AMERICAN CHEMISTRY COUNCIL LONG-RANGE RESEARCH INITIATIVE

Research Strategy 2024 - 2027

February 7, 2024

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Executive Summary

The American Chemistry Council's (ACC) Long-Range Research Initiative (LRI) Research Strategy 2024-2027 outlines a 4-year agenda that complements ACC's advocacy priorities, particularly those focused on strengthening the science needed for improving the implementation of the Toxic Substances Control Act (TSCA) and those focused on understanding and communicating chemical and non-chemical stressors in disadvantaged communities.

The LRI is the chemical industry's investment in research that affirms its commitment to product safety and stewardship. Through the LRI, our industry is actively engaging in scientific research, improving chemical safety assessment through development of methods with improved accuracy and efficiency and to reduce the need for conducting additional animal toxicity testing. Advancements in knowledge of environmental science, computational chemistry, exposure science, biological profiling using mechanistic assays, and dosimetry are brought together through the LRI research program to meet the expanding need for risk-based decision making to support product stewardship, regulatory actions, and sustainability activities. LRI's principles of transparency, peer review, full principal investigator (PI) independence, and public dissemination of all research studies are the foundation for the integrity and credibility of LRI funded research. The LRI is designed to address the challenges facing the industry in chemical safety assessment and is an essential component for ACC advocacy success.

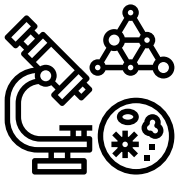
Summarized below are the six main components of this research strategy. The objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI Strategic Science Team (SST). Each project is monitored by a Project Monitoring Team (PMT), comprised of ACC LRI SST members, and where warranted, additional subject matter experts (typically drawn from ACC member companies). Projects are fully evaluated by the full SST membership at least once per year, and adjustments in scope are made accordingly.

Focus Area 1: Accelerating Exposure Science for Product Stewardship, Sustainability and Regulatory Decision-Making

The absence of exposure data for conditions of use is a significant obstacle that limits integration of hazard data with exposure information, impeding the effective implementation of risk-based decision making in TSCA and other safety evaluations. Without scientifically solid exposure data, decisions are likely to be driven by unrealistic overestimates of potential exposures, or by considerations of hazards alone, and not by scientifically defensible and reliable determinations of risks. Accordingly, to improve the availability and accuracy of exposure information, this research area focuses on developing tools and demonstrating their utility to provide exposure inputs into tiered risk assessment approaches for regulatory, product stewardship and sustainability applications.

The ACC LRI research program will:

- Develop and improve predictive models for generating exposure estimates for safety evaluations.
- Develop case studies that demonstrate the application of advanced exposure modeling tools for regulatory and product stewardship uses, including side-by-side comparisons to regulatory default approaches.
- Improve and expand exposure assessment tool for applications not only to workers, and consumers, but also to sensitive subpopulations and fence line communities.

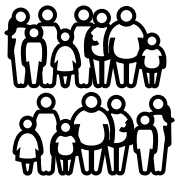


Focus Area 2: Advancing New Approach Methods (NAMs) for Application in Risk Assessment through Development of Scientific Confidence

New approach methodologies (NAMs) are defined as any technology or approach, or combination, which provide information on chemical hazard and risk assessment that avoids use of animals. NAMs are rapidly advancing, and some are beginning to gain regulatory acceptance in lieu of traditional tests for application in chemical safety assessment. NAMs offer the promise to make decisions more effectively and rapidly, in many cases using assays designed to be more accurate for a particular outcome with respect to human health and ecological effects. TSCA specifically requires use of such methods in lieu of traditional animal toxicity tests when they can provide relevant information of equivalent or better scientific quality for assessing risks. A NAM is rarely, if ever, a 1-to-1 replacement for a traditional lab animal toxicity test. Instead, NAMs are most often deployed in a tiered testing decision tree workflow as a battery or a sequential set of approaches. This research plan focuses on catalyzing collaborative research to actualize *in silico*, *in vitro*, and tiered testing and assessment workflows to increase the scientific confidence in NAMs for regulatory and product stewardship uses for human health and ecological safety evaluations.

The ACC LRI research program will:

- Support applied research to develop and demonstrate hypothesis-based integrated approaches for tiered testing and assessment using NAMs for complex adverse effect outcomes such as developmental and reproductive toxicities.
- Accelerate the development (and evaluation) of respiratory tract NAMs to pave the way towards risk assessments of chemical products without requiring inhalation testing in lab animals.
- Catalyze collaborative applications (and scientific publications) of a generally accepted set of Scientific Confidence Principles for establishing the readiness of NAMs for regulatory and product stewardship uses.



Focus Area 3: Strengthening Public Health Science Approaches for Evaluating Co-exposures and Cumulative Impacts in Communities

Increasingly, focus is being given to understanding and addressing health inequities across certain communities. Understanding and addressing the root causes of such inequities is challenging. Community health issues can be affected by socioeconomic status, psychological stressors, background health conditions, specific susceptibilities, and the physical environment, including potentially disproportionate exposures to environmental chemicals in air, water, soil, or dust. Accordingly, this research plan includes activities focusing on strengthening public health science approaches for evaluating co-exposures and cumulative impacts in communities.

The ACC LRI research program will:

- Develop (and catalyze dissemination and use of) a comprehensive set of key principles and elements of successful future Public-Private Partnerships (PPPs) for community environmental monitoring programs.
- Evaluate the scientific bases, strengths, and limitations of Environmental Justice (EJ) assessment methodologies to identify both short-term and long-term research areas, and then select the key research areas for LRI to pursue.
- Explore the feasibility of developing of an interactive visualization dashboard to improve communication of the scientific understanding of the weight of the evidence for each risk factor (biological, behavioral, physical/chemical, and social) for one or more health outcomes relevant to EJ communities.

Focus Area 4: Expanding Education, Outreach and Knowledge Transfer

The 2024-2027 LRI Research Strategy will continue to design and implement a proactive education program to help ACC members and ACC panels understand the application of NAMs and other new tools in support of their needs for chemical safety evaluations under TSCA and product stewardship.

The ACC LRI research program will:

- Continue (and consider expanding) the New Approach Methodologies (NAMs) 101 – survey course for ACC members and staff.
- Develop webinars and training on the tools, approaches and workflows needed to develop scientifically robust chemical categories for category-based safety evaluations.
- Develop and present webinars for ACC members on case examples using Read-Across, Threshold of Toxicological Concern (TTC), and other computational and bioactivity NAMs to fill data needs for new and existing chemicals.

Focus Area 5: Enhancing Stakeholder's Understanding of the ACC LRI Program

The ACC LRI program embodies ACC member's commitment to putting science at the forefront of improving chemical safety assessments that are protective of public health and the environment. Industry's dedication to innovation in developing and applying the best available scientific methods to product stewardship and regulatory decision making is the reason ACC members invest in the LRI. LRI's principles of transparency, full principal investigator (PI) independence, and public dissemination of all research studies are the foundation for the integrity and credibility of LRI funded research. At the same time, it can be challenging to communicate the value and importance of the work of the LRI to broader stakeholders inside and outside ACC member companies due to the highly technical nature and time horizons of the LRI research projects. This research plan includes activities to improve communicating LRI research (and the impacts of this research) to ACC members and other stakeholders.

The ACC LRI research program will:

- Continue with, and enhance, the publicly available ACC LRI research catalog of peer reviewed journal publications of LRI supported research projects.
- Increase internal and external awareness of ACC's research through platforms such as ACC Science and Research Highlights, research progress webinars (for regulatory science communities, including United States Environmental Protection Agency and academic programs), and presentations of LRI supported research at scientific conferences.
- Partner with the ACC Communications Department to develop a pilot communications program in 2024-2025 aimed at increasing the awareness of the ACC LRI and LRI's activities and scientific contributions with a select set of stakeholders.

