# Emerging Contaminants and Issues of Concern Program

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# **Problem Statement**

Emergency situations and novel human health concerns emerge unexpectedly, yet regularly, and decision makers depend on timely access to high-quality, actionable information to protect public health. Effective and rapid mobilization of scientific resources in response to such situations can be challenging due to their unpredictable nature. Programs that intend to be responsive to these concerns will have capabilities, capacity, and communication with pertinent organizations that enable rapid generation of translationally relevant data for public health decision-making.

# Objectives

The Emerging Contaminants and Issues of Concern (ECIC) program objectives are to:

- 1. Address emerging issues to which the Division of the National Toxicology Program (DNTP) may apply capabilities and expertise to effectively respond to public health issues in *a timely way* using a "Decision Framework." ECIC projects may include:
  - *Emergencies* that require a *rapid response* when members of the public have been exposed to a toxicological hazard for which there are insufficient data to adequately characterize potential harm.
  - *Emerging contaminants or issues of concern* for which there are insufficient toxicological information available for understanding key aspects of risk to human health for contemporary environmental concerns requiring a *prioritized response*.
- 2. Use "horizon-scanning"<sup>1</sup> or scoping<sup>2</sup> activities to identify ECICs, especially those affecting historically marginalized and underserved populations, and develop projects to *proactively* address the needs of our stakeholders.<sup>3</sup>
- 3. Formulate and apply strategic approaches, leveraging the breadth of DNTP capabilities, which allow for *fit-for-purpose research responses* to emerging contaminants, diseases, disasters, or other concerns. Development of response strategies is an iterative process and will include coordination and regular communication with internal and external organizational stakeholders and allow for the identification of capability and research gaps.

<sup>&</sup>lt;sup>1</sup>Organisation for Economic Co-operation and Development (OECD). Overview of Methodologies. <u>http://www.oecd.org/site/schoolingfortomorrowknowledgebase/futuresthinking/overviewofmethodologies.htm</u>. <sup>2</sup>Project Management Knowledge. Define Scope. <u>https://project-management-</u> knowledge.com/definitions/d/define-scope/.

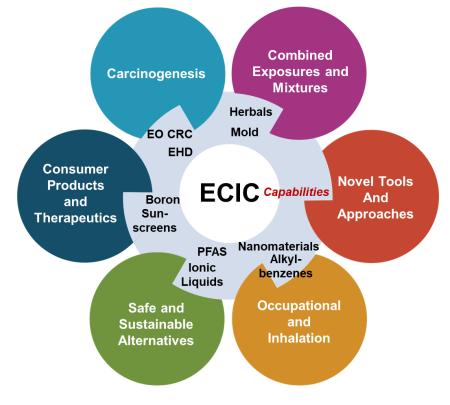
<sup>&</sup>lt;sup>3</sup>Horizon-scanning and scoping activities differ in that scanning efforts are more verbal and proactive—they engage experts in conversations *to predict* responses or capabilities that may be needed; scoping typically consists of compiling bits of information and working with a stakeholder to *satisfy their needs*.

# Rationale

Public health is increasingly affected by environmental issues, such as exposure to emerging contaminants, for which associated toxicological information is sparse. These exposures could be obvious, as with disasters such as chemical spills or intense weather events, or they may be less apparent, as when health conditions with unknown origins emerge rapidly, implicating potential environmental components. Published guidelines<sup>4</sup> have helped to define ECICs for this program:

- Contaminants that may have been in the environment for a while but for which concerns have been raised more recently and health data are lacking
- More traditional contaminants for which new facts or information warrant heightened concern
- Emergent health issues with potential connections to undefined environmental contaminant exposures

In these ECIC cases, existing toxicological data may be insufficient for establishing guidelines to limit exposure to hazardous substances. The West Virginia Elk River spill is an example of an emergency response for which NTP engaged DNTP, the Agency for Toxic Substances and Disease Registry (ATSDR), the Environmental Protection Agency (U.S. EPA), and the National Institute for Occupational Safety and Health (NIOSH) scientists to define the chemical of highest concern (CHC), obtain published information on the CHC, rapidly conduct in vitro and in vivo studies to address uncertainties around potential advisory levels, and communicate the data to stakeholders. Other ECIC projects requiring a timely response may first undergo scoping efforts to better understand our ability to provide the needed data or necessitate a tier of studies that may include several aspects of our capabilities pipeline.



