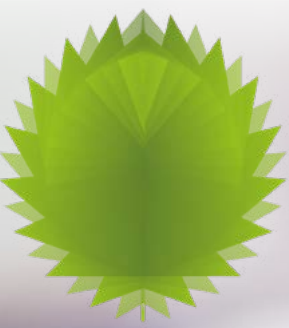


TCDD



T O X I C O L O G I E

NUMMER 49
OKTOBER 2026

SPECIAL THEME

Current Topics in Pharmaceutical Toxicology

- FLUORINATED PHARMACEUTICALS THAT MEET THE PFAS DEFINITION: A NEED TO WORRY?
- HOW TOXIC ARE WEIGHT-LOSS MEDICINES?
UNDERSTANDING THE RISKS OF GLP-1-BASED TREATMENTS
- FROM ANIMALS TO ALTERNATIVES: OPPORTUNITIES IN REGULATORY TOXICITY TESTING
- PROTECTING THE KIDNEY DURING DRUG DEVELOPMENT

Colofon

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Secretariaat

Hester Hendriks,
Rijksinstituut voor Volksgezondheid en Milieu
Postvak 1, Postbus 1, 3720 BA Bilthoven
E-mail: secretaris@toxicologie.nl

Redactie

Devon Barnes
Damiën van Berlo, *National Institute for Public Health and the Environment (RIVM)*
Jelmer Faber, *Maastricht University*
Barae Jomaa, *Colonial Chemical*
Héloïse Proquin, *National Institute for Public Health and the Environment (RIVM)*
Puck Roos, *Medicines Evaluation Board (CBG-MEB)*

Webredactie

webmaster@toxicologie.nl

Lidmaatschap en Adreswijzigingen

Ledenadministratie NVT, p/a KNCV
Postadres: Loire 150, 2471 AK, Den Haag
tel. 070 - 337 87 97
Via NVT website na inloggen
<http://www.toxicologie.nl>
E-mail: administratie@toxicologie.nl

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.

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- Gewoon lid: € 67 per jaar
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Marleen Mulder
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www.greenbeandesign.nl



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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.

Dear readers,

It is the time of year when everyone is back from their summer holidays and enjoying the last few days of good weather. In the TCDD we're celebrating this return to studies/work with a special issue related to pharmaceutical toxicology. There is an old adage that toxicology is the flipside of pharmacology and in some cases, they are one and the same. How safe are pharmaceuticals, which, after all, are chemicals designed to elicit a biological effect? This is something that this issue's contributing authors will be exploring.

Toxicology is dear to me. The appreciation for this science was instilled in me by a great lady by the name of Ivonne Rietjens. Professor Rietjens led me through every step of my PhD, taught me structure, discipline, perseverance and, most of

all, the many joys of research. Needless to say, my life would not have been the same without Ivonne. Along with all other toxicologists that have crossed her path, I will deeply miss her presence and wish all the strength to her loved ones.

As the leaves fall, we get ready to close one chapter and open a new one. I hope that you enjoy reading this special issue of the TCDD and would love to hear your thoughts. You can also share your insights and/or research with the rest of the Dutch toxicology community by sending us an email at redactie@toxicologie.nl

Sincerely,

Barae Jomaa



News from the board

This was a long and hot summer and we hope you all enjoyed it and that you made a fresh and inspiring start.

The board has not been sitting on their hands. Ongoing and upcoming activities include:

- A revision of our bylaws and internal regulations to comply with the current law
- To give substance to the 'future proofing' of our organisation
- New website
- Looking back at the NVT-2 day in June 2026 and making plans for the 2027 meeting
- Revising the regulations for supervisors

There is much to do in a society such as ours and much is done by volunteers. 'Many hands make light work' is a well-known Dutch proverb. Therefore, the board is looking for **young professionals** (both PhD students and early career colleagues) to help organise the NVT-2-day conference in June 2027. This will give you the opportunity to:

- Contribute to the annual meeting
- Think about the content of the scientific program
- Select and interact with the speakers

- Get experience in organising and chairing a session
- Broaden your toxicology network

If you are interested in contributing, please contact secretaris@toxicologie.nl

If you are a medior or senior toxicologist and would like to contribute, please don't hesitate to reach out!

Finally, we warmly encourage you to submit manuscripts to the Journal of the Netherlands Society of Toxicology (JNST). The Board wishes all members an inspiring start of 2026-2027.

Daan Touw
Chair



Call for submissions – next issues of TCDD

Are you interested in contributing to the next issues of TCDD? We welcome ideas and submissions on the following special themes. Please get in touch with us at redactie@toxicologie.nl.

TCDD #4, 2026: *Cosmetics and Consumer Products*

This issue will focus on the toxicology of substances in cosmetics, personal care and household products.

Submission deadline: 13 November 2026

TCDD #1, 2027: *Natural Disaster Toxicology*

This issue will explore the toxicological consequences of natural disasters. How can heavy rains or other natural disasters contaminate food, water and more?

Submission deadline: 12 February 2027



In memory of our beloved colleague Ivonne Rietjens

We received the sad news that emeritus professor Ivonne Rietjens passed away on 11th August 2026. Last year we learned that Ivonne was very ill, only months before her official retirement. Her passing comes as a shock and is extremely sad.

Ivonne was an inspirational chair of the Wageningen Toxicology department for almost 25 years, and she leaves an important legacy, not only scientifically but also personally. She has guided many of us through important steps in our careers, for which we are grateful. She has supervised more than 100 PhD students to a successful defense, which illustrates her drive to educate people and even more so her passion for research. In her work, Ivonne was extremely efficient and focused on results. This was a side of her which was well known to people. Perhaps less obvious is the fact that she was always very helpful to students and colleagues.

Ivonne was also renowned beyond Wageningen. Her scientific standing is illustrated by her membership in the Koninklijke Nederlandse Akademie van Wetenschappen (KNAW) and by the 2024 Merit Award she received – after nomination by the board of the NVT – from the Federation of European Toxicologists & European Societies of Toxicology (EUROTOX) in recognition of her extraordinary contribution to the field of toxicology.

Within the NVT Ivonne took on important roles, as chair and vice chair of the NVT board, as member of the

Concilium Toxicologicum and as educator for Toxicologist in Training. As an educator, she supervised the highest number of toxicologists in training over many years. Her dedication to mentoring young professionals is also evident from the interview she gave together with Jan Hendriks for the TCDD in 2014, which resulted in eleven pieces of career advice. Ivonne was also a highly visible and active presence at the annual meetings of the NVT. In 2017, she was invited to deliver the keynote lecture as a tribute to her extensive body of work and the many PhD students she had supervised. She was likewise committed to bringing international congresses to the Netherlands; for example, she served as secretary of the organizing committee for EUROTOX 2007 in Amsterdam. With Ivonne, we lose a remarkable person with kaleidoscopic qualities. We will miss her dearly. We wish her sons Kevin and Max, and their budding families, her partner Paul van Helvert, other family members and loved ones, much strength in dealing with this great loss. We hope they find consolation in knowing that Ivonne's heritage will endure. Through her influential scientific work and the many researchers she trained, who now carry her scientific legacy into laboratories, lecture halls and boardrooms across the world, she will continue to inspire generations to come.



The NVT board



PHARMACEUTICAL TOXICOLOGY

Spring symposium of the section pharmaceutical toxicology

New Meds, New Challenges – navigating risks, innovation, and sustainability

This summary provides an overview of the key presentations, discussions, and take-home messages from the Spring Symposium. The event brought together researchers, students, and professionals to share recent developments, exchange ideas, and discuss future directions within the field. The highlights below capture the main themes and findings presented during the symposium.

Charlotte de Wolf: Regulatory considerations in non-clinical development of new medicines.

An overview of the full non-clinical toxicology package needed for marketing authorisation application (MAA) was shown for small molecules. General toxicity studies are usually required in two species (rodent and non-rodent), in line with ICH guideline M3. In addition, the package should include *in vitro* and *in vivo* genotoxicity testing (ICH S2), *in vivo* carcinogenicity testing (ICH S1) and studies on reproductive and developmental toxicity (ICH S5). Different types of new medicines were introduced and what differs in the required toxicology package. For biologicals, like monoclonal antibodies (mAbs), that have higher specificity, tox studies in 1 species may be sufficient if there are no or only 1 pharmacologically relevant species (often monkeys). Guidance is found in ICH S6. Oligonucleotides (ONTs) are generally tested similarly to small molecules, although given their higher specificity sometimes an ICH S6 approach is used. A new guideline for ONTs, ICH S13, is being written.

Advanced therapy medicinal products (ATMPs) include tissue-engineered products, somatic cell therapy and gene therapy. Many different guidelines exist, though the non-clinical development is not standard and rather a case-by-case situation. ICH S12 is one of the relevant guidelines for (distribution of) gene therapy. For ATMPs, it is usually sufficient to perform a general toxicity study (combined with biodistribution) in a single animal species. Genotoxicity testing is usually limited to an assessment of vector integration risk or off-target site analyses (*in silico* and *in vitro*) in case of gene therapies. Tumorigenicity testing is mainly related to evaluation of potential proliferative signs at histopathology in the general toxicity study. Reproductive studies are often not required, though it depends on the biodistribution and integration risk in germline cells. Take home message; talk to the regulator for the optimal non-clinical package; examples of toxicology packages were discussed for ONTs, mAbs, ATMPs (such as gene therapies) and compared against small molecule standards.



Liesbeth Heijink: Insights in non-clinical development of AAV gene therapies.

Various aspects of gene therapy development were covered, supported with example therapies. AAVs (Adeno Associated Viruses) are selected as an example gene therapy. These vectors, containing the gene of interest, are administered only once and provide durable gene expression, resulting in long term efficacy. (Clinical) biomarkers are essential to understand biodistribution of the vector and efficacy of the transgene. Toxic immune responses are the main safety risks, especially when high doses of viral particles are needed for efficacy. 3Rs and platform approaches are important to reduce animal use. Where possible biodistribution, efficacy and safety assessments are combined in nonclinical animal studies.

Loan Honeywell: Impact of immunogenicity on clinical efficacy and safety of biological drugs.

Biological drugs can provoke an immune response, unlike small molecules. Clinical consequence of so-called anti-drug antibodies (ADAs) can range from no clinical effect to life threatening reactions. ADAs can lead to three types of clinical effects: PK (resulting in exposure changes with diminished or exaggerated pharmacology), efficacy (neutralizing antibodies leading to reduced efficacy), safety (e.g. acute reactions, non-acute ADA-mediated reactions, auto-immunity by cross-reactions). Risk of ADAs can be reduced by using immune-modulators. ADAs need to be sampled and characterized in clinical trials. It is important to investigate and monitor the clinical consequences of immunogenicity throughout the entire life cycle of biological drugs.

Caroline Moermond: Environmental risks of pharmaceuticals: current methods and future developments.

