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A roadmap for risk

Chemicals risk is really the intersection of toxicity and exposure. The traditional regulatory paradigm calls for tests to understand the exposure, or dose, of an agent that could cause harm and, more importantly, the dose at which no harm would occur.

For the last four decades, animal testing has been the primary method of identifying chemical toxicity. As the need to test more and more chemicals grows, this approach of testing for toxicity without due consideration to potential exposure is becoming increasingly inefficient and unsustainable.

In recognition of these concerns, several influential reports by the US National Academy of Sciences (NAS), the Canadian Academies, and the European Union, have called for a marked change in exposure assessment, toxicity testing, and human health risk assessment. These reports, among others, clearly ask for change that will bring greater efficiency and transparency to human health risk assessments.

To catalyse change and improvements, the ILSI Health and Environmental Sciences Institute (HESI), a global organisation based in Washington, DC, US, created the Risk Assessment in the 21st Century (RISK21) Project, a multi-sector programme with participants from government agencies, academia, industry, and other areas (www.hesiglobal.org). More than 120 participants from 12 countries, 15 government institutions, 20 universities, and two non-government organisations have been engaged in the project since it started in 2010. RISK21 provides a conceptual framework whereby both exposure and toxicity are evaluated efficiently and transparently, using all relevant and reliable data. The programme aims to reduce unnecessary resource utilisation, while providing sufficient precision and accuracy in support of decisions that protect human health.

RISK21 provides a method to synthesise current knowledge by using evolving science and technology, a vision shared in reports from the US National Academy of Sciences and numerous other publications by forward-thinking scientists. It provides a flexible framework for bringing together knowledge to enable effective decision-making.

This approach is based on four principles:

1 Focus on problem formulation. Establish a purpose, scope, and plan for collecting and evaluating information that will guide the effective use of resources at each stage of the assessment process and ensure the right data are collected for the right reasons.
2 Use existing information. Collate and mine the extensive knowledge that now exists on chemistry, fate, use characteristics, and toxicity to group chemicals by similar characteristics. This may allow sufficient estimates for a decision about the risk of a particular chemical based on known data about other substances in its group without additional testing.
3 Start with exposure rather than toxicity. Develop an early estimate of potential human exposure in relevant populations, including susceptible populations. Chemicals with exceedingly low potential exposure should engender more frugal allocation of toxicological resources than those with higher exposure.
4 Use a tiered approach to data development and decision-making. Prioritise both exposure and hazard assessment, which allows for optimisation of limited resources and establishes an approach for decision-making that considers the quality of information, not just the quantity.

Once the data are collected using these basic principles, they are plotted on a RISK21 matrix that integrates both toxicity and exposure in a way that allows for uncertainty and provides flexibility in assigning dose metrics. This dynamic illustration also makes it clear that as toxicity or exposure changes, so does the risk.

The RISK21 roadmap has the potential to be a major step forward in human health risk assessment. The principles and methodology of RISK21, including the roadmap and matrix, will be published in mid-2014 and will include case studies and a unique methodology for assessing risk to multiple chemicals. These papers signal a major transition toward ensuring that the benefits of chemistry and scientific innovation are appropriately weighed against the risks.

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