidence Level 3, or a tentative structural candidate identification (see Figure 3, Analytical Methods Fact Sheet). Schymanski Confidence Levels are defined solely by HRMS information and chromatography data (e.g., retention time at Schymanski Confidence Level 1) about the candidate molecule and do not account for structural confirmation using alternative instrumental techniques. The fact that this study confirmed the structure of the causative toxicant using NMR would place the confidence in its structure at a higher confidence level that is not mapped by the Schymanski Confidence Level Scale (see Figure 3, Analytical Methods Fact Sheet). Note that no analytical reference standards for 6PPD-q were commercially available by the end of the experimental study to help improve confidence in the structural information of the CEC to Schymanski Confidence Level 1 using UHPLC-HRMS or high-performance liquid chromatography (HPLC)-HRMS data.

3. Next Steps

The NTA case study described above used an EDA approach coupled with physical simplification processes for environmental mixture complexity reduction and UHPLC-HRMS, to determine the molecular formula of the toxicant responsible for URMS in coho salmon. Once the molecular formula was identified, the chemical structure was elucidated by testing an ozonation hypothesis using multiple instrumental analysis tools (HRMS and NMR).

The next challenge after determining the identity of a previously unknown CEC (i.e., molecular formula and chemical structure) is the development of a targeted quantitative analytical method that can determine concentrations of the toxicant in environmental media at trace levels. This challenge usually takes the following steps:

1. Chemical synthesis and purification of an analytical reference standard (note that for 6PPD-q, the chemical synthesis could be from the proto-toxicant, 6PPD, which is widely available)

2. Development of an analytical method for identification and quantitation of 6PPD-q within environmental media (note that HPLC-MS/MS is considered the “gold standard” for the most reliable and sensitive targeted analysis of semi- and nonvolatile organic compounds)

3. Addressing any environmental media-specific issues, including stability and adsorption, that might require more specialized approaches such as derivatization or isotope dilution to account for potential matrix bias

4. Epilogue

EDA is only one NTA method. In the study reported here, EDA worked well as the CEC induced rapid and acute mortality in the test organisms at low concentrations. It should be noted, however, that most environmental toxicants demonstrate nonlethal chronic effects and, therefore, may not be amenable to such an approach. In such cases, other NTA methods, including chemistry driven approaches (e.g., search for particular chemical signatures) and statistically driven approaches (e.g., spatiotemporal trends) (Hollender et al. 2019), might be more suitable to determine CEC that induce chronic toxicity effects.

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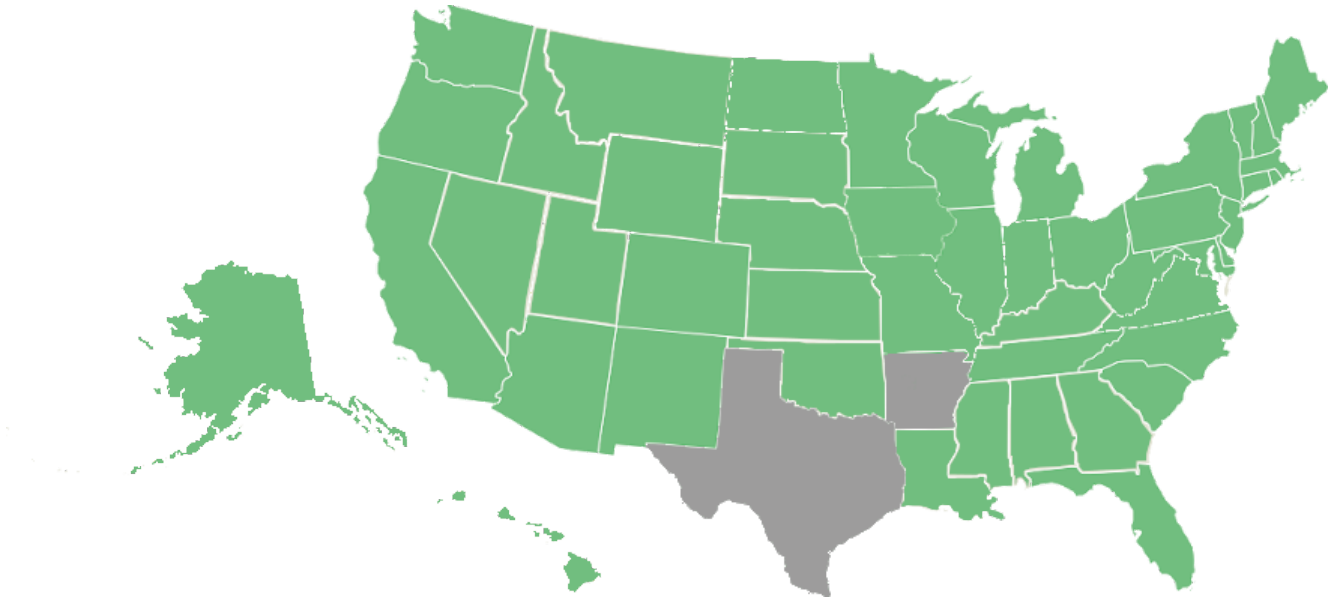
CEC Monitoring Programs Fact Sheet

US



Washington

WA Department of Ecology State of Washington - Other
https://ecology.wa.gov/Research-Data/Monitoring-assessment/toxics-monitoring

WA Department of Ecology State of Washington - Other
https://ecology.wa.gov/About-us/Who-we-are/Our-Programs/Environmental-Assessment

Oregon

Oregon Health Authority - Drinking water
https://www.oregon.gov/oha/PH/HEALTHYENVIRONMENTS/DRINKINGWATER/OPERATIONS/Pages/EmergingContaminants.aspx

California

State Water Resources Control Board - Drinking water https://www.waterboards.ca.gov/pfas/
https://waterboards.ca.gov/water_issues/programs/#cec

California Department of Pesticide Regulation - Air Quality Pesticide Air Monitoring Results Database

California Department of Pesticide Regulation, Groundwater Protection Program (GWPP) - Groundwater Groundwater Monitoring, Analyses, and Assessments

California Department of Pesticide Regulation, Surface Water Protection Program - Surface water Surface Water Database

California - Biomonitoring Biomonitoring California's Results Database

Idaho

Idaho Department of Environmental Quality — Drinking Water Bureau - Drinking water
https://www.deq.idaho.gov/water-quality/drinking-water/pfas-and-idaho-drinking-water/

Nevada

Nevada Division of Environmental Protection - Multiple
https://ndep.nv.gov/uploads/documents/DRAFT_75-percent_NDEP_PFAS_Action_Plan_20220405.docx

Montana

Montana Department of Environmental Quality - Multiple https://deq.mt.gov/cleanupandrec/Programs/pfas

Utah

Utah Department of Environmental Quality - Drinking water https://deq.utah.gov/drinking-water/drinking-water-pfas

Arizona

Arizona Department of Environmental Quality - Wastewater and biosolids https://www.azdeq.gov/node/7940

Arizona Department of Environmental Quality - Stormwater https://www.azdeq.gov/node/7940

Arizona Department of Environmental Quality - Environmental protection
https://azdeq.gov/press-releases/press-release-adeq-committed-protecting-arizonans-and-assisting-public-water-systems

Arizona Department of Environmental Quality - Drinking water https://www.azdeq.gov/node/7940

Colorado

Colorado Department of Public Health and Environment - Multiple
Main program page: https://cdphe.colorado.gov/toxic-algae
Data specifically:
https://cohealthviz.dphe.state.co.us/t/EnvironmentalEpidemiologyPublic/views/newhab_draft/HABdash?%3AshowAppBanner=false&%3Aorigin=viz_share_link&%3Adisplay_count=n&%3AshowVizHome=n&%3AisGuestRedirectFromVizportal=y&%3Aembed=y

Colorado Department of Public Health and Environment - Multiple https://cdphe.colorado.gov/pfas

City of Fort Collins - Drinking water
https://www.fcgov.com/utilities/what-we-do/water/water-quality/source-water-monitoring/special-studies/emerging-contaminants

New Mexico

New Mexico Environment Department - https://www.env.nm.gov/

South Dakota

South Dakota Department of Agriculture & Natural Resources - Drinking water

Kansas

Kansas Department of Health and Environment / Division of Environment - Drinking water
https://www.kdhe.ks.gov/635/Per--Polyfluoroalkyl-Substances

Oklahoma

Oklahoma Department of Environmental Quality - https://www.deq.ok.gov/asd/about-deq/#

