

Hazardous Substances Advisory Committee (HSAC)

Meeting Minutes – 46th HSAC Meeting

3rd June 2025

Item 1 Welcome by the chair and CPHW Deputy Director

- 1.1 The Chair, Professor Iseult Lynch, welcomed all attendees to the meeting (see Annex A).
- 1.2 The draft agenda was approved with no additional items added under any other business. No conflicts of interest were declared with items on the agenda.

Item 2 Approval of the minutes from the 45th meeting, and review of actions - Iseult Lynch, Chair

- 2.1 The minutes from the 45th meeting have been actioned and accepted without objections. The actions from the last meeting are as follows:
 - **Follow up discussion on the priority areas of uncertainty in the work to value environmental risk from chemical pollution.**
Julia confirmed the project is close to being published and she is taking forward the immediate next steps of how they are going to use that information. These next steps will be brought to a future meeting.
 - **HSAC to provide written responses to Keegan's questions on biodiversity.**
This action item is completed.
 - **HSAC to write three 100 word case studies on usage of New Approach Methodologies (NAMs).**
This action item is completed.

Item 3 Forward look, upcoming meeting topics & commissions in progress – Yasmin Wright, Secretariat

- 3.1 Yasmin Wright presented upcoming meeting topics for the meeting in September, which include a presentation on the latest NAMs survey from the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), the Environment Agency (EA) water quality team on characterising chemical exposure, and open-source Polychlorinated biphenyls (PCBs). She also gave an update on the flame retardant scoping review the HSAC provided comment on for the EA. The EA was grateful for the comments and have plans to publish the review in the summer. Finally she informed HSAC that the Pro-oxidant Additive Containing (PAC) plastics report is going through Defra internal review ahead of publication.

- **Yasmin to share responses from the EA on the flame retardant scoping review.**

Item 4 Activity in other chemicals-related advisory committees – Julia Sussams, Evidence Strategy Lead, Chemicals Science & Environmental Impacts Team

- 4.1 Five chemicals-related science advisory councils across Government meet quarterly to share updates and identify collaborative opportunities. These are the committees on mutagenicity, carcinogenicity, toxicology, chemical safety of non-food and non-medicinal products, and the HSAC. These meetings ensure that the committees collectively consider broader strategic themes of shared relevance—such as the role of generative AI tools. Julia asked the HSAC for feedback on other areas of relevance.
- 4.2 Jason Weeks suggested that more committees may be relevant to include, such as REACH Independent Scientific Expert Pool (RISEP), Veterinary Products Committee, Pharmaceuticals in the Environment (PIE) Group (chaired by Jason) and the Interagency Chemicals Group. The joint secretariat will consider expanding to include these groups.
- 4.3 Charlie Stevenson asked if we have heard anything more about the progress of the latest draft of a NAMs roadmap or how it interacts with the UK government phase-out strategy.
 - **Julia to contact Olivia Osbourne at the Food Standards Agency to provide an update**
- 4.4 Iseult Lynch suggested a draft of the next NAMs policy paper is shared with the other committees. This was agreed by the HSAC.

Item 5 Endocrine Disruptor Predicted No Effect Concentrations (PNECs) derived using mammalian datasets – *Morné Van Der Mescht, Environment Agency*

- 5.1 Morné Van Der Mescht presented the above report to the HSAC and asked for feedback.
- 5.2 Stewart Owen questioned why a model requiring more animal testing is being pursued when the government and European policies aim to reduce such testing. He highlighted that the approach would necessitate additional data from animals like mammals and fish. He challenged the exclusion of in vitro data, arguing that scientists have the ability to establish consensus on its use. Stewart suggested that instead of relying on animal models, there should be a stronger push towards adopting New Approach Methodologies (NAMs) as alternatives.
- 5.3 In response to Morné's questions, Stewart Owen made the following points:
 - **On the assessment factor:** He argued that choosing a factor of 10 implies high uncertainty, and applying an additional factor of 10 usually results from extra information leading to further uncertainty. He suggests that this approach might not be useful.

- **On selecting more compounds:** He expressed hesitation about funding additional compounds, stating that while more data-rich and widely studied compounds might exist, their presence in the environment is uncertain.
- **On fish plasma:** With two decades of experience working on it, Stewart confirmed that the method is effective but stressed the importance of accounting for ionisation and water chemistry. He believes these considerations allow for a reliable margin within a factor of 3.

