



## Annual Conference 2021 of the European Partnership for Alternative Approaches to Animal Testing (EPAA)

*'How can EPAA help the successful implementation of the EU Chemical Strategy for Sustainability'*  
(27 October 2021, online)

### Summary

*The partners pool their knowledge and resources to accelerate the development, validation and acceptance of alternative approaches at national, European and global levels.*

The EPAA annual conference, taking place (remotely) on 27 October saw delegates give their thoughts and insights on EPAA's achievements in 2021, announce the EPAA Refinement Prize winner, and discuss the Partnership's role in the EU Chemical Strategy for Sustainability.

### Opening remarks

Welcoming participants to the event, conference moderator **Brian Maguire** walked through the agenda for the day. He reminded them that a key element of the event was to look at how the EPAA can help ensure the successful implementation of the EU chemical strategy for sustainability.

In pre-recorded comments, Deputy Director-General DG GROW **Hubert Gams** thanked participants for dedicating their time to this conference and apologised that he could not be present in person. On behalf of the European Commission overall, and DG GROW, in particular, he wanted to stress how much the work of the EPAA was valued. Abolishing animal testing, as soon as the science made it possible, had always been high on the Commission's agenda. In pursuit of this, EPAA's contribution to cross-sectoral dialogue has been substantial, not only through the partnership between industry and regulators but also through its outreach to academia, animal welfare organisations, consumers and patient groups via its mirror group.

### The future for NAMs (New Approach Methods)

The first keynote speaker, **Dorothee Funk-Weyer** of BASF, focused on the potential role for NAMs (New Approach Methods) in the CSS (Chemical Strategy for Sustainability), which is part of the European Green Deal. This strategy will see changes to the chemicals market, and will present both an opportunity and a challenge for industry. The CSS will trigger more than 80 changes to chemical legislation in the next few years.

She posed the question of what the role for EPAA would be in this. In terms of the main challenges and opportunities, it was clear that it was always best to rely on the best available science as well as to continue to develop up-to-date risk assessment tools. This would not happen without strong collaboration between NGOs, regulators and industry; in EPAA there was the ideal platform to make this a reality.

Looking at how toxicological data is currently generated; it was clear that there was still a long way to go to move away from reliance on animal testing. Looking at how regulatory requirements are likely to evolve, there would be a considerable increase in demand, requiring a further 2 million animals to be used for testing as a result. It must be time to revisit testing strategies; NAMs offer the potential to do this. They also provide a range of advantages, including no interspecies extrapolation and well-defined applicability. In addition, they will be cheaper, faster and suitable for adaptation to high-throughput screening and automation. However, NAMs still have their limitations; they cannot substitute for higher-tier animal studies, nor can they cover all adverse events. There needs to be suitably funded research to bridge this gap.

She stressed the need to further develop and validate NAMs; they also need to be accepted more quickly at OECD level. There should be a dialogue on the pressing need to modernise approaches to testing and the regulatory implementation of NAMs, both here in the EU and in the rest of the world.

**Kristin Schreiber**, Director at DG GROW, said that the debate has gained fresh momentum, following the European Parliament's recent Resolution on accelerating the switch away from animal testing. This transition was a shared goal for the institutions, and the Commission was pleased that the Parliament had specifically – and rightly – highlighted the role of EPAA; this is something that would be discussed further during the upcoming sessions of the conference.

The EU CSS takes into account the need to innovate, both in order to be able to move away from animal testing and to improve the quality, efficiency and speed of chemical hazard and risk assessments; the Strategy sets out a range of actions to this end. She stressed that the EU had been at the forefront of promoting alternative approaches, funding some €800 million in research over the last 20 years and establishing its own alternatives reference laboratory in Italy. In addition, many EU Regulations now specify the use of animal alternatives.

Until recently, she pointed out, the tools to provide the required information were lacking; this, she felt, could be about to change for the better. The challenge is to connect and coordinate activities. EPAA could play a key role in this, particularly as it already brings together the various Commission services involved and its mirror group as a consultation platform. She was pleased to announce that the EPAA co-chair would participate in the REACH and CLP (Classification Labelling and Packaging Regulation) competent authority expert groups (CARACAL) as an ad hoc observer for any aspects relating to alternatives to animal testing.