Texas

State program(s) not identified by the CEC Team at the time of publication

Minnesota

Minnesota Pollution Control Agency - Environmental protection
https://www.pca.state.mn.us/waste/mpca-pfas-monitoring-plan

Minnesota Pollution Control Agency - Air Quality https://www.pca.state.mn.us/waste/mpca-pfas-monitoring-plan

Minnesota Pollution Control Agency - Wastewater and biosolids
https://www.pca.state.mn.us/waste/mpca-pfas-monitoring-plan

Minnesota Pollution Control Agency - Solid and haz wastes
https://www.pca.state.mn.us/waste/mpca-pfas-monitoring-plan

Minnesota Pollution Control Agency - Stormwater https://www.pca.state.mn.us/waste/mpca-pfas-monitoring-plan

Minnesota Pollution Control Agency - Remediation https://www.pca.state.mn.us/waste/mpca-pfas-monitoring-plan

Minnesota Department of Health - Drinking water
https://www.health.state.mn.us/communities/environment/water/unregcontam.html

Minnesota Department of Health - Drinking water
https://www.health.state.mn.us/communities/environment/water/pfas.html

Minnesota Pollution Control Agency - Water resources
https://www.pca.state.mn.us/water/contaminants-emerging-concern

Iowa

Iowa Department of Natural Resources - Drinking water
https:/https://www.iowadnr.gov/About-DNR/DNR-News-Releases/ArticleID/4446/Iowa-Department-of-Natural-Resources-releases-summary-of-PFAS-sampling

Arkansas

State program(s) not identified by the CEC Team at the time of publication

Wisconsin

Wisconsin Department of Natural Resources - Drinking water
https://docs.legis.wisconsin.gov/code/admin_code/nr/800/80

https://dnr.wisconsin.gov/sites/default/files/topic/PFAS/LabUpdate20210301.pdf

Wisconsin Department of Natural Resources - Ecology https://dnr.wisconsin.gov/topic/Fishing/consumption

Wisconsin Department of Natural Resources - Surface water
https://docs.legis.wisconsin.gov/code/register/2022/799b/register/final/cr_21_083_rule_text/cr_21_083_rule_text

Illinois

Illinois Environmental Protection Agency - Groundwater
https://www2.illinois.gov/epa/topics/water-quality/groundwater/Pages/620-Groundwater-Quality.aspx

Tennessee

TN Department of Environment and Conservation - Other
https://www.tn.gov/environment/policy/pfas/tdec-sampling-for-pfas.html

Michigan

Michigan Department of Environment, Great Lakes, and Energy - Multiple https://www.michigan.gov/pfasresponse

Kentucky

Kentucky Energy and Environment Cabinet / Department of Environmental Protection - Multiple
https://eec.ky.gov/Environmental-Protection/Water/Protection/Pages/PFAS.aspx

Alabama

Department of Environmental Management - Drinking water
http://ademmail2.state.al.us/programs/water/drinkingwater/pfaspage.cnt

Ohio

Ohio Environmental Protection Agency - Drinking water
https://epa.ohio.gov/monitor-pollution/pollution-issues/pfas-action-plan

Georgia

Georgia Environmental Protection Division - Environmental protection
https://gaepd.maps.arcgis.com/apps/MapSeries/index.html?appid=e8f2c6a51c1c41088002350f1eabe598

Florida

Florida Department of Environmental Protection - Drinking water
https://floridadep.gov/comm/press-office/content/regulated-drinking-water-contaminants-and-contaminants-emerging-concern

Florida Department of Environmental Protection - Drinking water
https://www.floridahealth.gov/environmental-health/private-well-testing/index.html

West Virginia

West Virginia Department of Environmental Protection - Environmental protection
https://dep.wv.gov/key-issues/Pages/PFAS.aspx

North Carolina

North Carolina Environmental Quality - Environmental protection
https://deq.nc.gov/news/key-issues/emerging-compounds

South Carolina

South Carolina Department of Health and Environment - Environmental protection
https://scdhec.gov/BOW/perfluoroalkyl-substances-pfas

Pennsylvania

Pennsylvania Department of Environmental Protection - Water resources
https://www.dep.pa.gov/Business/Water/CleanWater/WaterQuality/Pages/CECs.aspx

Maryland

Maryland Department of Environment - Groundwater
https://mde.maryland.gov/PublicHealth/Pages/PFAS-Landing-Page.aspx

Delaware

Department of Natural Resources and Environmental Control - Water quality
https://dnrec.alpha.delaware.gov/waste-hazardous/remediation/watar/

Delaware River Basin Commission - Water quality https://www.nj.gov/drbc/programs/quality/cecs.html

New Jersey

New Jersey Department of Environmental Protection - Remediation
https://www.nj.gov/dep/srp/srra/listserv_archives/2021/20210805_srra.html

New Jersey Department of Environmental Protection - Drinking water
https://nj.gov/dep/wiip/docs/njwb_ffy22-sfy23-cw-dw_finaliup_propamend-pubnotice.pdf

Connecticut

Department of Energy and Environmental Protection - Remediation
https://portal.ct.gov/DEEP/Remediation--Site-Clean-Up/Contaminants-of-Emerging-Concern/Contaminants-of-Emerging-Concern

Massachusetts

Massachusetts Department of Environmental Protection - Multiple
https://www.mass.gov/info-details/emerging-contaminants

Northeastern University's Social Science Environmental Health Research Institute (SSEHRI) - Multiple https://pfasproject.com/pfas-sites-and-community-resources/

New Hampshire

New Hampshire Department of Environmental Services - Multiple https://pfas.des.nh.com

Rhode Island

Vermont

Agency of Natural Resources - Water resources https://legislature.vermont.gov/statutes/section/10/047/01283a

Maine

Maine Department of Environmental Protection - Multiple https://www.maine.gov/dep/spills/topics/pfas/index.html

New York

New York State Department of Environmental Conservation - Remediation https://www.dec.ny.gov/docs/water_pdf/emergingcontaminants.pdf

New York State Department of Environmental Conservation - Water resources https://www.dec.ny.gov/docs/water_pdf/emergingcontaminants.pdf

New York State Department of Health - Drinking water https://dos.ny.gov/system/files/documents/2022/10/100522.pdf

Virginia

Virginia Department of Health
Virgia Department of Environmental Quality
Office of Drinking Water
Drinking water https://www.vdh.virginia.gov/drinking-water/pfas/

Indiana

Indiana Department of Environmental Management - Ecology http://www.in.gov/idem/nps/files/ir_2022_report.pdf

Mississippi

Mississippi Department of Environmental Quality - Groundwater https://www.mdeq.ms.gov/water/groundwater-assessment-and-remediation/pfas-information/

Louisiana

Louisiana Department of Environmental Quality - https://deq.louisiana.gov/subhome/water

Missouri

Missouri Department of Natural Resources - Multiple
https://modnr.maps.arcgis.com/apps/webappviewer/index.html?id=386c71927569476ebd2d0e6910424d17

Nebraska

Nebraska Department of Environment and Energy - http://dee.ne.gov/NDEQProg.nsf/Home.xsp

North Dakota

North Dakota Department of Environmental Quality - Multiple
https://deq.nd.gov/Publications/MF/PFAS_Report_2021.pdf?v=1

Wyoming

Pending Additional Input - https://deq.wyoming.gov/water-quality/groundwater/pfas/

Alaska

Department of Environmental Conservation - Spill prevention https://dec.alaska.gov/spar/csp/pfas

Hawaii

Department of Health - Multiple https://health.hawaii.gov/heer/environmental-health/highlighted-projects/pfas/

Federal

Association of State and Territorial Solid Waste Management Officials, Inc.
Solid and haz wastes -
https://astswmo.org/webinar-how-to-develop-a-state-led-contaminants-of-emerging-concern-cec-program/

Centers for Disease Control and Prevention (CDC)
National Biomonitoring Program (NBP) Health - National Biomonitoring Program

USDOD
U.S. Department of Defense Environment, Safety & Occupational Health Network and Information Exchange
Hazardous substances - https://www.denix.osd.mil/cmrmp/index.html

USEPA
U.S. Environmental Protection Agency Remediation -

https://www.epa.gov/fedfac/emerging-contaminants-and-federal-facility-contaminants-concern

U.S. Environmental Protection Agency CEC including pharmaceuticals and personal care products - https://www.epa.gov/wqc/contaminants-emerging-concern-including-pharmaceuticals-and-personal-care-products

U.S. Environmental Protection Agency Drinking water - https://www.epa.gov/system/files/documents/2022-03/combined_srf-implementation-memo_final_03.2022.pdf

