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TCDD

TOXICOLOGIE

SPECIAL THEME

QSARs, AI and Read-Across

- QSARS, MACHINE LEARNING AND LLMS: WHAT “AI” REALLY MEANS IN TOXICOLOGY
- VIRTUAL CONTROL GROUPS: CAN DIGITAL ANIMALS REPLACE REAL ONES?

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Toxicologische Communicatie, Data en Documentatie (TCDD)

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Het lidmaatschap wordt automatisch verlengd tenzij de NVT-ledenadministratie vóór 1 december van het lopende jaar schriftelijk of per e-mail een opzegging heeft ontvangen. Hiervan ontvangt u een bevestiging.

Contributie NVT
Incl. abonnement TCDD 50,= euro
(extra kosten EEMS: 10,= euro)

Indien u ervoor kiest zelf uw contributie over te maken, dan worden € 5,- administratiekosten in rekening gebracht.

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TOXICOLOGIE

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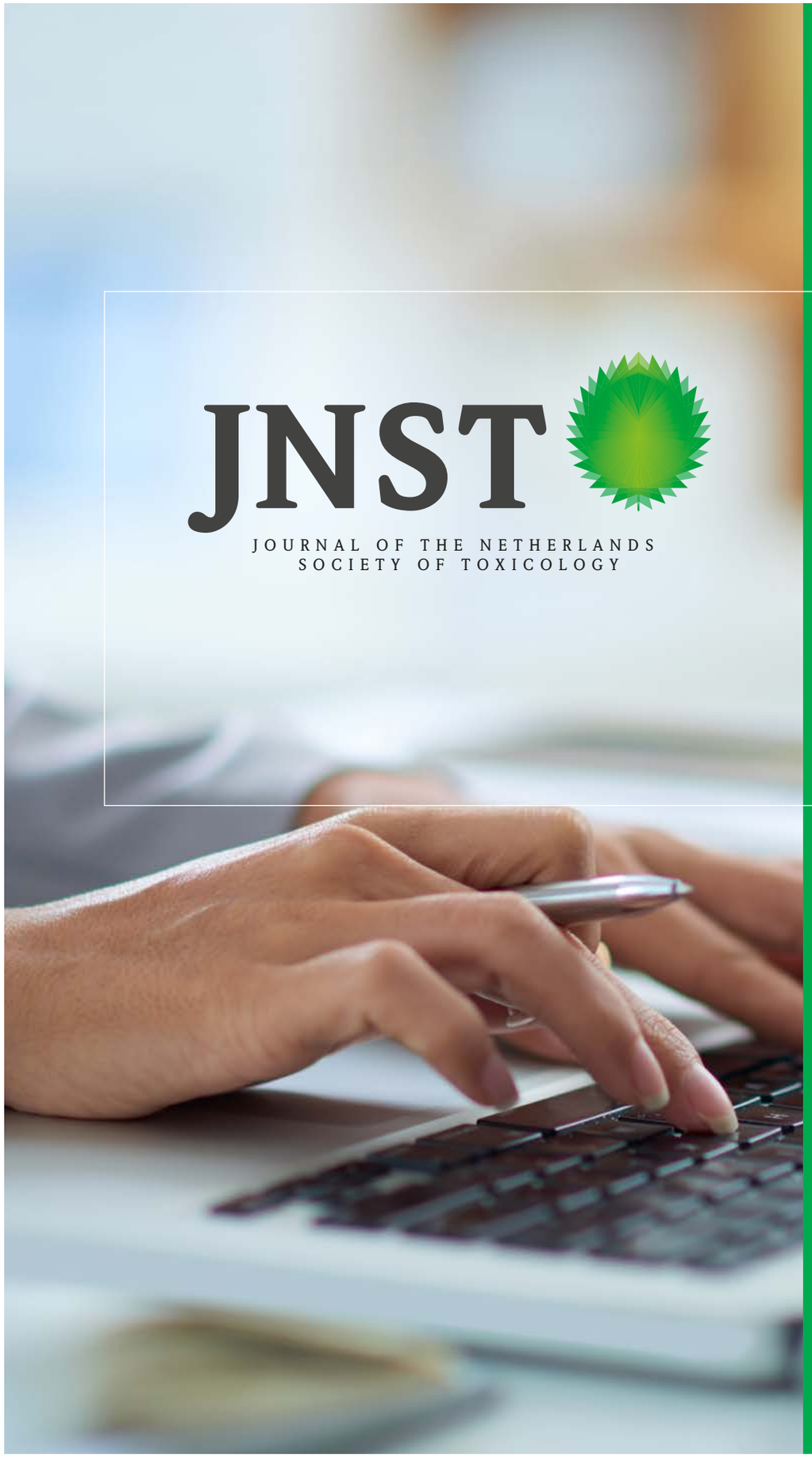

JNST

JOURNAL OF THE NETHERLANDS SOCIETY OF TOXICOLOGY

Submit your paper!

Call for submissions

to the Journal of the Netherlands Society of Toxicology

- Submissions can be made through ScienceOpen.
- A free account must be made with ScienceOpen prior to submission.
- Author guidelines can be found by following this link: Journal of the Netherlands Society of Toxicology – ScienceOpen.
- There is no deadline for submission.
- Once the submitted papers are accepted and have completed the peer review process, they will be available online and the journal entries will be appended to the TCDD.

TERUG NAAR INHOUD

Editorial

With sadness in my heart, I say goodbye to the TCDD readers and the lovely editorial staff. My life is taking me in a new direction. After a decade in Toxicology, I am taking the next step in my career by moving into Reproductive Medicine, where I will work on genetic clinical applications in early human development (e.g., PGT and NIPT) to help give babies the best possible start in life.

I have truly enjoyed being part of the TCDD editorial team, especially the lively brainstorming sessions for new topics and the chance to explore toxicological subjects beyond my own field. Each issue brought something new to discover and learn, and that has been incredibly rewarding. I recommend joining this wonderful team to scientists, young and old. If you feel inspired, please reach out to redactie@toxicologie.nl.

This will be my final issue, and it is a particularly enjoyable one about Computational toxicology. We will explore QSARs, Machine Learning, LLMs and Read-Across and Virtual Control Groups. Additionally, this issue includes an interview with Flemming Cassee and Rob Vandebriel is looking back on his 35-year journey. Of course, we also have a Toxafette by Kirsten Lassing and Toxicology in the news about the baby formula recalls.

Thank you all, and I hope you enjoy diving into the articles ahead!

Sincerely,

Marcha Verheijen

Photo by Jess Bailey on Unsplash

Call for New Editorial Team Members – TCDD Newsletter

The editorial team of TCDD, the newsletter of the Netherlands Society of Toxicology (NVT), is looking for new members to join us.

All NVT members are welcome to apply, including PhD students, early career professionals, and experienced toxicologists working in academia, industry, or government.

Are you interested in following developments in toxicology? Do you enjoy writing, interviewing colleagues, or helping shape the content and direction of a professional newsletter? Joining the editorial team is a great way to contribute to the community and stay closely connected to what is happening within the field.

TCDD is published four times a year. To prepare each issue, the editorial team meets twice, once in person and once online. In total, we meet eight times per year. The overall time commitment is manageable and can be combined with your professional responsibilities.

If you are interested or would like more information, please send an email to redactie@toxicologie.nl. We look forward to hearing from you.

Spring updates from the NVT Board

Spring has arrived, bringing fresh energy and a sense of renewal.

Welcoming a New Treasurer

We are pleased to welcome Marten Schults as our incoming treasurer. Over the coming months, Marten will work closely with the current treasurer, Laura Hondebrink, to ensure a smooth handover. He will officially take on the role as of 1 June 2026. We are grateful to Laura for her support during this transition and wish Marten every success in his new position.

Join Us at the NvT Annual Meeting – 23–24 June 2026

We warmly invite you to the NvT Annual Meeting, which will take place on 23–24 June 2026 at a new location: De Eenhoorn in Amersfoort.

This year's theme, *"Toxicology at every scale: from molecules to ecosystems," will be explored through four subthemes: small molecules, big consequences; small to big data; life in formation; and our planet under pressure.*

Both days are intended for the full toxicology community and will feature inspiring presentations, lively discussions, and many opportunities to connect.

Be sure to **register and submit your abstract before 31 March** — we hope to see many of you there.

Joep van den Bercken Prize

Several excellent PhD theses have been nominated for this year's Joep van den Bercken Prize, and a jury will soon begin the evaluation process.
If you are interested in contributing as a jury member, please let us know — your expertise would be highly appreciated.

NVT at the German Pharma-Tox Summit

The NVT is co-organizing the 11th German Pharma-Tox Summit (GPTS), taking place 17–20 March 2026 in Düsseldorf. If you are interested in attending, please visit: https://gpts-kongress.de/

Board Vacancies – Get Involved!

