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Society of Toxicology
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AI will only replace toxicologists, who don't use it

The advent of Artificial Intelligence in daily life is also impacting on toxicology. In fact, it prompts a scientific and technological revolution. You just heard examples of what is happening and what is likely to come. Let's use a real case to sharpen our discussions:

The Elk River chemical spill occurred on January 9, 2014, in Charleston, West Virginia, when a storage tank at Freedom Industries leaked a chemical mixture, primarily consisting of 4-methylcyclohexanemethanol (MCHM), into the Elk River. This spill contaminated the water supply for over 300,000 residents, leading to widespread panic, water use restrictions, and a significant public health emergency. The incident highlighted the vulnerabilities in chemical storage and water safety regulations and underscored the need for improved emergency response and contaminant detection methods. The use of AI in toxicology could greatly enhance the speed and accuracy of detecting and analyzing chemical spills, aiding in quicker decision-making and potentially mitigating the impact of such environmental disasters.

At the time of the incident, toxicological information on MCHM was limited, leading to challenges in assessing the chemical's health risks and setting safe exposure levels. Available data primarily came from material safety data sheets (MSDS) and essemtially one LD_{50} study in rats, but these offered insufficient detail on the compound's effects on human health, highlighting the need for more comprehensive toxicological evaluations and rapid evidence integration in such emergencies. In response to the Elk River chemical spill, risk assessment efforts were initiated despite the sparse toxicological data on MCHM. These efforts involved gathering all available information on MCHM, including any existing studies and its MSDS, to estimate potential health risks. Agencies like the CDC and local health departments worked to establish provisional guidelines for safe water use, based on conservative estimates of toxicity and exposure levels. This approach aimed to protect public health while acknowledging the limitations and uncertainties due to the lack of comprehensive toxicological data on MCHM.

Table Discussion

1. What is the risk assessment possible with these data in 2014? What could be done to support decisions with *in vivo* and *in vitro* tests?

Discussion points:

- What are available test methods?
- What are duration and costs?

Answer:

- In vivo: years and millions in costs
- In vitro: months and ten thousands in costs, limited for chronic systemic effects

2. How can AI help information retrieval in such cases nowadays? What are the problems?

Discussion points:

- Where do we find toxicological information?
- How much is public?
- What are the problems in finding information?
- Large Language Models (LLM) for information retrieval

Answer:

- Data retrieval takes time
- Scientific papers, databases, public parts of registrations (especially REACH), safety data sheets
- AI is a premier tool to find machine-readable information
- Information is scarce and dispersed
- Reporting is little standardized
- Underreporting of negative effects

3. Information is often contradictory and comes from very different sources. How does this impede emergency risk assessments? How can AI help to integrate information?

Discussion points:

- What are information types?
- Where do Big Data needed for AI come from?
- AI combining multi-modal information in Large Language Models (LLM)

Answer:

- Chemico-physical properties, animal (guideline) studies, *in vitro*, QSAR, human case studies, epidemiology, biomonitoring
- Big data come from databases, ~omics, high-throughput testing, high-content-imaging, sensor technologies, literature, internet
- LLM combine information

4. How can AI fill data gaps and predict toxicity by automated read-across in such cases?

Discussion points:

- What is read-across?
- Read-across and its automation

Answer:

- Use of data from similar chemicals as substitute
- Moving from single or few source chemicals to many to predict target chemical's properties.

5. Why are big data and transfer learning superior to traditional computational methods?

Discussion points:

- Network effects
- Transfer learning
- Foundational models to pre-train for specific uses and plug-in own data

Answer:

- The more data points the more connections between them strengthening AI; deep learning gets better with more data
- Different properties inform each other (transfer learning) strengthens AI

6. What are hallucinations in AI? How can these be mitigated? What would this mean in an emergency case?

Discussion points:

- AI presenting wrong information as factual
- Examples: invented references.
- Better false information than no information? Precaution as consequence of false-positives. How to handle false-negatives?

Answer:

- Responsibilty for end-product; checking sources
- Combine AI with search engines
- Human-in-the-loop, expertise
- AI not as the only source for decision-taking

7. What is the black box problem of AI and how can it be mitigated? Is this important in an emergency risk assessment?

Discussion points:

- AI does not show how it integrates information and comes to conclusions
- Can regulatory decisions be taken based on black box methds?
- Are animal tests less black box approaches?
- Is this a problem in emergency cases?

Answer:

- Explainable AI is developing
- Sensitivity analysis
- Comparing to traditional methods – validation
- Less important for emergency cases

8. Can AI support mechanistic and systems toxicology? Is this important for emergency situations?

Discussion points:

- What is systems toxicology?
- Is this helpful to emergency situations?
- How is it helping method development?

Answer:

- Systems toxicology is an approach that integrates classical toxicology with quantitative analysis of large networks of molecular and functional changes occurring across multiple levels of biological organization. This method combines bioinformatics, systems biology, and traditional toxicology to understand the complex mechanisms of toxicity induced by exposures to chemicals or environmental factors. It aims to provide a more comprehensive understanding of how substances affect human health and the environment, enabling the prediction of toxicity and the development of safer chemicals and therapeutic strategies.
- Relevance of methods, when based on mechanism
- Mechanism translates between species or shows that something is not relevant
- Less important for emergency situations but indicrectly through improvement of tools

9. How fast can we expect AI to develop in toxicology? How can it be used already?

Discussion points:

- AI as a co-pilot vs. autonomous AI
- Extremely fast progress (why is this a problem in safety sciences?)
- Emergency cases like the Elk River case
- Green Chemistry (Green Toxicology): Benign by Design, early detection of problems, finding alternative chemistry

Answer:

- AI doubles in capacity every three months.
- Use of AI outside the regulatory toxicology (product development, investigative toxicology)
- AI lends itself to support decisions (dara retrieval, filling data gaps, priority setting, plausibility checks
- Green Chemistry benefits enormously from predictive toxicology through AI

10. What are the bottlenecks for AI use? How can we overcome them?

Discussion points:

- AI literacy
- Proprietary data
- Lack of reporting standards
- How to validate?
- Regulatory acceptance

Answer:

- Education
- Data sharing, reporting standards, machine-readable publisihing
- Open-access publishing
- Revision of validation process, explainable AI
- Vocational training for regulators