Where marketing authorization depends on the use of the substance or product (e.g. industrial chemicals or human pharmaceutical), environmental quality legislation is based on the environmental compartment, e.g., soil or water. Retrospective risk assessment (actual exposure measurements) does not feed back into prospective risk assessment (based on estimated use) as performed for marketing authorisation. For marketing authorisation of human pharmaceuticals, an environmental risk assessment (ERA) is performed, but with current legislation there is no consequence (not part of the risk/benefit assessment). With the revised pharmaceutical legislation, a suboptimal ERA or insufficient risk mitigation will on its own be grounds for refusing market authorization. New information, e.g., from water legislation, can be a reason for re-evaluation. Redesigning of drugs to minimize environmental impact

does not seem a promising avenue if the focus is only on degradation. Environmental sustainability assessments, regarding ERA and other aspects of the environmental footprint, need to be harmonized across Europe.

Mirjam Luijten: New Meds, and thus new safety assessments?

(Human health) next-generation risk assessment takes advantage of scientific insights for new methods of toxicity testing, with the aim to enhance mechanistic understanding and to further reduce animal use. A large variety of case studies have provided insight into the applicability of next-generation risk assessment (NGRA). NGRA requires flexibility for the use of *in vitro* and/or *in silico* new approach methodologies (NAMs). Barriers hampering the implementation of NGRA include end-users not understanding NAM data, and a too large number of NAMs being included in a dossier. The Horizon 2020 project “RISK-HUNT3R” has developed a workflow that serves as guidance on data generation and data interpretation; it involves a tiered approach for which NAMs to include for hazard, ADME and exposure. The exact steps to be followed in the workflow depend on the problem definition at hand. Data from the different NAMs together feed into final data integration, uncertainty compilation and risk assessment. Documentation of both the data used and the rationale for various decisions made in the risk assessment process needs to be clear, to ensure a structured and transparent process. Dedicated case studies to evaluate the applicability of the NGRA workflow are underway and will advance the acceptance of NGRA approaches for regulatory decision-making.



Fluorinated Pharmaceuticals that Meet the PFAS Definition: **A Need to Worry?**

Per- and polyfluoroalkyl substances (PFAS) are everywhere, and that much has been made amply clear in both the wider news media and in toxicology journals. There is no debate about their persistence since the carbon fluorine bond is the strongest single bond that carbon forms, which is what makes highly fluorinated molecules resistant to microbial degradation and therefore persistent in the environment and in our bodies (Wackett, 2021). Much has been circulated about the deleterious health effects of PFAS, with PFOS and PFOA used as examples to come to the conclusion that PFAS may cause cancer and disrupt our hormonal system. While widely known as “forever chemicals”, pharmacologists may instead be more familiar with the potency and metabolic stability that the carbon fluorine bond confers on common pharmaceuticals such as fluoxetine (Prozac) and sitagliptin. Around 15 to 20% of marketed small molecule drugs incorporate at least one fluorine atom. In 2025, 14 of the 29 small molecule entities approved by the FDA contained fluorine, the highest proportion over the 2021 to 2025 period (Mishra et al., 2026). Many of the fluorine-containing medicines, including fluoxetine and sitagliptin, fall under the 2021 OECD definition of what constitutes PFAS. But how can PFAS be both harmful chemicals and simultaneously thoroughly tested and approved medicines? The short answer is that PFAS is a category that encompasses more than ten thousand diverse chemicals (ECHA, 2023) and just because PFOS and PFOA have been associated with cancer and endocrine disruption does not automatically mean that all the other PFAS molecules also carry the same hazards. But what about persistence? The very bond that makes these molecules metabolically stable also makes them persist in the environment. One of the arguments is that environmental contamination with PFAS from pharmaceuticals is a small portion of overall PFAS contamination. This invites another question, do the benefits outweigh the risks? Given that these pharmaceuticals are still on the market, the answer from the regulators appears to be yes.



By Barae Jomaa

Sign posted on a bridge over a river in Michigan, USA: “Avoid Foam. Foam may have high amounts of PFAS.” Photo by MountaineFae, CC BY-SA 4.0.



Defining PFAS

The OECD definition of PFAS is the one most widely used: a PFAS is a fluorinated substance containing at least one fully fluorinated methyl or methylene carbon with no hydrogen, chlorine, bromine or iodine attached, so that almost any chemical with a -CF₃ or -CF₂- group qualifies (OECD, 2021). The proposed EU universal restriction on PFAS, an Annex XV dossier submitted by five national authorities in 2023, highlights the limitations of the OECD definition as it is “based on chemical structure” and “hazardous properties or risks are not part of it”, whereas the scope of their own proposal is “additionally a concern-based one”, intended to cover PFAS that are very persistent (ECHA, 2023). The proposed EU universal restriction on PFAS excludes from the scope a few subgroups that are shown to mineralise fully to CO₂, H₂O and HF, leaving no persistent perfluoroalkyl acid degradation products (ECHA, 2023). The restriction on PFAS in firefighting foams, by contrast, applies the OECD formulation with no such exclusion (European Commission, 2025). EPA’s Office of Pollution Prevention and Toxics (OPPT) applied a narrower definition in 2021, requiring the unit R-CF₂-CF(R₁)(R₂) with a saturated carbon-carbon bond, which a lone trifluoromethyl group does not satisfy (US EPA, 2021). The 2023 TSCA section 8(a) (7) reporting rule replaced that with three explicit structural classes, and acknowledged that the definition “may not be identical to other definitions of PFAS used within EPA and/or other organizations” (US EPA, 2023a).

In the preamble to that reporting rule, the EPA estimated that roughly 23,000 additional substances would be captured by the OECD definition, and that about 17,000 of them would qualify only due to the presence of one terminal CF₃ group with no other fluorine in the molecule (US EPA, 2023b). Interestingly, the presence of only one terminal CF₃ group is the bucket into which most fluorinated pharmaceuticals fall.

State legislation diverges even further. Washington, Vermont, Maine, California and the federal National Defense Authorization Act all rest on the “at least one fully fluorinated carbon” formula, while Delaware and West Virginia require at least two fully fluorinated carbon atoms and exclude gases and volatile liquids, and Maryland simply names thirteen substances.

Hammel et al. (2022) screened 360 organofluorine pharmaceuticals approved globally between 1954 and 2021 against nine published PFAS definitions. Depending on which definition is applied, between 1% and 100% of these fluorinated pharmaceuticals are considered PFAS. The 2021 OECD definition captures 107, fluoxetine among them. The cholesterol-lowering drug atorvastatin further highlights the problem with varying definitions. It has an aromatic ring bound directly to a single fluorine atom, which does not fulfil the PFAS definition on its own (OECD, 2021). However, even though its single aromatic fluorine falls outside every perfluoroalkyl based definition, the phrase “at least one fully fluorinated carbon” used in the US National Defense Authorization Act and in several state laws does not specify saturation, so atorvastatin can be captured. That definition is so broad that it covers 337 of the 360 medicines screened in the Hammel et al. study.

A definition written to identify substances that are likely to be extremely persistent may therefore have the unintended effect of capturing essential substances, including medicines whose safety under prescribed use is proven, in the process. That is the logic of the “P-sufficient” approach, under which high persistence alone is taken to justify regulation irrespective of measured toxicity (Cousins et al., 2019a; Jomaa, 2021). Fluorine blocks sites of oxidative metabolism, modulates pKa, adjusts lipophilicity and improves target binding. About one third of the antiretrovirals approved since 1981 contain it (Han and Lu, 2023; Ismail and Ayoup, 2022).

Not all fluorinated pharmaceuticals fall under the OECD definition of PFAS

Much of the fluorine in medicines sits as a single aromatic fluorine or an isolated C-F bond. Those substituents are not captured by the OECD definition and do not behave like perfluoroalkyl acids (PFAAs). What is captured is the trifluoromethyl group, intended to resist metabolic breakdown, and that stability carries downstream to eventual environmental degradation, or lack thereof.

TFA

Degradation is also not a silver bullet when it comes to PFAS due to their potential to break down into trifluoroacetic acid (TFA), which is a highly mobile, non-degradable ultra-short-chain perfluoroalkyl substance. Scheurer et al. (2017) subjected a mixed set of -CF₃ bearing compounds to biodegradation and ozonation, including fluoxetine and sitagliptin alongside fluorinated pesticides, and observed formation of trifluoroacetate, the anion of TFA, identifying wastewater treatment plants as an overlooked TFA source rather than a sink. This is because treatment plants cannot degrade most PFAS sufficiently (Nguyen et al., 2022). TFA forms from some -CF₃ compounds under defined conditions, and yields are compound specific. In most pharmaceuticals the -CF₃ group sits on an aromatic or heteroaromatic ring, so release requires degradation of that ring rather than cleavage of a side chain. Guo et al. (2025) traced that sequence for fluoxetine, following a ¹³CF₃ isotopologue of its transformation product 4-(trifluoromethyl)phenol through hydroxylation, ring opening and oxidative cleavage to TFA, with a steady state yield of 8.0% under acidic conditions (Figure 1). TFA is a terminal degradation product where a C-CF₃ moiety resists biochemical and photochemical degradation (Arp et al., 2024). The pathway is therefore real, but requires ring degradation rather than side chain cleavage, and that is a much slower process.

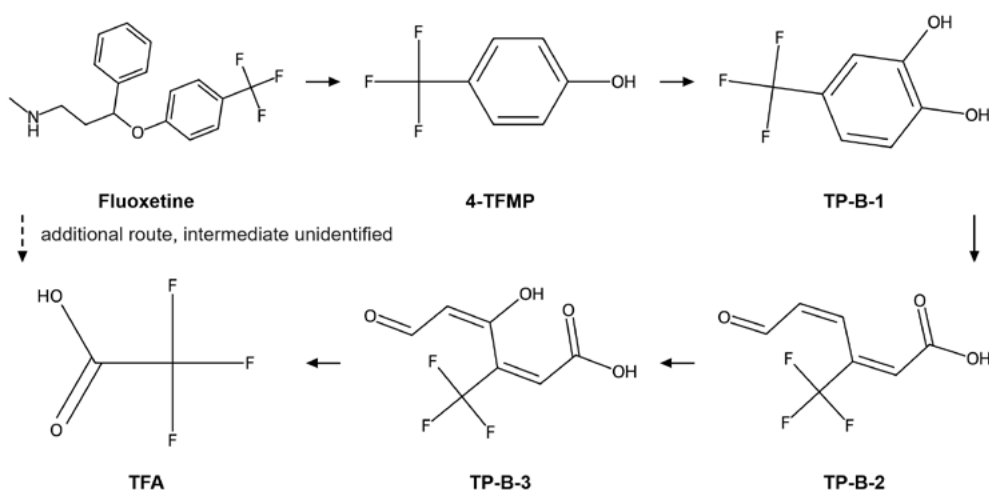


Figure 1. Photochemical formation of TFA from fluoxetine via 4(trifluoromethyl)phenol (4TFMP) and the oxidation products TPB1 to TPB3. The CF₃ carbon is carried through unchanged; the dashed arrow marks a second route bypassing 4TFMP. Adapted from Guo et al. (2025).