In the coming years, some board members will step down as their terms come to an end. One of them is Anne Kienhuis, who will leave the board as of 1 June. We would like to sincerely thank Anne for her excellent contributions, dedication, and active involvement over the past years.

Her departure also means there will be opportunities for new members to join the board. Please consider putting yourself forward or contact us to learn more about what being a board member involves.

Future-Proofing the NVT – Very Short Update

The future-proofing working groups have provided valuable input on how to strengthen the NVT. Key themes include increasing interaction among members, improving internal communication, enhancing the visibility and added value of the sections, and reflecting on the balance and positioning of the society. The board will further consider these recommendations and explore how to integrate them into our future plans. We thank Anne Kienhuis, Joanne Salverda, and all members who contributed to this effort.environment, and protecting all living creatures - including ourselves.

Closer Collaboration with the KNCV

We are currently in discussion with the KNCV about expanding their support for operational activities, including membership administration, financial processes, support for the registration committee, and website management. Strengthening this collaboration could help reduce the operational workload for members of the board and sections allowing more time and focus on content and strategy. The possible use of the KNCV's event management module is also under consideration.

We **wish** you all an inspiring and productive spring season and look forward to seeing many of you in Amersfoort in June.

SECTION
RISK ASSESSMENT

January symposium 2026

Risk is not just a number - How to communicate accurately and understandably in complex cases?

On the 20th of January 2026 the section Risk Assessment from the Dutch Society for Toxicology (NVT) organized a symposium on the importance of accurate and understandable risk communication. Speakers from RIVM, TNO, GGD and NVIC were invited to share their experiences.

The symposium started with a presentation from Tom Jansen, a social psychologist and communication scientist from the National Institute for Public Health and the Environment (RIVM). His presentation focussed on how the public perceives risks and which factors influence their risk perception. It is important to keep these factors into account as current risk communication practices often lead to misinterpretation.

The use of a video exposure monitoring tool to gain better insight in occupational risks was presented by Sander Ruiter from TNO. He explained how this tool identifies activities that produce peak exposures and how it can be used for a dialogue with workers to together identify and understand those activities that should be avoided with the aim to reduce occupational exposure and thus risks.

Manon Vaal and Marja Gelders from the GGD Gelderland-Midden highlighted important factors that influence risk perception, e.g. volunteerism, advantages, trust in authorities. One of the key messages was that it is important to have an open dialog with the public to understand the context and reasons why people are concerned. An intriguing example was the case of PFAS in which the perceived risk was higher compared to the estimated risk by experts due to the context of the PFAS being in the soil of a playground for children. While in another case the perceived risk was lower in the context that people valued swimming during a warm day as more important compared to their exposure to PFAS in the water. Besides open dialog, it is also important to pay attention to the process, be clear about what you know on the risks but might still be uncertain, keep people informed throughout the process and let them know which steps are being taken.

The final presentation was provided by Chantal Roelen from the Dutch National Poison Information Centre (NVIC) who provided examples of how important it is to clearly and understandable communicate on risks. In an example of product recalls, unclear communication on potential health risks led to unnecessary public concern as was highlighted by the number of times the NVIC was contacted by health physicians. On the other hand, communication by the NVIC about actual risks of an unregistered sleep drink with an active component was perceived by part of the public as alarmist as it went against peoples interests and expectations.

More details are provided in the presentations from the speakers.

You are welcome to join the risk assessment section
Our risk assessment section consists of 7 dedicated people from different backgrounds, including governmental organisations, consultancy, research organisations and industry. We have an open position specifically for someone working either in industry or in academia. If you are enthusiastic about risk assessment and enjoy organizing symposia together with a dedicated team, please reach out to Marjolijn Woutersen marjolijn.woutersen@rivm.nl.

SECTION
PHARMACEUTICAL
TOXICOLOGY

PET Course

The PET course “Pharmaceutical Toxicology” has been confirmed for this year and will be held on **June 15th-19th 2026**. Please visit https://toxcourses.nl/ for more information.

On **April 14th 2026** the section Pharmaceutical Toxicology will hold their annual scientific spring meeting with the theme:

New Meds, New Challenges
Navigating Risks, Innovation, and Sustainability

Agenda and registration details will follow through the regular NVT communication channels.

SECTIE
ARBEIDS-
TOXICOLOGIE

De toekomst van biomonitoring op de werkplek: een onmisbare stap vooruit?

Datum: donderdag 26 maart, 13:30 – 16:30
Locatie: Aristo Eindhoven, Vestdijk 30, 5611 CC Eindhoven

Biomonitoring biedt vele mogelijkheden. Tegelijkertijd roept het fundamentele vragen op over de praktische toepasbaarheid, betrouwbaarheid, effectiviteit, privacy, ethiek en de gevolgen voor beleid en praktijk. De ontwikkelingen rond biomonitoring op de werkplek gaan snel. Het advies van de Gezondheidsraad (https://www.gezondheidsraad.nl/adviesonderwerpen/schadelijke-stoffen/meetprogramma-voor-blootstelling-aan-chemische-stoffen) en van de Europese onderzoeksprogramma’s HBM4EU (https://www.hbm4eu.eu/) en PARC (https://www.eu-parc.eu/), laat zien hoe biomonitoring een centrale rol kan gaan spelen in de vroeg-signalering en preventie van beroepsziekten.

Tijdens het symposium ‘De toekomst van biomonitoring op de werkplek: een onmisbare stap vooruit?’ nemen vijf sprekers u mee in de actuele stand van zaken, praktijkervaringen, (inter) nationale richtlijnen en nieuwe technieken.

Aanmelden kan op de CGC website via de volgende link: https://p.easydus.com/project/c7b6744f-e5aa-43f9-a50c-0013eb78efd2/form/2?sig=ec53f81108a0dd4393c936020e10816d625df2470b290cef82a31be0e8690f99

Op de CGC website (https://www.contactgroep-gezondheid-en-chemie.nl/26-maart-2026-de-toekomst-van-biomonitoring-op-de-werkplek-een-onmisbare-stap-vooruit/) is ook de routebeschrijving naar Aristo in Eindhoven te vinden.

Programma:

13:00	Inloop met koffie en thee
13:20	Inloggen via Teams met de persoonlijke link (sound/video check)
13:30 - 13:45	Opening (CGC en NVT)
13:45 - 14:00	Introductie (Nicole Palmen)
14:00 - 14:15	Recente ontwikkelingen beleid en onderzoek (Jelle Vlaanderen)
14:15 – 14:45	Methods and guidelines (Maryam Zare Jeddi)
14:45 - 15:00	Pauze
15:00 - 15:30	Biomonitoring in de praktijk (Rik Menting + Jolanda Willems)
15:30 - 16:00	Biomonitoring in de toekomst en de rol van vroeg-signalering (Bernice Scholten
16:00 - 16:30	Paneldiscussie

QSARs, Machine Learning and LLMs: **What "AI" Really Means in Toxicology**

By *Barae Jomaa*

Artificial Intelligence (AI) is being adopted across most industries[1] and its increased use is raising widespread concern about its role in society[2]. "AI" is a catchall term covering a hierarchy of related but distinct techniques. These range from rule-based Symbolic AI and traditional Quantitative Structure-Activity Relationship (QSAR) models to modern Machine Learning (ML), Artificial Neural Networks (ANNs), Deep Learning (DL), and generative systems including Large Language Models (LLMs).