**Figure 1.** Examples of DNTP projects across several research programs demonstrating some connectivity (light blue/gray circle) with the ECIC program. Other ECIC projects are detailed in Table 2.

ECIC: emerging contaminants and issues of concern; EHD: environmental health disparities; EO CRC: early onset colorectal cancer; PFAS: per- and polyfluoroalkyl substances.

<sup>&</sup>lt;sup>4</sup>Sauvé S, Desrosiers M. (2014) A review of what is an emerging contaminant. Chem. Cent. J. 8:15. <u>https://doi.org/10.1186/1752-153X-8-15</u>.

Projects may fall under the purview of more than one program. It is anticipated that projects identified as most closely aligned with the ECIC program may also have connections to other programs, and projects that begin with ECIC may help to inform new research projects that fit other programs (Figure 1). The ECIC program aims to provide decision makers with actionable data—*as a prioritized response*—to support regulations or guidelines limiting exposure to hazardous substances and to protect public health in response to emerging *environmental issues that may not fit into other DNTP programs, and which may require new capabilities or fit-for-purpose approaches*.

### **Public Health Context**

With an increasing number of accidental exposures, discoveries of industrial contamination, and natural disasters—combined with erosion of public health protection and increasing reliance on limited state resources to manage regulatory requirements—the general population may be increasingly exposed to substances for which toxicological data are limited. High-quality, reliable data are necessary to assess which substances have hazard potential so that measures can be enacted to limit exposure and risks to the public. Engagement with the affected communities and translation of data, particularly when those communities would be most exposed or most susceptible if exposed, are necessary so that action(s) such as intervention, remediation, and litigation will be well informed.

### Alignment with Mission, Goals, Strategic Pipeline

Aligned with DNTP goals, the ECIC program will foster collaboration and employ capabilities and expertise to provide trusted science to support decision-making in a prioritized manner for emergency or emerging environmental health issues of concern. This program directly aligns with the DNTP mission to improve public health through data and knowledge development that is translatable, predictive, and timely. DNTP is positioned to provide a variety of actionable and informative data quickly in response to stakeholder requests due to 1) maturation of a broad suite of testing capabilities, 2) organization of the research portfolio into defined programs with focused goals, and 3) increasing avenues of coordination with stakeholders reacting to similar ECIC. DNTP has continued to broaden its testing program beyond the 2-year cancer bioassay to include an expansive suite of various short-term testing strategies and mechanistic capabilities designed to characterize environmental exposures more quickly and efficiently. Leveraging multiple capabilities and data streams, as outlined in the Translational Toxicology Pipeline, will improve the contextualization of toxicological data for understanding the effects of exposures on human health. In addition to facilitating completion of ongoing projects, this program will foster crossdisciplinary collaborations among DNTP staff and help shape strategies for timely responses of new projects that include innovative tools and approaches. To increase emphasis on transdisciplinary approaches, the ECIC program will seek out partnerships with U.S. and international researchers conducting human exposure and molecular epidemiology studies.

## Stakeholder Interest and Engagement

Stakeholder interest and engagement are critical for the success of DNTP programs. Continued discussions with stakeholders will enhance the use of limited resources by avoiding duplication of effort, increasing productivity, and identifying/engaging communities and groups requesting the needed data. The ECIC program categorizes stakeholders as "program" or "project" stakeholders, the definitions of which are provided below.

### **Program Stakeholders**

Program stakeholders are agency, institute, or organizational liaisons also involved in ECIC-related projects that have a vested interest in particular areas that need further research to inform their policy and regulatory decision-making. Because this program would oversee projects based on the need for fit-for-purpose responsive research to fill data gaps on a wide range of exposures, we have initiated communication with a variety of stakeholders (see Table 1). To date, the ECIC program has engaged with and plans to collaborate with other National Institutes of Health (NIH) and National Institute of Environmental Health Sciences (NIEHS) programs related to disasters, emergency response, or emerging contaminants (e.g., the National Emerging Contaminants Research Initiative [NECRI], Disaster Research Response [DR2], Division of Extramural Research and Training, and Superfund Research Program [SRP]). We also have initiated outreach with numerous categories of stakeholders to advance ECIC program Objectives 2 and 3.