### **View from the industry co-chair**

Outgoing EPAA co-chair, **Rob Roggeband** of P&G, said he would provide an 'at a glance' overview of the current status of the EPAA and its likely future developments. However, as this was his last conference as co-chair, he hoped people would understand if he also took a slight retrospective of his tenure.

He felt that with the upcoming policies such the new EU CSS and the revisions of REACH and the CLP, the EPAA stood at a crossroad as regards the '3Rs'. It now had a unique opportunity to ensure 'best-in-class' science was leveraged in making safety-related decisions and in reducing animal testing overall. EPAA had initiated a new project this year, to address the question of whether it was possible to make these safety decisions on ingredients without further new animal testing and whether it was possible to integrate these learnings into the REACH and CLP revisions.

Rob Roggeband announced that Gavin Maxwell of Unilever would take over his role as co-chair from 2022, and would do so with EPAA well positioned for continuing success. The Partnership continued to make strong progress, despite the challenges of COVID. There is an excellent working relationship among the industry and the Commission partners and the Mirror Group, under the chair of Marina Pereira; the Parliament also thinks highly of EPAA, and the secretariat provides excellent support. The core of the work – the projects – continued to make strong progress, with around ten running in 2021. He highlighted a number of project activities, as well as the communication and dissemination activities on the 3Rs that EPAA had undertaken. There was also its presence at the World Congress on Alternatives and Animal Use in Life Sciences, as well as other external events. EPAA had also published four peer-reviewed papers and expanded its number of members.

In terms of the outlook, he stressed again that this looked bright; the core of this being the ongoing dialogue between industry and the regulators on how to best protect consumers and workers through using state-of-the-art approaches. The immediate emphasis would be on the new NAMs project, to help contribute to the successful implementation of the CSS. The existing strong dialogue and relationship with the Commission would be an asset here. However, he stressed the need to integrate exposure into risk assessment and management; otherwise, there is a threat that important chemical ingredients may be lost. The guiding principle should be to protect the worker and consumer. Validation needed to be faster, and classification of chemicals could be improved.

The only route to progress, he stressed, is partnership and dialogue; he thanked the members, Commission and the Mirror Group for the open dialogue that they had created. In conclusion, he pointed out that EPAA's work was more important than ever; the collaboration must continue!

### **View from the Mirror Group**

**Emily McIvor** from PETA – a member of the Mirror Group for 16 years and a member of the Commission's high-level round table on the CSS strategy – provided the Mirror Group's perspective. She too agreed that it was a suitable time to be looking for workable solutions together, and thanked her fellow Mirror Group members for their expertise when preparing the collective input. She also singled out Sirpa Pietikäinen MEP for her support in the European Parliament.

As well as addressing the theme of the meeting, she also wanted to raise concerns over the current direction of travel; what happens next will shape the future, she said. For the last 16 years, the EPAA has provided a forum where scientists and partners could collaborate with the Commission on pursuing the 3R principles. There was a clear focus on the practical application of that work. Part of EPAA's role in the CSS implementation was to scrutinise and highlight that scientific development should, where possible, drive policy and regulatory change. Given that animal protection is a priority for both the public and the Parliament, pursuing specific objectives seems logical; actions such as achieving the bans on animal testing for cosmetics have delivered better science and wider understanding.

She noted that, in the CSS, the European Commission had set a series of short - and long-term actions and policy objectives. As a stakeholder in the negotiations around REACH and the 7<sup>th</sup> amendment to the Cosmetics Directive, she was in no doubt that legislators had intended the REACH data requirements to apply a stepwise manner and that animal testing for cosmetics should cease. However, there seems to be efforts to prioritise substances for testing simply because they can be used for similar purposes as substances of concern; this has led to several ingredients that were used exclusively in cosmetics now being subject to animal test requests without a clear scientific justification. ECHA's requests for clarification of REACH testing requirements may even seem a divergence from OECD guidelines, potentially leading to repeated testing. However, questions from stakeholders on these points so far remain unanswered. ECHA's requests to test exclusive-use cosmetic ingredients on animals is currently the subject of a case at the European Court.