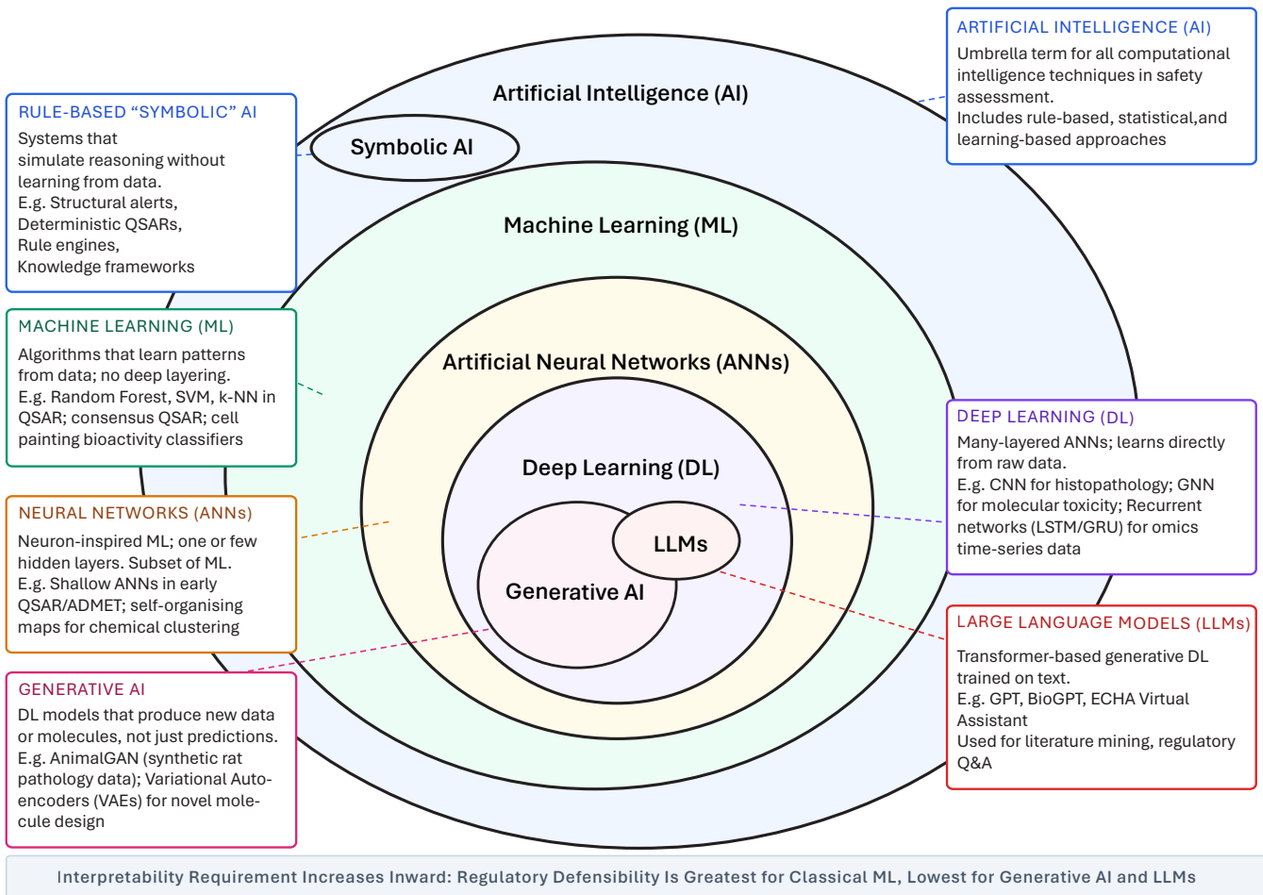

Figure 1: Hierarchical relationships between artificial intelligence categories relevant to toxicology.

AI forms the broadest category, within which ML represents a subset. ANNs are a class of ML model; DL refers to multi-layered ANN architectures; and LLMs are a specialised form of generative AI built using deep learning methods (Figure 1). Symbolic AI, which operates through hand-coded expert rules rather than learning from data, sits within AI but outside ML entirely. Although these approaches are frequently grouped together under the label "AI," they differ substantially in architecture, function, and application. Clarifying these distinctions is important for toxicologists when interpreting methodological claims, selecting appropriate tools, and explaining their reasoning to regulators[3].

Growth of AI Terminology in Toxicology Literature

Over the past decade, publications linking toxicology with AI-related terminology have increased markedly (Figure 2). ML publications show the earliest and most sustained growth, rising gradually from 2010 and accelerating sharply from around 2019 to reach the highest counts of any term by 2025. AI as a search term follows a similar but later trajectory, remaining low until around 2020 before rising steeply, suggesting that the field began adopting

ML methods before it consistently labelled them as AI. DL emerges as a distinct topic around 2019 and grows steadily, reflecting the uptake of more complex architectures in recent years. ANNs, by contrast, show a low and flat publication count throughout the entire period, consistent with their status as an established but narrowly described methodology that predates the current wave of interest. Mentions of LLMs appear only from around 2022 and remain comparatively limited, reflecting their very recent entry into toxicological practice. Taken together, these trends illustrate both increasing methodological adoption and expanding terminological overlap within the field, making it all the more important to be precise about what each term refers to.

Symbolic AI and Rule-Based Systems

Some of the oldest computational tools in toxicology belong not to ML but to Symbolic AI. The first QSAR publication indexed in PubMed dates from 1971[4] , and structural alert systems such as Derek Nexus have been in regulatory use since its original description in 1991 as a computer-based expert system that perceives chemical substructures and relates them to a rulebase linking those substructures with likely types of toxicity[5]. In Derek Nexus, the authors of the alerts first establish the mechanistic basis of an alert, then review a training set of compounds to identify the activating and deactivating structural features, and encode those findings as explicit rules that are applied deterministically to any new structure submitted by the user. The pattern recognition is performed by the author of the alert rather than by an algorithm, and the system is explicitly knowledge-based rather than statistically based: standard robustness metrics are not applicable. Outputs take the form of expert-assigned confidence levels derived through a logic of argumentation, and the derivation of each alert is documented with supporting references, making the reasoning fully inspectable. Deterministic QSARs and rule engines work on the same principle. These systems remain widely used in regulatory practice precisely because every prediction can be traced back to an explicit, human-readable reasoning step, which makes them highly defensible in submissions. Understanding that they occupy a different category from ML is important. Their transparency and regulatory defensibility are strengths that most learning-based models cannot yet match, but their coverage is bound by what the alert authors have encoded, and they cannot identify structural patterns that lie outside their existing rulebase.

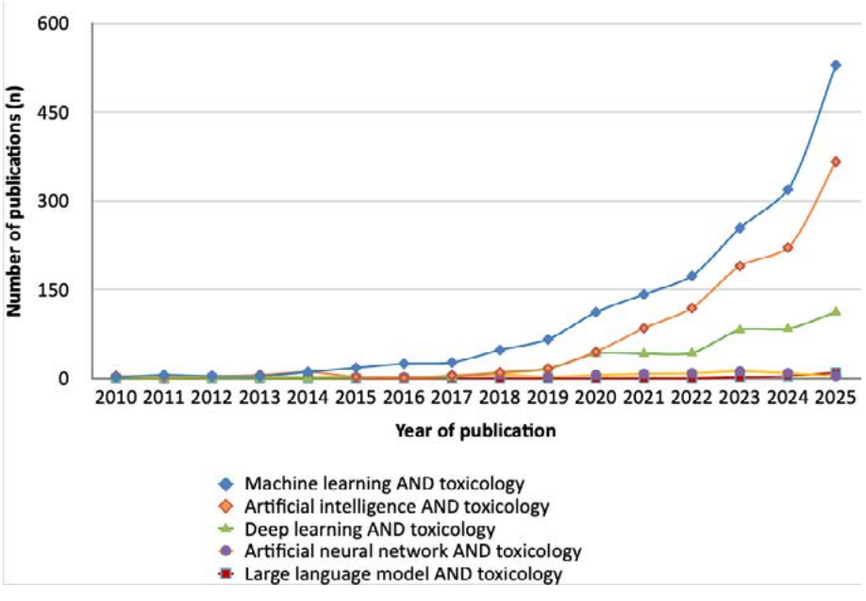

Figure 2: Number of publications mentioning toxicology and one of the following terms “machine learning”, “artificial intelligence”, “deep learning”, “artificial neural network” or “large language model” based on a PubMed search.

Machine Learning in Toxicological Modelling

ML refers to computational algorithms that learn patterns from data to generate predictions or classifications. In toxicology, ML methods are widely used in QSAR modelling, toxicokinetic prediction, read-across support, and hazard classification. Common approaches include Random Forests[6], Support Vector Machines (SVMs)[7], k-Nearest Neighbours (k-NNs)[8], and gradient boosting algorithms[9]. These models typically rely on predefined molecular descriptors such as physicochemical parameters, structural fragments, or fingerprint representations. Because descriptor spaces are explicitly specified, many traditional ML models are more readily interpretable than deeper architectures, which is particularly relevant to satisfying OECD Principle 2, requiring an unambiguous algorithm, and OECD Principle 5, which calls for a mechanistic interpretation of the model[10]. ML methods can also classify bioactivity patterns in high-content screening data such as cell painting bioactivity classifiers, extending their reach well beyond classical QSAR endpoints such as mutagenicity, skin sensitisation, and acute oral toxicity.

Artificial Neural Networks and the Emergence of Deep Learning

ANNs are a class of ML model composed of interconnected computational nodes organised in layers, with connection weights adjusted during training to minimise prediction error. Early toxicological applications generally involved shallow architectures of one or two hidden layers, applied

in QSAR development and other predictive tasks where nonlinear relationships were expected. DL refers to ANN architectures with multiple stacked hidden layers that enable hierarchical representation learning. The distinction between ANNs and DL is therefore one of architectural depth rather than principle. Increased depth allows DL systems to learn progressively abstract features from structured or semi-structured input data without relying exclusively on predefined descriptors.