5.4 Luigi Margiotta-Casaluci acknowledged that the proposed approach in the report makes sense but raised concerns about the use of PNECs to guide inter-species comparison/extrapolation exercises, as the derivation of PNECs is not a rigorous data driven approach but reflects how the operator decides to deal with uncertainty. He highlighted the importance of assessing how uncertainty is propagated throughout the process and the relevant mathematical equations. He argued that focusing on effect concentrations (rather than no effect concentrations) may lead to more reliable scientific predictions. He also observed a (welcome) shift in focus from population-level effects to individual-level mechanistic considerations (typical of human risk assessment). He cautioned, however, that this shift may warrant a broader discussion of current ERA protection goals (beyond the scope of the report). He shared the example of scientific publications reporting sustained fish populations in English rivers despite EDCs-induced intersex at individual level. This transition, he argued, aligns with a growing reliance on New Approach Methodologies (NAMs), to fill data gaps. He concluded by highlighting the importance of validating reverse pharmacokinetics (PK) approaches to maximise the value and usability of fish in vitro NAMs. These approaches would also be useful to integrate the risk derived from dietary exposure with the risk arising from waterborne exposure to the same compound.

5.5 Jason Weeks agreed with previous points and argued that assessment factors create excessive complexity, especially when additional mixture factors are introduced. He praised the report for including climate-scored data but suggested limiting studies to those with the highest scores to reduce uncertainty. He raised concerns about test methodologies focusing exclusively on males, pointing out that the absence of female data overlooks a significant portion of potential impacts. He highlighted differences in hormonal systems across species and questioned whether mammalian data can effectively be extrapolated to fish and ecosystem effects. Overall, Jason expressed uncertainty about the ultimate goal of setting a level of protection.

5.6 John Colbourne praised the report for its detail but expressed concern about the transitional phase in which decisions must be made based on current data, despite an impending shift in approach. He highlighted the valuable insights gained from discussions and suggested that incorporating these learnings into the report could enhance its long-term relevance. Rather than treating it as a finalised document, he proposed adding a third objective: identifying lessons from the exercise that could refine future thinking and guide the next steps. John also suggested that the HSAC make reference to this report when writing the paper on NAMs.

Action

- **The committee has three weeks to provide written feedback**

Item 6 Update on per-and poly fluoroalkyl substances (PFAS) work - *Ed Latter, Chemicals Policy Lead*

- 6.1 Ed Latter gave the HSAC an update on the PFAS work his team is currently undertaking.
- 6.2 John Colbourne felt that PFAS regulation is significantly behind where it should be. He suggested using PFAS as a case study to understand whether regulatory decisions could have been made differently, whether missing data played a role and what should be considered moving forward to learn from past mistakes. John argued that PFAS presents a unique opportunity, as all major regulatory agencies are currently focused on it, and suggests the work currently underway by Defra should be UK-focussed should ensure its approach is distinct from other global efforts to restrict PFAS.
- 6.3 Jason Weeks highlighted how certain issues, such as PFAS, are not necessarily *new* but re-emerging. He noted that other substances, like lead and heavy metals, remain unresolved and will likely demand attention again. Jason stressed the need to address uncertainty in regulatory decision-making, particularly when faced with significant gaps in available information to ensure more effective long-term solutions.
- 6.4 John Colbourne suggested that PFAS presents an opportunity to explore the value of grouping substances for regulatory purposes. He highlighted past work by the HSE and Environment Agency on grouping strategies and encouraged critical thinking about whether regulating PFAS as a group could effectively minimise harm while aligning with broader policy goals, such as avoiding regrettable substitutions. He proposed a radical approach, where industry would need to prove that specific substances should not be grouped, using their own data to demonstrate differences. John believes that PFAS regulation could serve as a model system for future chemical regulation, as lessons learned from its regulation could be applied to other classes of substances in the future.
- 6.5 Stewart Owen highlighted the UK's strong history of innovation in chemical research, noting that many PFAS compounds originated in this country. He felt this means there is an opportunity to leverage this expertise to drive solutions and advocate for further research efforts. He suggested that the UK could play a leadership role in finding solutions to PFAS-related challenges.
- 6.6 Stephanie Metzger questioned if the PFAS policy options report includes an analysis of the options in general or will it also indicate which options that Defra is interested in pursuing? Ed explained that the report is purely analytical for now, but the team is taking time to review the findings, consult across government, and determine a clear direction—aiming to offer more insight when it's published later this year.