Category	Stakeholder	Issue	Role of Stakeholder
NIH	Superfund Research Program (SRP)	Geospatial mapping	Partner
	Disaster Research Response (DR2) Program	Emergency response strategy development	Collaborator
Cross-federal Agency Programs	Interagency Working Group on Emerging Contaminants and National Emerging Contaminants Research Initiative (NECRI)	Drinking water contaminants; emergency response research development	Collaborators
Federal Agency	U.S. EPA: Center for Public Health and Environmental Assessment (CPHEA), Chemical and Pollutant Assessment Division (CPAD)	Horizon scanning	Partners
	CDC: National Institute for Occupational Safety and Health (NIOSH)	TBD	Partner
	CDC: Agency for Toxic Substances and Disease Registry (ATSDR)	Emerging contaminants biomonitoring; horizon scanning; prevention	Collaborator
	United States Geological Survey	Geospatial mapping	Collaborator
State Agencies	CalEPA: Office of Environmental Health and Hazard Assessment (OEHHA)	Strategies aligned with ECIC program Objective 3; mapping projects	Partner and User
	North Carolina Departments of Environmental Quality (NCDEQ) and Health and Human Services (NCDHHS)	Toxicology study expertise	User
Non-governmental Organization (NGO)	Environmental Working Group (EWG)	TBD	User

#### Table 1. Current and Planned Engagements with Program Stakeholders

Stakeholder definitions: CDC = Centers for Disease Control and Prevention; CalEPA = California Environmental Protection Agency.

TBD = to be determined.

A wide range of additional stakeholders have also been identified, including the various types of organizations listed below. Near-term future efforts will focus on engaging with these groups.

- National environmental advocacy groups: For example, National Research Defense Council; Environmental Defense Fund; Silent Spring Institute
- Regional environmental advocacy groups: For example, Cape Fear River Watch; Collaborative on Health and the Environment
- State public health agencies: For example, North Carolina Department of Health and Human Services' Division of Public Health; Department of Environmental Quality's Division of Waste Management
- State- or national-level NGOs focused on specific health outcomes: For example, California Breast Cancer Research Program; the Society for Birth Defects Research and Prevention
- Environmental justice advocacy groups: For example, North Carolina Environmental Justice Network
- International organizations: For example, Female Reproductive toxicity of Endocrine disrupting chemicals: a human evidence-based screening and Identification Approach (FREIA) a European Union's Horizons 2020 Program; Health Canada

#### Input Received from Program Stakeholders

Through our scheduled information-gathering meetings and planned participation in national meetings, such as the Emerging Contaminants in the Environment Conference, Society of Toxicology, and International Society of Environmental Epidemiologists, we plan to develop a list of ECICs that are a priority for many organizations yet lack the toxicological data needed for public health hazard identification. As evident from Table 1, some of the program stakeholders have expressed an interest in having the DNTP ECIC program as a collaborator for specific cross-agency and cross-divisional activities in support of their new avenues of public health protection.

To date, interest has been substantial in proposed horizon-scanning efforts, information sharing on emerging contaminants, convening a workshop focused on ECIC proactive/prevention approaches, and development of cross-agency capabilities and strategies for emergency response.

### **Project Stakeholders**

As DNTP has been conducting studies in the area of ECICs for some time, a wide range of projects are ongoing that originate from various stakeholders' requests. In general, communication with the project stakeholders is initiated and continued by the project leads. Stakeholders for current ECIC projects in the program portfolio are listed in Table 2.

Project Focus	Study Type	Status	Stakeholders
Boron Compounds	Developmental exposures in rodent models	Conducting Reporting	Minnesota Dept. of Health
Cyanotoxins (Microcystin-LR)	Mouse and rat evaluations	Conducting Review	U.S. EPA
Deoxynivalenol (DON)	Rat MOG DRF	Reporting	FDA and NTP
Glyphosate	In vitro studies	Reporting	U.S. EPA
Pyriproxyfen (MPEP)	Rat 28-day and teratology studies	Conducting	Physicians and CDC