This comes at the cost of interpretability. A traditional QSAR model can often point to the specific structural features driving a prediction, whereas a deep neural network may perform accurately yet offer little insight into why. In regulatory toxicology, where predictions must be biologically plausible and defensible, this black box problem is not trivial, and maps directly onto the mechanistic interpretability requirement of OECD Principle 5 for QSAR model validation10. Ongoing work in explainable AI (xAI) is addressing this through tools such as SHAP values, saliency maps, and counterfactual explanations[11].

Deep Learning for Complex Toxicological Data

DL has expanded modelling capacity in toxicology, particularly where large and complex datasets are available. Applications include high-content screening, transcriptomic profiling[12], and structure-based molecular modelling. Where analysis is applied directly to raw imaging data rather than to extracted feature profiles, as in end-to-end cell painting pipelines, convolutional neural network (CNN) architectures are increasingly preferred over classical ML classifiers[13]. Recurrent architectures including Long Short-Term Memory networks (LSTMs) and Gated Recurrent Units (GRUs), commonly associated with natural language processing, are also being applied in toxicological DL modelling, for instance in the prediction of key events within Adverse Outcome Pathway frameworks for cardiotoxicity[14]. Graph Neural Networks (GNNs) represent a DL architecture especially relevant to chemistry and toxicology. Molecules are encoded as graphs of atoms and bonds, allowing the network to learn structural features directly from connectivity information without hand-selected descriptors or fingerprints. GNNs have demonstrated strong performance across multiple toxicity prediction benchmarks including Ames mutagenicity, skin sensitisation, DILI, and acute oral toxicity[15,16], and represent an important bridge between classical QSAR thinking and modern deep learning practice. Despite their flexibility, DL models typically require substantial training data and computational resources, and in regulatory contexts where reproducibility and justification are formal requirements, the lack of transparency remains a challenge.

Generative AI and Large Language Models

Generative AI systems are designed to produce new outputs based on patterns learned from data. In toxicology, this opens a dimension distinct from prediction. Generative Adversarial Networks (GANs) can produce synthetic data that closely mimics real experimental observations. The Animal-GAN model, for instance, was trained on rat clinical pathology data from the TG-GATEs database and generated profiles closely comparable to real experimental observations[17]. These capabilities offer real prospects for reducing animal testing and filling data gaps in regulatory submissions, but they also raise serious questions about data provenance. If AI can generate data that looks identical to what comes out of a laboratory, ensuring the origin of data in a regulatory dossier is always transparent becomes critically important. Generative models compound the black box problem found in predictive DL. Not only is the internal reasoning of the model opaque, but the outputs themselves are synthetic constructs that carry no inherent indication of their artificial origin or the uncertainty underlying them. Unlike a QSAR prediction, which can in principle be traced back to a training set and an applicability domain, a GAN-generated dataset leaves no such audit trail by default.

LLMs are a form of generative AI trained on an extensive body of text. Unlike QSAR, ML, or DL models used for hazard prediction, LLMs do not estimate toxicological endpoints from chemical structure. Their function is linguistic rather than predictive in the toxicological sense. Potential applications include literature summarisation, extraction of study details, drafting of technical documents, and interrogation of regulatory guidance. The ECHA Virtual Assistant is an applied example of this kind of tool operating within a regulatory context, alongside research-oriented systems such as GPT and BioGPT. LLMs carry two behavioural tendencies that are particularly consequential in a scientific context. The first is hallucination: the generation of plausible-sounding statements that are factually incorrect, with no internal signal to alert the user. The second is sycophancy: a trained disposition to align outputs with what the user appears to want or believe, which can cause the model to confirm a flawed premise, validate an incorrect hypothesis, or soften a critical assessment rather than contradict it. Both tendencies arise from how these models are trained and optimised, and neither is reliably detectable due to the fluency and confidence of the output. LLMs are tools for efficiency, not for scientific judgement, and expert review of every output remains essential.

Responsible Use and the Question of Trust

The question of trust runs through all of these applications. A recent ECETOC workshop that brought together experts from academia, industry and regulatory bodies arrived at a useful framing: AI should be viewed as "augmented intelligence," a tool aimed at enhancing human assessment rather than replacing it[18]. The workshop emphasised that the reliability of any AI tool depends fundamentally on the data behind it. The FAIR principles, requiring that data be findable, accessible, interoperable and reusable, are not merely

best practice but a prerequisite for trustworthy AI. Without high-quality, well-curated training data, even sophisticated algorithms will produce unreliable results.

Conclusion

The practical takeaway is that "AI" encompasses a layered set of computational approaches with distinct capabilities. Rule-based Symbolic AI tools remain valuable because they are transparent and traceable. ML methods, including shallow neural network architectures, are established tools for predictive modelling, and DL extends these architectures to enable more complex representation learning when large datasets are available. Generative AI can produce synthetic experimental data but demands rigorous governance of data provenance and explicit documentation of the artificial origin of any outputs. LLMs are language-based systems that assist with information synthesis but do not perform toxicological prediction, and their tendencies toward hallucination and sycophancy mean that fluent, confident output is not a reliable indicator of accuracy.

A structural alert system, a Random Forest QSAR model, a GNN trained on molecular graphs, a GAN generating synthetic clinical pathology data, and an LLM drafting a summary are all described as "AI" in the current literature, yet each operates on fundamentally different principles, requires different validation, and is suited to a different task. Clear understanding of this hierarchy allows toxicologists to evaluate AI more critically, apply appropriate methodologies to specific scientific questions, and avoid conflating predictive modelling with generative language systems. In practical terms, responsible use means evaluating each tool for fitness of purpose, documenting its limitations and training data alongside the output, and preserving the human judgement that no algorithm can currently replace.

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Virtual Control Groups: can digital animals replace real ones?

When it comes to replacement of animal testing, most people have heard about *in vitro* models such as organ-on-a-chip models, or *in silico* models to predict adverse outcomes. But what if we could replace whole animals with virtual ones? With Virtual Control Groups (VCGs), researchers try to do just that: replace a live Concurrent Control Group (CCG) with a virtual one. Is this possible? How would it work? And what would be the drawbacks?

By *Puck Roos*

VCG, or synthetic control arms, have been used in clinical research for some time [1]. For example, data from electronic health records can be used as a control when a live control group is not feasible or not ethical. More recently, the concept of VCGs has also gained attention in the toxicology community [2]. In toxicology, Historical Control Data (HCD) is already collected and used to interpret rare findings. The hypothesis is that a VCG, constructed from animals from the HCD that are matched to the live animals in a certain study, could replace the CCG. Since conventional animal toxicology studies have one control group and three dose groups, replacing the CCG with a VCG could lead to 25% reduction of animal use.

Several studies have retrospectively compared outcome of original toxicity studies (with a CCG), to the same toxicity studies in which the CCG was replaced by a VCG. Wright *et al.* (2023) evaluated the interpretation of histopathological findings in repeat-dose toxicity studies when using a CCG versus a VCG [3]. First, they established a database of histopathology findings from >1000 rat and dog toxicity studies. Next, for each study, they generated a VCG by aggregating the HCD from studies other than the original study. They matched the animals in the VCG to the animals from the original study for strain, sex, administration route and vehicle, or a smaller subset of these parameters. Then, they statistically predicted whether the histopathology findings were treatment-related, using the original study's CCG or the generated VCGs. Last, they

compared the statistical predictions to the study director's interpretation of the original study report. The authors found that the balanced accuracy *[(true positive rate + true negative rate) / 2*] of the statistical predictions vs the study director's interpretation was higher when using a CCG than when using a VCG: 0.704 for rats and 0.628 for dogs. However, when the VCG matched the CCG for most parameters, the balanced accuracy was only slightly lower for rats (0.702). When the VCG matched the CCG for fewer parameters, the balanced accuracy dropped: for example, 0.679 for rats when only strain and sex were the same. This drop was likely caused by increased variability in the HCD. For dogs, no clear trend was observed. The authors concluded that VCGs are not ready for implementation in regulatory testing yet. Furthermore, they recommended more granular documentation of HCD, to match VCGs to the live study animals on more parameters.

In another study, Andaya et al. (2025), compared the interpretation of a 7-day repeat-dose toxicity study in rats with a CCG, versus when a VCG replaced the CCG [4]. Animals were matched for more parameters (for example test site, age, diet, blood collection method, clinical

pathology method). Scientist blinded to the nature of the control group analysed the data. They found no differences between the CCG and VCG analyses for changes in body weight, organ weight, and macro- and microscopic findings. However, the VCG could not replicate the interpretation of the clinical chemistry and haematology findings from the original study. The interpretation of the effects at the high dose was similar, but in the VCG analysis, effects at the low and mid dose were inconsistent with effects at the high dose. According to the authors, this inconsistency may have raised concerns about the reliability of the study in a real-world setting. Even though the study evaluation with a VCG established the same NOAEL as the original study (with a CCG), the authors concluded that more work is necessary before VCGs can be used in a regulatory setting.