Focus Area 6: Leading the ICCA LRI to Advance Innovative Risk-Based Science Globally

Around the world, the chemical industry currently faces multiple challenges. Sound science is essential for addressing these challenges and for providing the basis for decision making about chemical safety and innovation. The LRI is a global program implemented through three International Council of Chemical Associations (ICCA) member organizations – the European Chemical Industry Council (Cefic), the American Chemistry Council (ACC), and the Japan Chemical Industry Association (JCIA). Through the ICCA, these regional LRI research programs support complementary areas of research that target the science-policy interface to improve chemical safety and reduce uncertainty in risk evaluations.

The ACC LRI research program will:

- Continue to lead and coordinate the regional LRI programs through chairing the ICCA LRI Planning Group. Coordination of the three LRI programs and development of complimentary research projects is emphasized. This is accomplished through proactive review of each program's new research strategies and new research concept papers to identify opportunities to collaborate or leverage across LRI programs on areas of mutual interest.

- Leverage the three LRI Program's NAMs activities by initiating and conducting ICCA LRI international conferences focused on key risk science areas.

A. Introduction: Addressing Challenges Faced by the Chemical Industry

The ACC LRI program is industry's investment in research that affirms its commitment to determine the safety of its products and supports responsible product stewardship. The LRI research program advances chemical safety assessment through innovative approaches and methodologies for evaluating chemicals and products. ACC member companies can apply these new approaches and methodologies as part of their own efforts to address issues in hazard, exposure, and risk assessment for their products and to meet the public demands for product safety information. The scientific research supported by, and advanced through, the ACC LRI program has global relevance.

LRI strives to forge collaborations among industry, governmental and regulatory agencies, and academia. In doing so, LRI works to develop effective partnerships that provide collective voices across the regulatory science community for improvements to science-informed decision making. These collaborations have facilitated acceptance of LRI outcomes in the regulatory science community, in TSCA modernization, and are influencing chemical safety assessments today.

The research supported by the LRI is directly relevant to chemical risk management and science policy advocacy initiatives within the ACC. This specifically includes addressing some of the most significant challenges for improving the implementation of the modernized TSCA, such as the need to improve exposure modeling to enable more accurate risk-based decision making for both new and existing chemicals, and the need for tiered, scientifically solid, risk-based testing and assessment technologies to rapidly and efficiently fill data needs to reduce or eliminate unnecessary testing in laboratory animals.

ACC advocates for a risk-based, holistic approach to sustainability. While such risk-based decision making requires integrating hazard information with exposure information, for new chemistries, or potential substitutes for an existing substance, traditional approaches to testing for potential hazards would be too time consuming and costly. Further, these traditional animal studies may have issues of human relevance and may not fully reflect current toxicological knowledge. LRI activities to catalyze advances in exposure prediction modeling, NAMs, and *in vitro* to *in vivo* extrapolation can play a central role in product innovation and sustainability - these tools can enable side by side risk-based comparisons to be made within life cycle and sustainability analyses.

Corporate social responsibility programs in ACC, and in ACC members' companies, continue to evolve and grow to address stakeholders' expectations and ACC has committed to engaging with communities and creating a cleaner, safer, and more sustainable future. In addition to advancing Responsible Care®, through the LRI and efforts with the Foundation for Chemistry Research and Initiatives (FCRI), ACC continues to invest in science, research, and education relevant to communities. ACC's collaboration with FCRI provided a grant to Harris County (Texas) to purchase air monitoring equipment to enhance their local community air monitoring program. This is one such example of community focused actions by ACC. LRI's research to identify key components of successful public private partnerships will help improve community environmental monitoring programs. Similarly, LRI's research

to improve the scientific basis of environmental justice community cumulative impact assessments will help to support engagement by ACC and ACC members with local communities, regulators, and policymakers to continue to develop and share accurate environmental and human health risk information.

The risk-based methods developed through LRI research can be applied by specific panels in ACC's Chemical Product and Technology Division (CPTD) and the Plastics Division, and in ACC's Sustainability Program. In each of these areas, the need for high quality and reliable exposure modeling tools and approaches is paramount to ensuring that risk which accounts for differences in potency and exposure among chemicals, and not hazard alone, is the basis for decision-making about chemicals, whether by regulators, retailers, or the public. In addition, each of these programs face the challenge of understanding and communicating in a risk context the deluge of "hazard and effects" data from new approach methods (NAMs), such as high throughput screening, transcriptomics, and in silico prediction models. In the months and years ahead, ACC members and CPTD panels will likely find themselves in a position of needing more up-to-date hazard and exposure information to support risk-based decision making in TSCA and for product stewardship. The LRI research projects outlined in this generate LRI Strategy 2024-2027 are designed to meet many of these needs.

Current challenges to be addressed in the LRI program via the 2024-2027 strategy include:

- The need for publicly available exposure information (e.g., modeled estimates) for conditions of use, including exposures to workers, consumers, sensitive subpopulations, and fence line communities.
- The increase in public demand for safe products, and insistence by some groups to rely solely on hazard data for decision making.
- The need for scientifically sound methods to conduct risk-based prioritization of the 20,000 – 30,000 chemicals on the existing TSCA inventory to permit United States Environmental Protection Agency (US EPA) to more rapidly identify low risk substances for which comprehensive risk evaluations are not warranted currently.
- The importance of developing and applying tiered risk-based evaluation approaches in TSCA that use NAMs (in place of, or to more appropriately apply, traditional animal toxicity tests), for both human health and ecological effects.
- The need for scientific tools to enable integration of biological activity data with exposure information at each decision node within a tiered testing and assessment framework to support advanced risk-based decision making.
- The requirement to establish scientific confidence in new approach methods for intended applications and decision contexts of use for application to chemical safety assessment.
- The need to improve design, conduct, and communication of community exposure assessments.
- The challenge of improving the scientific basis of cumulative impact assessments for evaluating both chemical and non-chemical stressors in communities.

- The need to help ACC panels and members keep up with the rapid pace of development of NAMs and exposure science tools.

The LRI Research Strategy 2024-2027 was developed by the ACC's LRI SST, which provides oversight and direction for the program. The LRI SST is comprised of senior scientists and science managers from ACC member companies as well as from outside of industry. The SST's deliberations to develop the LRI Research Strategy 2024-2027 were informed by review of research plans and strategies from US EPA and other organizations. Presentations and discussions with ACC staff from the Chemical Product and Technology Division and the Plastics Division; the Sustainability Program; and the Regulatory and Scientific Affairs Department as well as LRI investigators helped to provide valuable insight. The SST is responsible for managing the LRI and for implementing the research strategy.

B. Research to Support Science Policy Advocacy Success

The LRI Research Strategy 2024-2027 integrates research areas that focus on developing solutions for the challenges facing the chemical industry. The LRI program will help to demonstrate the industry's value as a constructive partner for providing credible scientific research that focuses on solutions. LRI plays an important contributing role and makes a difference in the development and implementation of new technologies for chemical safety assessment. The following principles are the basis of the LRI program and ensure that LRI funded research meets the highest quality standards:

- **Scientific Excellence:** The best research proposals and most-qualified scientists will be selected for funding.
- **Transparency:** Research will be conducted openly, and the results will be publicly available.
- **Fair and Unbiased Conduct**: Potential conflicts of interest will be rigorously evaluated.
- **Relevance to the Chemical Industry**: Research will address the potential health and environmental impacts of chemicals.

The LRI model for success is depicted in Figure 1. The goal is to provide timely and relevant research that can be translated into policies and practices for product stewardship and regulatory decision making. In developing and carrying out the 2024-2027 LRI Research Strategy, the LRI will:

- Leverage ACC research funds and research uptake through strategic collaborations.
- Optimize use of financial and scientific resources for research in key areas of mutual interest for chemical safety assessment with governmental agencies.
- Foster transparency of information related to methods development and data generation.