U.S. Environmental Protection Agency Wastewater and biosolids - https://www.epa.gov/system/files/documents/2022-03/combined_srf-implementation-memo_final_03.2022.pdf

U.S. Environmental Protection Agency Drinking water - https://www.epa.gov/dwucmr/learn-about-unregulated-contaminant-monitoring-rule

Canada

Environment and Climate Change Canada - Others National Pollutant Release Inventory - Canada.ca

Environment and Climate Change Canada - Others Water Quality Monitoring and Surveillance Program

Europe

European Chemicals Agency

Pending Additional Input

Australia

Department of Climate Change, Energy, the Environment and Water - Multiple
https://www.dcceew.gov.au/environment/protection/npi/data

New South Wales Environment Protection Authority - Multiple
https://www.epa.nsw.gov.au/your-environment/contaminated-land/pfas-investigation-program

Australia's National Science Agency - Multiple
https://www.csiro.au/en/research/natural-environment/ecosystems/Emerging-contaminants

State Program has been identified by ITRC's CEC Team

State Program has **not** been identified by ITRC's CEC Team

1. Introduction

This Fact Sheet consists of a table containing representative contaminants of emerging concern (CEC) programs from state, federal, local, and international programs, along with associations with CEC monitoring programs in place at the time of this publication. The purpose of the table is to provide high-level information to help states and other stakeholders plan their own CEC monitoring programs to monitor the impact of CEC in the common environmental matrices. The White Paper defines the CEC, but the CEC selection criteria to be included in the state-based CEC monitoring program can vary from state to state subject to the state CEC selection criteria, regulations, and policy. For instance, in some states, 1,4-dioxane might be regulated and no longer considered a CEC for drinking water; at the same time, it may be considered to be a CEC for soil and groundwater. When this publication was prepared, the programs included in the CEC monitoring spreadsheet were searchable and had open-source information and were expected to remain accessible.

This Fact Sheet does not include CEC programs that only include introductory information to generally communicate what a CEC is and where a CEC comes from (e.g., CEC-containing products) or do not have CEC monitoring programs.

Details about how to use the table are below.

1.1 How to Use the Table

Each column can be sorted and filtered. Each column is described below. Blank cells indicate no information was identified at the time this table was created.

1.2 Column Details

State/Fed/Others = name of the state or federal agency or association

Agency = full agency name

Agency Acronym = agency acronym

Program area (categories) = Air Quality, Biomonitoring, Drinking water, Ecology, Environmental protection, Groundwater, Hazardous substances, Health, Multiple (see description), Other (see description or notes), Remediation, Solid and hazardous wastes, Spill prevention, Stormwater, Surface water, Wastewater and biosolids, Water quality, Water resources

Focus Area = additional details of program area, if applicable

Monitoring Media (categories) = Air, Biological tissues, Drinking water, Groundwater, Human Health, Multiple (see description or notes), Other (see description or notes), Solid waste, Stormwater, Surface water, Wastewater

CEC = description of which contaminants of emerging concern are addressed in the monitoring program

Description = short description of the monitoring program and additional details, if needed

Legislation or Executive Order = reference to legislation, if applicable

Web link = link to home of the monitoring program

CEC database = link to specific database, if applicable for the CEC

1.3 Types of Programs That Are NOT Included in This Table

The following types of programs are not included in the table:

- Those geared toward only public education, such as “What are PFAS?”
- Those that detail sampling methods, analytical methods, and compliance limits.
- Those that are specific to one site.
- Those that describe just physical and chemical properties.
- Those that list toxicity values or derivations of toxicity values.
- Those that regulate and monitor parent compounds that have the potential to degrade or break down to a CEC.
- Those that monitor products, such as personal care products

1.4 Limitations of This Table

This table does not address biological and radionuclide CEC.

This table does not report monitoring programs related to personal care or consumer products such as paper, textiles, or others within the built environment.

Download table

CEC Monitoring Programs Video

This video consists of a tutorial of the CEC Monitoring Programs Table. It discusses the types of programs and media covered by the table, as well as its limitations. A walk-through on how to use the table is included toward the end of the video.
CEC Monitoring Table Tutorial Video.mp4

ITRC (Interstate Technology & Regulatory Council). 2023. *Contaminants of Emerging Concern Framework* CEC-1. Washington, D.C.: Interstate Technology & Regulatory Council, CEC Team. https://cec-1.itrcweb.org/.

Hypothetical Case Study

This Case Study has been organized into the following subsections:

- Section 1: Introduction
- Section 2: Background Information
- Section 3: Key Variables Evaluation Using the Process Flowchart
  - Section 3.1: Occurrence Criterion
  - Section 3.2 Human Health and Ecological Effects (Toxicity Criteria)
  - Section 3.3 Physical-Chemical Properties Criterion
  - Section 3.4 Overall CEC Recommendation and Data Evaluation Based on Process Criteria
- Section 4: Risk Perception and Communication

1. Introduction

The White Paper and the four associated contaminants of emerging concern (CEC) Fact Sheets are intended to provide a framework that states may consider when undertaking or developing a CEC program to identify, evaluate, and monitor potentially harmful substances in the environment. Addressing CEC is a complex process that requires consideration of many factors. This hypothetical case study shows how a CEC may be evaluated using the approach illustrated in the Identification of Key CEC Variables Fact Sheet Flowchart.

2. Background Information

Chemical Name: Chloro-α,α,α-trifluorotoluene
CASRN: 98-56-6
Chemical Formula: $C_7H_4ClF_3$
Molecular Weight: 180.56

The potential CEC was originally observed as a tentatively identified compound (TIC) in wastewater during full-scan GC-MS analysis with a >85% spectral match against the Wiley–National Institutes of Standards and Technology GC-MS mass spectral library (for example guidance on TICs see (USEPA 2020)). The potential CEC was also detected in the property well used as a drinking water source at the site. The laboratory identified the TIC as chloro-α,α,α-trifluorotoluene or para-chlorobenzotrifluoride, one of several compounds in a chemical mixture that is being used as a solvent substitute for xylene. This chemical is not listed in any of the Resource Conservation and Recovery Act, Comprehensive Environmental Response, Compensation, and Liability Act, or state lists of chemicals monitored or analyzed in environmental media (see the CEC Monitoring Programs Fact Sheet). A reference analytical standard was obtained to confirm the identity of the TIC. Once confirmed, the analytical method was updated using calibration information for the CEC to enable its quantitation (see the Analytical Methods Fact Sheet). With an identified CEC, evaluation can proceed using the process flowchart.

3. Key Variables Evaluation Using the Process Flowchart

3.1 Occurrence Criterion

The CEC was identified in wastewater and drinking well water samples but not measured in other environmental media. An additional four samples each from the wastewater and drinking well water including quality control samples were collected each month for three consecutive months and submitted to the laboratory that initially detected and identified the CEC.

Using the CEC prioritization flow chart, the following considerations indicate sufficient evidence of the presence of the CEC in

the environment (wastewater and drinking water). Further evaluation of its hazards, physical-chemical properties, presence in other environmental media (soil and air), and presence at other sites is required:

- The wastewater data and the company's process and safety information indicate that the presence of the CEC in wastewater came from the waste stream of the industrial process used at the site.
- The CEC is a component of a solvent and an intermediate in pesticide production.
- The CEC was detected in all but one sample from the drinking water well, indicating groundwater contamination.
- Drinking water is a direct exposure route for the workers at the site. The extent of contamination on site and off site is not known and requires further investigation.
- Soil and ambient air concentrations of the CEC are not known and require further investigation.
- The volatilization from groundwater to indoor air pathways also requires evaluation. The CEC is a solvent used in some caulks, paints, and coatings and is found in some fabric stain removers. Therefore, it is possible that the chemical could migrate into indoor air.
- The European Chemical Agency reports this chemical is used (1) in consumer products such as coating products, inks, and toners; (2) in the manufacture of other chemicals, machinery and vehicles, plastic products, and mineral products (e.g., plasters, cement); (3) in scientific research and development; and (4) as an intermediate step in the manufacturing of another substance. Release to the environment of this substance can occur from industrial use and release to the environment may occur from indoor or outdoor use as a processing aid (ECHA 2022).