Animal protection organisations are deeply disappointed by the lack of a mention of animal test bans for cosmetics in the CSS or in the impact assessment consultation for the revision of the Cosmetics Regulation. The Commission has already conducted public consultations on many aspects of the CSS; animal protection organisations have responded to all of them. A detailed response from PETA on numerous aspects had been - to all intents - ignored, reduced to only a couple of sentences amounting to "we want to phase out animal testing and increase investment in development of non-animal methods". Other aspects had been omitted. She hoped that this was not the path for the coming months.

There was a fear among animal protection organisations and regulatory scientists within the Mirror Group that the 'one substance, one assessment' approach will see the expertise in using non-animal approaches developed over the years in the SCCS lost in favour of ECHA evaluators with a different record. There was some cause for hope with standard information requirements to identify endocrine disruptors that were being investigated in the REACH and CLP revision impact assessments. The CSS also envisages increasing the scope of REACH, and to include impacts on animal testing has been promised. However, it appears that the broader scope will increase animal testing without any impact assessment.

For the time being, all she could do is to ask these questions and, more importantly, ask when the course will be corrected. While the EU may transition to a more modern and effective system, it speaks volumes that the question of whether the ban on animal testing of cosmetics ingredients will continue still needs to be asked. Despite support from various influential quarters, their insights had not been applied during the CSS discussions. The

EPAA may have a role to play in sharing these insights, helping ensure that both today's and tomorrow's thinking rely on the best available science.

She concluded by expressing her personal disappointment that the European Commission and the ECHA seemed not to be listening. "We can do better", she believed, and the EPAA was part of this.

### **EPAA Refinement Prize**

**Rob Roggeband** then announced the EPAA Refinement Prize winner for 2021; the award, worth €6000, is presented every other year and is for a laboratory technician animal, caretaker or technologist who has demonstrated outstanding achievements in new and novel approaches to advanced implementation and/or awareness raising of refinement of animal testing.

This year's contest had received nine high-quality entries. The jury, made up of two members each from industry, the European Commission and the Mirror Group, selected **Inês Preguiça**, from the faculty of medicine in Coimbra, Portugal as the winner. Inês said it was an honour to be present at the EPAA conference and thanked the selection committee and the supervisor for making it possible.

She presented her winning case study entitled 'HaPILLness: precise voluntary oral drug dosing in rodents - an innovative 3Rs approach'. The objective had been to avoid the stress of oral gavage when routinely administering drugs in laboratory animals by developing a truly voluntary, stress-free, precise and metabolically inert alternative in the form of a versatile, semi-solid matrix. During the study, Inês and her team were able to validate voluntary consumption, the precision of dosing, whether the process was genuinely stress free, its lack of metabolic impact and its safety. The pill technology developed as a result is now undergoing evaluation for a European patent, but hopes to publish this for the scientific community shortly.

**Rob Roggeband** congratulated Inês on her prize and the clarity of her presentation. He wanted to know how she had come with the idea. She explained that it had been born out of necessity; she had been confronted with having to conduct an extensive gavage protocol spanning several weeks. Given the potential for harm to the animals, they needed a viable alternative in order to be able to proceed. Finally, they found one that had worked.

Rob wanted to know about any planned dissemination activities; Inês said she was keen to undertake these. This approach, she felt, could change the entire dynamic of performing pre-clinical studies. She was asked whether there were limitations to the applicability of the approach, in terms of the chemical substances and mixtures; she said she hadn't found one as yet, but of course this could change.

**Rob Roggeband** was asked whether NAMs were compared to earlier-requested animal studies or whether they can be compared to human data. He responded that validating against animal studies was no longer necessary; human data should be considered state-of-the-art where possible. As NAMs approach, validation could be faster.