In the same year, Gurjanov *et al.* (2025), investigated whether a VCG could replace a CCG in 4-week rat toxicity studies [5]. They picked three studies with a CCG, in which different levels of toxicity were observed. Similar to Wright *et al.*, they first analysed whether the analysis with a VCG could replicate the statistical results of the original studies (with a CCG). Next, they asked experts to evaluate whether the statistical differences were treatment-related. As a final step, they compared the outcome of the studies with a VCG could replicate the conclusions of the original studies. Study conclusions were defined as the No Observed Adverse Effect Level (NOAEL), Severely Toxic Dose to 10% of the population (STD10), target organs of toxicity, and safety biomarkers for clinical monitoring. Analysis with a VCG could not reproduce the statistical analysis of the original studies: only for 22% of the parameters, VCG analysis obtained the same statistical findings as the original analysis with a CCG. However, not all statistically significant findings were treatment-related, according to the experts. Treatment-relatedness was more consistent between VCG and CCG analyses than statistical differences, although some differences were still observed for clinical chemistry, food consumption and organ weight. Still, for all three studies, analysis with a VCG could replicate the conclusions of the analysis with a CCG: the NOAEL, STD10, target organs and safety biomarkers remained the same.

As a final example, Bowman *et al.* (2026), investigated the use of VCGs for Fertility and Early Embryonic Development (FEED) studies [6]. They compared the analysis of 12 FEED studies with a CCG, or when a CCG was replaced with different types of VCGs. Similar to the other examples, they compared the statistical analyses of the original studies versus statistical analysis with a VCG. Then, they compared the statistical analyses to the interpretation in the study report. They evaluated different VCG sizes (5-20 animals) and full versus hybrid VCG (*N* VCG animals + 5 CCG animals). They observed that sensitivity and specificity increased as the size of the VCG increased. When using a VCG of 15 or 20 animals, sensitivity and specificity were equal to or better than in the original study (with a CCG) for most endpoints. These effects were similar for full and hybrid VCGs. Only for the number of oestrous cycles and oestrous cycle length, VCGs performed worse than CCGs. According to the authors, this may be due to variability in how oestrous cycles are measured, which would lead to more variability in the HCD from which the VCG animals are drawn. As a case example, they compared the conclusions of one original FEED study to the same FEED study when analysed with a VCG. Similar to previous examples, the same NOAEL was determined with a VCG as with the CCG.

These examples demonstrate that (partly) replacing a CCG by a VCG may be a promising way to reduce animal use. However, some challenges need to be addressed. First, databases with large amounts of HCD are needed, which use standardised terminology to allow for consistent analysis and interpretation [2, 7]. Second, more granular documentation of HCD might be needed. Traditionally, it is preferred to compare in-study data only to HCD that is matched for species, strain, testing facility, housing conditions, animal age, and time window in which the study is performed [3]. In the case studies described above, it was not always possible to match VCG to the study animals for all desired parameters, such as body weight (Wright *et al.*)

or vehicle (Andaya *et al.*). In addition, Gurjanov *et al.* noted that, since most inconsistencies between CCG and VCG analysis were found for clinical pathology, matching animals more closely on these parameters would be beneficial. However, clinical pathology parameters are usually not measured prior to study initiation and could therefore not be used as a parameter to match [5]. Furthermore, assay kits to analyse clinical pathology may differ between labs, and are usually not recorded in HCD [8].

Even if VCGs perform equal to or better than CCGs, full replacement of the CCG is probably not possible. Due to genetic drift or changes in test facilities over time, replenishment of the HCD would be needed. This could be achieved through hybrid control groups (as discussed by Bowman *et al.* [6]), or by using the same CCG for multiple studies that are conducted at a testing facility at the same time [2].

Furthermore, VCGs may be more applicable in studies where large differences are expected, rather than subtle pathological changes. For example, they could be used in dose-range finding studies, which aim to establish a maximum tolerated dose [8, 9]. Another possibility to use VCGs would be in non-human primate (NHP) studies. Because of ethical considerations and a shortage of NHPs, there is a need to reduce NHP use. However, biologically, NHPs are more variable than rodents, especially when using NHPs from different origins [8]. This might hamper the use of VCGs in NHP studies.

Still, the case studies have shown that analysis with VCGs can replicate the analysis of original studies with a CCG. To further investigate the regulatory applicability of VCGs, the VICT3R (Developing and implementing VIrtual Control groups To reducE animal use in toxicology Research) project is currently ongoing. The goal of VICT3R is to develop a database with historical control data from various animal testing facilities, using controlled terminologies, and including links to digital histopathological images. They aim to assess the performance of VCGs by comparing the outcome of studies before and after replacement of CCG by VCG, similar to the examples described above. Finally, they aim to obtain global regulatory acceptance of VCGs [10].

In conclusion, full replacement of real control animals with virtual ones may not be possible yet, but VCGs offer a promising way to reduce animal use. With more standardized documentation of HCD, more granular documentation of parameters (e.g. clinical pathology analysis), and more understanding of inherent variability in animal studies, VCG might be constructed that can perform as well as CCG and could reduce animal use in regulatory toxicity testing.

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Interview with Flemming Cassee, IUTOX's New Secretary General

Flemming Cassee, Chief Science Officer at RIVM National Institute for Public Health and the Environment, professor of Inhalation Toxicology at Utrecht University, Institute for Risk Assessment Science and Secretary General at IUTOX.

1. Background & Role

TCDD Editorial: Could you briefly summarise your career path and how you came to specialise in inhalation toxicology?

Flemming Cassee: I started my career as an inhalation toxicologist towards the end of my biology master's at the Utrecht University. I had done an internship under the supervision of Bas Blaauboer and Heleen Wortelboer, as well as Hein Falke at TNO in Zeist. Based on that I was asked by Vic Feron to do my writing assignment on aldehydes and from there I was asked to become a PhD study on the combined effects of aldehydes on the upper respiratory tract. After receiving my PhD degree, I could start as an inhalation toxicologist at the National Institute for Public Health and the Environment – RIVM- in Bilthoven. At that time there was a big knowledge gap on the causal relationship between particulate matter (inhalable particles, fibres and droplets) in ambient air and the associated health effects and premature death. Under the leadership of Peter Rombout and Leendert van Bree, we focused on the effects of secondary aerosols (mainly nitrates and sulfates) whereas Jos Arts at TNO did work using carbonaceous particles. We soon moved to using the real-word particles, by using specially designed concentrators to increase the concentrations for *in vivo* studies. This was an interesting time as we also put everything in a mobile lab to do these studies for example near a motorway tunnel rather than the relatively clear air in Bilthoven. After several years we also used the technology for controlled human exposures and when about 15 years ago the so-called air liquid interface cell models and exposure equipment became widely available, we also went in the direction of *in vitro* exposure. Interestingly, when doing the PhD project at TNO, we already tried to expose explant of nasal tissues to aldehydes, I would say, pioneering work. Anyhow, from air pollution we expanded the work towards nanomaterials and more recently to micro- and nano-sized plastics and advanced materials whereas others benefit from our inhalation toxicology infrastructure to study effects of e.g., sensitizers.

TCDD Editorial: What motivated you to accept the role of Secretary-General of IUTOX — and what does this role mean to you personally?

Flemming Cassee: At RIVM we do our own research, by and large oriented towards providing support for policy development and regulation. Yet, we rely a lot on the knowledge from others, which is why I have a very large network across the globe and good collaboration with many groups outside the institute. Positions as international organizations will strengthen that position and vice versa. Now, IUTOX also aims to support toxicology in less well-developed countries or at least in countries where toxicology should or is expanding. After 35 years of doing toxicological research, I want to reach out to those that can benefit from my knowledge. After all, I am also a professor at the Institute for Risk Assessment, so teaching and knowledge transfer is part of the job.

TCDD Editorial: For readers less familiar with IUTOX: what is the core mission of IUTOX, and how do you see the role of a Secretary-General in advancing that mission (especially in the coming years)?

Flemming Cassee: IUTOX (International Union of Toxicology) exists to advance toxicology worldwide in a way that protects human health and the environment. At its core, the mission can be summed up as:

- Promoting excellence in toxicological science across regions
- Supporting education and capacity building, especially in low- and middle-income countries
- Facilitating global collaboration among toxicologists, societies, and institutions
- Ensuring toxicology informs public health, environmental protection, and policy in an ethical and evidence-based way

In other words, IUTOX is about connecting science to global well-being, while making sure toxicology expertise is shared equitably, not concentrated in only a few parts of the world. The Secretary-General is less about setting scientific direction and more about making the mission operational and sustainable. The Secretary-General helps ensure the union consistently delivers on how that happens—through coordination, credibility, inclusiveness, and long-term momentum. In times when science is not always appreciated or even not trusted, we have to make sure that what we can offer to the society is made possible by education and training.