Recommendation

The CEC was detected in drinking water, but other environmental media were not analyzed. Exposure to a contaminant in drinking water is a direct human exposure. Proximity of the CEC to sensitive receptors (e.g., children) is a critical consideration for occurrence evaluation. The drinking water data quality is adequate; however, the environmental characterization of the site in relation to impact on soil, ambient air, and nearby surface water is lacking. The CEC evaluation should move to the evaluation and determination of other key variables (hazard/toxicity and physical-chemical properties) and additional occurrence characterization data to determine whether the CEC is a low-, medium-, or high-priority CEC. The occurrence of a contaminant in soil may lead to a higher priority assignment depending on several factors. See the Identification of Key CEC Variables Fact Sheet for additional explanation.

3.2 Human Health and Ecological Effects (Toxicity Criteria)

3.2.1 Available Human Health Toxicity Values (Hazard Criteria—Human Health)

Group 1 and Group 2 sources of toxicity values were searched. See the Identification of Key CEC Variables Fact Sheet for additional details on these sources. The Group 1 and 2 oral and inhalation toxicity values are available for this CEC (Table 1).

Table 1. Available toxicity values

Sources	Chronic RfD	CSF	Chronic RfC	IURF
Group 1	3×10^{-3} mg/kg-day (USEPA 2007)	NA	3.0×10^{-1} mg/m^3 (USEPA 2007)	NA
Group 2	NA	3.0×10^{-2} (mg/kg-day)$^{-1}$ (CalEPA, OEHHA. 2019)	NA	8.6×10^{-6} (µg/m^3)$^{-1}$ (CalEPA, OEHHA. 2020a)
Others	NA	NA	NA	NA

CSF = oral cancer slope factor; IURF = inhalation unit risk factor; mg/kg-day = milligrams per kilogram per day; mg/m^3 = milligrams per cubic meter; $\mu g/m^3$ = micrograms per cubic meter; NA = no information available currently; RfC = inhalation reference concentration; RfD = oral reference dose Note: The CSF value is an inhalation CSF. The National Toxicology Program (NTP. 2018) study used as the basis of the CSF and IURF is an inhalation study, and the inhalation CSF was developed by the California Environmental Protection Agency as part of the development of the IURF. The inhalation-based CSF may be used as a screening oral toxicity value to develop a drinking water screening value. Evaluation by toxicologists could be needed to determine whether route-to-route extrapolation (i.e., use of the inhalation CSF as an oral CSF) is scientifically supportable for development of a guidance value or criterion.

The United States Environmental Protection Agency's (USEPA's) Provisional Peer-Reviewed Toxicity Value (PPRTV) assessments (derivation details, (USEPA 2007)) developed subchronic and chronic noncancer oral reference dose (RfD) and inhalation reference concentration (RfC) toxicity values based on a 28-day oral study in rats (Macrí et al. 1987) and a 13-week inhalation study in rats (Newton et al. 1998), respectively. The critical noncancer effect was liver effects.

The California Office of Environmental Health Hazard Assessment (OEHHA) based its cancer toxicity values on the published chronic inhalation toxicity study by the National Toxicology Program (NTP 2018), NTP Technical Report on the Toxicology and Carcinogenesis Studies of p-chloro-α,α,α-trifluorotoluene (CalEPA 2020b). For chemicals with an oral cancer slope factor (CSF), inhalation CSF, or inhalation unit risk factor (IURF), the weight of evidence information or cancer classification (i.e., suspected/suggestive, likely/presumed, or known to cause cancer to humans) should be presented, if available. The OEHHA assessment did not specify a cancer classification.

3.2.2 Available Ecological Health Information (Hazard Criteria—Ecological Health)

According to the ECHA Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) registrations (ECHA 2022), the CEC is "toxic to aquatic life with long lasting effects" (see ECHA Brief Profile in the references section for more details). Hazards for aquatic organisms may be represented by the predicted no effect concentration (PNEC) values. The PNEC is the concentration below which adverse effects are not likely to occur (see the Risk Perception and Communication Fact Sheet for more information on ecological health endpoints). ECHA has listed PNEC values for aquatic and terrestrial (soil) organisms. Impacts to fish and aquatic invertebrates in relation to short-term toxicity (lethal concentrations) were also noted.

3.2.3 Hazard Information Summaries

Additional hazard information is summarized in Table 2 and the text below.

Table 2. ECHA identified hazards

Properties (Hazards)	Code	Hazard Description
Flam. Liq. 3	H226	Flammable liquid and vapor
Eye Irrit. 2	H319	Causes serious eye irritation
Skin Irrit. 2	H315	Causes skin irritation
STOT SE 3	H335	May cause respiratory irritation
Aquatic Chronic 2	H411	Toxic to aquatic life with long-lasting effects
Skin Sens. 1B	H317	May cause an allergic skin irritation
Carc. 2	H351	Suspected of causing cancer
Aquatic Chronic 3	H412	Harmful to aquatic life with long-lasting effects
STOT RE 2	H373	May cause damage to organs through prolonged or repeated exposure
Repr. 2	H361	Suspected of damaging fertility or the unborn child
Aquatic Chronic 1	H410	Very toxic to aquatic life with long-lasting effects
Skin Sens. 1	H317	May cause an allergic skin reaction
Carc. 1B	H350	May cause cancer (presumed human carcinogen)

STOT SE 3	H336	May cause dizziness or drowsiness

Information taken from https://echa.europa.eu/information-on-chemicals/registered-substances:
Hazard Class and Category Codes and Hazard Statement Codes

- California Environmental Protection Agency (CalEPA) (CalEPA 2019; 2020a):
  - Can pass from mother to baby during pregnancy.
  - Exposure occurs by breathing the CEC in air and skin contact with products containing the CEC.
  - Human cancer potency.

- ECHA (See ECHA Identified Hazards Table for breakdown of hazards and their classification):
  - Hazard classification and labeling: "Warning! According to the classification provided by companies to ECHA in REACH registrations this substance is toxic to aquatic life with long lasting effects, is a flammable liquid and vapor, is suspected of causing cancer, is suspected of damaging fertility or the unborn child, causes serious eye irritation, may cause an allergic skin reaction, causes skin irritation, and may cause respiratory irritation" (CalEPA, ECHA. 2022).

- Fluoride Action Network Project (Fluoride Action Network Project 2023):
  - Volatile, aromatic liquid used as a chemical intermediate in the manufacture of dinitroaniline herbicides. Also used as a dye intermediate, solvent, and dielectric fluid.
  - NTP 14-day toxicity studies on rats and mice indicated effects on the liver (liver hypertrophy), kidney (hyaline droplet nephropathy), and adrenal changes in rats (Jameson and Yuan 1992; USDHHS 2009).

Recommendation

Human health: The hazard/toxicity evaluation identified human health toxicity endpoints from Group 1 and 2 sources that could be used for calculation of risk estimates and preliminary risk characterization. The NTP study and ECHA information provide evidence of human health effects (developmental-reproductive and potential cancer effects) that require attention. The contaminant is detected in drinking water but not measured in other media. The detected CEC levels in groundwater should be evaluated against a cancer-based drinking water screening level or criterion developed using the Group 2 CSF to determine the risk of drinking the contaminated water. Note that the available CSF developed by CalEPA is an inhalation CSF; therefore, the extrapolation of inhalation toxicity data to develop an oral toxicity value requires further evaluation. The inhalation-based CSF could be used to develop an interim or provisional drinking water screening value. Environmental characterization of the site soil and ambient air for CEC concentrations is recommended. The detection of the CEC in surface water will require data on potential human indirect exposure through fish consumption, including information on bioaccumulation of the CEC in aquatic organisms. The CEC evaluation should move to the evaluation of physical-chemical properties. Additional studies are needed to more conclusively determine the human health toxicity relating to developmental-reproductive effects.

Ecological health: Based on data from REACH registrations for the CEC, ECHA concluded that the CEC poses a hazard for aquatic organisms and terrestrial organisms. Although there is no report of bioaccumulation, there is a potential short-term toxicity to fish and indirectly to human consumers of fish. To understand the direct effect on aquatic species and indirect risk to fish consumers, additional data on ecological impacts on fish and other aquatic species would be helpful.

Summary: Overall, the CEC poses human and ecological health effects of concern; however, noncancer toxicity data are not available to allow the evaluation of other potential noncancer endpoints (e.g., acute skin irritation [unlikely to be a concern at levels found in the environment] and reproductive-developmental effects). Because inhalation toxicity data indicate the importance of the inhalation exposure pathway, toxicity via indoor air inhalation exposure should be evaluated.

3.3 Physical-Chemical Properties Criterion

Further research on the chemical using the available database (Table 3) found the following physical-chemical information on the CEC. California (CalEPA 2020a) compared the vapor pressure and boiling point of the CEC to petroleum-based

solvents and found similarities with xylene isomers and ethylbenzene (Table 4). This indicates that the CEC is a volatile compound.