TFA is not as well-known as other PFAS compounds such as PFOA and PFOS, both of which carry harmonised classifications as Carc. 2 and Repr. 1B under Annex VI to CLP (European Union, 2008), but deserves closer attention. Arp et al. (2024) report concentrations in rain, soil, plants, serum and drinking water orders of magnitude above other PFAS, accumulation that is effectively irreversible because emissions continue while degradation does not. In June 2026 ECHA's Risk Assessment Committee (RAC) adopted an opinion supporting Germany's proposal to add Repr. 1B to TFA's existing Annex VI entry, together with persistent, mobile and toxic (PMT) and very persistent, very mobile (vPvM) designations (ECHA, 2026b). The concern with PFAS pharmaceuticals is therefore not necessarily with the active compounds but rather with their potential degradation products.

The share of PFAS from pharmaceuticals

Chemical regulations such as EU REACH are tiered by

tonnage with the degree of oversight being commensurate with the quantities placed on the market. Among substances carrying only a single -CF₃ group, and therefore potential TFA precursors, the EU PFAS Restriction proposal lists fluorinated gases, biocides, plant protection products and "pharmaceuticals containing a -CF₃ group bound to an aromatic ring". The proposal also underlines that fluorinated gases "form the largest contribution by production volume to this subgroup" (ECHA, 2023). Arp et al. (2024), citing the German Environment Agency inventory of national TFA emissions, state that in Germany, refrigerants and blowing agents are the largest quantifiable source at roughly 2,000 tonnes per year, with pesticides following at roughly 457

tonnes per year, dominated by flufenacet, diflufenican and fluazinam. Human pharmaceuticals account for roughly 29 tonnes per year. That is around 1% of the quantified total, which is a relatively minor amount. Several further sources, including direct TFA production, biocides, veterinary medicines and fluorochemicals in articles, could not be quantified at all.

In our blood

PFAS are in our blood, but targeted analysis explains only part of the extractable organofluorine (EOF) in human serum. Individual PFAS are quantified against authentic standards by LC-MS/MS, which cannot be done across thousands of substances, so total organic fluorine serves as the aggregate measure and the difference between the two is what goes unassigned. Pennoyer et al. (2023) analysed 44 PFAS and found the unexplained organofluorine fraction ranged from 15% to 86% of EOF in commercial U.S. donor serum. Using pharmacokinetic estimates, they estimated

that organofluorine attributable to pharmaceuticals could reach tens of nanograms of fluorine per millilitre of serum. Nonetheless, the observed association between self-reported pharmaceutical use and unexplained organofluorine was weak and not statistically significant. In a separate study, ultrashort and short-chain PFAAs, particularly TFA and PFPrA, have been found to dominate measured PFAA burdens in U.S. homes and residents (Zheng et al., 2023).

Safety or essential use?

The EU universal PFAS restriction takes advantage of the essential use concept in order to identify uses that can be phased out. The concept was developed and applied to PFAS uses, categorizing uses as non-essential, substitutable, or essential (Cousins et al., 2019b). The Restriction Dossier Submitters proposed time unlimited derogations for PFAS used as active substances in medicinal, biocidal and plant protection products. RAC accepted the overarching derogation in principle but held that the medicinal products framework does not fully address emissions of persistent PFAS, and recommended sector specific measures to minimise them. SEAC, the Committee for Socio-economic Analysis, found a time unlimited derogation for active substances to be unjustified and inconsistent with the rest of the restriction. It noted that the impacts of a ban on these uses had not been assessed, so it could not conclude that costs would outweigh benefits (ECHA, 2026a). SEAC's recommendation involves a general concentration-based ban with tailored, time-limited derogations where the socio-economic case for continued use is demonstrated. Its conclusions on medical uses are mixed rather than negative: most derogations for medical devices are deemed to be justified or likely justified while packaging for medical devices was only deemed to be partly justified. For the eight sectors added in 2025, which include other medical applications, SEAC could not reach a conclusion and

recommends interim time limited derogations until those uses are evaluated. Its final opinion is expected by the end of 2026.

A medicine containing a -CF₃ group will not be exempt from a future restriction because the chemistry is benign. After all, pharmaceuticals are meant to be bioactive and, as Paracelsus would say, it is the dose that makes the poison. An eventual exemption will also not rely on the lack of persistence, given the resilient nature of the carbon-fluorine bond. Whether or not we continue using fluorinated pharmaceuticals that fall under the OECD definition of PFAS will boil down to the socioeconomic case.

Conclusion

“It is a drug, therefore safe under all settings and throughout the lifetime of the substance” and “it has a -CF₃ group, therefore is similar in its health hazards to PFOA” are both misconceptions. Of the 360 drugs screened by Hammel et al. (2022), 50% carry a single fluorine atom including 35% where that single fluorine is aromatic, only 10% contain more than three fluorine atoms, 88 carry at least one trifluoromethyl group, and only four are fully or nearly fully fluorinated aliphatic compounds. An aromatic fluorine, a -CF₃ group and a perfluoroalkyl chain have different metabolic and safety profiles. The concern with fluorinated actives has little to do with patient safety and a great deal to do with manufacturing emissions and wastewater, where medicines remain a minor contributor. Regulatory attention will most likely take the form of emission minimisation obligations, management plans and reporting, rather than a ban on the prescription of these currently essential substances.

References

- Arp, H.P.H., Gredelj, A., Glüge, J., Scheringer, M., Cousins, I.T. (2024). The global threat from the irreversible accumulation of trifluoroacetic acid (TFA). *Environmental Science & Technology* 58(45), 19925–19935. [doi:10.1021/acs.est.4c06189](https://doi.org/10.1021/acs.est.4c06189)
- Cousins, I.T., Ng, C.A., Wang, Z., Scheringer, M. (2019a). Why is high persistence alone a major cause of concern? *Environmental Science: Processes & Impacts* 21, 781–792. [doi: 10.1039/c8em00515j](https://doi.org/10.1039/c8em00515j)
- Cousins, I.T., Goldenman, G., Herzke, D., et al. (2019b). The concept of essential use for determining when uses of PFASs can be phased out. *Environmental Science: Processes & Impacts* 21, 1803–1815. [doi: 10.1039/c9em00163h](https://doi.org/10.1039/c9em00163h)
- ECHA (2023). Annex XV restriction report: proposal for a restriction. Per- and polyfluoroalkyl substances (PFASs). Version 2, 22 March 2023. Dossier Submitters: BAuA (Germany), RIVM (Netherlands), KEMI (Sweden), Norwegian Environment Agency, Danish EPA. European Chemicals Agency, Helsinki.
- ECHA (2026a). RAC final opinion (2 March 2026) and SEAC draft opinion (10 March 2026) on the proposed universal restriction of per- and polyfluoroalkyl substances under REACH. European Chemicals Agency, Helsinki; consultation launched 26 March 2026.
- ECHA (2026b). Minutes of the 77th meeting of the Committee for Risk Assessment (RAC-77): opinion on the harmonised classification and labelling of trifluoroacetic acid and its inorganic salts. European Chemicals Agency, Helsinki, 5 June 2026.
- European Commission (2025). Commission Regulation (EU) 2025/1988 of 2 October 2025 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council as regards per- and polyfluoroalkyl substances in firefighting foams. Official Journal of the European Union.
- European Union (2008). Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (CLP), Annex VI, Table 3. Consolidated version. Official Journal of the European Union.
- Guo, Z., Attar, A.A., Qiqige, Q., Lundgren, R.J., Joudan, S. (2025). Photochemical formation of trifluoroacetic acid: mechanistic insights into a fluoxetine-related aryl-CF₃ compound. *Environmental Science & Technology* 59(2), 1367–1377. [doi:10.1021/acs.est.4c10777](https://doi.org/10.1021/acs.est.4c10777)
- Hammel, E., Webster, T.F., Gurney, R., Heiger-Bernays, W. (2022). Implications of PFAS definitions using fluorinated pharmaceuticals. *iScience* 25(4), 104020. [doi:10.1016/j.isci.2022.104020](https://doi.org/10.1016/j.isci.2022.104020)
- Han, S., Lu, Y. (2023). Fluorine in anti-HIV drugs approved by FDA from 1981 to 2023. *European Journal of Medicinal Chemistry* 258, 115586. [doi:10.1016/j.ejmech.2023.115586](https://doi.org/10.1016/j.ejmech.2023.115586)
- Ismail, M.M.F., Ayoup, M.S. (2022). Review on fluorinated nucleoside/non-nucleoside FDA-approved antiviral drugs. *RSC Advances* 12(48), 31032–31045. [doi:10.1039/d2ra05370e](https://doi.org/10.1039/d2ra05370e)
- Jomaa, B. (2021). Organohalogens and our persistent ski wax problem. *Toxicologische Communicatie, Data en Documentatie (TCDD)* 4, 12–13. Nederlandse Vereniging voor Toxicologie.
- Mishra, S., Jadala, C., Cardoza, S., Potuganti, G.R., Velma, G.R. (2026). Fluorine-containing FDA-approved small-molecule drugs in 2025: significance, synthetic insights, and therapeutic applications. *RSC Advances* 16(15), 13830–13850. [doi:10.1039/d6ra01711h](https://doi.org/10.1039/d6ra01711h)
- Nguyen, H.T., McLachlan, M.S., Tschärke, B., et al. (2022). Background release and potential point sources of per- and polyfluoroalkyl substances to municipal wastewater treatment plants across Australia. *Chemosphere* 293, 133657. [doi:10.1016/j.chemosphere.2022.133657](https://doi.org/10.1016/j.chemosphere.2022.133657)
- OECD (2021). Reconciling Terminology of the Universe of Per- and Polyfluoroalkyl Substances: Recommendations and Practical Guidance. OECD Series on Risk Management No. 61, ENV/CBC/MONO(2021)25. Organisation for Economic Co-operation and Development, Paris.
- Pennoyer, E.H., Heiger-Bernays, W., Aro, R., Yeung, L.W.Y., Schlezinger, J.J., Webster, T.F. (2023). Unknown organofluorine mixtures in U.S. adult serum: contribution from pharmaceuticals? *Toxics* 11(5), 416. [doi:10.3390/toxics11050416](https://doi.org/10.3390/toxics11050416)
- Scheurer, M., Nödler, K., Freeling, F., Janda, J., Happel, O., Riegel, M., Müller, U., Storck, F.R., Fleig, M., Lange, F.T., Brunsch, A., Brauch, H.-J. (2017). Small, mobile, persistent: trifluoroacetate in the water cycle. Overlooked sources, pathways, and consequences for drinking water supply. *Water Research* 126, 460–471. [doi:10.1016/j.watres.2017.09.045](https://doi.org/10.1016/j.watres.2017.09.045)
- US EPA (2021). Definition of PFAS used by the Office of Pollution Prevention and Toxics. United States Environmental Protection Agency, Washington DC.
- US EPA (2023a). Instructions for reporting PFAS under TSCA section 8(a)(7). EPA-705-G-2023-3727. United States Environmental Protection Agency, Washington DC.
- US EPA (2023b). Changes to reporting requirements for per- and polyfluoroalkyl substances and TSCA section 8(a)(7); final rule. Federal Register, 11 October 2023. Available at <https://www.govinfo.gov/content/pkg/FR-2023-10-11/html/2023-22094.htm>
- Wackett, L.P. (2021). Why is the biodegradation of polyfluorinated compounds so rare? *mSphere* 6, e0072121. [doi:10.1128/mSphere.00721-21](https://doi.org/10.1128/mSphere.00721-21)
- Zheng, G., Eick, S.M., Salamova, A. (2023). Elevated levels of ultrashort- and short-chain perfluoroalkyl acids in US homes and people. *Environmental Science & Technology* 57(42), 15782–15793. [doi:10.1021/acs.est.2c06715](https://doi.org/10.1021/acs.est.2c06715)

How Toxic Are Weight-Loss Medicines? Understanding the Risks of GLP-1-Based Treatments

Weight-loss medicines have become increasingly prominent in the treatment of obesity. The most widely discussed products include semaglutide, liraglutide and tirzepatide, which act through the incretin system. Semaglutide and liraglutide are GLP-1 receptor agonists, while tirzepatide activates both the GIP and GLP-1 receptors.