Project Focus	Study Type	Status	Stakeholders
		Reporting	
Sulfolane	Multi-model 28-day, immunotoxicity studies	Review Reporting	State of Alaska, ATSDR, U.S. EPA
Tris(4-chlorophenyl) methanol (TCPMe)	DRF	Review	NIEHS and HESI
Thallium Compounds	Mouse and rat evaluations	Conducting Reporting	U.S. EPA
Sodium Tungstate	PN rat/mouse chronic DW	Reporting	U.S. EPA
Vanadium Compounds	Rat and mouse DW studies	Conducting Review	U.S. EPA
3,3'-dicholorobiphenyl (PCB 11)	In vitro screening	Review	U.S. EPA, NIEHS
Chronic Kidney Disease of Unknown Origin (CKDu)	Kidney pathology; analyze human samples, compare with rodent	Reporting	NIEHS Director initiated project. DHHS, FDA, FCC, Industry
	Potential origins: 1 – analyze for human pathogens, genetic susceptibility, disease etiology/prognosis 2 – literature search	Planning	
	Circulating free DNA	Planning	
Infant Exposures and Environmental Health Disparities	Cord blood hazard ID	Planning	Duke University, FDA CBER, CDC

Note: Several compounds had multiple studies, at different stages of completion.

Study definitions: PN = perinatal; DW = drinking water; DRF = dose range-finding; MOG = modified one-generation; ID = identification.

Stakeholder definitions: FDA = U.S. Food and Drug Administration; HESI = Health and Environmental Sciences Institute; DHHS = U.S. Department of Health and Human Services; FCC = Federal Communications Commission; CBER = Center for Biologics Evaluation and Research.

#### Input Received from Project Stakeholders

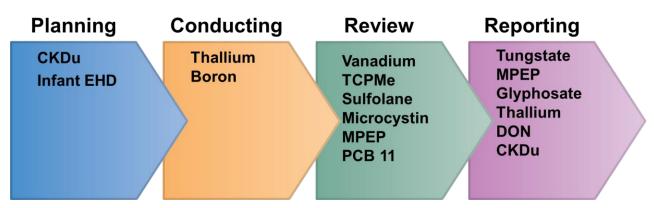
Communication with project stakeholders has been established already because we are conducting studies that have been nominated by those stakeholders. Stakeholder input is taken into consideration during project development and when project updates are provided. This process of interaction is iterative during the project life cycle. Project leads communicate with their stakeholders periodically (how often is dependent on the stakeholder and the project), provide updates on timelines and deliverables, and inform the ECIC program when requested. Projects without actionable data may be retired.

### **Milestones and Metrics**

#### **Current Project Milestones**

The current ECIC portfolio covers a diverse range of projects that vary in topic, approach or model system, endpoints (e.g., general toxicity, specific adverse outcome), and complexity. Current ECIC projects, with relevant details presented in Table 2, are in various stages of completion and summarized

in Figure 2. The expected outcomes of the projects are peer-reviewed DNTP reports or journal publications.



**Figure 2.** A synopsis of the status of individual projects within the ECIC portfolio is indicated in various phases. Details of these projects can be found in Table 2, along with full project names. Projects listed in more than one phase indicates that more than one study type was conducted for that chemical and that they are in different phases of completion.

CKDu = chronic kidney disease of unknown origin; EHD = environmental health disparities; MPEP = pyriproxyfen; TCPMe = tris(4-chlorophenyl) methanol; PCB 11 = 3,3'-dicholorobiphenyl; DON = deoxynivalenol.

### **Strategic Objective Milestones**

### Objective 1: Select Projects in ECIC Program

We have developed a draft Decision Framework to meet ECIC program Objective 1 (see the Appendix of this program concept). In addition, we have drafted a project review protocol (PRP) for providing consistent feedback to project leads (not shown).

- Short term Share the Decision Framework with the other DNTP programs to gather constructive comments on its content and utility. In the meantime, we are testing the effectiveness of our Decision Framework and the draft PRP on ECIC project proposals.
- Midterm Revise the Decision Framework and PRP using internal comments, have the documents reviewed by leadership, and finalize.
- Long term Standardize application of the final Decision Framework and PRP for all projects coming to the ECIC program to maintain consistency.

### Objective 2: Select ECIC Projects Proactively Using Horizon-scanning or Scoping Activities

A plan for horizon-scanning and scoping activities is expected to be iterative and will be developed and improved via conversations with the various contributors. This work has just begun and will evolve significantly over the next year (see the Appendix for more details).

- Short term Continue to meet/communicate with stakeholders and leads from other agencies, NGOs, and advocacy groups to understand their issues of highest concern.
- Midterm Develop a plan or methods to conduct horizon-scanning and scoping activities in collaboration with our program stakeholders, which could include a cross-agency workshop or think-tank approach to generate proactive projects or methodological needs.
- Long term Apply the methods to identify new emergency contaminants and issues. Develop a system of cross-agency communication to share information that will let us all be more proactive in response to ECIC and share methodology/capabilities.