2. Science & Society — inhalation toxicology / air pollution / nanomaterials

TCDD Editorial: Your work spans inhalation toxicology, air pollution, particulate matter, and nanomaterials — could you outline what you see as the most pressing scientific challenges in these fields today?

Flemming Cassee: The *in vitro* approaches are considered to be promising for many years now, but there are only a few *in vitro* test for which the derived data are using in risk assessment and regulation. It seems that the predictive value for human health, the reproducibility and the transferability are still key issues that must be solved

TCDD Editorial: Recent years have seen increased attention to ultrafine particles, nanomaterials, and “new-approach methodologies (NAMs)” in toxicology (e.g. in hazard screening of particles). How do you view the promise and limitations of such NAMs — and what remains important in terms of *in vivo* or real-world studies?

Flemming Cassee: Just looking at the respiratory tract, with at least 40 different cell types, the composition that change from the nose to the alveoli, the impact of the morphology and function (breathing patterns) that have a major impact on the dose and dose rate, the interaction with the immune and nervous system makes it still a major challenge to mimic this in *in vitro* models. On top of that, our and other studies have demonstrated that inhaled substances may not affect the lung but they can affect other organs as well as fetuses. From e.g. air pollution we know that chronic exposure has a significant stronger impact on human health than day-to-day variation. On top of that it shows that susceptibility can vary a lot between groups. All these challenges are not easy to address by using only *in vitro* and modeling approaches, so that is the scientific challenge.
So, even though a rat, mouse or rabbit is not the same as a human, we probably have to rely on *in vivo* approaches for some time. Ideally, you’d like to gain a lot of insight using *in vitro* methods, read-across approaches, put the endpoint into the perspective of quantitative adverse outcome pathways and use controlled human exposures to verify the predictions that are based on non-animal testing.

TCDD Editorial: How can toxicologists better bridge the gap between complex scientific findings (e.g. about air pollution, particle toxicity) and public health policy — especially in the Netherlands and Europe?

Flemming Cassee: What remains important is that we train young researchers not only as toxicologists who do excellent science but also teach them how to translate their findings in the language of stakeholders such as citizens, policymakers and regulators.

3. On IUTOX & International Collaboration

TCDD Editorial: As Secretary-General of IUTOX, how do you envision balancing global toxicology priorities (e.g. capacity building in under-represented regions) with the needs and issues in developed countries like the Netherlands / EU?

Flemming Cassee: Balancing global and EU toxicology priorities is not a trade-off, because chemical risks are global while capacities differ. By strengthening toxicology capacity in under-represented regions and sharing EU expertise in regulation, new methodologies, and risk assessment, we create mutual scientific benefit and more robust global chemical safety. This approach allows countries like the Netherlands to remain leaders in innovation while contributing to a safer, more harmonized global system.

TCDD Editorial: What key initiatives or projects do you hope IUTOX will focus on during your tenure — and how can NVT members contribute or benefit from those?

Flemming Cassee: This remains to be seen, we have our first executive board meeting just prior to the Annual Meeting of the Society of Toxicology in San Diego in March where we will do exactly that. IUTOX offers its members a global platform that amplifies scientific impact beyond national or regional boundaries. NVT is member of IUTOX and the NVT members gain access to international networks, world congresses, education and training initiatives, and opportunities to shape global standards in toxicology. I'd say that we enable members to both contribute to and benefit from capacity building, scientific collaboration, and policy-relevant dialogue that strengthens toxicology worldwide.

TCDD Editorial: How did you navigate a career combining academic research (at Utrecht University / IRAS) with regulatory science and public-health advisory work (at RIVM)? What advice would you give early-career toxicologists considering a similar path?

Flemming Cassee: Can be very short on that: decide what you like to do and what in the context of the organization you work for is good for the mission and act. Don't wait for others to help you, but find your own way, dare to do things differently. And above all, create a good network.

From descriptive to mechanistic toxicology, looking back on my 35-year journey

By *Rob Vandebriel*

Coming from a PhD in immunology in an era (the late eighties) when breakthroughs came at a breathtaking pace, when I entered toxicology it seemed like a quiet place. The common approach was exposing animals and measuring a multitude of parameters, such as organ weights, blood parameters, lymphocyte surface markers, and immune function that required *ex vivo* culture of immune cells. The data were collected and put into a paper. The studies were descriptive, and mechanistic understanding was seldom achieved.

35 years ago

My first project measured cytokine production by lymphocytes *ex vivo*, my second a similar question but instead doing the exposures *in vitro*. In the early nineties, these were the first steps towards animal-free toxicology. At that time, most toxicologists felt that animal-free toxicology was impossible. At the turn of the century the human genome was sequenced, paving the way for a comprehensive analysis (microarrays, later RNA-sequencing) towards mechanistic understanding. This progress made me feel that animal-free toxicology based on mechanistic understanding could eventually become feasible. However, for this not only genetics but also *in vitro* models needed a leap forward. Organ-on-chips respond to that need, although much development is still needed. Transition to mechanistic toxicology and advanced *in vitro* models is illustrated by AOP and NAM, words that soon after being coined became centre-stage.

Recent years have seen a re-appraisal of (developmental) immunotoxicology. The developing immune system is sensitive to immunotoxic compounds, and exposure may lead to adverse effects later in life. The developing immune system is complex because of its constant changes in composition in time after conception, and difficult to study in humans for ethical reasons. Nonetheless, techniques such as single-cell RNA-sequencing, *in vitro* B- and T-cell differentiation, and *in vitro* immune responses using cells obtained from tonsillectomy, enable mechanistic, human-centred studies. A re-appraisal is also seen for vaccine studies, significantly driven by the effects of pre- and postnatal PFAS exposure on vaccination responses.

15 years ago

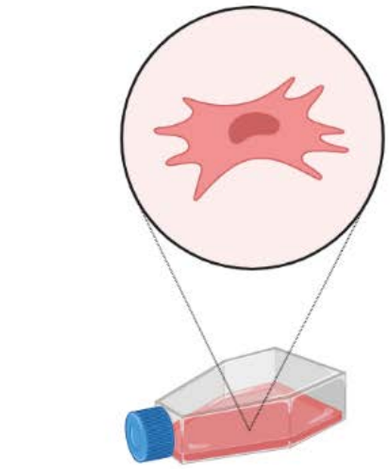
Over the past 15 years, besides small molecules I also worked on nanomaterials and advanced materials. This field of toxicology is particularly challenging because experimentally, many more variables should be taken into account, such as physical-chemical characterisation and absence of endotoxins. Regarding exposure, obtaining adequate dispersions and aerosols, especially of hydrophobic materials such as carbon nanotubes and graphene is challenging.

10 years ago

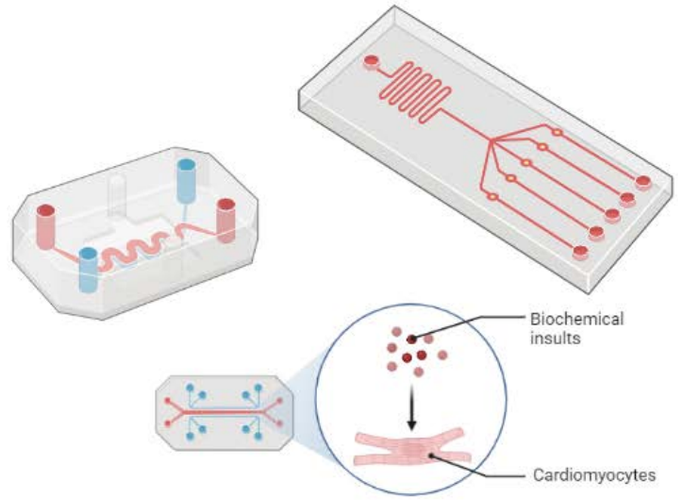
Over the past 10 years, I devoted part of my work on animal-free alternatives in vaccine development and regulatory acceptance. Vaccine immunogenicity and safety is studied in experimental animals. Human 3D *in vitro* models can be used to answer questions that animals cannot, such as effects of age, genetics, and comorbidity, or comparing vaccinated and unvaccinated *in vitro* models derived from the same individual in a vaccination cohort.

The 3D *in vitro* mucosal models used to study airborne pathogens and effects of vaccines resemble those used for testing chemical respiratory sensitization, an endpoint for which no test guideline currently exists. Cross-fertilization of models between these fields is apparent.

Looking back, two things come to mind. First, the constant discovery of immune mechanisms and the incredible developments in molecular biology and cell culture made this journey a very dynamic one. Second and most important, I had the privilege of meeting many kind, generous, and inspiring colleagues, working together at the lab bench or new insights from famous researchers. I will cherish these memories the rest of my life.