By Héloïse Proquin



These medicines can produce substantial weight loss and may improve several obesity-related health outcomes. However, their growing use has also raised concerns about toxicity. The appropriate question is therefore not whether these medicines are “toxic” in general, but under what circumstances their risks may outweigh their benefits.

What do these medicines do?

GLP-1 drugs, also called GLP-1 agonists, are shortened names for glucagon-like peptide-1 receptor agonists. GLP-1 receptor agonists mimic the GLP-1 hormone that is naturally released in the gastrointestinal tract in response to eating. GLP-1-based medicines reduce appetite, increase feelings of fullness and slow the movement of food through the stomach. They can also affect blood-glucose regulation because GLP-1 triggers the release of insulin from your pancreas¹.

What are the possible side effects?

Although serious side effects are rarely reported, up to 50 percent of people will experience some degree of nausea, constipation or diarrhoea while taking these drugs. The European Medicines Agency – Digital Application Platform (DAP) also reports side effects like irritability, anxiety and/or

sleep problems². More serious side effects that may occur with long-term use include cardiovascular issues, pancreas inflammation, liver damage or gastroparesis, a condition in which the stomach muscles don’t function properly to move food into the intestines.

Literature shows that some patients report more severe problems, including persistent early satiety, inability to tolerate normal meals or fluids, marked weakness, and dehydration³. These effects may be particularly relevant during dose escalation and can impair nutritional intake and daily functioning. In addition, a study analysing discussions on Reddit, YouTube, and TikTok found that users reported both positive experiences, such as improved mood and reduced cravings, and negative effects, including insomnia, anxiety, fatigue, panic symptoms, and depression⁴. However, because these reports were self-reported and collected from social media, they cannot establish that GLP1 medicines caused the physical or psychological effects. The frequency and causal relationship of these less commonly reported problems remain uncertain, highlighting the need for further clinical research into the gastrointestinal and psychiatric safety of GLP1 medicines and their possible effects on compulsive behaviours.

Furthermore, because these medicines delay gastric emptying, rare complications such as severe gastric motility disorders or obstruction-like symptoms may occur, and retained stomach contents can increase aspiration risk during sedation, endoscopy, or surgery. Other important potential risks include gallstones or gallbladder inflammation, acute pancreatitis, temporary worsening of diabetic retinopathy when blood glucose improves rapidly, and hypoglycaemia when combined with insulin or sulfonylureas. Thyroid C-cell tumour warnings are based on animal findings, and a comparable human risk has not been established; nevertheless, these medicines are generally avoided in people with a personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2⁵. Additional safety concerns arise from overdosing or using unapproved or compounded products, which have been associated with severe gastrointestinal symptoms, dehydration, pancreatitis, gallstones, and hospitalisation.

What are the risks of use in individuals without obesity?

There is a trend on social media to use these medicines to lose weight by people who do not have obesity. This trend is not without risks.

The emerging use in individuals without obesity for modest, primarily cosmetic weight loss raises important risk–benefit and ethical concerns. In nonobese populations, the risk-benefit balance tips towards the risk: the absolute health benefit of small weight changes is limited, whereas exposure to adverse effects—gastrointestinal symptoms, gallbladder disease, pancreatitis, and potential kidney injury—remains^{5,6}. Appetite suppression may also lead to disproportionate loss of lean mass and possible nutritional compromise, particularly in the absence of structured diet and resistance training interventions.

At a population level, widespread cosmetic use may medicalize normal bodyweight variation, reinforce

unrealistic body ideals, and exacerbate access issues for patients with evidence based indications. This population is not targeted by the medicine, therefore they search for many online sources which operate with limited oversight, offering prescription-only GLP1 agents without rigorous clinical assessment or appropriate monitoring⁷. This raises concerns about counterfeit or substandard products, inaccurate dosing, contamination, and lack of screening for contraindications such as pancreatitis, gallbladder disease, renal impairment, or eating disorders.

Conclusion

Weight-loss medicines are not harmless. Their most common harms are gastrointestinal and dose-related, while severe dehydration, gallbladder disease, kidney injury, pancreatitis and complications related to delayed gastric emptying are less common but clinically important.

The risk–benefit balance depends on appropriate patient selection, licensed products, gradual dosing and medical follow-up. The greatest avoidable dangers arise from unsupervised use, dosing errors, rapid dose escalation and products obtained through unreliable sources

References:

¹ <https://www.health.harvard.edu/healthy-aging-and-longevity/glp-1-diabetes-and-weight-loss-drug-side-effects-ozempic-face-and-more>

² European Medicines Agency – Digital Application Platform (DAP). https://dap.ema.europa.eu/analytics/saw.dll?PortalPages&PortalPath=%2Fshared%2FPHV%20DAP%2F_portal%2FDAP&Action=Navigate&P0=1&P1=eq&P2=%22Line%20Listing%20Objects%22.%22Product%20High%20Level%20Code%22&P3=1+107527486

³ Olubodun T, Osundina MA, Soyoye DO, de Oliveira NMB, Olubodun AB, Ogundele OO (2026) Gastroparesis induced by glucagon-like peptide-1 receptor agonists: A systematic review of clinical features, diagnosis, management, and outcomes. PLoS One 21(8): e0354497. <https://doi.org/10.1371/journal.pone.0354497>

⁴ Arillotta D, Floresta G, Guirguis A, Corkery JM, Catalani V, Martinotti G, Sensi SL, Schifano F. GLP-1 Receptor Agonists and Related Mental Health Issues; Insights from a Range of Social Media Platforms Using a Mixed-Methods Approach. Brain Sci. 2023 Oct 24;13(11):1503. doi: 10.3390/brainsci13111503.

⁵ FDA prescribing information for semaglutide products (Ozempic/Rybelsus) https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/213051Orig1s030lbl.pdf

⁶ Savla R, Van Hoven AM, Pilkington B. Ethical Considerations in the Use of Weight Loss Medications. J Gen Intern Med. 2026 Feb;41(3):852-855. doi: 10.1007/s11606-025-10026-6

⁷ Kindel TL, Wang AY, Wadhwa A, Schulman AR, Sharaiha RZ, Kroh M, Ghanem OM, Levy S, Joshi GP, LaMasters T; Multi-society clinical practice guidance for the safe use of glucagon-like peptide-1 receptor agonists in the perioperative period. Surg Endosc. 2025 Jan;39(1):180-183. doi: 10.1007/s00464-024-11263-2.

From animals to alternatives: opportunities in regulatory toxicity testing

In 2023, approximately 8 million animals were used in animal studies in the European Union, and almost 500,000 of these in regulatory toxicology studies for pharmaceuticals [1]. Regulatory toxicology tests for pharmaceuticals are guided by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines [2]. These are global guidelines that direct which toxicity studies should be conducted and how. Specific guidelines exist for specific types of toxicology studies, for example the ICH S1 guidelines for carcinogenicity testing, or specific types of pharmaceuticals, for example the ICH S6 guideline for biopharmaceuticals. Usually, regulatory toxicology studies involve animal testing, although alternatives are possible. Over the past years, societal and political pressure to reduce animal testing is increasing, not only for pharmaceuticals. When it comes to replacing or reducing animal testing in toxicity studies for pharmaceuticals, what is already being done, what is possible, and how to get there?



By Puck Roos



Organ-on-a-chip by NASA Headquarters / Emulate, Public domain, via Wikimedia Commons

To reduce animal testing in regulatory toxicity studies for pharmaceuticals, two main approaches are New Approach Methodologies (NAMs) and a Weight-of-Evidence (WoE) approach. NAMs can include in vitro models, such as organ-on-chip systems, in silico models, such as PBPK modelling, and more. A WoE is an integrated approach in which all available data on a pharmaceutical are considered to characterize the toxicity risk and determine the need for an animal study. This can include data on the mechanism of action, data from other toxicity studies, data from similar products, etc. Data generated from NAMs can also be part of a WoE approach.

WoE approaches are already used a lot and are integrated in several regulatory guidelines. For example, carcinogenicity studies for pharmaceuticals are generally performed in

both rats and mice, but a WoE approach can be used to determine the need for a 2-year rat carcinogenicity study [3]. Similarly, a WoE approach can be used to determine the need for juvenile toxicity studies, taking into account data on the intended patient age, effects on developing organ systems, existing non-clinical and clinical data, the pharmacological target, selectivity and specificity of the pharmaceutical, and the clinical treatment duration [4].

NAMs, on the other hand, are much less frequently used. For example, despite NAMs being included in the guideline on developmental toxicity testing as a possible alternative to animal testing, no pharmaceutical companies use NAMs for that purpose [5]. In 2025, the European Medicines Agency (EMA) published an overview of their experience with NAMs [6]. They encountered some use

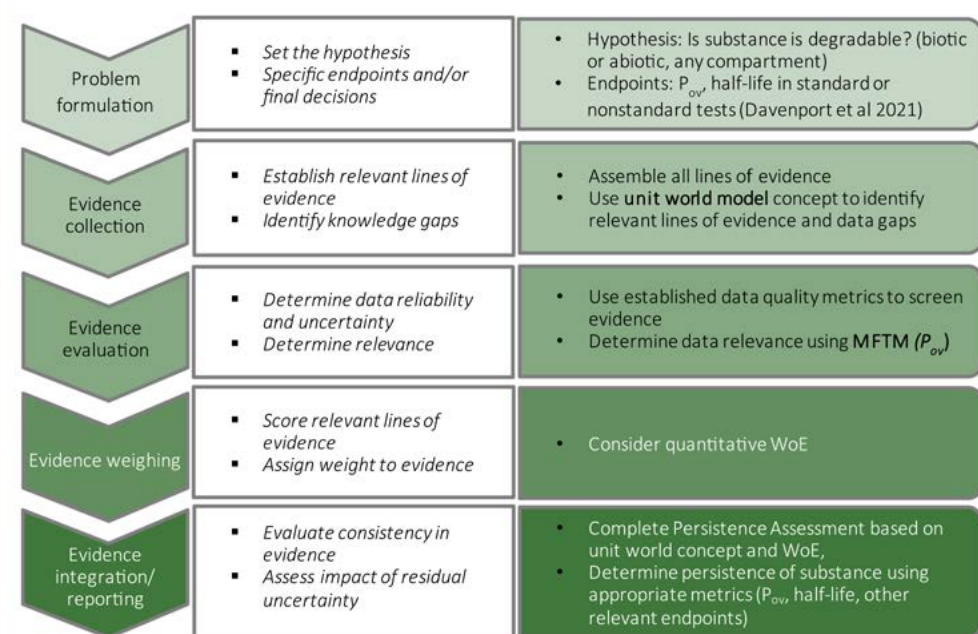


FIGURE 1 Schematic of a weight-of-evidence approach adapted for persistence assessment (adapted from OECD (2019) Reproduced from Redman et al. (2022), Integrated Environmental Assessment and Management 18(4): 868–887, <https://doi.org/10.1002/ieam.4548>, under a CC BY-NC-ND 4.0 licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)).

of NAMs by pharmaceutical companies in Innovation Task Force meetings or Scientific Advices, which are opportunities for pharmaceutical companies to interact with the EMA before they submit a drug for marketing authorization. More recently, the United States Food and Drug Administration (FDA) published an overview of NAMs in study reports submitted by pharmaceutical companies to the FDA [7]. They described that only 0.24% of all non-clinical study reports submitted between 2011 and 2025 contained a NAM. Of all the NAMs studies submitted to the FDA, only 19.5% were used in toxicology studies, while NAMs were used more frequently for pharmacology or pharmacokinetics testing. The majority of these NAMs (87.6%) were used in Investigational New Drug (IND) applications, which are applications for first-in-human

clinical trials, and only a small part for New Drug Application (NDA) or Biologics License Applications (BLA), which are marketing applications. When NAMs were used for toxicity testing, these were most often stem cell-derived models, reconstructed tissue models or 3D models, such as organoids. In short, both of these publications indicate that use of NAMs remains limited, and when they are used, it is usually in earlier stages of drug development, and not yet to support marketing applications.