Table 3. Properties

Source: PubChem (2023)

Chemical formula	**$C_7H_4ClF_3$**
CAS Number	98-56-6
EC Number	202-681-1
Synonyms	4-chloro-a,a,a-trifluorotoluene 4-chloro-α,α,α-trifluorotoluene 1 chloro-4-trifluoromethyl benzene benzene 1-chloro-4-(trifluoromethyl)- 4-chlorobenzotrifluoride para-chlorobenzotrifluoride p-chloro-a,a,a-trifluorotoluene
IUPAC Name	1-chloro-4-(trifluoromethyl)benzene
Molar Mass	180.55 g/mol
Appearance	colorless liquid
Odor	aromatic
Density	1.33 g/mL at 25°C
Melting Point	−33°C
Boiling Point	138.5°C
Vapor Pressure	7.6 mm Hg at 25°C
Solubility in Water	29 mg/L at 25ºC
Log Octanol/Water Partition Coefficient (6now)	3.60 at 25ºC (estimated)

Note: CAS . = Chemical Abstract Service, EC = European Community, g/mL = grams per milliliter, g/mol = grams per mole (molar mass), IUPAC = International Union of Pure and Applied Chemistry, mm Hg = millimeters of mercury.

Table 4. Vapor pressure and boiling point of similar compounds

Solvent	**Vapor Pressure (mm Hg, 25°C)**	**Boiling Point (°C)**
Ethylbenzene	9.6	136.2
p-Xylene	8.8	138.3
m-Xylene	8.3	139.1
Chloro-α,α,α-trifluorotoluene	7.6	138.5
o-Xylene	6.7	144.5

Note: mm Hg = millimeters of mercury.

Recommendation

In addition to solubility, other fate and transport properties that impact the CEC's mobility or ability to migrate (Henry's Law Constant, K_{oc}) and exposure potential (volatility, persistence half-life, bioaccumulation, and biomagnification factors) should be identified or estimated. The quality and correctness of the physical-chemical information gleaned from ECHA through its REACH registration data would need validation because ECHA emphasizes that the correctness of the REACH information is not guaranteed. Completion of the information gaps on the physical-chemical features of this chemical will inform its fate and transport characteristics (persistence, bioaccumulation, and mobility). Understanding fate and transport would lead to a better understanding of all potential exposure pathways and consequently the risk to sensitive human and ecological receptors.

3.4 Overall CEC Recommendation and Data Evaluation Based on Process Criteria

Based on the results of the evaluation of the CEC using the flowchart's three criteria (occurrence, hazard/toxicity, and physical-chemical factors), the CEC is: (1) found in drinking water, an exposure pathway of concern; (2) a hazardous substance (carcinogenic, irritant, and suspected reproductive toxicant); and (3) volatile and soluble in water. Occurrence in other environmental media (soil and air), noncancer health effects (especially those linked to reproductive and developmental impacts), and physical-chemical characteristics that may impact exposure through additional exposure pathways (indoor air) require further investigation. Therefore, we would classify this emerging contaminant as a **medium priority CEC** because additional information is needed to determine whether there is widespread concern, which would move it to a high priority. Such additional information would include characterization in other environmental media, continued drinking water monitoring and identification of the CEC in drinking water sources, investigation (toxicity and fate/transport), and data and risk reevaluation. The CEC classification does not negate the need to evaluate the extent of contamination in various environmental media and assessment of the risk posed by the CEC to human and ecological receptors. The three criteria provide a process for prioritizing CEC and identifying scientific information and data needed to fully characterize human health and ecological risks.

Throughout the evaluation of the CEC using the three criteria (see flowchart), this question is asked before proceeding to the next evaluation: ***"Are the data sufficient to make a technical assessment?"*** For occurrence data, this question seeks to answer analytical methods validity, data sufficiency, reproducibility, and other data-relevant issues (see Box 1 of the Identification of Key CEC Variables Fact Sheet). For toxicity or hazard data, this question will identify whether additional data are needed to support the health effects used to establish the toxicity values (cancer, skin irritation, or aquatic short-term toxicity) and identify other health concerns, especially those for sensitive humans (e.g., developmental effects). It is equally important that uncertainties, assumptions, and data sources are considered in the evaluation of hazard or toxicity data. Similarly, the physical-chemical properties of a contaminant reflect its potential to remain in the environment or cause increased exposure and risk to human and ecological receptors (see Box 2 of the Identification of Key CEC Variables Fact Sheet). Therefore, the data quality and sources supporting these physical-chemical properties should be part of the CEC evaluation.

For this case study, the basis of the toxicity endpoints are peer-reviewed studies, and the assessments were conducted by reliable scientific agencies. The oral and inhalation noncancer values derived from the PPRTV were based on oral and inhalation studies, but no cancer values were developed. CalEPA used an NTP 2018 inhalation study as basis for its inhalation cancer toxicity value (IURF). CalEPA also derived a CSF based on the NTP study to develop a No Significant Risk Level (CalEPA 2019). Because the CSF is based on an inhalation value (i.e., based on inhalation-to-oral route extrapolation), its use as an oral CSF may need to be evaluated for scientific validity. Although the California assessment did not specify a cancer classification, ECHA reported that this CEC is a likely or presumed human carcinogen. Health-based screening levels or criteria developed using this cancer toxicity value should be used to evaluate the risk posed by CEC levels in groundwater and other environmental media (e.g., air, soil) to human receptors. The findings of the evaluation should be used to inform regulators and decision-makers on the management of the CEC (e.g., source reduction, exposure prevention, etc.) to protect public health and the environment.

The ecological health impacts were based on data from REACH registrations. As ECHA indicated, the correctness or accuracy of these data may require validation. The physical-chemical information is not sufficient to characterize the chemical's properties and fate and transport characteristics. Characterization of the CEC occurrence in other media and at other sites is also needed. Overall, additional data are required to sufficiently evaluate this CEC and properly define whether the priority level of this CEC remains moderate or changes to high. High-priority substances are evaluated for additional steps that include expanded surveillance, additional risk evaluations and legislative actions (federal or state rulemaking). Regardless of priority level, CEC should be adequately characterized in various environmental media and evaluated for potential risks to human and ecological receptors.

4. Risk Perception and Communication

This part of the case study addresses risk communication messaging—specifically, the who, what, and when and the challenges and considerations, including uncertainties, unknowns, fast-evolving scientific information, and moving and varying risk estimates. As mentioned in the Identification of Key CEC Variables Fact Sheet, a CEC can be shifted between priorities (low, moderate, high) at any time depending on the unique circumstances of the CEC in relation to other competing communication priorities, and the risk communication challenges and strategies will be influenced by the resulting priority designation.

Based on available information identified in the key variables, evaluation, occurrence data, hazard/toxicity values, and physical-chemical factors are available for this chemical. The CEC is considered to be a medium priority CEC, and risk communication becomes more involved than for a low-priority CEC. At this stage, there may already be some public awareness and/or outrage.

For risk communication purposes, an updated version of the chemical Fact Sheet with the most recent occurrence, hazard/toxicity, and physical-chemical factors should be used. The Fact Sheet should also note that the chemical is not adequately characterized in various environmental media. Minimizing exposure by advising the community to not drink well water while the agency monitors drinking water for two consecutive rounds (3 weeks apart for the next 6 weeks) is recommended to the community at a community meeting along with next steps based on sampling results. The Fact Sheet is shared with decision-makers, internal agency stakeholders, and the community to educate them on both the knowns and unknowns about the chemical.

The goal of the risk communicator at this stage is to review and update any educational materials. A risk communicator focusing on precaution advocacy may continue to pressure decision-makers to find more data, but there is already enough information to recommend precautions that individuals can take to protect themselves. There may also be enough new data indicating that specific communities may be uniquely susceptible to the contaminant. At such a time, it is imperative to communicate both the knowns and unknowns to ensure honesty, transparency, and empathy for those involved. A Frequently Asked Questions document should also be developed to proactively address community comments, questions, and concerns. If not already developed, a communication team should be formed, and a communication plan completed. This will support effective communication of key messages. More information can be found in the Interstate Technology and Regulatory Council's Risk Communication Toolkit (ITRC 2020).

More details on risk communication and risk perception challenges that may be considered are presented in the Risk Perception and Communication Fact Sheet.

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Glossary

A

Adaptive Management

Adaptive management, also known as adaptive environmental assessment and management, is a structured, iterative process of robust decision-making in the face of uncertainty with the aim of reducing uncertainty over time via system monitoring.