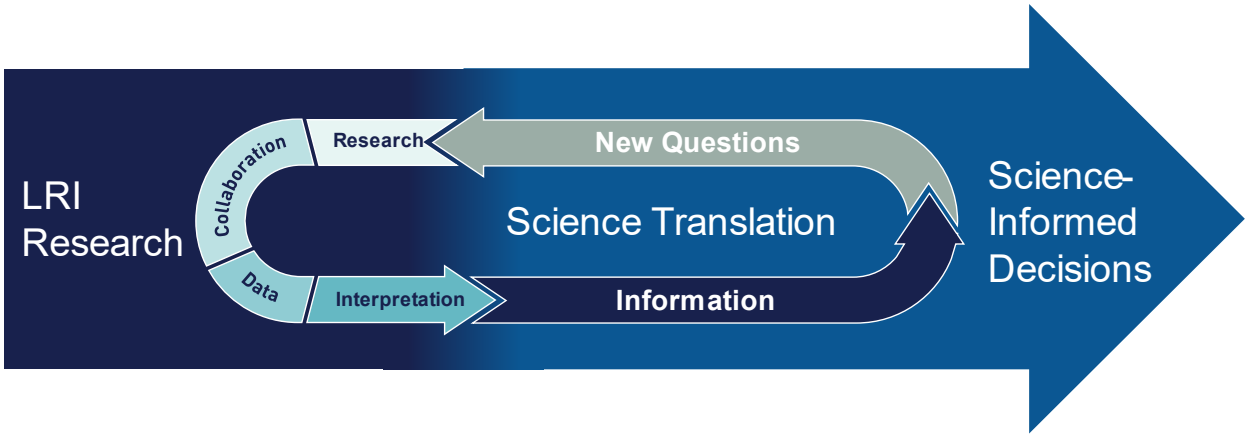


Figure 1. The LRI Model: Science to Inform Policy

In 1999, when the ACC LRI program was initiated, the LRI partnered with the Chemical Industry Institute of Technology (CIIT), which conducted the vast majority of LRI research on behalf of ACC. CIIT transitioned to the Hamner Institute, which then was subsequently acquired by ScitoVation, a for-profit research organization. The 2019 review of the ACC LRI program concluded that, over the course of the ensuing 4 years, LRI should work to rebalance its research portfolio, and LRI has substantially implemented this recommendation. By the end of 2023, all ScitoVation LRI research projects have been successfully completed, with the exception that a few scientific research papers are slated to be submitted and published in the first part of 2024.

Going forward, the LRI 2024-2027 Research Strategy is designed to further actualize these objectives by 1) broadening engagement with scientists from other institutions, 2) working to foster greater collaboration of LRI researchers with government scientific projects, and 3) expanding access of LRI to individuals and institutions who possess the high degree of expertise and scientific creativity needed to address the complex challenges faced in modernizing chemical safety evaluations.

C. The Six Focus Areas of the 2024-2027 LRI Research Strategy

The LRI Research Strategy 2024-2027 outlines a 4-year agenda that complements ACC's advocacy priorities, particularly those focused on strengthening the science needed for improving the implementation of TSCA and those focused on understanding and communicating chemical and non-chemical stressors in disadvantaged communities.

1. Accelerating Exposure Science for Product Stewardship, Sustainability and Regulatory Decision-Making

The absence of exposure data is a significant obstacle that limits the ability to conduct risk-based prioritizations, make risk-based decisions for new chemicals, and develop accurate in-depth risk assessments for workers, consumers, sensitive subpopulations, and fence line communities. In the absence of exposure information and tiered exposure modeling, worst case exposure assumptions in chemical regulatory programs such as TSCA are likely to be used which potentially leads to overestimates of risks.

To overcome such limitations requires development, demonstration and uptake of scientifically sound and reliable exposure tools that support tiered approaches, appropriately address workers, consumers, sensitive subpopulations, communities, and ecological receptors.

A key focus of the LRI Research Strategy 2024-2027 is on supporting the Exposure and Safety Estimate (EAS-E) Suite Platform for Exposure Modeling. The EAS-E Suite project is focused on developing and disseminating exposure tools for simulating (i) chemical emissions throughout their life-cycle; (ii) chemical fate and transport and persistence in natural and manufactured (e.g., indoor) environments; (iii) toxicokinetics in humans, rodents, and ecological receptors as well as *in vitro* bioassays; (iv) exposures and bioaccumulation to a broad range of organisms, including humans. This platform is used by Canadian regulatory agencies and has the interest of US and EU regulators. Predictions from the platform's tools are included in the US EPA SEEM -3 high throughput exposure assessment approach.

EAS-E Suite is a free, user-friendly online platform of new and existing data and exposure models. Over the last 4 years, the development of EAS-E Suite has been supported, in part by funding from the ACC LRI. This platform includes curated databases, OECD validated QSARs, and environmental fate and exposure models to aid chemical assessments for ecological and human health evaluations. These tools and methods can also be deployed in sustainability studies. The EAS-E Suite platform includes numerous models from US EPA, and other organizations, including:

- US EPA's OPERA QSAR models for chemical properties and half-lives
- Dermal exposure models: the "AIHA IH-SkinPerm" model, the US EPA CEM, and the ECETOC TRA consumer & worker models, and the EAS-E model
- US EPA-ORD's High-Throughput Toxicokinetc (HTTK) model and the EAS-E HTTK

The platform also includes models more current than existing regulatory tools, such as the updated Bioaccumulation Assessment Tool (BAT) (developed under the Cefic LRI program), and PROTEX-HT which enables life cycle exposure predictions based upon a substance's structure, function, and production volume.

The range of models present in the EAS-E Suite platform supports human and ecological exposure assessment throughout a substance's life cycle. A very useful aspect of the platform is its inclusion of an extensive curated database of physical chemical properties; these properties are the basis for many exposure model predictions. A user can assess the range of measured and modeled physical-chemical property values for a substance of interest.

The vision for EAS-E Suite is to continue to grow and evolve to be able to provide users the ability to readily access and run both regulatory agency exposure models as well as other equivalent or better exposure models, to enable side-by-side comparisons of results. In addition, the EAS-E Suite platform can be expanded to include tiered exposure models, to support tiered risk-based assessments for chemical regulatory programs as well as for product stewardship and sustainability uses by industry. Exposure models that will be considered for addition to EAS-E Suite may include PACEM (aggregate model), ConsExpo, Chemsteer, and EFAST.

Additional LRI exposure science projects will focus on exposure model verification and expansion. For example, a pilot project is currently in progress to collect empirical exposure data for specific conditions of use by using robots simulating human activities using chemical products in exposure chambers. The aim is to use this data for model verification and potentially model improvement or expansion, if applicable. This project is using the emerging capabilities of robotics technology to better understand exposure potential during paint use. If this research proves promising, it could allow for better understanding and predicting more accurate human exposures for a number of chemical products and their specific conditions of use.

Other innovative areas in exposure prediction include US EPA-developed Quantitative Structure Use Relationships (QSUR), in which molecular structure and physical-chemical properties are used to predict the function of a substance. This predicted function can then be used to develop other important exposure parameters, such as presence and weight fraction in product categories. A number of potential research areas to improve and/or expand QSUR predictive capabilities emerged from the 2022 ACC LRI sponsored QSUR Summit. Potential areas include further development of frame formulations which can assist in refining weight fraction upper bounds, and case studies evaluating QSUR performance, possibly utilizing the EAS-E Suite Platform. QSUR -predicted functions are useful for chemical screening and are included in tools found in EAS-E Suite and in the SEEM-3 suite of tools.