Item 7 Multi- and transgenerational effects of EDCs literature review – Yasmin Wright, Secretariat

- 7.1 This agenda item was presented by Yasmin Wright on the upcoming literature review on the multi- and trans-generational effects of endocrine disrupting chemicals (EDCs).
- 7.2 Jason Weeks expressed concern about the quality of literature reviews, arguing that the real issue lies in the credibility of the sources used rather than the sheer volume of existing studies. He stated it was important to ensure that only robust and useful studies are included to avoid wasting time and resources. Additionally, he highlighted the sex-related gap in toxicity data, cautioning that a failure to account for these differences could lead to significant missing information.
- 7.3 John Colbourne also flagged the importance of robust and reliable evidence in literature reviews.
- 7.4 Ed Latter highlighted key policy challenges related to endocrine-disrupting chemicals (EDCs), particularly emerging scientific uncertainties around low-dose and synergistic effects. He explained that the goal is to break down these complexities through evidence assessments to improve regulatory risk management. Given the uncertainties, decisions must balance precaution, protection, and strategic significance. He sees the evidence review process as a way to refine judgment and fill gaps in understanding, rather than dictate specific regulations. Ed emphasised that this approach complements existing rigorous testing methods and regulatory frameworks rather than replacing them.
- 7.5 Luigi Margiotta-Casaluci emphasised the importance of defining the difference between multi-generational and trans-generational effects from the outset. He acknowledged that there may be limited evidence from large-scale studies but suggested that researchers can explore mechanistic endpoints within the first generation as potential indicators of trans-generational risks. He proposed examining factors such as sperm quality, epigenetic modifications, and mutagenesis in gametes (sperm and eggs) to gain insight into possible long-term effects. Luigi argued that even if comprehensive studies are lacking, focusing on lower-layer mechanistic endpoints could still provide valuable information relevant to understanding trans-generational hazards.

Item 8 Next HSAC paper on New Approach Methodologies (NAMs) – HSAC, led by Iseult Lynch

- 8.1 A recent kick-off meeting in Birmingham helped refine the report structure, ensuring specific regulatory mapping and strategic decision-making. It was agreed that the report needs to contain concise, evidence-based recommendations, questioning how best NAMs should be used in chemical regulation. With diverse opinions, particularly in Brussels as the European Commission develops its roadmap, John Colbourne sees an opportunity for the UK to lead in NAMs adoption, making bold regulatory decisions that could position it ahead of other countries.

- 8.2 Stewart Owen opined whether animal studies were truly necessary for regulators to make safety decisions and whether regulators could determine acceptable chemical limits without relying on animal data. He explored whether assessment factors—which already help set thresholds—could replace traditional studies, effectively allowing decisions to be made without animal testing. Finally, Stewart raised the idea that AI-powered software could potentially replace animal studies, providing an alternative method for assessing chemical risks.
- 8.3 Susan Chilton discussed the concept of acceptability thresholds in regulatory decisions. She acknowledged that risk thresholds will likely vary across different NAMs and that the cost of not relying on animal test data plays a role in decision-making. She suggested that a higher threshold would be acceptable in cases of personal health risks, while environmental concerns could be valued higher or lower depending on societal priorities. She argued against assigning individual values for every NAM, instead advocating for broad thresholds based on risk types and associated costs, ensuring a more practical regulatory approach.
- 8.4 Morné Van Der Mescht clarified that smaller assessment factors indicate a better understanding of uncertainty, which regulators prefer. Large assessment factors are applied only when uncertainty is high. Regarding NAMs, he stressed that they must be reliable, repeatable, relevant and supported by rigorous validation rather than merely presenting new techniques. He criticised some NAM developers for prioritising innovation over demonstrating applicability across chemical spaces and species. He highlighted the need for strong validation efforts, particularly in the human health space. Morné emphasised the challenge of bringing all research together cohesively. He pointed out that applying assessment factors to NAMs remains uncertain, though they often detect mechanistic effects before adverse impacts appear, which may justify smaller factors. He felt that the key challenge is ensuring NAMs correctly model sensitive species, tying into precision toxicology efforts. Finally, he called for practical testing, urging researchers to submit dossiers with NAMs so regulators can assess their effectiveness in characterising risk.
- 8.5 Stewart Owen emphasised the importance of understanding the consequences of regulatory decisions, particularly when determining safe concentration levels. He questioned how often regulators might be wrong when relying on animal data, and what happens in cases where environmental changes suggest the need for lower protection goals, even if test data doesn't support it. He argued that without clear documented examples, the impact of errors is difficult to assess, which reinforces continued reliance on animal studies for confidence. He tied this to Sue's argument, which explored the trade-offs of making decisions with less data—whether granting the benefit of the doubt in uncertain cases carries greater risk or acceptable uncertainty. Stewart suggested that further discussion is needed to explore these consequences more deeply.
- 8.6 Luigi Margiotta-Casaluci argued that the focus should be on the purpose of a NAM rather than just the method itself, emphasising its role in the weight-of-evidence assessment. He cautioned against expecting a single method to resolve all challenges, as variability and uncertainty in in vitro studies remain problematic. Luigi stressed the importance of data-driven decision-making, pointing out that many assumptions in the field lack actual supporting data. While