So, what is holding back the use of NAMs? On one hand, there are the technical challenges surrounding NAMs, such as low

throughput compared to cell lines, a lack of standardization and limited reproducibility. Furthermore, one NAM cannot replace a whole-organism animal study; instead, a battery of NAMs representing different endpoints may be required. On the other hand, there are regulatory challenges surrounding NAMs. For example, regulators generally have limited experience with NAMs, and NAM developers generally have limited experience with regulatory testing, and regulatory acceptance may differ from one region to another. Besides, NAMs may be more predictive for human outcomes than animal models, because they are generally based on human cells, but limited comparative studies have been done. [8,9,10]

Despite these challenges, regulatory agencies do allow for the use of NAMs. Last year, the FDA published their Roadmap to Reducing Animal Testing in Preclinical Safety Studies for monoclonal antibodies, in which they state that in 3-5 years, they aim to make animal toxicity studies the exception rather than the norm [11]. To achieve this, they plan to identify pilot cases in which animal studies could be waived in favor of NAMs, develop regulatory guidance

on NAMs, support the development of NAMs and organize training workshops on NAMs for their staff. Earlier this year, they published a draft guidance on the use of NAMs in drug development [12]. This guidance outlines 4 principles to enhance the interpretability and reliability of NAMs: context of use, defined as the intended use and regulatory purpose of the NAMs in a decision-making context in drug development; human biological relevance, described as how the information generated from NAMs could impact the assessment of the drug and predict toxicities that cannot be measured in clinical trials; technical characterization, described as establishing scientific confidence and ensuring the NAM is robust, reliable and reproducible enough; and lastly, fit-for-purpose, meaning that it can either replace traditional methods, fill a data gap when traditional models are unavailable or insufficient, or confirm and/or complement findings from traditional methods.

In 2024, the EMA published a reflection paper on the implementation of the 3Rs in drug development [13]. This paper outlines what is already possible under current regulatory guidelines and where the EMA sees opportunities to further reduce animal testing. As mentioned above, when pharmaceutical companies want to use a NAM for regulatory testing, they can apply for an Innovation Task Force meeting or a Scientific Advice at the EMA [14]. In addition, the EMA has a qualification procedure in which drug developers or NAM developers can request qualification of their NAM in a specific context of use, meaning that the EMA considers the NAM acceptable to use in that specific context. However, no NAMs have been qualified to date. More recently, the EMA started a pilot for voluntary data submission [15]. In this pilot, pharmaceutical companies, NAM developers, academic labs and other stakeholders can submit and discuss NAMs data with the EMA, outside of a marketing authorization application procedure. The goal is to provide a platform for discussion about NAMs, for regulators to gain experience with data

generated using NAMs and for NAM developers to receive feedback on the relevance of their NAMs for regulatory testing.

In conclusion, despite the abundance of NAMs that have been developed over the past years, the use of NAMs in regulatory toxicity testing for pharmaceuticals is lagging behind. Yet, regulatory agencies are opening up the possibilities to use NAMs and other alternative approaches to animal testing in toxicity testing. This may provide opportunities to move the use of NAMs to the next stage, from their use in early drug development to regulatory testing.

References:

1. [ALURES database](#)
2. [ICH Official web site : ICH](#)
3. [ICH S1B\(R1\) guideline](#)
4. [ICH S11 guideline](#)
5. Powles-Glover et al. 2025 (<https://doi.org/10.1016/j.reprotox.2025.109035>)
6. Edwards et al. 2025 (<https://doi.org/10.1038/d41573-025-00052-8>)
7. Hao et al. 2026 (<https://doi.org/10.1016/j.yrtph.2026.106246>)
8. Komarnisky et al. 2025 (<https://doi.org/10.1039/d5lc00426h>)
9. Oyetade et al. 2025 (<https://doi.org/10.14573/altex.2505281>)
10. Edwards et al. 2025 (<https://doi.org/10.1038/d41573-025-00053-7>)
11. [FDA Roadmap to Reducing Animal Testing in Preclinical Safety Studies](#) (2025)
12. [General Considerations for the Use of New Approach Methodologies in Drug Development | FDA](#) (2026)
13. [EMA Draft reflection paper on opportunities for implementation of the 3Rs](#) (2024)
14. [Regulatory acceptance of new approach methodologies \(NAMs\) to reduce animal use testing | European Medicines Agency \(EMA\)](#)
15. [New approach methodologies to replace and reduce animal testing: Voluntary data submission pilot | European Medicines Agency \(EMA\)](#)



Protecting the Kidney During Drug Development

A medicine's journey through the body can place considerable demands on the kidney. Filtration and tubular transport help remove drugs and their metabolites, but these same processes can expose renal cells to substances capable of damaging them. For pharmaceutical toxicology, this creates a persistent challenge: how do we identify kidney injury early enough to influence drug development, and how do we determine what an experimental finding means for the people who may eventually receive the treatment? Answering those questions requires an understanding of the relationship between exposure, injury, and the models used to study them.



By *Devon Barnes*



The proximal tubule illustrates this challenge particularly well. Its transport systems move substances between blood, cells, and urine, making cellular exposure dependent on more than the concentration measured in plasma. Cisplatin provides a familiar example. Research using human transporters and isolated human proximal tubules demonstrated that organic cation transporter 2 contributes to cisplatin uptake and toxicity (1). This has an important implication for safety testing: a model that poorly represents the relevant uptake process may underestimate injury even when the cells themselves are capable of responding. The biology responsible for exposure is part of the toxicological question.

Recognising injury also depends on what we choose to measure. Serum creatinine remains central to assessing renal function, but it does not directly describe the cellular processes through which a drug damages the kidney. Urinary injury biomarkers can provide complementary information. Recent clinical development case studies have shown how a qualified kidney biomarker panel can

support risk assessment and dose selection alongside conventional monitoring (2). These measurements still require interpretation in the population and exposure setting in which they are used. An abnormal result becomes useful when it helps explain what is happening and informs a decision about what should happen next.

Animal studies allow renal effects to be investigated in intact organisms, in which circulation, metabolism, immune responses, and interorgan interactions contribute to the outcome. Histopathology can identify the location and character of injury, while repeated measurements help establish its development over time. Translating those observations to humans, however, requires consideration of differences in exposure and biological response. Renal transporter expression and substrate handling can vary between species (1). A finding in an animal therefore needs a reasoned assessment of its human relevance, just as an absence of injury needs to be interpreted within the conditions actually tested.

Human in vitro models offer a complementary way to investigate that relevance. Renal cell cultures allow researchers to examine drug uptake, cellular stress, and loss of viability under controlled conditions, and to test whether changing a suspected mechanism alters the response. Yet human origin alone does not establish that a model represents the necessary biology. Work on the widely used HK-2 cell line, for example, identified limitations in its expression and function of key proximal tubular drug transporters (3). Model selection must therefore begin with the process being investigated. For a transport-dependent toxicant, a convenient viability assay may be difficult to interpret if the cells do not reproduce the route by which the compound reaches its intracellular target.

More complex systems broaden the range of questions that can be asked. Proximal tubule chips introduce fluid flow and controlled tissue organisation, while kidney organoids contain multiple renal cell populations. Early work with a human proximal tubule chip demonstrated that flow could improve aspects of tubular function and the response to cisplatin (4). Organoid studies have also reproduced aspects of cisplatin-induced injury (5). These are useful advances, but their value remains tied to a defined purpose. Researchers still need to establish whether the relevant cells are sufficiently mature, whether exposure reaches the intended compartment, and whether the response is reproducible. Adding complexity is worthwhile when it resolves a biological limitation that matters for the decision.

Mechanistic frameworks can help connect these different sources of evidence. Adverse outcome pathways organise knowledge about the sequence of biological events linking an initiating interaction to an adverse effect (6). Applied to kidney toxicity, this approach can guide the selection of measurements spanning early disturbances and later injury.

For example, a proposed role for mitochondrial dysfunction can be examined alongside subsequent changes in cell integrity, with attention to the order and exposure levels at which they occur. A pathway also makes gaps visible. Evidence that two events occur together does not establish that one causes the other, and a cellular change does not automatically predict impaired kidney function in a patient.

For drug development, the practical value lies in bringing these observations together. An early cellular signal might justify further work on exposure or mechanism. A transporter-dependent response might help explain a difference between models. A urinary biomarker might inform monitoring in a clinical study. Each addresses part of a larger assessment, and the weight given to it should reflect how well the method has been characterised for that purpose. Mechanistic evidence can make a safety finding more actionable while also clarifying the limits of the interpretation.

The kidney's role in pharmaceutical development therefore extends well beyond measuring how quickly a compound is eliminated. It asks toxicologists to consider how the processes that handle a medicine also shape its potential to cause harm. Progress will depend on selecting models that capture the relevant biology and connecting their results to realistic exposure and meaningful outcomes. The aim is to recognise renal liabilities early enough to guide better choices, while retaining a clear account of what the evidence can support. That is how kidney safety assessment can contribute to the development of medicines whose benefits can be realised with a better understanding of their risks.