Exposure Science

Focus Area 1
Research Objectives

- Develop and improve predictive models for generating exposure estimates. Exposure estimates can be used for developing a practical and useful tiered framework for:
  - risk-based prioritization of 20,000 – 30,000 chemicals under TSCA to permit low risk substances to be rapidly de-prioritized; and
  - integration of exposure modeling estimates with NAMs to enable risk-based integrated testing and assessment approaches; and
  - tiered predictive exposure modeling for substances with limited data for use in screening and refined assessments for new chemicals and for sustainability evaluations; and
  - more accurate exposure estimates for in depth safety evaluations of high priority substances under TSCA (for workers, consumers, sensitive subpopulations, communities, and ecological receptors).
- Develop case studies, with input from expert stakeholders (e.g., US EPA, OSHA, industry, etc.), that demonstrate the application of the EAS-E Suite Platform for Exposure Modeling, or other advanced exposure modeling tools, to calculate estimated exposures to workers, consumers, sensitive subpopulations, and fence line communities.
  - These case studies will exemplify the use of EAS-E Suite and other advanced exposure modeling tools for product stewardship and regulatory decision making and form the basis of education and outreach webinars and training sessions. The outreach and training sessions will include ACC members, regulatory agency scientists, and others in the regulatory science community.

Exposure Science

Focus Area 1
Value to Chemical Industry

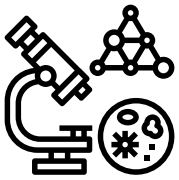
- LRI research can verify and refine exposure models that can be used to produce more accurate exposure estimates for TSCA and product stewardship assessments of the potential health and environmental risks from chemicals that are the basis for concerns about industry's products, both for new and existing chemicals.
- LRI applications of tiered predictive exposure models support efficient and cost-effective generation of exposure estimates for workers, consumers, subpopulations, and environmental receptors for TSCA with sufficient precision to support prioritization and safety decisions and decrease the likelihood of premature decisions about chemical substances based on hazard data alone. This information is relevant to regulatory determinations, marketplace product defense, and company product stewardship and research efforts.
- Exposure science research can accelerate risk-based evaluation of alternative chemicals and green chemistry products by more rapidly identifying those new chemical products and processes that meet safety criteria and support sustainable chemical products design. The EAS-E Suite platform incorporates the ability to predict physical chemical properties and a range of exposures based upon chemical structure, enabling rapid screening level assessments of new chemicals that fall within its predictive domain.

The ACC LRI 2024-2027 exposure science research project areas are summarized in Table 1. The objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI SST. Each project is monitored by a Project Monitoring Team (PMT), comprised of ACC LRI SST members, and where warranted, additional subject matter experts (typically drawn from ACC member companies). Projects are fully evaluated by the full SST membership at least once per year, and adjustments in scope are made accordingly.

Table 1. Accelerating Exposure Science for Product Stewardship, Sustainability and Regulatory Decision-Making

Research Project	2024	2025	2026	2027
ES 1. Expand and improve the EAS-E Suite platform for exposure modeling (complete Phases I&II)				
ES 2. Initiate new exposure science research projects: A. Strategic review of exposure science opportunities by the SST, the SST Exposure Science Sub team and ACC's Exposure Work Group to ensure LRI exposure projects are focused on high priorities and sufficiently diversified B. Initiate new exposure science research projects (e.g., expand and improve the EAS-E Suite Platform to include other EPA models, models, community and fence line models, etc.)				
ES 3. Convene an Expert Stakeholder Science Group to provide input on, and review of, case studies and other aspects of advanced exposure models, e.g., EAS-E Suite, to address product stewardship regulatory needs				
ES 4. Develop case studies applying EAS-E Suite or other advanced exposure models focused on regulatory, product stewardship and sustainability applications as well as education/ outreach/ training				
ES 5. Complete the pilot experiment using a robot to apply a chemical product to obtain real time measurement data to verify exposure models. Then evaluate potential future applications of robotic technologies for exposure model verification				
ES 6. Collaborative research on fate, transport, exposures, risks etc. of microplastics				
ES 7. Review of LRI's exposure science research program SST, the SST Exposure Science Sub team and ACC's Exposure Work Group to e to develop recommendations for future exposure science research				RfP Development

Note: green (■) indicates planning, blue (■) indicates implementation, and gray (■) indicates potential activities.



2. Advancing New Approach Methods (NAMs) for Application in Risk Assessment through Development of Scientific Confidence

The LRI 2024-2027 Research Strategy is designed to advance the development of tiered, risk-based methods and approaches to be used to address relevant toxicity and exposure information needs focused on an individual chemical or a chemical group. This research is intended to provide scientifically sound and credible information in a timely and targeted manner to inform chemical risk management decisions by developing and building confidence in hypothesis-based integrated approaches for tiered testing and assessments in lieu of traditional empirical animal toxicity data.

The development of NAMs to evaluate the biological activity of chemicals is rapidly advancing. TSCA now requires use of such methods in lieu of traditional animal toxicity tests when they can provide information of equivalent or better scientific quality and relevance for assessing risks under TSCA.

US EPA is also required to implement a strategic plan to develop and integrate NAMs into decision making under TSCA. This effort includes the New Chemicals Collaborative Research Program, initiated in 2023 by the TSCA Program and ORD, to accelerate the development and uptake of NAMs within TSCA's New Chemicals division. In addition, US EPA's Agency-wide NAMs Work Plan appropriately focuses on, among other things, the need to develop and implement a Scientific Confidence Framework to evaluate the quality, reliability, and relevance of NAMs for specific applications. This framework may be available in 2024.

To cover the biological space represented in traditional lab animal tests, a suite or battery of NAMs linked to one another to emulate an *in vivo* biological pathway (or pathways), such as an Adverse Outcome Pathway (AOP), are often proposed. Accordingly, the LRI Research Strategy 2024-2027 seeks to support collaborative work to actualize and illustrate the use of NAMs (*in silico*, *in vitro*) in a tiered testing and risk-based integrated approaches to testing and assessment (IATA) framework.

The modernized TSCA gives US EPA authority to require toxicity testing by simply issuing test orders directly to manufacturers. This is a more rapid procedure than in the past when US EPA had to issue a formal test rule. For chemicals with sparse toxicity data and for complex substances (UVCBs), US EPA's initial evaluation will likely reveal gaps in traditional animal toxicity data sets. When it's determined that there's a need for additional toxicity data (e.g., when US EPA is contemplating issuing testing orders under the new TSCA), integrated approaches for tiered testing and assessments should be available to be used by ACC members in lieu of traditional animal toxicity tests for human health and ecological safety evaluations. Such an approach needs to 1) be tiered and fit for purpose (align with the decision context), 2) begin with least costly, less complex in silico methods and proceed, if warranted, to more complex tests and models 3) use NAMs that provide scientifically relevant data for the decision to be made and the degree of confidence needed for that decision; and 4) integrate knowledge of exposure at each tier to enable a risk-based determination to be made as to whether the margin of exposure is sufficiently large to support stopping at that tier, or if the next level of testing is warranted. It is important to illustrate how pivotal exposure knowledge/modeling is in this tiered and risk-based

approach and how an acceptable margin of exposure can occur at lower tiers without always advancing to higher tiers of testing.

Matching these new tools and methods up to the specific decision contexts (e.g., candidate selection, risk-based prioritization, screening level risk assessments, in-depth and refine risk evaluations) and demonstrating the scientific confidence needed for different decision contexts are critical needs. Hence, LRI research will include developing and demonstrating proof-of-concept applications and procedures to actualize a flexible Scientific Confidence Framework (SCF) for fit-for-purpose (FFP) "validation" of NAMs. Once sufficient confidence is established for the application of NAMs in different decision contexts, the appropriate NAMs can be applied to generate more rapid, cost effective and less animal intensive data for various applications including priority setting, screening, and filling relevant data needs. This research will focus on developing and demonstrating hypothesis-based integrated approaches for tiered testing and assessment, with knowledge of exposure being integrated at each tier to enable risk-based determinations with stopping points at each tier (Figure 2).