tools for data analysis are improving, he highlighted a major issue: there is no centralised database for NAMs, making it difficult to ensure consistency and reliability in their application.

- 8.7 Anthony Wilson highlighted the challenge of certainty and acceptance in regulatory decision-making, especially when NAMs are used as evidence in dossiers. He explained that whilst companies may submit robust scientific justifications, regulators might reach different conclusions—creating potential for legal disputes. Beyond scientific certainty, he stressed the importance of understanding whether a method is broadly accepted as a valid and reliable basis for risk assessment, noting that differing interpretations can undermine the perceived validity of the evidence.
- 8.8 John Colbourne emphasised the need to clearly define the essential requirements for the report, arguing that successful recommendations must be actionable and prioritised. He encouraged identifying what could not be achieved without NAMs, aiming to streamline regulatory processes for both human health and environmental protection. He highlighted the importance of understanding shared biomolecular processes across species, interpreting mechanistic data using molecular biomarkers, and shifting toward probabilistic risk assessments. John also called for realigning protection goals, breaking down conceptual barriers, and improving clarity on the causal links between exposure and adverse outcomes. Ultimately, he suggested that the next NAMs policy paper should present a focused set of recommendations—anchored in scientific and strategic priorities which could guide the UK's transition toward integrated NAMs adoption.
- 8.9 Stewart Owen emphasised the importance of understanding the consequences of regulatory decisions—particularly where there is uncertainty. He highlighted that the stakes can be high, involving serious harm to human health or the environment, and argued that managing uncertainty is essentially about risk tolerance. He proposed including a dedicated section in the work to explore the *value of getting decisions right or wrong*, suggesting that societal perspectives—what risks people are willing to accept—should inform this analysis, potentially with support from experts in public acceptability.
- 8.10 Iseult Lynch suggested that for each component or methodology under consideration, it's important to identify the inherent uncertainties and understand how these may propagate through the overall process. She emphasised that as uncertainty decreases, so does the need for large safety margins or assessment factors, ultimately leading to greater confidence in the resulting risk evaluations. This approach reinforces the value of systematically tracking and addressing uncertainty throughout regulatory assessments.
- 8.11 Morné Van Der Mescht explained that a standard assessment factor of 10 accounts for uncertainties between lab and environmental conditions, and across species. He emphasised that very large factors, like 1000, are inappropriate, signalling misuse of a method. While both regulators and industry prefer smaller factors, their motivations differ: industry may use large factors to flag potential toxicity, whereas regulators see small factors as a sign of greater confidence in the data. Morné concluded that anything above 100 is unjustifiable.

8.12 Iseult Lynch concluded that there is now enough to take forward and can touch base in a virtual meeting to decide exact timeline.

- **Yasmin Wright to setup a meeting for the committee in a few weeks' time**

Side discussion (occurring concurrently with the item above) : Horizon Scanning – Environmental Impacts of Chemicals – HSAC, *Julia Sussams*

8.13 Julia Sussams summarised discussions with those not involved in the above item around horizon scanning, focusing on its purpose, potential applications, and the role of HSAC. She noted the value of recent tools like Feedly for aggregating public data and highlighted parallels with the Environment Agency's Prioritisation and Early Warning System (PEWS). She emphasised the need to re-engage with PEWS developers to understand current methods, possible AI integration, and internal usage. Julia stressed that understanding the intended audience is key to shaping the scope and usefulness of horizon scanning, especially when results fall outside the commissioning body's remit. She proposed exploring different use cases, including regulatory customers like UK REACH, and suggested involving stakeholders and NGOs to improve both data collection and uptake—possibly through a public-facing horizon scanning process for broader utility. She plans to revisit these ideas with HSAC for further discussion.