References

1. Ciarimboli G, Ludwig T, Lang D, Pavenstädt H, Koepsell H, Piechota HJ, et al. Cisplatin nephrotoxicity is critically mediated via the human organic cation transporter 2. *Am J Pathol.* 2005;167(6):1477-84.
2. Ravindra KC, Fader KA, Potter D, Radi ZA, Friedman GS, Brennen KA, et al. Qualified kidney injury biomarkers demonstrate value during early clinical drug development. *Toxicol Sci.* 2024;201(2):206-15.
3. Jenkinson SE, Chung GW, van Loon E, Bakar NS, Dalzell AM, Brown CDA. The limitations of renal epithelial cell line HK-2 as a model of drug transporter expression and function in the proximal tubule. *Pflugers Arch.* 2012;464(6):601-11.
4. Jang KJ, Mehr AP, Hamilton GA, McPartlin LA, Chung S, Suh KY, et al. Human kidney proximal tubule-on-a-chip for drug transport and nephrotoxicity assessment. *Integr Biol (Camb).* 2013;5(9):1119-29.
5. Digby JLM, Vanichapol T, Przepiorski A, Davidson AJ, Sander V. Evaluation of cisplatin-induced injury in human kidney organoids. *Am J Physiol Renal Physiol.* 2020;318(4):F971-8.
6. Ankley GT, Bennett RS, Erickson RJ, Hoff DJ, Hornung MW, Johnson RD, et al. Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment. *Environ Toxicol Chem.* 2010;29(3):730-41.

Environment as a determinant of birth outcomes: new Dutch data from Amsterdam Zuidoost

Researchers at Erasmus MC have mapped health outcomes around birth in the twenty most vulnerable neighbourhoods in the Netherlands, all of them covered by the National Programme for Liveability and Safety (NPLV). Their analysis draws on data from 2015 to 2021. That more babies are born with health disadvantages in poorer areas was hardly news. What the study adds is the map: nobody had charted the pattern neighbourhood by neighbourhood in the Netherlands before, and the spread between them turns out to be wide.



By Barae Jomaa; summary of original article "Al voor de geboorte gezondheidsachterstand bij kinderen Zuidoost: "Schrikbarend resultaat" published online by AT5



Amsterdam Zuidoost stands out even in this company. Perinatal mortality there is roughly 8 per 1,000, about twice the rate in the rest of the country. One baby in five is born underweight, against one in ten nationally. Preterm births run at 7 per cent, where the national figure is 5. Measured against the rest of Amsterdam the gap widens further, because the city as a whole does better than the country. Nieuw West shows the same tilt less sharply, with 5.6 perinatal deaths per 1,000 births and 123.4 underweight births per 1,000.

Individual factors, maternal age and migration background among them, were deliberately adjusted for, and the neighbourhood differences survive that adjustment. So the researchers look outward, to air quality, noise and the state of the housing. Heat stress and crime may matter too, by a slower route. Both feed chronic stress, and chronic stress is known to impair placental function, cutting the supply of nutrients and oxygen that reaches the baby. Which of these weighs heaviest is not yet known. A follow up study on their relative contribution is under way.

The full article in its original form and language can be found [here](#).

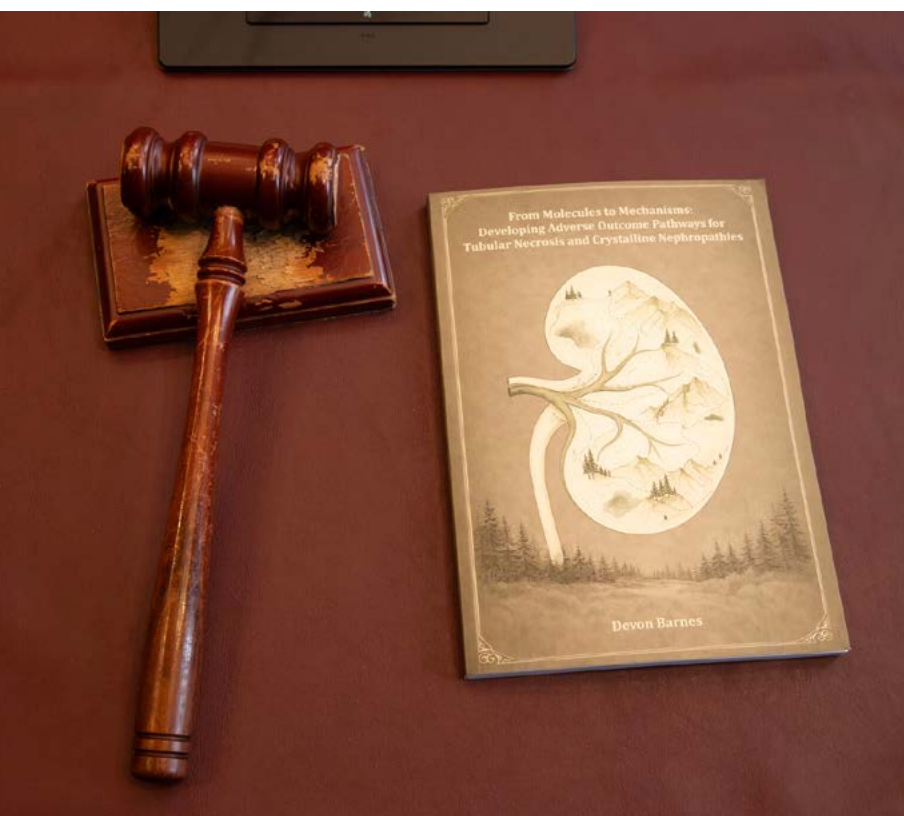
From Molecules to Mechanisms

Developing Adverse Outcome Pathways for Tubular Necrosis and Crystalline Nephropathies

This thesis explores how computational prediction, adverse outcome pathways, and experiments with human kidney cells can be combined to investigate nephrotoxicity. Studies of platinum-based chemotherapy and uric acid-associated injury identified early cellular disturbances and highlighted how different stressors can converge on related mechanisms of damage. The findings provide a foundation for developing more informative, animal-free approaches to kidney safety assessment, while identifying the further work needed to connect experimental responses with adverse outcomes in humans.



By *Devon Barnes*



In my PhD research, I investigated how different causes of kidney injury can be understood through the biological events that connect exposure to damage. The kidney presents a particular challenge for toxicology because its functions in filtration, transport, and maintenance of the body's chemical balance also influence its exposure to and susceptibility to harmful substances. Understanding an effect therefore requires attention to both the mechanism of injury and the conditions under which it develops.

Adverse outcome pathways, or AOPs, provided the organising framework for this work. They bring together evidence about the sequence of events linking an initiating interaction to an adverse outcome. In my thesis, this framework helped connect computational predictions with existing mechanistic knowledge and experimental observations. It also provided a way to identify gaps and decide which biological processes to investigate further.

The computational part of the research involved models developed from a dataset of 565 compounds to predict nephrotoxic potential from chemical structure. This work offered a starting point for prioritising compounds for further investigation. Alongside it, we constructed an AOP network for nephrotoxicity, bringing together evidence on interconnected injury mechanisms, and developed a more specific pathway describing how DNA adduct formation can lead to kidney failure. These frameworks helped organise findings that would otherwise have remained scattered across different studies and experimental systems.

To investigate key events experimentally, I used conditionally immortalised human proximal tubule epithelial cells, known as ciPTECs. An AOP-guided assay battery measured mitochondrial disturbances, reactive oxygen species, lysosomal leakage, and cell viability following exposure to cisplatin, carboplatin, and oxaliplatin. Measuring responses across concentrations and exposure

times allowed us to examine how injury developed. Mitochondrial dysfunction emerged as an early response, preceding later indicators of cellular damage. This supported the relevance of measuring early disturbances alongside cell viability and provided evidence for assessing the proposed relationships between events.

RNA sequencing added a complementary view of the cellular response. Across the three platinum compounds, the analysis identified shared changes in gene expression associated with processes including DNA damage responses, protein homeostasis, and mitochondrial translation. These findings suggested additional candidate events for the AOP network. Because the experiments examined conditions with limited cytotoxicity, the results also required careful interpretation: early molecular responses may reflect attempts to adapt to stress as well as processes contributing to injury. Distinguishing these possibilities remains an important step in developing predictive approaches.

The final part of my thesis examined uric acid and crystalline nephropathies. Experiments in ciPTEC-OAT1 cells showed that acidic conditions increased uric acid-associated toxicity even in the absence of crystal formation. This finding highlighted how the local chemical environment can influence injury and why crystal formation alone may not explain the observed response. A complementary, literature-based AOP organised evidence on the progression from crystal formation and tubular interactions to oxidative stress, inflammation, and fibrosis. Together, these studies examined distinct initiating conditions that can converge on related mechanisms of kidney damage.

The approaches developed in this thesis provide tools for studying specific parts of a complex process. Human proximal tubule cells allow controlled investigation of cellular responses, but they cannot reproduce all the

interactions present in an intact kidney. Further work is needed to account for immune and vascular contributions, establish quantitative relationships between events, and demonstrate reproducibility across laboratories. The methods therefore provide a foundation for further development rather than a complete prediction of clinical kidney injury.

I defended this thesis at Utrecht University on 5 June 2026, following research in the Division of Pharmacology under the supervision of Roos Masereeuw and Frank Redegeld. The work contributes to the ONTOX ambition of developing

mechanism-based, animal-free toxicity assessment. A central lesson from bringing these approaches together is the importance of asking what each result adds to the biological explanation. Computational predictions can guide priorities, AOPs can structure questions, and experiments can test specific parts of the proposed mechanism. Connecting those contributions makes it possible to see more clearly both what the evidence supports and what remains unresolved. That is the contribution I hope this work makes to a more informative kidney safety assessment.



AIO toxafette – Olivia Klatt

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 passes the baton to a fellow PhD-student. This time Olivia Klatt, from Vrije Universiteit, tells us about her project.

Can you introduce yourself?

Hi, I'm Olivia and I'm currently a fourth-year PhD candidate at Vrije Universiteit (VU) Amsterdam. My research focuses on the absorption, distribution, metabolism and excretion (ADME) of different chemicals in various human and rat renal in vitro systems. When I'm not in the lab, I like to stay active by playing tennis, going for a run or hike, doing a workout class with a friend and in the winter I enjoy skiing (which is a bit difficult in the Netherlands I know :D). On the weekends you can also find me exploring new areas in and around Amsterdam or in one of the city's amazing cafés with friends or a good book.

How would you explain the subject of your research to a layperson?

When chemical or pharmaceutical companies want to bring a new drug or pesticide to the market, a large number of tests for the risk assessment are done in animals such as rats or mice. This process raises a lot of ethical concerns, is costly and the accuracy of the results is questionable with around 90% of drugs previously appearing safe and effective in animals not reaching the market. This is largely due to species differences between humans and these lab animals and thus alternatives, such as cell-based models, are being further developed, characterised and validated to hopefully one day replace the current common testing strategies. My research focuses on kidney cell models of the proximal

tubule, which is the main site of reabsorption in the kidney and thus especially vulnerable to drug-induced toxic effects. I work with stem cell derived models, cell lines and cells directly isolated from a human and I'm trying to understand better how well these systems predict the metabolism and toxicity of chemicals. For that I expose the different renal systems to pesticides, environmental toxins and drugs with well documented human exposure data due to long market access and determine if and at what concentrations we can see similar metabolism and toxic effects compared with the human data. This will allow us to understand better how well these cell-based systems emulate what is happening in the human body and will hopefully help us pick more accurate systems for our risk assessment than the current practice of animal testing.

How is your research related to the field of toxicology, and why did you choose this subject?