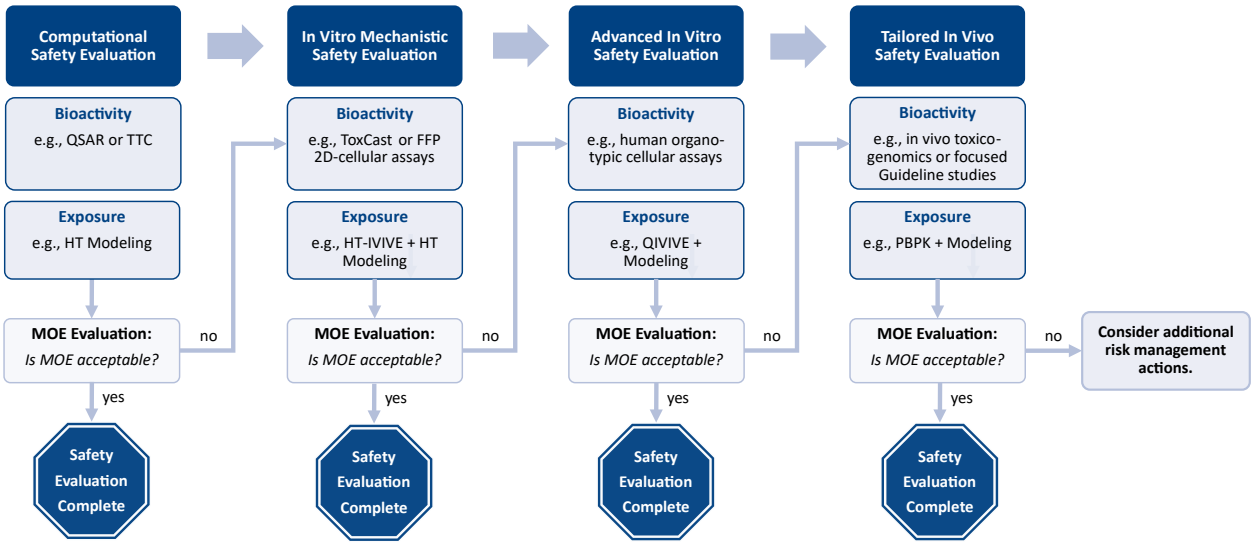


Figure 2. Tiered, risk-based approach to integrated testing for chemical safety evaluations (adapted from *Andersen et al., 2019*)

New Methods

Focus Area 2
Research Objectives

- Provide research funding to scientists/scientific institutions with the requisite degree of expertise and scientific creativity needed to address the complex challenges faced in modernizing chemical safety evaluation.
  - Focus on developing and demonstrating hypothesis-based integrated approaches for tiered testing and assessment, with knowledge of exposure being integrated at each tier to enable risk-based determinations with stopping points at each tier (see Figure 2).
  - For the commodity chemical and consumer chemical sectors, there is a pressing need to develop alternative models to replace biologically complex apical endpoints in laboratory animal studies for effects such as repeat dose systemic toxicity and development / reproductive toxicities.
- Extend the development (and evaluation) of approaches that use organotypic respiratory tract cell-based assays and high content endpoints to generate dose-response data for deriving points of departure that can be used with *in vitro* to *in vivo* extrapolation modeling to enable risk-based decision making. Such an integrated approach to testing and assessment would be used in lieu of conducting traditional inhalation toxicity tests in lab animals. Expanding this current research that has mainly focused on gases/vapors to address aerosols and particulates.
- Explore areas for future collaborative research to improve Read-Across methods, including US EPA's GenRA. Initiate collaborations to address one or more of the priority research areas identified in the QSUR Summit.
- Catalyze collaborations, and support the development of case examples, applying the Scientific Confidence Framework principles to NAMs for both hazard and exposure) and for the types of decisions and the confidence needed (e.g., risk-based prioritization of existing chemicals, or filling a toxicity endpoint data need, or developing a risk-based rationale for a test order waiver).

New Methods

Focus Area 2
Value to Chemical Industry

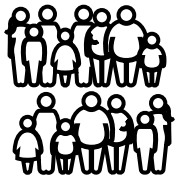
- Innovations in IATAs will expedite new product development, sustainable design of new materials, and development of new chemical solutions by shortening testing times and increasing cost efficiencies.
- LRI research of organotypic respiratory tract cell-based assays and high content endpoints will be a key resource for ACC companies and US EPA to address potential requirements under the TSCA for chemicals where respiratory tract effects are of interest. This research will also be an important resource for other regulatory authorities (e.g., Health Canada, ECHA, etc.) and OECD.
- Application of the Scientific Confidence Framework principles will provide trust in the application of these NAMs to generate more rapid, relevant, predictive, cost effective (and less animal intensive) data and information for chemical safety determinations.
- Collaborations to advance the next generation of sophisticated NAMs (e.g., human organs on a chip to simulate a response of an organ, use of points of departures based on transcriptomics) will help to elucidate the utility of these assays, explore strengths and limitations of such approaches, and document the scientific confidence for specific uses in regulatory and product stewardship decision making.

The ACC LRI 2024-2027 advancing risk assessment science project areas are summarized in Table 2. The objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI Strategic Science Team (SST). Each project is monitored by a Project Monitoring Team (PMT), comprised of ACC LRI SST members, and where warranted, additional subject matter experts (preferably drawn from ACC member companies). Projects are fully evaluated by the SST at least once per year, and adjustments in scope are made accordingly.

Table 2. Advancing New Approach Methods (NAMs) for Application in Risk Assessment through Development of Scientific Confidence

Research Project	2024	2025	2026	2027
RA 1. Research grant for development and demonstration of hypothesis-based integrated approaches for tiered testing and risk assessment using NAMs (multi-year grant focusing on complex challenges faced in modernizing chemical safety evaluation)	RfP			
RA 2. Extend the organotypic respiratory tract assays/ IATA to aerosols and particulates				
RA 3. NAMs for ecological risk assessment: strategic review of needs for ecological risk assessment NAMs by the SST and ACC Ecotoxicology workgroup. Then development of RfP and initiation of research project(s)	RfP	Potential launch of new project(s)		
RA 4. Plan and convene the Read-Across Summit of invited expert meeting to identify areas for future collaborative research – to be followed by initiation of research project(s)			Organize and host the Summit; publish results	Consider and initiate research project(s) to address Summit recommendations
RA 5. Support advanced approaches to safety assessments (with annual -or more frequent- updates to LRI SST) 1. HESI-OASIS consortium (phenomics, transcriptomics, and proteomics) 2. Tex-Val Tissue Chip Consortium (human tissue chips)				
RA 6. Explore the potential to develop a program for awarding an annual "Innovative Young Investigator Award" to acknowledge and support risk-based NAMs research	Design of procedures and adoption of annual schedule – then open for submissions	Potential launch and implementation		
RA 7. Develop case studies (collaborations) applying Scientific Confidence Framework principles to NAMs	RfP			
RA 8. Review of LRI's Risk Assessment Research Program by the SST to Develop Recommendations for Future Risk Assessment Science Research				RfP development

Note: green (■) indicates planning, blue (■) indicates implementation, and gray (■) indicates potential activities.



