

# Chemical Pollution and One Health – from Reactivity to Proactivity October 2023

## Testing our way to a safe environment?

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### Background

There are about 140,000 individual synthetic chemicals in commerce worldwide<sup>1</sup>. The relative few that have been evaluated for safety were tested by a system that is known to be both slow, expensive and insensitive to certain kinds of toxicity<sup>2</sup>, despite a consensus on the scientific principles by which chemicals can produce toxicity through endocrine pathways<sup>3</sup>. There are major currently ongoing efforts to update the testing system, to make it more protective of public health and to require the use of fewer animals in toxicity testing.

### Approach

Recognizing that there is no single toxicity test, and that there will not be in the future, we have the obligation to develop toxicity testing strategies in ways that could make the environment safer. These strategies will require a multi-pronged approach, including improved chemical testing strategies, analysis and interpretation of the resulting data, changes to the regulatory system(s) to limit exposures and encourage innovation, and others. Thus, the aim of this workshop was to categorize the different perspectives on strategies for improving chemical testing, as they relate to the goal of a toxic-free future, and to identify obstacles to achieving each of these strategies.

The workshop was introduced by two inspirational speakers, Anne Gourmelon, principal administrator for the test guidelines program at the OECD in Paris, and Professor Laura Vandenberg of the School of Public Health at the University of Massachusetts Amherst. Participants included scientists, chiefly from academia but also from various government agencies and from civil society; they came from 8 countries.

First, the group identified the most important issues that need to be addressed to create a safer environment. The workshop continued with recommendations on how to move forward

with these questions. The four questions identified were:

1. How can regulations be used to create a safer environment?
2. Can New Approach Methodologies (NAMs) enhance toxicity testing?
3. How can conflicts of interest be managed to navigate the scientific landscape?
4. What is the role of the public in improving safety?

### Recommendations

#### Recommendation 1: Tighten the relationship between regulations and the testing strategy.

The system of chemical testing should change fundamentally, from the default – according to which chemicals are innocent until proven guilty – to the opposite. Currently, some applications for new chemicals do not require authorization. Testing new chemicals must necessarily be “agnostic” with respect to hazard, so it is important to define what kinds of toxicity should be tested for. Major systems like ToxCast and Tox21 can play a role here, and a system like that described as the Tiered Protocol for Endocrine Disruption (TiPED)<sup>4</sup> can improve the logic employed in the analysis of test results.

Testing of existing chemicals that have some toxicity data needs to be more hypothesis-directed. This approach can take advantage of the academic community. A recent experiment entitled “The Consortium Linking Academic and Regulatory Insights on Bisphenol A Toxicity (CLARITY-BPA)” supported by the US FDA and the National Institute of Environmental Health Science (NIEHS), represents a prototype in which traditional guideline regulatory studies can be supplemented by collaborating with academic scientists. Bringing independent academic science into the regulatory arena requires that academic scientists be more fully apprised of the data requirements regulators have. Regulatory agencies have been



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employing systematic evidence mapping and reviews that will enhance this relationship – although it is not currently without controversy<sup>6</sup>.

There is currently little to no incentive structure to support academic scientists in their effort to inform risk assessments with “discovery science” approaches to identifying chemical hazards and risks. This needs to change, so that public funds are employed to link more directly to public health improvement.

**Recommendation 2: New Approach Methodologies (NAMs) need to be more fully developed along with improved interpretation.**

In principle, NAMs include tests at all levels of organization, from in silico modeling through biochemical and cell-based assays to the use of complex tissue models and novel endpoints (e.g., genomics) in animal testing. It is important to focus on assays where the data can be most directly applied to human and/or animal risk, i.e., focus NAM development where animals are poor predictors of human endpoints.

Data from NAMs need to be used for regulatory purposes. This will require an increased understanding of the relevance of specific endpoints (the endpoint measured by a test such

as an enzyme or hormone receptor) and human and wildlife health.

Although there is a consensus on reducing animal testing, there is also recognition that non-animal NAMs, or other non-animal tests, are not ready to replace animal testing completely.

Given that current testing strategies are not sensitive predictors of human health endpoints, the development of new and more advanced NAMs will be part of the solution.

**Recommendation 3: Eliminate the role of conflicted interests in the goal to improve chemical testing.**

Better manage conflicts of interest in chemical safety assessments; the current system is not transparent enough. Chemical testing by the producing industry represents a private exchange between the industry and regulatory agency and, as such, is not privy to the kind of scrutiny required to identify flaws in the information. This could be eliminated by having these tests performed by an independent entity.

Better ways to identify and eliminate scientific misinformation. The chemical industry not only invests heavily in direct lobby-

ing of regulatory agencies<sup>7</sup>, but also commissions “scientific” papers designed to interfere with the regulatory system<sup>8,9</sup>. The case of the deceptive practices of the chemical flame-retardant industry was revealed by the Chicago Tribune<sup>10</sup>. These deceptive practices constituted not only a successful business model, but also a public health catastrophe<sup>11,12</sup>.

#### Recommendation 4: Involve the Public.

Public opinion strongly influences industries and regulatory agencies. Transparent reporting on environmental chemicals is crucial, yet incomplete disclosures persist, especially in cases like shale oil fracking, where many undisclosed chemicals affect water sources. Achieving full disclosure remains a pivotal goal in addressing this issue.

Communicating hazard and risk to public fora effectively. This means that the public should understand the issues without reacting in a way that is counter to public health.

Communicating hazard and risk to policymakers and regulators. These two groups represent public interests, but do not always act accordingly. Thus, it is important to communicate effectively and publicly, recognizing that monied special interests have an inside track to these groups.

## Conclusion

It is paradoxical that there is greater trust in the current system, despite the recognition that this system has allowed human exposures that greatly exceed safe levels, contributing to global disease trends and incurring healthcare costs well into the billions. We owe it to future generations to create the changes necessary to protect human and environmental health.

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