Published in EuroScientist magazine on 7th September 2015 via SciencePOD

Summary

To date, most toxicology tests have not been validated but they are still mandated by regulatory agencies. The question is to find suitable ways of modernising toxicology testing in the 21st century in a structured, consistent, transparent way.

In this article, Thomas Hartung, Founder Evidence-Based Toxicology Collaboration (EBTC), at Johns Hopkins University Bloomberg School of Public Health, and colleagues, examine what remains to be done to address the mounting pressure exerted on industries and food and drug regulators worldwide to bring their decision-making process up-to-date with modern science.

This calls for the use of a rigorous appraisal of the value of past studies under the umbrella of what has been dubbed evidence-based medicine (EBM), to be adapted in toxicology, to guarantee the safety of drug and consumer products.

Thomas Hartung was the first Professor of Evidence Based Toxicology at John Hopkins University

Evidence-base safety science is nigh

Modernising toxicology tests could help improve the safety of new drug approval and better clinical practice

Translating the evidence provided by science into policy has always been challenging. This is particularly true when integrating scientific evidence into safety sciences.

As surprising as it may appear, most of the tests that are currently used in the decision-making process used for the approval of new food, drugs and chemicals by regulatory agencies worldwide have not all been validated. Current test methods for prediction of hazardous effects, experts agree, are not always adequate to ensure the safety of consumers exposed to medicines and other chemicals. Today, pressure is mounting on industries and food and drug regulators worldwide to improve the safety of consumer products and bring regulatory batteries up to date with modern science.

The solutions may lie in following principles used in evidence-based medicine (EBM). EBM relies on a core tool, namely systematic reviews. These have been developed for clinical research to add rigour to appraisals of the value of evidence presented in past studies. Reviews of the available literature on a given topic are at heart of decision-making in science. They answer questions like: What do the studies on a specific topic collectively indicate? Systematic reviews constitute therefore a standardised approach for addressing this question.

Their advantages is that they yield transparent, robust conclusions. And they provide a convenient means for scientists and regulatory decision-makers to gain a condensed snapshot of the literature findings on their topic of interest.

Today, EBM principles need to be adopted in safety sciences like toxicology--a field known as evidence-based toxicology (EBT). Ultimately, adopting EBT principles will yield fully validated safety testing methods into the regulatory approval process for new drugs, food and chemicals.

The dawn of modern toxicology

Transparency, objectivity and consistency are the three principles of EBM, collectively referred to as the Cochrane principles. Using these criteria has strengthened the scientific foundation of decision-making in clinical medicine and healthcare. The idea was to assess the bearing of available evidence on healthcare questions in a structured way.

Moreover, bestowing such EBM approach to previous studies inevitably encouraged improvements in the design and reporting of new studies. As a result, clinical research has undergone a fundamental improvement in quality in the last few decades. This has led to an increased transparency and rigour in all aspects of research, from study design to reporting of the outcomes.

While EBM and systematic reviews are well established approaches in clinical medicine, traditional narrative reviews are still the norm in toxicology. While such reviews still have their place, they lack many of the features of a systematic review. Besides, they are prone to author bias in selecting,

synthesising and interpreting studies under review. Consequently, these traditional practices can compromise decision-making.

Fortunately, this situation is now changing. Prominent agencies around the world, including the European Food Safety Authority (EFSA), the US National Toxicology Program (NTP), and the US Environmental Protection Agency EPA with its Integrated Risk Information System (IRIS program), have embraced the systematic review framework. Already early applications of such reviews are focusing on hazard identification and risk assessment, as well as test method performance. What is more, applying systematic review to test method performance offers opportunities to provide a new and more robust framework for assessing evidence in the contentious area of toxicology tests validation.

Shift from medicine to toxicology

Historically, the translation of evidence-based approaches from medicine to toxicology has already been underway for a decade. Around 2005 as the term EBT emerged. Together with colleagues, we noted the potential value in translating evidence-based assessments of diagnostic measures in medicine to assessments of test methods in toxicology. We went on to further elaborate the conceptual underpinnings of EBT and coordinated the first international conference on EBT, held in Italy in 2007.

This led one of us--Thomas Hartung--to later found the Evidence-Based Toxicology Collaboration (EBTC). This is an initiative based at Johns Hopkins University Bloomberg School of Public Health, located in Baltimore, Maryland, USA. It aims to advance EBT and gather all the international EBT efforts under one roof. The collaboration has brought together stakeholders from government, non-government organisations, academia and industry to accelerate the transition of toxicology from expert judgement-based narrative to evidence-based science.

The collaboration ultimately aims to address directly all the challenges of translating EBM principles to toxicology and to reach consensus on draft of a primer and handbook of EBT and systematic reviews in toxicology. This information will then be disseminated among the members of the toxicology community, while taking the lead to write systematic reviews in chemicals%E2%80%99 and test performance assessment under the newly developed guidelines.

Next steps

We believe that one of the first applications of EBT could be in validation of safety assessment methods. EBT and systematic reviews can serve as key tools to help accelerate transition of new safety technologies into a quicker qualification stage. In addition, this approach can give confidence to the regulators to start using these technologies for regulatory decision making. With their emphasis on transparency, objectivity, and consistency, evidence-based approaches offer a tremendous potential to transform and modernise toxicology.

Thomas Hartung

Founder Evidence-Based Toxicology Collaboration (EBTC)

This article has been co-written with contributions from EBTC colleagues including: Katya Tsaioun, Director EBTC, Martin Stephens, Founding Director EBTC, and Sebastian Hoffmann, Research Staff, European Affairs EBTC, at the Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.

Photo credit: John Hopkins University