3. Strengthening Public Health Science Approaches for Evaluating Co-exposures and Cumulative Impacts in Communities

Understanding and addressing the root causes of health inequities in disadvantaged communities is challenging. Community health status can be impacted by socioeconomic and psychological stressors, background health conditions, the physical environment, specific susceptibilities of members of the community, and exposure to local environmental chemical stressors in air, water, soil, etc. For the chemical industry, community concerns around the nexus of health inequities and potential exposures from chemical and industrial facilities are important considerations in permit processes and can impact the broader social license of companies to operate in those communities.

However, evidence-based understanding of the relative contributions of specific health risks associated with experiencing environmental chemical and non-chemical stressors in combination is currently lacking. For this reason, the approaches being used today for evaluating co-exposures to chemical and non-chemical stressors and potential cumulative impacts in communities use primarily qualitative or semi-quantitative indices. These sets of indices have been constructed largely on a foundation of assumptions. But the impact of such assumptions is often lost when such community health impacts are communicated to stakeholders and decision makers. Accordingly, the LRI Research Strategy 2024-2027 will include projects to strengthen public health science approaches for evaluating and communicating co-exposures and cumulative impacts in communities, as summarized below.

As technologies advance, community exposure monitoring and modeling approaches have emerged as key components of community impact assessments. As key stakeholders in these communities, chemical industry facilities (and the broader manufacturing sector) can have the opportunity to constructively participate in scientifically sound fence line and community monitoring programs. To this end, the LRI Strategy includes 1) development of a comprehensive set of key principles and elements to enable successful future Public-Private Partnerships (PPPs) for environmental monitoring programs, and 2) education and outreach activities at scientific conferences to reach academics and explore strategic partnership opportunities for translating PPP principles into actual practice (such as development of a pilot web-based infrastructure).

It is also important to recognize the growing emphasis on Citizen Science initiatives – which are now often referred to as Participatory Science initiatives. US EPA and a number of other federal agencies are funding participatory science initiatives (e.g., NIEHS, NSF, NOAA, USGS and NASA).[1,2] In addition to these government initiatives, the Association for Advancing Participatory Sciences focuses on "advancing knowledge through research and monitoring done by, for, and with members of the public." This society has its own journal, "Citizen Science: Theory and Practice," and hosts conferences and webinars. LRI will explore

[1] https://citizenscience.org/home/events/webinars/ - A Conversation on the Federal Funding Landscape for Citizen Science and NIEHS provided examples of the impacts of these programs, including a community air monitoring network that led to California State legislation AB 617 (https://community.valleyair.org/#:~:text=What%20is%20AB%20617%3F,pollution%20exposure%20in%20disadvantaged%20communities).

[2] US EPA has developed guidance documents and toolkits and is currently establishing technical assistance programs across the US – see https://www.epa.gov/participatory-science

opportunities to catalyze participation of LRI researchers to communicate the application of PPP principles within the citizen science sector.

Scientific understanding of the relative contributions that different determinants of health have on specific health impacts and disease causation is often limited. Nevertheless, community impact assessments are proceeding; these can include multiple exposure pathways across media, impacts across multiple chemical and non-chemical stressors, and multiple sources of stressors from the built, natural, and social environments. It's axiomatic that unless the major contributors of health impacts are addressed, actions taken on lesser or perceived contributors would have substantially less, or maybe even no, measurable effect on improving health. Stated differently, actions focused on ameliorating a set of overstated putative risk factors would be expected to have little likelihood of successfully improving community health. The current LRI project focused on understanding the scientific bases, strengths, and limitations of EJ assessment methodologies is expected to identify both short-term and long-term research areas that the LRI SST may elect to consider for future LRI projects.

The LRI will explore initiation of a pilot project to develop qualitative approaches that can display and communicate the data quality and putative causal understanding of the relative contributions of the four intersecting determinants of health — biological, behavioral, environmental (chemical and physical), and social — make to a health impact/disease outcome of concern in EJ communities. Following the pilot, if the SST determines it is feasible, the LRI will explore developing an RfP for one or more public health academic groups (e.g., at, or in collaboration with, historically black colleges and universities public health program) to review and refine the pilot approach and then conduct case examples for one or more health outcomes relevant to EJ community assessments.

There is recognition that chemical exposures do not occur in isolation, and exposure to multiple chemicals is more reflective of environmental and human exposures. Such exposures are from the natural constituents of foods, air, and water, as well as the chemicals encountered in our environment from products used in the home and workplaces, from pollutants in the air, and trace contaminants in drinking water and foods. These cumulative exposures have typically been dealt with in risk assessment and public health evaluations using tiered approaches – approaches that have been designed to account for toxicity thresholds and health guidance values of individual substances alone and in combination. Theoretically, effects to such combined exposure to chemicals can be independent, additive, antagonistic, or synergistic. Recently, the European Commission has introduced requirements to address the issue of unintentional exposures to "mixtures" of different chemicals in the environment by requiring the use of a "Mixture Assessment Factor" – essentially an additional, precautionary safety factor – that would be applied to all chemical risk assessments to lower the permitted levels of exposures to substances in such unintended mixtures. From a public health perspective, overly broad applications of the precautionary principle may seem at first to be beneficial. However, the unintended consequences of such a broad approach could result in unnecessary regulations, impact many beneficial uses of substances, and spend scarce resources towards addressing such perceived risks.

In late 2023, the LRI initiated a research project to investigate if dose addition, independent action, synergism, or antagonism are the primary drivers for chemicals that are unintentionally co-occurring. This project will address the mechanism of action and mixture behavior of individual chemicals (that are common to both human and environmental biomonitoring) within and eventually across chemical subclasses using the embryonic zebrafish assay. The embryonic zebrafish assay is a cost and time effective NAM which is widely recognized as a good screening model of developmental toxicity given that many genes and critical pathways are highly conserved between humans and zebrafish. This project will be completed in 2024 and, based on the results, the LRI SST will review options for follow up or additional studies. As artificial intelligence methods advance and are applied to data mining and analysis, and as exposure data sets continue to develop, future opportunities to better identify factors associated with the subset of co-exposures in which traditional single-chemical assessment approaches may need to be pursued or augmented.

Public Health

Focus Area 3
Research Objectives

- Complete the LRI research project "Creating and Sustaining Successful Public-Private Partnerships (PPPs) for Environmental Monitoring Programs: Principles and Elements" in 2024. Then conduct education and outreach efforts to communicate the research results to stakeholders in industry, communities, government, and NGO sectors. Seek opportunities to catalyze uptake and application of the key elements of successful PPPs into new environmental exposure PPPs.
- Complete the LRI research project "A Comprehensive Review and Appraisal of Frameworks, Methods, Metrics, and Data Used in Assessments of Communities with Environmental Justice Concerns" in 2024. Then identify research areas that the LRI SST may elect to consider for future LRI projects.
- Explore initiation of a pilot project to develop qualitative approaches that can display and communicate the data quality and putative causal understanding of the relative contributions of the four intersecting determinants of health —biological, behavioral, environmental (chemical and physical), and social — make to a health impact / disease outcome of concern in EJ communities. Following the pilot, if the SST determines it is feasible, the LRI will explore developing an RfP for one or more public health academic groups (at, or in collaboration with, a HBCU public health program) to review and refine the pilot approach and then conduct case examples for one or more health outcomes relevant to EJ community assessments.

Public Health

Focus Area 3
Value to Chemical Industry

- Public perception of industry's operations in communities depends, in part, on dealing with communities' concerns of the potential health impacts of industrial activities in their communities. These LRI research projects will improve:
  - Approaches for design, implementation, and evaluation of community environmental monitoring programs, including public private environmental monitoring partnerships; and
  - Understanding of ways to evaluate and visualize relative contributions that chemical and non-chemical stressors may have on specific health impacts.
- Through a systematic analysis of scientific bases, strengths, and limitations of EJ and community impact assessment methodologies, this LRI research will identify the key future research areas that are most critical to focus on to ensure solid, science-based analyses and decision making.