**Tilly Metz MEP**, provided the European Parliament perspective. She reminded attendees that since the last EPAA conference, the Parliament had adopted - in September 2021 - an ambitious resolution on the phasing out of animal testing. She thanked the stakeholders

who had provided input to her working group. Although the resolution was not perfect, it represented a strong call to action and a clear statement that the pace of change was too slow. It highlighted the potential of NAMs and called for greater funding. The Commission's response is yet to be given.

In terms of the EPAA, the resolution called on the European Commission to establish a high-level interservice task force to work with Member States and stakeholders. Given that it already has many relevant stakeholders around the table, it seemed possible that EPAA could fill this role. It would make sense for the scientific dialogue that was taking place on this platform to be translated into future policy.

The Parliament has a specific focus on the CSS, as regulatory testing is where policymakers can have the most direct impact on the numbers of animals being used. She said it was important, therefore, to secure the shift to non-animal methods before any fresh regulation; if it is not implemented correctly, the number of animals used could increase. As a Green MEP, she supported the Green Deal and a high level of protection for human health; however it should be possible to do this better using modern scientific methods that NAMs offer. We therefore need to promote their use; this is an approach that many companies now support.

As an example, she highlighted the anomaly of a situation where there was a ban on animal testing for cosmetics, but that cosmetics companies still may have to undertake such testing as a requirement of REACH. The industry had demonstrated that it wanted to leave animal testing behind, was committed to NAMs, yet the CSS could require more animal testing for their ingredients. She felt it was time to press 'pause' on any new animal testing and find a solution.

The EPAA project on non-animal science in regulatory decisions for chemical safety was, she felt, exciting. This aims to identify the major challenges facing policymakers and NAMs users; when to embrace them, the competency of the risk assessor in using NAMs and – perhaps most importantly – how to build trust in their use in risk assessment. Stakeholder discussions should be able to develop scientific, legal and political recommendations for increasing confidence.

She closed by recalling the speech that ECHA's Director Bjorn Hansen recently gave to the ENVI Committee. He said that ECHA needed to 'up its game' on the recognition and use of NAMs; this provided her with hope. She felt that candidates for the new ECHA director should be committed to animal testing as a last resort and open minded on how to make that happen.

### **View from PARC (Partnership for the Assessment of Risk from Chemicals)**

**Pascal Sanders**, coordinator of PARC (Partnership for the Assessment of Risk from Chemicals). This is a PPP funded by Horizon Europe, which has been established to provide an interagency body to perform toxicological studies on substances of concern for public health; one that would be able to engage at different EU levels. The programme will be vital for the human biomonitoring of chemicals, and will create a robust dialogue between scientists and policymakers.

The PARC project is a network of 200 partners made up of 28 participating countries, three agencies – EEA, EFSA and ECHA – and five DGs; R&I, ENV, SANTE, GROW and the JRC.

He saw a clear role for EPAA in the work of PARC; they shared similar objectives on the 3Rs. It was important to continue the dialogue between the risk assessors, industry and the risk managers as well as other stakeholders responsible for reducing animal studies. It would therefore be important to see how best to collaborate on identifying the pressing needs and gaps as well as on the different case studies.

He explained that a partnership proposal had already been submitted to the European Commission; this was being evaluated; they were working on the various consortia and grant agreements required. The recommendations by the international experts would need to be incorporated. The expected start date would be around Q2 of 2022.

### **Panel discussion**

The panel discussion, on the topic of "The role of EPAA in CSS", was moderated by Brian Maguire. As well as featuring the earlier contributors - Tilly Metz MEP, Emily McIvor, Dorothee Funk-Weyer - Katrin Schutte from DG ENV, Brigitte Simon-Hettich from Merck and Maurice Whelan from the Commission's JRC were invited to take part. The moderator invited all participants to give a short 'snapshot' of their thoughts on the role of the EPAA in this.

**Tilly Metz** felt that a key role of the EPAA in the CSS was to 'spread the word' that it was possible to pursue safety without having to rely on animal testing. It should be pushing for training on the topic and for funding for NAMs. Perhaps most importantly, it should be highlighting the efficiency gains in the 3Rs and maintaining a dialogue on the topic, ultimately leading to a change in the regulations.