During my master's, I did an internship at Amsterdam UMC (AMC), where I worked with coronary artery cells under flow conditions. That time in the lab showed me how much I enjoy cell-based research, especially working out how a compound affects cells at the mechanistic level, which led me to my PhD in toxicology.

In my PhD, I work with several renal cell models, in both static cultures and microfluidic devices, and expose them to environmental toxins and pesticides. I combine

transcriptomics, LC-MS and fluorometric assays to understand how these compounds affect kidney cells in terms of which molecular pathways they influence and disturb and how they're taken up and metabolised by the cells.

What was your motivation for starting a Ph.D. programme?

I have always enjoyed a challenge and the chance to keep expanding my knowledge. The research internships during my master's showed me how exciting and varied lab work



can be, and how much there is to learn. At the same time, the six- to seven-month projects always left me feeling that I had only scratched the surface, and I wanted to dig deeper. A PhD gives me several years to explore one topic in depth and master a wide range of techniques, which made it the perfect fit for me.

How do you see the future of your research topic (follow-up research / social impact)? What do you hope for?

With my PhD work, I hope to expand our knowledge of kidney cell models and to clarify which model is best suited to which context. I also hope to help build confidence in NAMs, so that animal tests can gradually be reduced and eventually replaced. I don't think this change will happen overnight, but recent years, and 2026 in particular, have shown that regulators are moving in that direction. The FDA has updated its regulations to explicitly allow non-animal methods, the European Commission has published a roadmap towards phasing out animal testing, and agencies such as EMA, ECHA and EFSA are creating pathways to assess and accept NAM data. These developments make me hopeful that we're on the right track to reduce animal testing without jeopardising human health risk assessment. I hope that one day human-relevant kidney models like the ones I work with will become a standard part of how we assess the safety of chemicals.

How do you ensure that others can replicate your experiments and achieve the same results?

Most of my work is based on cell-based assays. Many studies have highlighted how difficult it can be to reproduce published results in this field, so ensuring reproducibility is very important to me. Before each experiment, I carefully check the health and maturity of the cells, make sure I include enough replicates, and document the exact exposure conditions and durations in detail. Where available, I include positive and negative controls to make

sure the assay performs as expected and my results are reliable. Every step of the data analysis is tracked and recorded, including the software versions used. Both raw and processed data are uploaded to my consortium's data platform. Together, these steps should allow others to reproduce my experiments and obtain the same results.

How do you combine your PhD project with your personal life? Are there choices you have to make?

I think one of the most difficult parts of doing a PhD is balancing work and personal life. At times, the amount of work and deadlines can feel overwhelming, and it can seem as if your whole life revolves around your PhD project. Over the years, I have learned that physical activity and spending time with friends keep me motivated and productive. So even when the work feels never-ending, a workout class, a run, or a coffee or dinner with a friend leaves me more energized and focused afterwards. Of course, this also means making choices. Sometimes I have had to say no to social gatherings, but that has made me enjoy the ones I can join even more. Keeping my days well-structured also helps me fit more into them, both at work and outside of it. I think it's important to find your own outlet and the things that recharge your battery. Otherwise, four years can feel very long and become more draining than it needs to be.

What is the biggest challenge for you in doing PhD research?

The biggest challenge for me has been staying motivated after many failed experiments, and knowing how long to pursue a direction before it's time to drop it or try a new angle. As many of us have experienced, it can be very draining to work long and hard to test a hypothesis, only to find that it doesn't show the effect you expected. What helps me is to step back from the project for a while and clear my head with a physical activity, so I can look at it more objectively. I then discuss the options with my supervisor, who has much more experience. I have learned

that it's important to be honest in these conversations, both about whether it makes scientific sense to continue and about whether I personally have the energy to try again, or whether I need a change of direction. Over time, I have also learned that negative results are still results, and that each failed experiment teaches me something about the system I'm working with.

What actions do you take if you encounter unexpected or questionable data in your research? How do you address these issues?

When I encounter unexpected results, I first make sure that what I'm seeing is real and not an artefact, by checking that I have enough replicates, appropriate controls and consistent experimental conditions. Next, I go back to the literature to see whether anyone has reported similar findings that I may have missed. I then discuss the results with my PI and my professor. If we're still unsure why we're seeing certain effects, I reach out to other experts in the field, either within my consortium or through contacts from other projects. Once we have a new hypothesis about why this result might occur in this specific setting, we brainstorm new experiments to test it. Often, this opens up new and exciting directions for my project.

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?

At the moment, I expect my future career to be outside academia, as I'm more drawn to team-based and applied work at a regulatory body or in industry. That said, it's difficult to say for sure at this stage, as it will largely depend on the job market and which positions and projects seem the most exciting and the best fit for me. I would definitely consider going abroad. I'm not originally from the Netherlands, and I could see myself moving closer to my family again. As an EU citizen, I could also easily see myself

moving to another European country, although for now I'm not considering moving outside the EU. In the end, it will depend on where the most exciting opportunities are and where my partner and I want to live. Either way, I'm excited to see where my PhD will take me when my contract ends in mid 2027.

Please answer the question from the last toxafette PhD-candidate: What do you think is the biggest barrier to implementing alternative test methods in regulatory toxicology, and how can we overcome it?

One of the biggest barriers, in my view, is our reliance on animal studies as the "gold standard" in risk assessment, even though their translatability to humans is uncertain for many endpoints. At EUROTOX 2026, Professor Thorhallur Halldorsson gave a keynote lecture showing how unreliable some controlled animal studies can be, and how some have produced false negatives. For example, animal studies on smoking underestimated how harmful it is to human health. He also highlighted how NAMs can help integrate epidemiological data into risk assessment. Because of these interspecies differences, I believe we need to gradually move away from animal-based testing to obtain more human-relevant data.

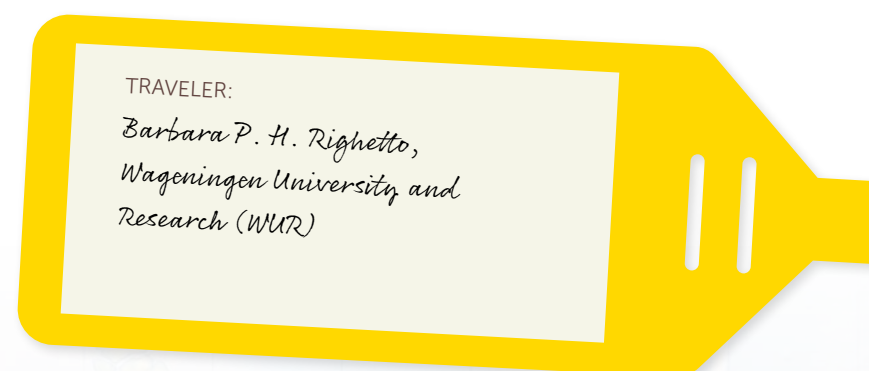
To overcome this barrier, we first need to build more confidence in the results obtained with NAMs, and European and Dutch-funded projects in this area play an important role here. Second, many of the NAMs currently in use still need to be improved to better reflect what happens in the human body. We need a combination of scientific innovation, willingness from industry, and openness from regulators, for example by requiring or accepting more NAM-based data for market approval. Together, this will help us understand how and when to use which NAM best. Regulatory bodies have taken important steps in this direction lately, but there is still more work to be done.

23rd Pollutant Response in Marine Organisms Conference (PRIMO23)

Hamilton, Canada, 2nd-5th of June 2026

At PRIMO23 I presented a poster with preliminary data from a project that I am developing in collaboration with a research group in Brazil. The overall goals of this project are: 1. To understand how the transfer of contaminants (current-use pesticides, metals and organic contaminants) occurs in an estuarine system with a focus on the role of biotransformation pathways and 2. To estimate the health risks associated with consumption of seafood containing such contaminants, for both local human populations and the resident population of bottlenose dolphins.

In this conference, I presented data regarding the levels of current-use pesticides in several estuarine organisms, selected due to their importance as food items and their range of ecological niches, and the activities of key enzymes involved in biotransformation processes, namely cytochrome P450s (CYP450), Glutathione S-transferases (GST) and carboxylesterases (CBEs). The data shows an evident distinction between species regarding both the pesticides detected and biotransformation activity. CYP450 is the primary phase I route for fish species, whereas CBEs seem to play that role in invertebrates, especially crabs



and oysters. Pesticide detection also varied between species, with morpholines only detected in crabs, and catfish being the species with the highest rate of detection and levels of current-use pesticides.

Despite the marked differences, neither biotransformation nor trophic level seem to be the only drivers of pesticide accumulation, exemplified by the distinction between catfishes and flatfishes: both species occupy a similar ecological niche and have a similar biotransformation capacity. Nonetheless, all pesticides were <LOD in flatfish, while catfishes were the most contaminated organism among those sampled. Other factors, like seasonality or excretion rates might play a role in the patterns observed for pesticide accumulation.

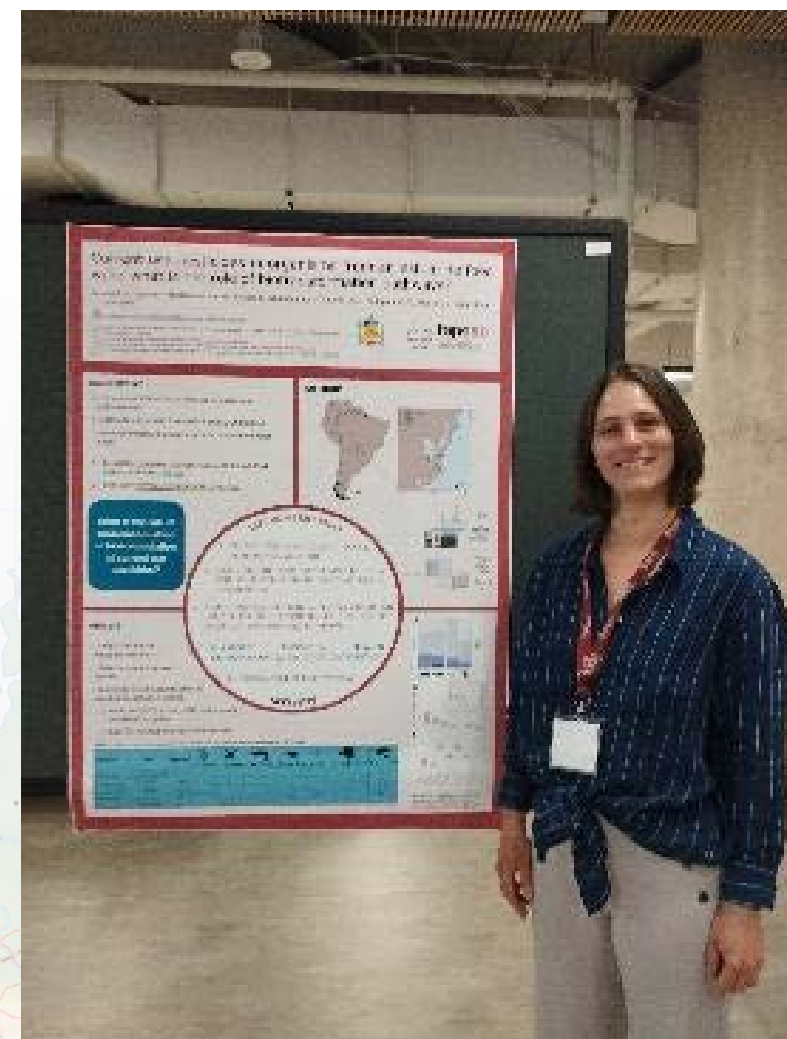
The conference was also a great opportunity to reconnect with former collaborators from Brazil, make new contacts with researchers working on ecotoxicology and get inspired by work being presented by other people.