The ACC LRI 2024-2027 public health science research project areas are summarized in Table 3. The objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI Strategic Science Team (SST). Each project is monitored by a Project Monitoring Team (PMT), comprised of ACC LRI SST members, and where warranted, additional subject matter experts (preferably drawn from ACC member companies). Projects are fully evaluated by the SST at least once per year, and adjustments in scope are made accordingly.

Table 3. Strengthening Public Health Science Approaches for Evaluating Co-exposures and Cumulative Impacts in Communities

Research Project	2024	2025	2026	2027
PH 1. Complete the research project "Creating and Sustaining Successful Public-Private Partnerships (PPPs) for Environmental Monitoring Programs: Principles and Elements"	Outreach			
PH 2. Complete the research project "A Comprehensive Review and Appraisal of Frameworks, Methods, Metrics, and Data Used in Assessments of Communities with Environmental Justice Concerns"	Outreach			
PH 3. Design follow-on projects to PH1 and PH2 – improving the science of community exposure studies – and initiate new projects: to include consideration of citizen science, wearable/hyper local sensors, and interpreting human and environmental biomonitoring		RfP develop-ment		
PH 4. Explore initiation of a pilot project to develop qualitative approaches that can display and communicate quality and putative causal understanding of chemical and non-chemical stressors	Possible RfP	Potential launch of new project		
PH 5. Develop the Artificial Intelligence Research Assistant – Phase 1 - to automate author pre-review and application of critical thinking to causal analyses/claims. Explore testing the tool by peer reviewers of articles submitted to an epidemiological journal				
PH 6. Investigate mechanisms of action and mixture behavior of individual chemicals that are common to both human and environmental biomonitoring within, and eventually across, chemical subclasses using the embryonic zebrafish assay		Potential launch of new project		
PH 7. Review of LRI's Public Health Science research activities to identify future focus areas and review options for follow up or additional studies				RfP development

Note: green (■) indicates planning, blue (■) indicates implementation, and gray (■) indicates potential activities.

4. Expanding Education, Outreach and Knowledge Transfer -- Transferring Knowledge to ACC Members and ACC Panels

Currently, it is very challenging for ACC panels and many member company scientists to keep pace with the rapid advancements in NAMs, as well as understand the strengths, limitations and beneficial applications of new hazard and exposure methods for product stewardship and regulatory decision making. Typically, scientific venues such as professional society meetings do not focus on use of these tools and methods for TSCA applications or product stewardship.

The 2024-2027 LRI Research Strategy will continue to design and implement a proactive education program to help ACC members and ACC panels become proficient in applying NAMs and other new tools in support of their needs for chemical safety evaluations under TSCA and product stewardship. These education and outreach efforts will go well beyond simply presenting webinars. For example, work products may include development of user guidelines, instructional web videos, and hands-on webinar-based training exercises. Consequently, the LRI Research Strategy 2024-2027 includes knowledge transfer activities that will be specifically designed to meet the needs of ACC panels and members to understand these advanced approaches so that they can be applied to address the chemical hazard, exposure, and safety challenges efficiently and effectively they face.

Knowledge Transfer

Focus Area 4
Research Objectives

- Design and implement a proactive education program to help ACC members and ACC panels become proficient in applying NAMs and other new tools in support of their needs for chemical safety evaluations under TSCA and product stewardship.
- Address key knowledge transfer project areas summarized in **Table 4**. The focus areas were selected by the ACC LRI SST with input from the ACC groups. The focus areas are those envisioned to be most important in terms of their readiness for use in TSCA, and product stewardship related to TSCA.
- Develop education and outreach efforts beyond simply presenting webinars. For example, work products may include development of user guidelines, instructional web videos, and hands-on webinar-based training exercises. The ACC LRI has developed and publicly disseminated such approaches for the "Prediction Analytic Toolkit", "How to Use ToxCast Data", "Use of the TTC", etc., and will build from these successes. Again, the objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI SST.

Knowledge Transfer

Focus Area 4
Value to Chemical Industry

- Member companies and panels will be able to better understand these methods, and where applicable, confidently employ these approaches in their product stewardship programs and or regulatory comments or submissions.
- Member companies and panels will also gain knowledge that will be useful to understanding potential misuses or scientifically flawed interpretations of these methods, and thus can document and communicate a scientific rationale why such misrepresentations are inappropriate.

The ACC LRI 2024-2027 expanding education research project areas are summarized in Table 4. The objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI Strategic Science Team (SST). Each project is monitored by a Project Monitoring Team (PMT), comprised of ACC LRI SST members, and where warranted, additional subject matter experts (preferably drawn from ACC member companies). Projects are fully evaluated by the SST at least once per year, and adjustments in scope are made accordingly.

Table 4. Expanding Knowledge Transfer to ACC Members and ACC Panels

Research Project	2024	2025	2026	2027
EDU 1. Continue with the New Approach Methodologies (NAMs) 101 – a survey course for ACC members and staff				
EDU 2. Develop a strategic approach to knowledge transfer to ACC members				
EDU 3. Exposure assessment 1. Determine ACC members need for the Exposure Assessment 101 course, and update course, if needed 2. Present EAS-E Suite case study training webinars and videos				
EDU 4. Develop and present education & outreach and training on chemical category formation				
EDU 5. Develop and present case examples of the use of bioactivity and exposure NAMs to fill data needs for new and existing chemicals				

Note: green (■) indicates planning, blue (■) indicates implementation, and gray (■) indicates potential activities.

5. Outreach to Enhance Stakeholder's Understanding of the ACC LRI Program

The ACC LRI program embodies ACC member's commitment to putting science at the forefront of improving chemical safety assessments. ACC's investment in the LRI for the express purpose of advancing new scientific approaches for increasing the understanding of chemical exposures, hazards and risks clearly shows industry's dedication to innovation in developing and applying the best available scientific methods to product stewardship and regulatory decision making. The LRI principles of transparency, full Principal Investigator (PI) independence, and public dissemination of all research studies, further this mission.

Since its inception, the ACC LRI has focused engagement with, and dissemination of LRI science to, the regulatory science community (industry scientists, government agency scientists, academic researchers, etc.). This focus will continue as part of the LRI 2024-2027 Research Strategy.

Focus Area 5
Research Objectives

- Continue to disseminate research studies through the publication by PIs in the open scientific peer reviewed literature. And LRI will make these publications accessible through the LRI Research Catalog on the LRI public web site.
- Publish ACC Science and Research Highlights (at a pace of approximately once per quarter) to communicate scientific accomplishments of LRI research with ACC members and ACC staff.
- Distribute quarterly research progress reports to SST members that highlight accomplishments of each LRI project during the past quarter and outline upcoming planned research for next quarter.
- Continue to refresh and update LRI's public website, to include, but not limited to, descriptions of current research projects, the ACC Research Catalog, descriptions and links to LRI exposure and risk assessment tools, etc.
- Partner with the ACC Communications Department to develop a pilot communications program in 2024 aimed at increasing the awareness of the ACC LRI and LRI's activities and scientific contributions with a select set of stakeholders. If the pilot project proves successful, the effort will be expanded in 2025 and beyond to reach additional stakeholders.

Focus Area 5
Value to Chemical Industry

- Greater understanding and appreciation that LRI represents ACC members' commitment to invest in the development of scientific methods to improve our understanding of the potential impacts of chemicals on human health and the environment.
- Broader recognition by ACC members and other stakeholders of the specific research projects undertaken by LRI and the impact of these specific research projects in advancing scientific methods and data to create improvements in the efficiency and effectiveness of chemical safety assessments.