Adsorbable Organic Fluorine (AOF)

An organofluorine assay that first adsorbs these compounds from a sample onto polystyrene divinylbenzene–based activated carbon from which it is eluted and analyzed by combustion ion chromatography (CIC).

B

BP4NTA

Benchmarking and Publications for Non-Targeted Analysis is a working group formed to address challenges in nontargeted analysis studies using mass spectrometry (https://nontargetedanalysis.org/) (BP4NTA 2023).

C

Combustion Ion Chromatography (CIC)

A separation technique that first combusts organics at 900–1,000°C to inorganic ions that can be separated by ion (exchange) chromatography (IC).

Contaminant(s) of Emerging Concern (CEC)

Substances and microorganisms, including physical, chemical, biological, or radiological materials known or anticipated in the environment, that may pose newly identified risks to human health or the environment.

D

Dalton (Da)

A unit of mass that is equal to one-twelfth the mass of a free ^{12}Carbon atom at rest. The Dalton is also known as the unified atomic mass unit. One Dalton is approximately 1.66×10^{-27} kg.

Deconvolution

For gas chromatography–mass spectrometry (GC-MS) data, deconvolution is the process of computationally separating co-eluting components and creating a pure spectrum for each component. It is widely used to process complex data generated by high resolution mass spectrometry (HRMS).

Dynamic Light Scattering (DLS)

DLS is a noninvasive laser-based technique that is a useful tool for determining the hydrodynamic diameter and particle size distribution in suspension and for investigating colloidal properties of nanoparticles.

E

Effect-Directed Analysis

Effect-directed analysis is an emerging strategy for environmental profiling of complex samples that brings together

biological-effects testing using bioassays, sample preparation and fractionation, and chemical analysis to evaluate environmental toxicity and identify toxic pollutants.

Electrochemical Methods

These methods are based on the direct impact of individual nanoparticles in a suspension on the electrode surface. This leads to current spikes as a function of time that can correlate to various characteristics of an engineered nanoparticle's (ENP's) property.

Electron Impact (EI)

A strong gas-phase ionization technique applied widely in GC-MS that uses highly energetic electrons at 70 electron volts to produce ions from sample molecules. EI produces extensive but highly reproducible fragmentations of the parent molecule and yields mass spectra that can be easily compared across platforms.

Electrospray Ionization (ESI)

ESI is a technique used in mass spectrometry to produce ions using an electrospray in which a high voltage is applied to a liquid to create an aerosol. It is especially useful in producing ions from macromolecules because it overcomes the propensity of these molecules to fragment when ionized. ESI is typically used in high-performance liquid chromatography–mass spectrometry (HPLC-MS).

Engineered Nanoparticles (ENPs)

Specially designed chemical substances or materials with particle size between 1 and 100 nm in at least one dimension.

Exposure

Contact with a substance by swallowing, breathing, or touching the skin or eyes. Exposure may be short-term (acute exposure), intermediate duration, or long-term (chronic exposure) (ATSDR 1994).

Exposure Pathway

The physical course or path that a chemical or pollutant takes from the source via air, soil, water, and food to humans, animals, and the environment (USEPA 2003). Each exposure pathway includes a source or release from a source, an exposure point, and an exposure route.

Extractable Organic Fluorine (EOF)

An organofluorine assay that first extracts these compounds from a sample using ion-pairing sample preparation methods and then analyzes the extract by CIC. The EOF sample preparation method is highly customizable.

F

Features (Chemical)

Any ion detected in a mass spectrum that may be of importance. Features are defined by the mass-to-charge ratio (*m/z*), chromatographic retention time, and mass spectral peak intensity. After a feature is selected to be important, it can be designated as an unknown, and the analyst can then take further steps to identify it.

Flow cytometry

Flow cytometry is a technology that provides rapid multi-parametric analysis of single cells in solution. Flow cytometers use lasers as light sources to produce both scattered and fluorescent light signals that are read by detectors. These signals are converted into electronic signals that are analyzed by a computer and written to a data file. Cell populations can be analyzed and/or purified via flow cytometry based on their fluorescent or light-scattering characteristics.

Fourier Transform Infrared (FTIR) Microscopy

FTIR microscopy is a combination of conventional light microscopy and clear chemical identification using FTIR spectroscopy. FTIR microscopy can yield chemical area maps or single point scans in an optical field.

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR is a vibrational spectroscopy technique that uses an infrared light source to induce vibrations. It is conducted in the frequency domain to rapidly produce infrared absorption spectra to identify organic, inorganic, and polymeric materials in a sample.

Full-Scan Mode

Full-scan mode is used in quantitative mass spectrometry to detect parent ions in a sample. A mass analyzer set to scan from the lowest to highest *m/z* ratio in a user-defined range.

G

Gas Chromatography–Mass Spectrometry (GC-MS)

A common hybrid analytical method that combines gas-phase chromatographic separation with a single mass spectrometer acting as a mass filter and detector. Once separated via GC, compounds can be identified by their full-scan EI ionization mass spectrum by a spectral match from a spectral library. A total ion chromatogram can be generated to document compound elution with time. Alternatively, more sensitive quantitation can be performed in selective ion monitoring (SIM) mode. GC-MS is typically used for the analysis of volatile and semi-volatile thermally stable compounds.

H

Hazard

A condition or physical situation with a potential for an undesirable consequence, such as harm to life or limb (ITRC 2020).

High Resolution Mass Spectrometry (HRMS)

HRMS is an analytical tool that measures the *m/z* ratio of ions to an accuracy of 0.001 Da or lower. These instruments can be used to distinguish between compounds with a similar nominal mass, determine elemental compositions, and identify unknowns. A type of HRMS widely used today is the quadrupole time-of-flight (QTOF) mass spectrometer.

Homologous Series

In organic chemistry, a homologous series is a group of compounds that contain the same functional group or structure and differ by a repeating unit (e.g., CH_2 or CF_2). Compounds in a homologous series tend to have similar chemical and physical properties.

I

Instrumental Neutron Activation Analysis (INAA)

A nuclear technique used to determine the concentration of trace and major elements in a variety of matrices. A sample is subjected to a neutron flux resulting in the production of radioactive nuclides, which upon radioactive decay, emit gamma rays whose energies are characteristic for each nuclide. Comparison of the intensity of these gamma rays with those emitted by a standard permit a quantitative measure of the concentrations of the various nuclides.

Ion Chromatography (IC)

IC is a separation technique that measures the concentration of ionic species using an ion exchange resin.

L

Laser Direct Infrared Microscopy

An infrared spectrometer using a quantum cascade laser coupled to a rapidly scanning imaging system.

Liquid Chromatography (LC)

LC is an analytical technique that separates compounds from their mixtures through a column or stationary phase using solvents or mobile phase. In the analytical chemistry realm, LC is typically performed at high pressure to shorten elution times and is more commonly known as high-performance liquid chromatography (HPLC).

M

Mass Spectrometry (MS)

Mass spectrometry is an analytical tool that measures the *m/z* ratio of ions.

Matrix-Assisted Laser Desorption or Ionization (MALDI)

An ionization technique for mass spectrometry that uses a laser-energy–absorbing matrix to create ions from large molecules with minimal fragmentation.

Metabolomics

Metabolomics is an emerging field and is broadly defined as the comprehensive measurement of all metabolites and low-molecular-weight molecules in a biological specimen using primarily mass spectrometry.

Metagenomics

Analysis of the genome of multiple organisms in bulk/environmental samples using next-generation sequencing (NGS) methods. Metagenomics is often used to study a specific community of microorganisms, such as those residing on human skin, in the soil, or in a water sample.

Metatranscriptomics

Metatranscriptomics is the science that studies gene expression of microbes within natural environments. It allows one to obtain whole gene expression profiling of complex microbial communities.

Microarray

A microarray is a laboratory tool used to detect the expression of thousands of genes at the same time. Deoxyribonucleic acid (DNA) microarrays are microscope slides that are printed with thousands of tiny spots in defined positions, with each spot containing a known DNA sequence or gene.

Microplastics (MPs)

Particles that are greater than 1 nanometer (nm) and less than 5 millimeters (mm) in their longest dimensions and are composed of solid polymeric materials to which chemical additives or other substances may have been added.

Molecular Ion Peak

In a mass spectrum, the peak representing the molecular ion is called the molecular ion peak. Excluding any peaks due to the presence of heavier isotopes, the molecular ion peak is the peak with the highest *m/z* ratio.