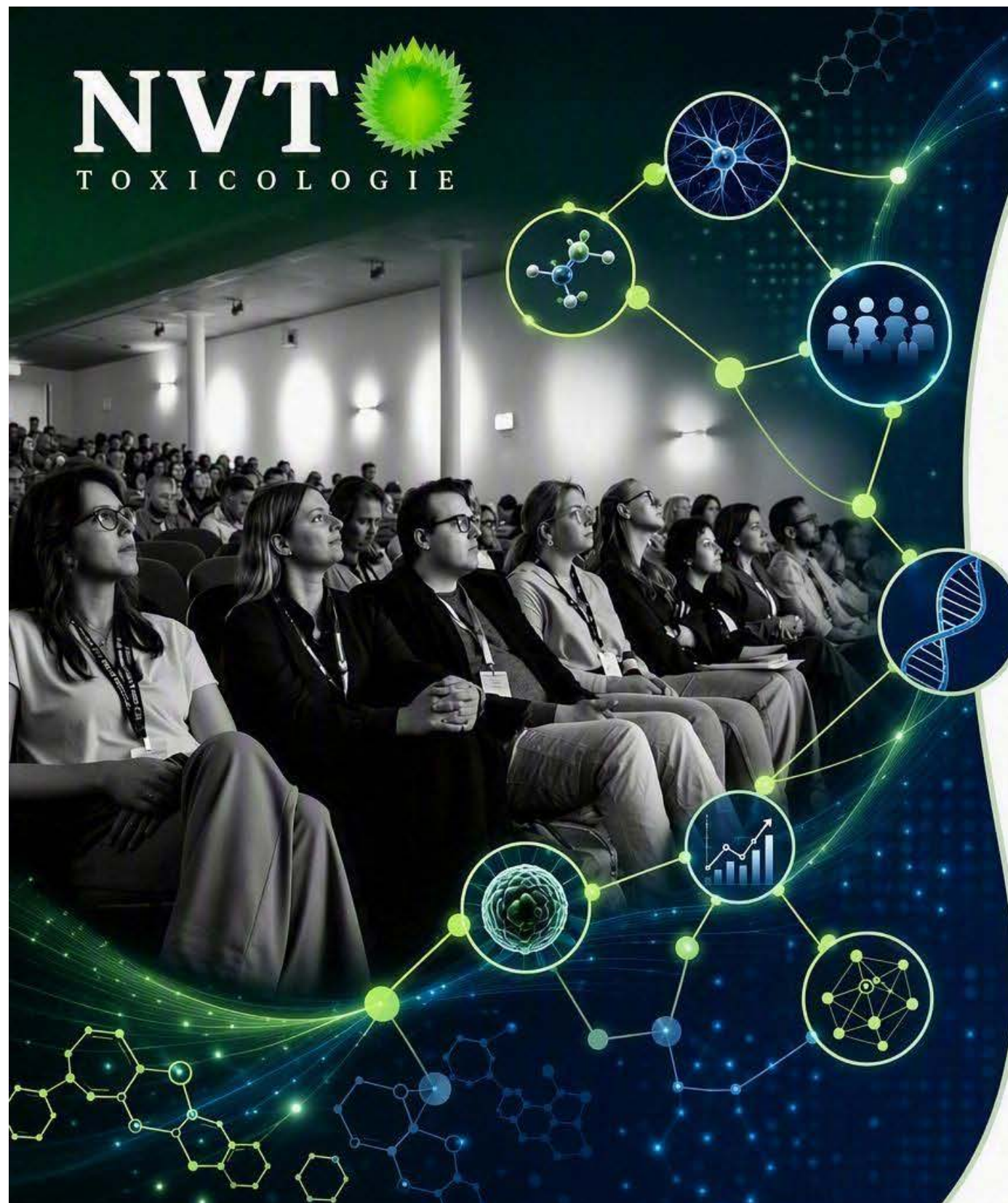
Specifically, there were quite a few presentations about the development and application of species-specific in vitro techniques for studies investigating the effect of chemicals in wildlife species. The new developments are really relevant because wildlife species are frequently endangered and in vivo work is not ethically sound. At the same time, relying on cell lines or in vitro tests designed for model organisms is not ideal, as species-specific differences in receptors and enzymes can greatly alter the interpretation of results. At PRIMO, two researchers from University of Bergen presented new techniques that they are developing for whale species: One is using COS-7 cells with recombinant whale receptors linked to a luciferase, effectively building a killer-whale species-specific luciferase reporter gene assay to evaluate the toxicity of pollutants. The other one is trying to develop a “receptor-on-a-chip” approach, called the TR-FRET assay, linking only the receptor LBD to an inorganic matrix. This would also work as a species-specific receptor binding assay, enhancing our capacity to establish cause-effect relationships for wildlife species. I found these talks particularly inspiring because

I am currently also working with wildlife. Part of my PhD at Wageningen will be to look at the potential effects of pesticides and PFAS on the black tailed godwit. However, as with any work with wildlife, establishing cause-effect relationships will be quite challenging. My initial plan was to do in silico predictions of toxicity and validate some of these predictions with in vitro work, mostly relying on chicken cell lines as representative of bird species in general. However, the approaches presented by both researchers seem a lot more adequate, albeit challenging. Nonetheless, both were very interested in the work I am developing and were open to discussing future collaborations.

Overall, the conference was very interesting, and presentations dealt with topics applicable to any ecotoxicology work focusing on effect responses. The main highlight for me was the importance of knowing your “model” organism, as species are very unique in their molecular apparatus and, hence, toxicological responses might differ greatly between them.

Though the meeting was held in Canada and I had, therefore, to take a flight there, I relied on the local system of shared bikes to attend the conference as a way to minimize my CO2 emissions.





NVT
TOXICOLOGIE

Help Shape the NVT Annual Meeting 2027

**Join the Organising Committee of the
NVT Annual Meeting 2027!**

Are you interested in toxicology and would you like to play an active role in the annual meeting of the Dutch Society of Toxicology (NVT)?

As a committee member, you will have the opportunity to:

- ✓ contribute to the scientific programme
- ✓ liaise with invited speakers
- ✓ help create an inspiring and successful annual meeting
- ✓ gain experience in moderating and facilitating sessions
- ✓ expand your professional network within the field of toxicology

.....

The practical and administrative support will be outsourced, allowing you to focus primarily on the scientific content and organisation of the conference.

.....

 **Interested in getting involved?**

 Contact the NVT Board at:
secretaris@toxicologie.nl

Current Topics in Toxicology

Utrecht University, November 5 and 6, 2026

If you would like to stay up to date in the field of toxicology while earning credits for your re-registration, please come and join the PET course Current Topics in Toxicology, offering a compact 1.5-day programme that this year will cover three cutting-edge areas: omics, particle & fibre toxicology and high-throughput screening.

01 OMICS IN TOXICOLOGY

Gain insight into the different types of 'omics techniques that are available for toxicological research, how these can be applied in the context of the development of NAMs, clinical and exposome research, and how 'omics approaches can contribute to toxicological risk assessment.

02 PARTICLE & FIBRE TOXICOLOGY

Learn about the latest developments in particle and fibre toxicology, exploring how particle properties, exposure, dosimetry and particle–biointeractions and the 5Bs (bioavailability, biopersistence, bioprocessing, biomodification and bioclearance) influence human health. There will be focus on advanced nanomaterials and microplastics, and challenges in interpreting in vitro/NAM data.

03 HIGH-THROUGHPUT SCREENING APPROACHES FOR CHEMICAL HAZARD CHARACTERIZATION

Learn how advanced mechanism-based screening methods based on high throughput imaging and transcriptomics can facilitate the characterization of hazards for safety assessment and be integrated in mechanism-based NGRA.

[Read the full program and apply.](#)



BelTox-BEMS Annual Scientific Meeting 2026 on Artificial Intelligence

Date: Monday 7th December 2026

Location: Auditorium BEL.Brussels

The Belgian Society for Toxicology and Ecotoxicology (BelTox) and the Belgian Environmental Mutagenicity Society (BEMS) are pleased to announce their 2026 Annual Scientific Meeting (AM26) in Brussels.

This year's theme focuses on the transformative role of Artificial Intelligence (AI) in toxicology, ecotoxicology, and health/environmental risk assessment.

Confirmed Keynote Speakers:

- Thomas Steger-Hartmann (Bayer AG): Discussing the VICT3R project, which aims to drastically reduce animal testing by implementing "Virtual Control Groups."
- Marc Teunis (Utrecht University): Presenting the ONTOX project, a generic strategy using non-animal methods (NAMs) and tailored exposure data to improve human risk assessment.
- Jian Jiang (VUB): Highlighting specific contributions to the ONTOX project.

- Lidwina Gerner (SCAHT): Introducing AI4AOP, an initiative using AI to translate massive mechanistic toxicology databases into structured Adverse Outcome Pathway frameworks.

Next to the keynote presentations, a demo/networking opportunity will be organized where AI tools will be showcased and can be tested by participants.

Pending Topics & Highlights:

The program will also feature sessions on the BIGPICTURE IMI (digitizing 3 million pathology slides for AI analysis), the regulatory and ethical implications of AI in the field, and BEMS-led discussions on AI in mutagenicity screening.



Foto: <https://beltox.be>

More details can be found by following [this link](#).

REGISTRATIE CIE

Inschrijving register

Voorletters	Achternaam	Datum inschrijving	Datum afloop registratie
N.	Zhang	09-06-2026	09-06-2031
H.	Brouwer	09-06-2026	09-06-2031
X.	Li	09-06-2026	09-06-2031
I.M.J.	Thoonen	09-06-2026	09-06-2031
L.V.J.	van Melis	09-06-2026	09-06-2031
S.	van Loon	09-06-2026	09-06-2031

Voorletters	Achternaam	Datum inschrijving	Datum afloop registratie
N.E.T.	Pinckaers	09-06-2026	09-06-2031
M.M.G.	Reijnaers	17-09-2026	17-09-2031
N.I.	Kramer	17-09-2026	17-09-2031
K.S.	Nitsche	17-09-2026	17-09-2031
T.J.H.	Jonkers	17-09-2026	17-09-2031
K.E.K.	Maudens	17-09-2026	17-09-2031

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

De Vereniging beoogt de belangen van het vakgebied Toxicologie in de ruimste zin te behartigen; de Vereniging heeft uitdrukkelijk niet de bedoeling de rechts-positionele belangen te behartigen van de individuele leden, tenzij deze belangen direct gerelateerd zijn aan de beoefening van het vakgebied. Gehele of gedeeltelijke overname van de inhoud van TCDD is alleen mogelijk met schriftelijke toestemming van de redactie.