The ACC LRI 2024-2027 outreach research project areas are summarized in Table 5. The objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI Strategic Science Team (SST). Each project is monitored by a Project Monitoring Team (PMT), comprised of ACC LRI SST members, and where warranted, additional subject matter experts (preferably drawn from ACC member companies). Projects are fully evaluated by the SST at least once per year, and adjustments in scope are made accordingly.

Table 5. Enhancing Stakeholder's Understanding of the ACC LRI Program

Research Project	2024	2025	2026	2027
OR 1. Continue with LRI's web-based communications to ACC members and the regulatory science community				
OR 2. Design, implement, and then evaluate a pilot to increase awareness LRI with a select set of stakeholders				
OR 3. Evaluate the effectiveness of LRI's outreach efforts and adjust activities as warranted				

Note: green (■) indicates planning, blue (■) indicates implementation, and gray (■) indicates potential activities.

6. Leading the ICCA LRI to Advance Innovative Risk-Based Science Globally

The chemical industry currently faces multiple challenges related to chemical safety evaluation procedures and regulatory decision making around the world. Sound science is essential for addressing these challenges and for providing the basis for decision making about chemical safety and innovation. Through the ICCA, the three LRI programs – the Cefic LRI, the ACC LRI, and the JCIA LRI support complementary areas of research that target the science-policy interface to improve chemical safety evaluation procedures and promote advanced approaches for hazard, exposure, and risk assessments.

Global

Focus Area 6
Research Objectives

Working with our LRI partners, the ICCA-LRI will co-sponsor workshops and conferences with scientific societies, international organizations, and governmental agencies to focus on timely issues of mutual interest to the LRI, co-sponsors groups and to policy makers. The primary goals are to foster interactions among researchers and stakeholders, to stimulate discussions that can improve the scientific basis for policymaking and to support consensus building that can advance the risk assessment process.

- Enhance coordination of the three LRI programs through the ICCA LRI Planning Group by exchanging research strategies to identify opportunities to collaborate across LRI programs on areas of mutual interest to avoid unneeded duplicative projects.
- Leverage the three LRI Program's NAMs activities by initiating and conducting ICCA LRI international conferences focused on key risk science areas.
- Working with the Microplastics Advanced Research and Innovation Initiative (MARII), leverage ICCA-LRI's experience in planning and holding global industry summits to work with MARII broadly examine scientific issues central to enabling risk-based decision making to address the potential for releases of all types of polymer products and their constituents into the environment (air, water, soil, biota) throughout a product's lifecycle.

Global

Focus Area 6
Value to Chemical Industry

- Enhance coordination of the three LRI programs through the ICCA LRI Planning Group by exchanging research strategies and research concept proposals to identify opportunities for potential collaborations across LRI programs will avoid unneeded duplicative projects.
- Global dissemination of the three LRI Programs' research activities demonstrates industry's substantial and sustained commitment to invest in chemical safety science research.

The ACC LRI 2024-2027 global advancement project areas are summarized in Table 6. The objectives, specific activities, milestones, and deliverables for each project will be developed by the ACC LRI Strategic Science Team (SST). Each project is monitored by a Project Monitoring Team (PMT), comprised of ACC LRI SST members, and where warranted, additional subject matter experts (preferably drawn from ACC member companies). Projects are fully evaluated by the SST at least once per year, and adjustments in scope are made accordingly.

Table 6. Leading the ICCA LRI to Advance Innovative Risk-Based Science Globally

Research Project	2024	2025	2026	2027
ICCA LRI 1. Continue to coordinate ICCA LRI activities via the ICCA LRI Planning Group to include exchange of research strategies, collaborations, and ICCA LRI communications (focus on NAMs in 2024)				
ICCA LRI 2. Initiate, design, and conduct ICCA LRI international conferences focused on key risk science challenges				
ICCA LRI 3. Collaborate in development and delivery of communication materials on the 25th Anniversary of the LRI (for audiences such as: 1) public 2) regulatory science stakeholders (industry, academia, reg agencies) focused on chemical safety sciences and 3) chemical industry sector leaders)				
ICCA LRI 4. Explore the opportunity to plan a global industry scientific summit to broadly examine scientific issues central to enabling risk-based decision making to address the potential for releases of polymer products and their constituents into the environment (air, water, soil, biota) throughout a product's lifecycle				

Note: green (■) indicates planning, blue (■) indicates implementation, and gray (■) indicates potential activities.

D. Defining Future Success for the LRI Program

The LRI Research Strategy 2024-2027 focuses on research results that can support many regulatory, science policy advocacy, and product stewardship needs. Figure 3 identifies areas where the ACC LRI program has been designed to be particularly impactful.

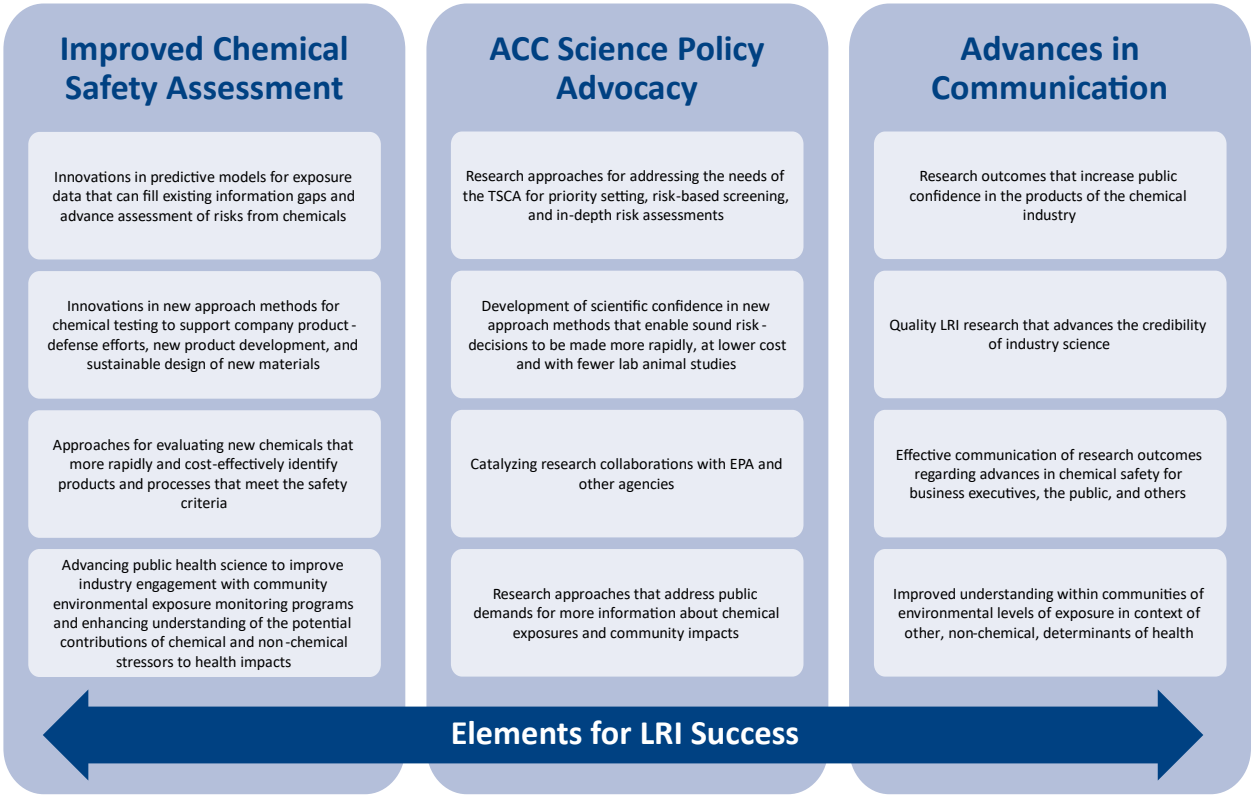


Figure 3. Elements for LRI Success