2D Cell Culture



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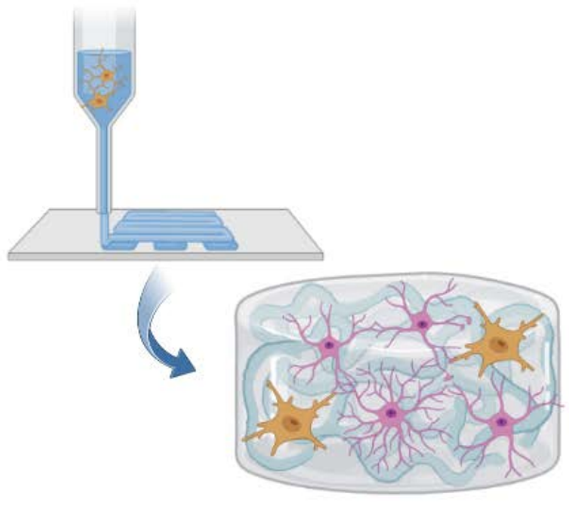
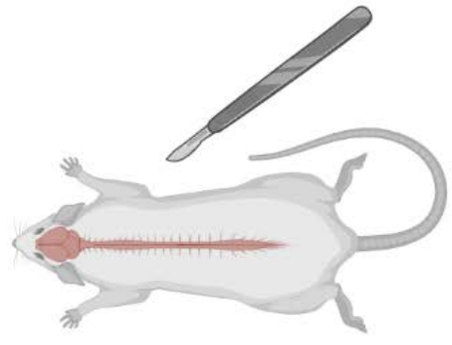


3D Cell Culture



Animal Study

Cereulide in Infant Formula: **Recalls, Risks, and Regulatory Response**

By *Marcha Verheijen*

It probably hasn't escaped your attention: recently there has been a lot of commotion about infant formula. It started with a recall by Nestlé, followed by Danone, Lactalis, Vitagermine, La marque en moins, Granarolo and Hochdorf [1]. The issue is the possible presence of the toxin cereulide.

Health problem: cereulide in infant formula

Cereulide is a toxin produced by certain strains of the bacterium Bacillus cereus. Bacillus cereus is a bacteria that can occur naturally in milk, dairy products and other raw products, but most strains do not pose a risk to food safety [2]. Cereulide, on the other hand, can cause nausea, stomach pain, vomiting, watery diarrhea and fever [3]. In young children and especially infants younger than 6 months, these symptoms may lead to severe dehydration [4]. Parents and caretakers are advised to pay attention to these symptoms and unusual restlessness that occur between 30 minutes and 6 hours after ingestion [2].

Affected infants

Cases of sick infants have been reported in several countries after consumption of potentially contaminated formula. In the Netherlands, the NVWA received six reports of babies who became ill after drinking products that were later recalled [5], while the Belgian FAVV (Federaal Agentschap voor de Veiligheid van de Voedselketen) is investigating around twenty suspected cases [6]; in three of nine tested powder samples cereulide was indeed detected, these positive powders were part of a recall batch. In France, the deaths of two infants are under investigation for a possible link with contaminated formula, although a causal relationship has not yet been confirmed [7].

Communication delays and recall dynamics

The first contamination was picked up by internal quality control at Nestlé at the end of November 2025 in a factory in Nunspeet the Netherlands, after which production on the affected line was halted for further investigation. Nestlé reports that authorities were informed around 9–10 December, but Foodwatch argues that broad public warnings and largescale recalls only really gathered pace weeks later, in January 2026, even though some products had been on the market since October. Foodwatch finds it unacceptable that information from Nestlé is only released at a late stage and that recalls appear to be being rolled out in stages and in a fragmented manner, leaving consumers unnecessarily uncertain for a long time [3].

Identification of the contamination source

Followup investigations showed that the primary source

was not the production line itself, but a contaminated ingredient: arachidonic acid oil (ARA), an omega6 fatty acid routinely added to infant formula [3]. This ARA oil was supplied by the Chinese company Cabio Biotech in Wuhan, one of the major producers serving hundreds of clients worldwide, including Nestlé and Danone [8]. Once Nestlé had identified this ingredient as the source, recall actions were expanded and other manufacturers and countries were notified, though with unnecessary delays [9,10], but again Foodwatch criticises the speed and transparency of informationsharing between companies and authorities and filed a criminal complaint [1].

EFSA actions and new threshold

In response to the multicountry recalls, the European Commission asked the European Food Safety Authority (EFSA) to perform a rapid risk assessment on cereulide in infant formula [11]. Furthermore, the Belgian research center Sciensano discovered that the older testing methods sometimes underestimated the amount of cereulide. According to their findings, measurements in dissolved milk could be up to 75 times higher than in the powdered form. EFSA therefore based its investigation on both the solid and the liquid form of the powder [12]. EFSA has now proposed an acute reference dose (ARfD) for infants of 0.014 microgram cereulide per kilogram body weight, based on vomiting as the critical effect and with additional safety factors for very young infants under 16 weeks [13]. Using high intake scenarios for formula, EFSA concluded that cereulide concentrations in reconstituted infant formula above roughly 0.054 microgram per litre (and slightly higher values for followon formula) raise safety concerns and should therefore trigger recalls. While the EFSA's advice is not legally enforceable, EU member States usually adhere to these values as a key benchmark when deciding on market withdrawals [12], and some countries, such as France, have already lowered their national thresholds to about half of their previous limits to avoid further incidents [14]. This lowered threshold may lead to additional recalls in the upcoming period.

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[12]https://www.hln.be/nieuws/nog-twee-soorten-babymelk-teruggeroepen-ook-in-ons-land-twintigtal-mogelijke-besmettingen~a0b44f33/?referrer=https%3A%2F%2Fwww.google.com%2F

[13] https://www.efsa.europa.eu/en/news/efsa-provides-rapid-risk-assessment-cereulide-infant-formula

[14] https://www.ad.nl/gezond/na-vele-meldingen-van-zieke-kinderen-wil-eu-autoriteit-lagere-drempel-voor-giftige-stof-in-babyvoeding~ab0e41c1/?referrer=https%3A%2F%2Fwww.google.com%2F

AIO toxafette - Kirsten Lassing

In the toxafette, PhD-students working in the toxicology field get the chance to open up about their experiences in performing research. Every issue a new candidate answers a series of questions, and then pass the baton to a fellow PhD-student. This time Kirsten Lassing, from Radboud University tells us about her project.

Can you introduce yourself?
My name is Kirsten. I obtained a Bachelor's degree in Biology and Medical Laboratory Research (HBO), after which I worked as a laboratory technician in medical diagnostics of infectious diseases during the COVID-19 pandemic. I then obtained a Master's degree in Biomedical Sciences, specializing in Drug Safety and Toxicology.

In July 2023, I started my PhD work at Radboudumc (Department of Medical Microbiology) and Radboud University (Department of Environmental Science) in Nijmegen. My work is part of the MIST project (see https://www.mist-project.nl/). This is an interdisciplinary research program supported by NWO Perspectief. This offers collaborations with researchers from fields such as physics, fluid dynamics, and architecture. I also have access to technology and knowledge from the industry. I am currently following the Postgraduate Education in Toxicology (PET) program aiming to become a registered toxicologist (ERT).

You may already know me as the chair of the committee organizing the NVT Annual Meeting in 2025. For the 2026 edition, I am involved supporting the new committee. Outside of my scientific work, you can find me on the ice skating rink or behind a camera. These hobbies give me the healthy distraction from my PhD work.

How is your research related to the field of toxicology, and why did you choose this subject?
My research is rooted in health risk assessment, a core discipline within toxicology. During the COVID-19 pandemic, toxicologists played a role in evaluating exposure risks for healthcare workers and other professionals who use respiratory protective equipment (RPE) to protect from airborne virus transmission.

In my work, I apply a risk assessment framework to study virus transmissibility via aerosols. Using both an experimental set-up in the laboratory and by performing human volunteer studies, I investigate how exposure, dose, and protective interventions (such as face masks) influence the risk of infection. An important part of this research focuses on improving our understanding of RPE performance against viruses and translating this knowledge to further improve guidelines for personal protection and decision-making on mitigation strategies during outbreaks or pandemics.

I chose this subject because it allows me to combine my background in laboratory science and toxicology with interdisciplinary approaches, bridging fields such as microbiology, exposure science, and physics, while highlighting the added value of toxicological thinking in managing infectious disease risks.

What was your motivation for starting a Ph.D. program?
During my Master's program, my main goal was to explore which skills I wanted to develop further and what type of work suits me best. Conversations with scientists in the field led me to the opportunity to start a PhD focusing on risk assessment. As an early-career researcher, I see a PhD as an ideal environment to develop my skills as a researcher as well as my personal competences.

What I found challenging is that this project did not focus on chemical risk assessment, as I had learned during my Master's, but rather on biological hazards. For me this turned out to be a good fit. The PhD work allows me to combine my background in laboratory diagnostics and biology with the toxicological knowledge gained during my Master's training. Working in medical microbiology on interdisciplinary themes felt like a natural continuation of my previous experiences and interests.