#### Objective 3: Develop Strategies for a Prioritized Response

The ECIC program has defined key elements to include in our strategies for a rapid response plan: 1) identify when rapid responses are required; 2) develop stakeholder networks, characterize current capabilities, and identify research gaps to enhance response time; and 3) facilitate fit-for-purpose prioritized responses that draw on a variety of DNTP resources (e.g., literature and evidence-based products, adverse health outcome studies, mechanistic studies). These key elements address emerging public health issues, without significant effect on the progress of ongoing research (see Figure 3).

The ECIC rapid response plan will use and integrate testing capabilities from a variety of resources that are already being compiled within DNTP, including contracted, in-house research, alternative models, and database capabilities. Additionally, lessons learned from previous DNTP approaches and responses to emergent and emergency projects (e.g., Elk River) and NIH-based disaster research responses (DR2) have been assessed by the ECIC program with significant input from project leaders involved with these responses. Our assessment focused on topics from previous experiences so that the ECIC program can guide future responses. Our queries (such as, "What was the question or goal?" "What was delivered?" "What were the timelines?" "What worked?" "What could have been done differently?" and "What different capabilities are now available?") yielded valuable information. These efforts complement the ongoing cross-agency NECRI activities the ECIC program has been asked to engage in to advance the science and technology research needs of contaminants of emerging concern.

- Short term Continue to meet/communicate with stakeholders on readiness to respond to emergencies. We will prepare a draft rapid response plan and share it with other agencies for comment over the next year.
- Midterm Develop a better understanding of which capabilities/tools for rapid response and fitfor-purpose approaches might be useful for risk assessors and of the gaps in capabilities/tools. We will coordinate with the DNTP Novel Tools and Approaches program to develop needed capabilities. Developing conversations with end users of the data that may come from these types of studies will inform future approaches. Develop internal guidance documents that can be used by the project leaders.
- Long term Prepare a cross-agency publication that outlines our strategies for rapid response as a follow-up from lessons learned, in coordination with NECRI, DR2, SRP, and others. Conversations with risk assessors on utility of fit-for-purpose approaches may lead to publications or development of studies to assess the predictive nature of new approach methodology for in vivo responses.



**Figure 3.** Approach for developing a project plan needed for a prioritized (emergency) response. Testing strategies and inventories of capabilities are being developed in collaboration with other programs and DNTP groups and are informed by stakeholder and Board of Scientific Counselors input and lessons learned from previous studies and the NIH DR2 team leads. Familiarity and ready access to these assets will facilitate a prioritized and timely response when needed.

### **Metrics**

One of our stated roles is to facilitate progress in all program projects that require a prioritized approach without negatively affecting the progress of other projects in the research pipeline. This means that we may assist with, find, or provide expertise needed to adhere to timelines, data release, reports, and other products to ensure that knowledge and data are provided to stakeholders in a timely manner. We have drafted guidelines for evaluating our success in many aspects of program management and project facilitation that we intend to share with other DNTP programs for input in the coming year.

#### Programmatic Success

- Program coordination is evident. Program team members work together to ensure the program projects include timely response, use of the right tools, actionable data, effective leverage of DNTP resources and are impactful, inform future projects, and satisfy stakeholders.
- Projects are aligned with program objectives.
  - Projects are coordinated and managed at all phases of the life cycle (initiation, conduct, reporting, and completion), which involves careful selection of projects that align with the DNTP mission and resources and undergo consistent, iterative review.
  - Knowledge (lessons learned) from past and ongoing projects is utilized to improve methods and approaches for future projects.
  - DNTP resources are leveraged effectively by consultation with resource managers (e.g., contracting officer's representatives, leadership) to enable an effective transit through the DNTP Translational Toxicology Pipeline.
- DNTP continues to be valued as a resource for generation of high-quality, actionable, and timely data.
  - Projects are successful (as described below).
  - Efforts are coordinated with limited risk to other DNTP projects.