Monoisotopic Molecular Ion

Ion composed of only the most abundant stable isotopes of its constituent elements.

N

Nanoparticle Tracking (NT)

NT passes a laser beam into the particle suspension. When the particles in suspension appear in the scattered light path, they can be clearly visualized and recorded frame by frame using a high-sensitivity camera or charged coupled device (CCD) detector. The motion trail of the particles is obtained and analyzed through the recorded frames by means of a microscope. Further calculation of hydrodynamic sizes is completed with the average distance between each particle, temperature, and solution viscosity through the Stokes-Einstein equation.

Nanoplastics

Plastic/polymeric particles less than 1,000 nm in their longest dimension.

Next-Generation Sequencing (NGS)

NGS is a massively parallel sequencing technology that offers ultra-high throughput, scalability, and speed. The technology is used to determine the order of nucleotides in entire genomes or targeted regions of DNA or ribonucleic acid (RNA).

Nominal Mass

Mass of a molecular ion or molecule calculated using the isotope mass of the most abundant constituent element stable isotope of each element rounded to the nearest integer value and multiplied by the number of atoms of each element.

Non-target Analysis or Screening (NTA or NTS)

NTA aims to detect "unknown-unknown" compounds without any *a priori* criteria to identify potential new molecules or molecular fragments. Because no structural information is available in advance, a full nontargeted identification starting from the exact mass, isotope, adduct, and fragmentation information needs to be performed using HRMS. NTA can result in acquiring structural information and compound identity but does not yield quantitative information with respect to concentration.

NORMAN Network (Network of Reference Laboratories, Research Centers and Related Organizations for Monitoring of Emerging Environmental Substance)

NORMAN is a network that facilitates the exchange of information and data collection of CEC, promotes method validation and harmonization, and shares knowledge of CEC across networks (https://www.norman-network.net/?q=NORMAN%20Network) (NORMAN 2023).

Nuclear Magnetic Resonance (NMR)

An NMR instrument allows the molecular structure of a material to be analyzed by observing and measuring the interaction of nuclear spins when placed in a powerful magnetic field.

P

Particle-Induced Gamma Ray Emission (PIGE)

PIGE spectroscopy is a surface analysis technique for quantification of elemental fluorine in which an accelerated beam of protons strikes the surface of the sample of interest, exciting ^{19}F nuclei. Gamma rays emitted upon de-excitation provide a unique signature proportional to the number of fluorine atoms on the surface.

Polymerase Chain Reaction (PCR)

PCR is a method widely used to rapidly make millions to billions of copies of a specific DNA sample, allowing scientists to take a very small sample of DNA and amplify it to a large enough amount to study in detail.

Proteomics

Proteomics is the systematic, large-scale analysis of proteins using techniques such as mass spectrometry. It is based on the concept of the proteome as a complete set of proteins produced by a given cell or organism under a defined set of conditions.

Public

A people as a whole; a populace having common interests (ITRC 2020).

Pyrolysis GC-MS

A GC-MS (see GC-MS) where samples are introduced via a pyrolizer, which provides a heated and inert environment where complex molecules are broken down into fragments/pyrolyzates.

Q

Quantitative Polymerase Chain Reaction (qPCR)

A laboratory analytical technique for quantification of a target gene. In qPCR, the accumulation of amplification nucleic acid product is measured as the reaction progresses, in real time, with product quantification after each cycle.

R

Raman Spectroscopy

Raman spectroscopy is a spectroscopic technique typically used to determine vibrational modes of molecules, although rotational and other low-frequency modes of systems may also be observed. Raman spectroscopy is commonly used in chemistry to provide a structural fingerprint by which molecules can be identified. Raman spectroscopy relies upon inelastic scattering of photons, known as Raman scattering.

Resolution (in mass spectrometry)

In mass spectrometry, resolution is defined as the ability of the mass spectrometer to separate ions of similar *m/z* ratio.

Reverse Transcription qPCR (RT-qPCR)

Reverse transcription qPCR (RT-qPCR) is used when the starting material is RNA. In this method, RNA is first transcribed into complementary DNA (cDNA) by reverse transcriptase enzyme from total RNA or messenger RNA (mRNA). The cDNA is then used as the template for the qPCR reaction.

Risk

The potential for realization of unwanted, adverse consequences to human life, health, property, or the environment. Estimation of risk is usually based on the expected value of the conditional probability of the event occurring multiplied by the consequence of the event, given that it has occurred (ITRC 2020).

Risk Communication

Actions, words, and other messages, responsive to the concerns and values of the information recipients, intended to help people make more informed decisions about threats to their health and safety.

Risk communication is the formal and informal process of communication among and between regulatory agencies and organizations responsible for site assessment and management, and the various parties who are potentially at risk from or are otherwise interested in the site.

S

Schymanski Confidence Levels or Scale

Schymanski Confidence Levels are used to communicate confidence in structural identification of compounds using HRMS. It is named after the first author of the paper (dx.doi.org/10.1021/es5002105) that first presented the scale (Schymanski et al. 2014).

Selective Ion Monitoring (SIM)

SIM is a mass spectrometry scanning mode in which only a limited *m/z* ratio range is transmitted/detected by the instrument, instead of the full spectrum range. This mode of operation typically results in significantly increased sensitivity.

Single Particle Inductively Coupled Plasma–Mass Spectrometry (ICP-MS)

SP ICP-MS is a type of mass spectrometry that uses an inductively coupled plasma to ionize the sample. It atomizes the sample and creates atomic and small polyatomic ions, which are then detected. It is known and used for its ability to detect metals and several nonmetals in liquid samples at very low concentrations. It can detect different isotopes of the same element, which makes it a versatile tool in isotopic labeling.

Solid-Phase Extraction (SPE)

SPE is a sample preparation technique used in analytical laboratories. It extracts and preconcentrates analytes from a complex liquid matrix prior to quantitative analysis.

Study Reporting Tool (SRT)

SRT is an open-source guide for reporting NTA data. It provides a framework for NTA design, data communication, and

reporting performance metrics to ensure high-quality data are gathered and interpreted.

Subpopulation

Groups of individuals who respond biologically at lower levels of exposure to a contaminant or who have more serious health consequences than the general population (USEPA, OW 2000).

Suspect Screening

Suspect Screening is a technique that uses HRMS to identify "suspect" compounds in a sample. Although reference standards may not be available for suspect screening, exact mass, mass fragmentation, and other experimental data can be used to increase the confidence of the identification.

T

Tandem Mass Spectrometry (MS/MS)

Mass spectrometry technique that breaks a precursor ion (parent ion) into fragments. These fragments are used to reveal the chemical structure of the precursor ion.

Target Screening or Target Analysis

Target analysis is a technique that uses tandem mass spectrometry to identify and quantify known compounds in a sample using available reference analytical standards and/or libraries.

Tentatively Identified Compound (TIC)

A compound detected in a sample, typically using a GC-MS method, that is not in the target analyte list for the method.

Thermal Desorption GC-MS

Uses heat and a flow of inert (carrier) gas to extract volatiles from a solid matrix (no solvent required), which is then analyzed via GC-MS. One such standardized method, USEPA Method 8275A, could be used to include the decomposition products of MPs.

Thermally Labile

Easily breaks down upon heating. The term also describes compounds not amenable to separation via gas chromatography because of the high temperature or thermal gradient applied to the GC. These compounds are usually separated using liquid chromatography.

Total Ion Chromatogram

A total ion chromatogram is the sum of the ion intensities versus time for a full chromatographic run.

Total Oxidizable Precursor (TOP)

The TOP assay is the most selective of perfluoroalkyl and polyfluoroalkyl substances (PFAS) surrogate analytical methods in that it selects only for compounds that can be oxidized to form targeted perfluoroalkyl acids (PFAAs). This method was developed to infer and indirectly quantify the total amount of chemical "precursors" to PFAAs in a sample by comparing the concentrations of specific PFAAs by HPLC-MS/MS both before and after oxidation of the sample by an excess of hydroxyl radicals.

Toxicological Reference Value or Toxicity Reference Value (TRV)

A concentration or dose that represents a threshold or defined level of toxic effects.

U

Ultra (High) Performance Liquid Chromatography (UPLC or UHPLC)

Liquid chromatography employing a shorter and more tightly packed analytical chromatography column (owing to smaller particle size of the stationary phase) that allows faster separation of analytes at a higher operating pressure than HPLC.

ITRC (Interstate Technology & Regulatory Council). 2023. *Contaminants of Emerging Concern Framework* CEC-1. Washington, D.C.: Interstate Technology & Regulatory Council, CEC Team. https://cec-1.itrcweb.org/.