How do you see the future of your research topic (follow-up research / social impact)? What do you hope for?
I envision that the data generated from the human volunteer studies will contribute to the development of integrated risk assessment models that account for multiple viruses, human characteristics, and intervention strategies, such as proper face mask use.

On the one hand, this research can help us better understand how facial features influence mask performance and what best practices are for effective use. On the other hand, considering the ongoing risk of large-scale epidemics or future pandemics, I hope that the knowledge gained through this project (and follow-up research) can help to reduce the overall burden of infectious diseases by improving preventive strategies.

What goals do you have regarding your career after finalization of your PhD? Would this be inside or outside academia, and why? Would you consider going abroad?
After finishing my PhD, my main goal is to find a position that gives me energy and allows me to contribute to work with societal relevance. As a future ERT, I believe that many roles (both inside and outside academia) can have meaningful societal impact. At this stage, I am open to both career paths, as each has its own advantages and challenges.

I value networking and exchanging ideas with others to identify new opportunities. I strongly believe that career development is something you do together. Regarding working abroad, I would be open to it in principle, but I also value my personal environment, so first I would like to explore opportunities closer to home.

How do you plan to share your research findings with both experts and non-experts?
I believe that effective dissemination is an essential part of research, especially when the topic has direct relevance for public health. For expert audiences, I share my findings through scientific publications, conferences, and discussions within interdisciplinary collaborations.

At the same time, I find it important to communicate results to non-experts in an accessible and transparent way. Within the MIST project, we have a dedicated work package focused on outreach and public engagement. The COVID-19 pandemic highlighted how crucial clear communication is for maintaining trust and ensuring that scientific knowledge can be translated into meaningful action.

How do you ensure that others can replicate your experiments and achieve the same results?
Reproducibility is a key principle in research, but in practice it requires constant attention and reflection. I find it important to carefully prepare experiments, often writing detailed Standard Operating Procedures, and I regularly ask my students for feedback on whether these protocols are clear and useful. In my own work, no two experiments are ever exactly the same, so I keep track of conditions like temperature, humidity, and wind speed. To draw meaningful conclusions, I try to repeat measurements whenever possible. This can be challenging when relying on human volunteers, so I make sure to first run pilot studies to refine procedures and ensure consistency.

Working in an interdisciplinary environment has strengthened my awareness of reproducibility even further, because clear communication across fields is essential. By being transparent about my methods and carefully documenting each step, I aim not only to make my work reproducible, but also to create something that others can learn from and build upon.

How do you expect society will benefit from your PhD research?
My PhD research aims to contribute to a better understanding of how airborne viruses are transmitted and how interventions such as face masks can reduce infection risk. By integrating experimental data into risk assessment models, this work can help inform evidence-based guidelines and preparedness strategies for future outbreaks or pandemics.

Ultimately, I hope that my research supports better protection of healthcare workers and the general population, reduces uncertainty during public health crises, and contributes to lowering the overall burden of infectious diseases.

How do you combine your PhD project with your personal life? Are there choices you have to make?
Combining a PhD with personal life requires conscious choices and setting boundaries. Research can be demanding and open-ended, which makes it important to create moments of rest and perspective outside of work. For me, activities such as ice skating and photography help me recharge and maintain balance.

I have learned that taking care of my personal well-being is not separate from doing good science, but rather a condition for it. Finding a sustainable balance helps me stay motivated, focused, and engaged throughout my PhD journey.

Please answer the question from the last toxafette PhD-candidate: Has your work in toxicology influenced your lifestyle in any way, for example, has it changed what food or products you choose to buy?
Yes, working in toxicology has definitely influenced my lifestyle, although in a balanced way rather than becoming fanatical. My interest in how substances affect the human body actually started even before my PhD, when I was highly involved in ice skating competition. During that time, I started taking food

supplements and became curious about what was truly beneficial and why. This initial interest later grew when I entered the field of toxicology, where I gained a deeper understanding of how and why some supplements may be healthy and others less so or even unnecessary.

When it comes to food and consumer products, I try to make conscious choices, for example by opting for more eco-friendly, biological, or locally produced products when possible. At the same time, I strive to maintain a realistic balance rather than being overly strict. My toxicology background has mainly helped me to make informed decisions instead of simply following market trends or assumptions.

Family, friends, and even acquaintances often ask me for advice about supplements, chemicals in products, or potential health risks, which I always find both amusing and rewarding. I see it as a positive side effect of my work that I can help others think more critically about these topics as well.

Changes to Travel Bursary Applications

Changes in the requirements for travel bursary applications and candidates for the Joep van den Bercken Prize Starting in 2027, the requirements for nominating a candidate for the Joep van den Bercken Prize will change. **Candidates must have been a member of the NVT for at least one year.** This requirement will also apply to travel bursary applications. We hope this will encourage more (young) toxicologists to become involved in the NVT.

Please inform your (fellow) PhD students/ Master's students! Membership is available through Membership - Nederlandse Vereniging voor Toxicologie and costs only €20 per year.

Spring is just around the corner and the registration to the NVT Annual Meeting 2026 is open!

We would like to invite you to this annual event. The NVT Annual Meeting 2026 will take place in the new venue, De Eenhoorn in Amersfoort on June 23rd (Tuesday) and 24th (Wednesday). The theme for this year is ''Toxicology at every scale: from molecules to ecosystems'' and features four subthemes: small molecules, big consequences; small to big data; life in formation; and our planet under pressure.

Registration opens on February 2 (Monday) via our website. The abstract submission deadline is March 31 (Tuesday) and early bird registration will be available until May 22 (Friday).

We also highly recommend booking your hotel accommodation in advance. Booking information is available here. The price per room is €125 per night for a single room, including breakfast. Please note that unused room allocations will all be released on May 22, 2026.

We will share further updates in the coming weeks. We look forward to welcoming you in Amersfoort!

On behalf of the organizing committee of 2026:

Sanah Majid Shaikh, Kirsten Lassing, Emmely Wagener, Can Jiang, Judith de Heer, Tim Verbruggen, Thijs Benschop, Bensu Tangil, Sara van Kaam, Milou Hendriks, Lucy Sinke

Laura Hondebrink, Joanne Salverda, Daan Touw, Hans Bouwmeester

P.S. Updates about the Annual Meeting will also be shared via LinkedIn. Follow our page to stay informed: https://www.linkedin.com/in/nvt-annual-meeting-78b52329a/

TERUG NAAR INHOUD

The TCDD Christmas Puzzle Contest Winner!

The winner of the 2025 Christmas Puzzle is **Jacqueline Steenbergen - Biesterbos!**

A randomizer was used to select the winner. Congratulations! Jacqueline wins a special prize!

International Conference on Environmental Mutagens 2026 Registration Open


By Ianlebruce - Own work, CC0

The NVT Section for Genetic Toxicology is pleased to remind you that registration for the 14th International Conference on Environmental Mutagens (ICEM 2026) is now open.

The Super Early Bird deadline (31 January 2026) has now passed, but **Early Bird registration rates are available until 31 March 2026 (23:59 GMT):**

Delegate – £725
PhD Students – £410
Fellow / Emeritus (Retired) Member – £410
Invited Speaker (Not Sponsored) – £380

Standard rates will apply from 1 April 2026 onwards.

Registration includes attendance at all scientific sessions, the welcome reception, and coffee breaks. Lunch is not included. Gala dinner tickets (held at the National Museum of Scotland) can be purchased separately.

Please note that the **abstract submission deadline is 31 March 2026 (23:59 GMT).**
If you require abstract acceptance before completing payment for registration, please contact the ICEM Office directly.

Register now via the ICEM website

The 14th International Conference on Environmental Mutagens (ICEM 2026) will take place from **6–10 September 2026** at the Edinburgh International Conference Centre (EICC), Scotland.

Organised jointly by the European Environmental Mutagenesis and Genomics Society (EEMGS) and the United Kingdom Environmental Mutagen Society (UKEMS), under the auspices of the International Association of Environmental Mutagenesis and Genomic Societies (IAEMGS), ICEM 2026 will focus on:

“Blending new technology with traditional genotoxicity approaches to solve real world problems.”

The scientific programme will feature:
- 30 symposia
- 10 plenary lectures
- Interactive poster sessions

Key themes include genome damage mechanisms, innovative *in vitro* models, artificial intelligence and bioinformatics applications, and regulatory advances in environmental mutagenesis and genomic health.
In addition to the scientific programme, delegates will enjoy extensive networking opportunities, social events, and a gala dinner at the National Museum of Scotland. A programme for accompanying persons will also be available, offering opportunities to explore Edinburgh and the surrounding region.

TERUG NAAR INHOUD

TCDD is de nieuwsbrief van de Nederlandse Vereniging voor Toxicologie (NVT).