#### Successful Projects

- Projects adhere to study designs, timelines (milestones), budget, and product deadlines.
- Project personnel effectively communicate with the stakeholders to determine whether the products and data provide useful, actionable, and translational data in a timely manner.
- Projects deliver impactful products, such as technical or research reports, monographs, peerreviewed manuscripts, citable data tables or interactive evidence maps. Products may also include:
  - Valued data that contribute to mechanism-based issues or hazard characterization or that answer the concerns of affected populations or stakeholders.
  - A timely deliverable based on expert opinion or weight of evidence, such as a workshop to address a specific issue or a literature-based search on a specific topic that includes a consensus decision on the issue of concern.
  - Any product that allows prediction of a related event that would avoid the issue of concern or emergency or prevent development of similar chemicals of concern in the future (e.g., computational models, exposure maps, methods, or adverse outcome pathways).

# Value Proposition and Summary

DNTP is a leader in the toxicology field, has considerable resources and expertise for solving complex toxicological problems, and is thus uniquely situated to work with a broad array of stakeholders to protect public health from emerging environmental hazards. The development and implementation of successful, timely, and responsive research requires cohesiveness, connectivity, and coordination across staff and resources. Building on prior experiences, the primary distinction of this program will be its ability to provide high-quality data in a reasonable amount of time in response to requests from stakeholders. Additionally, the program will meet the need of identifying testing approaches that do not currently have regulatory acceptance but may be of value for filling data gaps on chemicals with limited toxicological information in concert with collaborators/partners.

Responding to emerging environmental issues is a high-risk activity due to external pressures and internal rate-limiting factors. Emerging contaminant exposures or health conditions are typically highly visible issues that can be affected by outside factors, including political, legal, and societal considerations. While there are challenges in addressing time-sensitive issues of concern, there are also substantial rewards, including benefits to public health, the advancement of science, and expansion of collaborations. Engaging with other organizations focused on emerging contaminants will help to identify emerging contaminants/issues and knowledge gaps that might be amenable to potential collaborations at a program level. Continued discussions on national and state levels will enhance the use of limited resources by avoiding duplication of effort, increasing productivity, and identifying and engaging communities and groups advocating for scientific solutions to address human health concerns.

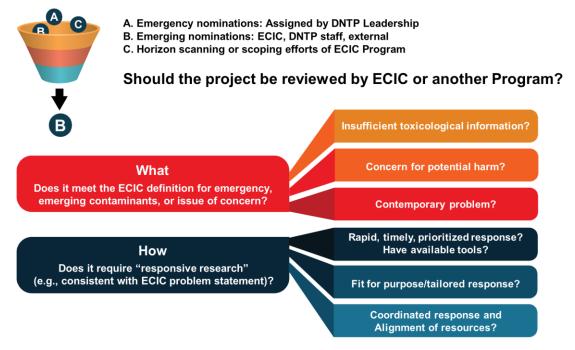
Lessons learned from past responses to emerging contaminants, such as the West Virginia chemical spill at Elk River, have shown that success depends on a prioritized, coordinated response with adherence to timelines. Ultimately, the program will strengthen the science base around ECICs, promote the use of DNTP resources to effectively respond to environmental health emergencies, and facilitate coordination with other federal programs, such as the legislatively mandated, cross-federal agency initiative (e.g., NECRI).

# Appendix

### **Objective 1: Decision Framework for ECIC Program Projects**

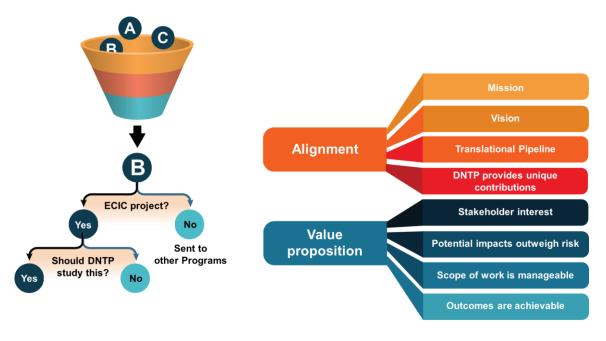
This framework, established to meet Objective 1, contains decision points that will be used to determine whether a project proposal fits within the purview of the ECIC program. ECIC project proposals include (A) emergency concerns typically assigned by DNTP leadership and (B) emerging contaminants and issues nominated by the ECIC program, other DNTP staff, or a variety of stakeholders. We anticipate that our scoping efforts (Objective 2) will also identify projects for consideration.