Acronyms

6PPD	N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine
6PPD-q	N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone
AFFF	aqueous film-forming foam
amu	atomic mass unit
AOF	adsorbable organic fluorine
ATSDR	United States Agency for Toxic Substances and Disease Registry
BAF	bioaccumulation factor
BCF	bioconcentration factor
BIL	Bipartisan Infrastructure Law
BP4NTA	Benchmarking and Publication for Non-Targeted Analysis
CalEPA	California Environmental Protection Agency
CCL	Contaminant Candidate List
CDC	United States Centers for Disease Control and Prevention
cDNA	complementary DNA
CEC	contaminant(s) of emerging concern
CIC	combustion ion chromatography
CMRM	Chemical and Material Risk Management
CSF	cancer slope factor
Da	Dalton
DLS	dynamic light scattering
DNA	deoxyribonucleic acid
DOD	United States Department of Defense
DOE	United States Department of Energy
DQRAchem	Detailed Quantitative Risk Assessment for Chemicals
EC	emerging chemical
ECHA	European Chemicals Agency
EDA	effect-directed analysis
EI	electron impact
EMD	Environmental Molecular Diagnostics
ENM	engineered nanomaterials
ENP	engineered nanoparticles
EOF	extractable organic fluorine

ERED	Environmental Residue Effects Database
ESI	electrospray ionization
ESOH	Environmental, Safety, and Occupational Health
EU	European Union
FAIR	Findability, Accessibility, Interoperability, Reusability
FDA	Food and Drug Administration
FTIR	Fourier transform infrared spectroscopy
GC	gas chromatography
GC-MS	gas chromatography-mass spectrometry
GenX	hexafluoropropylene oxide-dimer acid
HAL	health advisory levels
HFPO-DA	hexafluoropropylene oxide-dimer acid
HPLC	high-performance liquid chromatography
HPLC-MS	high-performance liquid chromatography-mass spectrometry
HRMS	high-resolution mass spectrometry
ICP	inductively coupled plasma
ICP-MS	inductively coupled plasma-mass spectrometry
IRIS	Integrated Risk Information System
ISO	International Organization for Standardization
ITRC	Interstate Technology and Regulatory Council
IUR	inhalation unit risk
IURF	inhalation unit risk factor
LC	liquid chromatography
LDIR	laser direct infrared microscopy
LSRP	licensed site remediation professional
MALDI	matrix-assisted laser desorption or ionization
MCL	maximum contaminant level
MDH	Minnesota Department of Health
MERLA	Minnesota Environmental Response and Liability Act
mg/kg-day	milligrams per kilogram per day
MI EGLE	Michigan Department of Environment, Great Lakes, and Energy
MIQE	minimum information of QPCR experiments
mm	millimeter
µg/m3	micrograms per cubic meter
µm	micrometer
MP	microplastics
MPCA	Minnesota Pollution Control Agency
MRL	minimal risk level
µs	microsecond
MS	mass spectrometry

MS/MS	tandem mass spectrometry
m/z	mass-to-charge ratio
ng/L	nanogram per liter
NGS	next-generation sequencing
NIST	National Institutes of Standards and Technology
nm	nanometer
NMR	nuclear magnetic resonance
NOAA	National Oceanic and Atmospheric Administration
NORMAN	network of reference laboratories, research centers and related organizations for monitoring of emerging environmental substances
NPRI	National Pollutant Release Inventory
NTA	nontarget analysis
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
OEHHA	California Office of Environmental Health Hazard Assessment
OPP	United States Environmental Protection Agency Office of Pesticide Programs
OSF	oral slope factor
OW	Office of Water, United States Environmental Protection Agency
PACT	Public Activities Coordination Tool
PAPM	Precaution Adoption Process Model
PBT	persistent, bioaccumulative, and toxic
PCR	polymerase chain reaction
PE	polyethylene
PFAA	perfluoroalkyl acids
PFAS	per- and polyfluoroalkyl substances
PFBS	perfluorobutanesulfonic acid
PFHpA	perfluoroheptanoic acid
PFHxS	perfluorohexanesulfonic acid
PFNA	perfluorononanoic acid
PFOA	perfluorooctanoic acid
PFOS	perfluorooctane sulfonic acid
PFP	pentafluorophenyl
PFPE	perfluoropolyether
PIGE	particle-induced gamma ray emission
PNEC	predicted no effect concentration
POPs	persistent organic pollutants
POTWs	publicly owned treatment works
PP	polypropylene
PPCPs	pharmaceuticals and personal care products
PPRTV	Provisional Peer-Reviewed Toxicity Values

PQRA	Preliminary Quantitative Risk Assessment
PS	polystyrene
PWS	public water systems
QA	quality assurance
QC	quality control
qPCR	quantitative polymerase chain reaction
QSAR	quantitative structure activity relationships
REACH	registration, evaluation, authorization and restriction of chemicals
RfC	reference concentration
RfD	reference dose
RNA	ribonucleic acid
RT	retention time
RT-qPCR	reverse transcription-quantitative polymerase chain reaction
SDWA	Safe Drinking Water Act
SIM	selective ion monitoring
SP ICP-MS	single particle inductively coupled plasma-mass spectrometry
SPE	solid-phase extraction
SWRCB	State Water Resources Control Board
TIC	tentatively identified compound
TOF	time of flight
TOP	total oxidizable precursor
TRRP	Texas Risk Reduction Program
TRV	toxicity reference value or toxicological reference value
TSCA	Toxic Substances Control Act
TWPL	tread wear particle leachate
UCMR	Unregulated Contaminant Monitoring Rule
UCMR 3	third Unregulated Contaminant Monitoring Rule
UCMR 5	fifth Unregulated Contaminant Monitoring Rule
UHPLC-HRMS	ultra-high-performance liquid chromatography-high resolution mass spectrometry
URMS	urban runoff mortality syndrome
U.S.	United States
USACE	United States Army Corps of Engineers
USEPA	United States Environmental Protection Agency
VOCs	volatile organic compounds
WWTP	wastewater treatment plant

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ITRC & Environmental Justice – A Commitment to Our Values

Environmental Justice is making its way to the forefront of today's environmental community following decades of documentation detailing the disproportionate burden placed on low-income and minority communities by pollution and environmental hazards. Failure to address EJ concerns has led to grave consequences for low-income or minority communities; without a voice, human health in these communities can suffer greatly as a result of poorly informed environmental decision-making.

Defined by the United States Environmental Protection Agency (EPA) as "…the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income, with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies," EJ can only be achieved when everyone has "the same degree of protection from environmental and health hazards, and equal access to the decision-making process to have a healthy environment in which to live, learn, and work." (USEPA, 2020a). Since its inception in the early 1980s, the field of EJ has grown to encompass a broad spectrum of other environmentally inclusive subjects, concerns and, ultimately, legislation; some of the terminology commonly used today includes Social Equity, Social Impact, and Environmental Equity.

Signed on February 16th, 1994, Executive Order 12898 officially recognized EJ on a federal level, directing agencies to focus attention on the environmental and human health effects of federal actions on minority and low-income populations (USEPA 2020b). Further executive action has been seen recently with the signing of Executive Order 13990, on January 20, 2021, which established White House and Inter-Agency Environmental Justice Councils, as well as the Justice40 Initiative for federal identification and investment in disadvantaged communities (Federal Register, 2021). Another milestone was met when New Jersey became the first state in the nation to adopt legislation on permitting requirements based on EJ. Signed on September 18, 2020, Senate Bill 232 requires the New Jersey Department of Environmental Protection "to evaluate the environmental and public health impacts of certain facilities on overburdened communities when reviewing certain permit applications." (O'Connor, 2020).

ITRC will continue to develop reference material for project managers and environmental professionals to consider in the use of current and future ITRC guidance materials in environmental decision-making and project design. ITRC will include the principals of EJ in future environmental products – working towards our mission while paying express attention to our core values of diversity, equity, inclusion and transparency. ITRC is excited to be a part of addressing environmental justice and bringing more voices to addressing the national and local environmental challenges.

ITRC Organizational Diversity, Equity & Inclusion

Diversity, equity, inclusion and transparency are embodied within the core values of ITRC. They are fulfilled in the pursuit of ITRC's mission and vision. ITRC's Membership Code of Conduct requires every member to benefit from team consensus and collaboration. ITRC requires diverse perspectives that provide the knowledge and skills to address all environmental challenges in pursuit of developing innovative products.

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