**Emily McIvor** agreed with Tilly Metz. She felt that ECHA had a greater role to play in boosting confidence in non-animal approaches. Given that ECHA claims to have the world's largest chemical database, she wanted to see that put to better use in making sure that knowledge gaps are bridged and the science base is improved. She felt that they were fighting against the regulatory tide but had the scientific tide at their back.

**Dorothee Funk-Weyer** felt that, given the objective of the CSS of driving the switch to more sustainable chemicals, we need to use and apply the best possible science. EPAA, with its broad stakeholder base, needs to communicate what the consensus is on this best science.

**Katrin Schutte** felt that the EPAA could help drive confidence in non-animal methodologies, and that its industry partners could play an important role in the adaptation of the strategy by sharing all their available case studies. This would help boost faith in NAMs.

**Brigitte Simon-Hettich** felt the investment in the 3Rs had delivered huge successes. However, as it was not possible to provide all the data for comprehensive risk assessment using only non-animal data, the rolling out of the CSS could actually see an increase in animal testing; here, the EPAA could foster stakeholder relations and champion non-animal methods in showing both the presence and absence of adverse effects. She also stressed that they could help by ensuring such methods are included in the policies, in order to provide greater certainty for industry when applying these approaches.

**Maurice Whelan** said that the EPAA should 'keep doing what it's doing'. EPAA project teams are unique because they combine extensive knowledge and knowhow on science, technology, regulation and policy, coming from industrial, regulatory and policymaking communities. The new project team on NAMs really illustrates this cross-disciplinary expertise. We have to look both at the reliability and relevance of the NAMs themselves, but also at how regulatory information requirements can be adapted to better match NAM data, and much more needs to be done to ensure NAMs are sufficiently standardised and validated for regulatory applications.

The moderator asked **Tilly Metz MEP** whether the EPAA's 'data firepower' impressed legislators and whether it brought weight to the arguments. She thought that it did; solid, reliable data was always valuable in developing and validating scientific arguments, particularly around NAMs. However, awareness of the existing NAMs was not widespread, they need to be given greater priority and visibility with funding to match.

**Maurice Whelan** felt that funding and resourcing was not necessarily the issue; in his view, research programmes did not always directly address the needs of the regulatory testing and thus results often lack impact. Newly funded research clusters should take on the real challenges, like delivering credible and viable NAM-based solutions that address complex toxicological effects of most concern. He stressed that it was important to work with what was already available now, in addition to pursuing new research.

**Dorothee Funk-Weyer** was asked about the validation of NAMs; were they requested to be compared to earlier-requested animal studies, or can they be compared to human studies? She pointed out that in chemicals, human data was not always available, so only animal data could be called upon. However, **Maurice Whelan** pointed out the challenges in developing any new validation strategy; it always created many contentious areas.

The moderator wanted to know how to build confidence in these new methodologies and ensure consensus among stakeholders. **Katrin Schutte** felt this was the key question; it required a great deal of dialogue and training on all sides. There was also the challenge of accelerating this process. It was also important to remember that these new methods are arguably more complex than those that preceded them, so ongoing training for method users as well as regulators is essential.

On the issue of improving communication on the change to new methods, **Brigitte Simon-Hettich** felt it was important to ensure the community understood what was – and what was not – possible; it wasn't feasible to reproduce all the reactions in a complex animal in an in vitro test. It might be necessary to accept some limitations to progress to NAMs. There needs to be consensus in order to progress. It was important to look at a number of approaches to find what worked best. However, she was not wholly optimistic that the change in attitudes was happening as quickly as she would like. **Tilly Metz MEP** added that animal testing had its limits in what could be achieved; for this reason new methods were needed. She also pointed out that companies needed to share their data; it should be a "quid pro quo" for accessing public funds.

For **Emily McIvor**, one of the problems was that the level of scientific understanding - and expertise - within the Commission was variable. Policy makers need greater support in this area, and it wasn't clear where the responsibility for providing training lay. Confidence could be improved through greater knowledge. **Katrin Schutte** agreed up to



a point, and said that this challenge was for the entire community, not just the Commission; that's why ongoing training was so important.