Within the framework, the process of approving ECIC projects takes into account not only what will be studied but also how it will be studied. Figure A1 gives an overview of guidelines for determining whether ECIC or another DNTP program should manage a project. For inclusion, the varied projects must first meet ECIC project definitions as iterated Objective 1 (contemporary need and rapid response set this program apart from others). Projects not fitting the "What" criteria are referred to another program. The "How" is more complicated and consists of not only the means to reach a goal, but also shared programmatic metrics to determine whether the goal can be accomplished in a timely manner, using DNTP resources and lessons learned.



**Figure A1.** Details on "Should ECIC Review this Project?" Contemporary issues with a need for rapid response and fit-for-purpose approaches set this program apart from other DNTP programs and are part of how we define an ECIC project.

Once a project is determined to fit within the program's purview, alignment with the DNTP mission and value proposition are considered to ensure that DNTP's reputation for excellence in toxicological data quality and commitment to communication are maintained (see Figure A2).



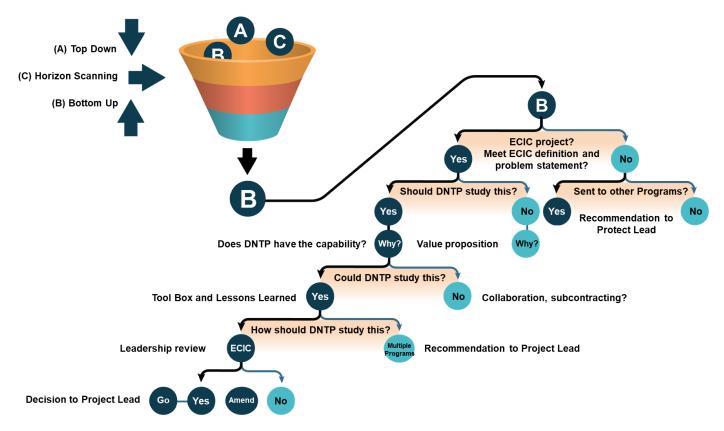
**Figure A2.** Details on relevance of projects to DNTP. The project value to DNTP and the stakeholders, along with alignment of the project with the DNTP mission and resources, are important considerations that will be evaluated as the project makes its way through the ECIC Decision Framework.

Emerging and emergency-based projects will be weighed for their fit within the ECIC program problem statement and topic definitions. DNTP leadership will usually refer emergency-based projects to the ECIC program (top-down approach). Many project proposals for emerging contaminants or issues of concern will be from stakeholder nominations and brought to the program by DNTP project leads (bottom-up approach), although some projects may be assigned/suggested by DNTP leadership and others will be developed by our team. In addition, some projects will be identified by horizon-scanning or scoping activities (see below for more detail).

Project concepts and proposals will be reviewed in a timely manner (ideally within one month) using our drafted PRP. Currently, project priority is determined using a scale of 1 (low degree) to 3 (high degree) for the following evaluation factors:

- **Importance**: Informed by perceived external impact and relevance to NIEHS strategic initiatives.
- **Difficulty**: Reflecting time and level of effort and ability to implement (plan, design, conduct, analyze, and report); also includes an assessment of whether it will require a specialized communication and/or reporting plan.
- **Risk**: Overall judgement on the program's capability and capacity to complete in a reasonable time without significant disruption to ongoing or planned work.

Once projects have moved through the Decision Framework (Figure A3) and are accepted, referred to another program, or rejected, they are entered into the project portfolio and managed along with other ongoing projects by the ECIC program.



**Figure A3.** Decision Framework depicting the entire process for determining a prioritized response and project managed by the ECIC Program.

### **Objective 2: Horizon-scanning**

This program has recently begun horizon-scanning or scoping activities to proactively identify research gaps related to ECICs (Objective 2). Horizon-scanning and scoping activities will identify environmental conditions that lead to release of new hazards, increases in exposure to previously contained hazards, increases in environmentally related disease, and gaps in capabilities that, if addressed, would improve response to issues of concern. One example is the increase in microplastics and nanoplastics in air, water, and food over the past decade that may be novel human exposures. Another example is our lack of data on environmental exposure disparities by race/ethnicity. Finally, there is a need to define the mixtures of contaminants in drinking water in the United States—what are they, where do they map to, and how do they overlap with areas of poverty/health concern "hotspots"? Many of our program stakeholders have expressed a joint interest in this project area, so we will work with them on future calls to extend this focus area.