Item 9 Presentation & discussion session - The use of generative AI and machine learning models in chemicals risk assessment – *Yasmin Wright, Secretariat*

- 9.1 This agenda item was presented by Yasmin Wright, Ollie Smith and Tony Wilson. Ollie Smith from the Government Office for Science presented slides on the work GO-Science is doing to look at effective usage of AI in the future.
- 9.2 Stewart Owen highlighted the importance of prompt-writing training, suggesting that weak prompts may lead to incomplete report outcomes. He urged formal training for teams—especially early career scientists—to fully leverage AI tools, warning that their potential will outpace traditional methods without proper guidance.
- 9.3 Jason Weeks emphasised that AI can filter data efficiently, but cannot replace expert judgment.
- 9.4 Tony Wilson from HSE presented slides on artificial intelligence: the potential to support plant protection product regulation.
- 9.5 Iseult Lynch raised concerns about the language limitations of current data sources, questioning how much valuable information may be missed by focusing solely on English. She also highlighted the need to assess the accuracy and trustworthiness of translation tools, especially when applied to scientific content.
- 9.6 Stewart Owen emphasised that the core issue is trust in the individual presenting the work, not whether AI was used. He argued that as AI becomes more widespread what matters is whether the person takes ownership and stands behind the final product.

- 9.7 Jason Weeks warned that AI models may carry inherent biases stemming from how they are trained, including racial or ideological leanings. He advised staying alert to these potential biases when interpreting AI-generated outputs.
- 9.8 Susan Chilton suggested not relying on a single tool for literature reviews and emphasised the value of built-in validation checks—such as running the same search across different systems to compare outputs. She questioned the repeatability and objectivity of such reviews, noting that true lack of bias is difficult, if not impossible, to measure.

Item 10 Emerging Evidence – HSAC Members

- 10.1 Susan Chilton shared an update from the OECD about a new environmental endpoints study—a companion to their earlier work on chemical morbidity values. The UK and Sweden are participating, and she highlighted the importance of liaising with those managing the study. She suggests Defra stay informed and involved, given the study's potential significance and scale.

Item 11 AOB

- 11.1 Yasmin Wright - Upcoming meeting dates. The next meeting will be in September. A Google poll will be sent around in due course to determine the exact date.

End of meeting – 4pm

ANNEX A

ATTENDANCE LIST

HSAC:

- Iseult Lynch
- Susan Chilton
- John Colbourne
- Stewart Owen
- Jason Weeks
- John Colbourne
- Luigi Margiotta-Casaluci

Secretariat:

- Yasmin Wright
- Julia Sussams
- Iqra Raja

Defra Policy Officials

- Mark Chandler (Evidence & Analysis Team Leader, Chemicals, Pesticides and Hazardous Waste)
- Ed Latter (Chemicals Policy Team, Chemicals, Pesticides and Hazardous Waste)
- Fatima Nasser (NAMs & OECD Team Leader, Chemicals, Pesticides and Hazardous Waste)
- Leon Jackson (Chemicals Hub, Chemicals, Pesticides and Hazardous Waste)
- Liz Lawton (Chemicals Hub, Chemicals, Pesticides and Hazardous Waste)
- Sarah Heathcote Jones (Chemicals Hub, Chemicals, Pesticides and Hazardous Waste)
- Jess Evans (Chemicals Hub, Chemicals, Pesticides and Hazardous Waste)
- Philippa Kearney (Chemicals Hub, Chemicals, Pesticides and Hazardous Waste)

Defra Agency Representatives

- Morne Van Der Mescht (Environment Agency)
- Luke Holmes (Environment Agency)
- Anthony Wilson (HSE)

Other Government Department and Agencies

- Ovnair Sepai (UKHSA)
- Britta Gadeberg (UKHSA)
- Ollie Smith (Go Science)

External Stakeholders

- Roger Pullin (Chemical Industries Association)
- Stephanie Metzger (RSC)
- Charlie Stevenson (Cruelty Free International)
- Mohamed Elkhailifa (BPF)