On the issue of using animal testing as a last resort, **Maurice Whelan** pointed out that as enshrined in EU law, when a scientifically valid non-animal alternative is available, it simply must be used. If it isn't then the relevant Member State should investigate and go after the transgressor. Katrin Schutte said she agreed fully, pointing out that ECHA is already required ECHA to assess any alternative approaches or adaptations under REACH today. However, **Emily McIvor** believed that requests for adaptations were regularly turned down because of a lack of resources at ECHA, so the 'last resort' requirement was not always being properly applied. **Katrin Schutte** explained that ECHA was not obliged to assist registrants in developing adaptations under the current REACH provisions. In addition, said **Brigitte Simon-Hettich**, not all regulatory regimes around the world were the same; some less-advanced systems may still require animal tests for a specific endpoint, creating a quandary for companies over whether (or not) to perform the in vivo test.

On the issue of protecting workers facing particularly high exposures to chemicals, and whether animal testing was needed to protect them, **Dorothee Funk-Weyer** felt it was possible to control this exposure in the workplace. **Brigitte Simon-Hettich** agreed, saying this was a normal issue for health and safety, and that there were approaches to ensure limited exposure.

Panellists were asked about their expectations for the potential collaboration with PARC. **Katrin Schutte** hoped that EPAA expertise would feed into this project. **Tilly Metz** MEP hoped that on a broader level, the French Presidency of the EU would see concrete steps and a timeline for finally phasing out animal testing completely. **Maurice Whelan** felt PARC was a huge opportunity with huge ambition.

On the question of a scientifically independent body to assess ECHA's rejections of non-animal testing approaches, both **Brigitte Simon-Hettich** and **Dorothee Funk-Weyer** were very much in favour. An independent body to give feedback would be very helpful. **Katrin Schutte**, however, had reservations – in order to achieve legal certainty for registrants, any such committee would need to have clear criteria to work by, very much like ECHA has got already today. The Commission was open to suggestions. **Emily McIvor** also thought such a committee was a good idea; she felt that ECHA was less rigorous than she would like, and that this could act as a check and balance.

Asked for their concluding remarks, **Tilly Metz** MEP said she was looking for a roadmap on phasing out animal testing in partnership with the EPAA. For **Emily McIvor**, EPAA should continue working across sectors; it was also important to look at the relevance of animal testing where possible and improve on current practice. **Dorothee Funk-Weyer** wanted to see the dialogue continued to build the confidence to see NAMs implemented. **Katrin Schutte** wanted to get into the 'meat' of the discussions with EPAA and look at as many case studies as possible. **Brigitte Simon-Hettich** felt there needs to be a clear strategy to achieving a science-based approach to eliminating animal testing. **Maurice Whelan** wanted to see greater visibility for the work that was being done at the moment; the EPAA was a potential showcase for that.

### **View from the European Commission co-chair**

**Giacomo Mattinò**, the EPAA co-chair on the European Commission's side, provided his closing remarks. He stressed it was his first time attending, and hoped that subsequent meetings would be face-to-face. He had been impressed by the breath of participation and by the level of interaction shown. He underlined the fact that the timing of the meeting was important. This was not simply because of the European Parliament resolution – which itself was a strong call for action – but also because of other legislation currently being discussed, in particular REACH and the CLP.

He had been particularly interested in the different areas of action that called for attention; this had been inspiring. Not just those for regulators in how to maximise the outputs of the research but also those on how to validate these new assessment strategies. He had particularly welcomed the inputs from Tilly Metz on this aspect.

On the role of NAMs, and of the EPAA in facilitating the process of transforming research into something that can be inserted into the legislation; this, he believed, was the core challenge. There was also the need to prioritise the topics into the various Commission actions streams in order to maximise the efforts and their success.

Another area he wanted to address was the perception of a lack of response from the Commission's side. Here, he said, he wanted to underline the complexity of the legislative process - it was important not to jump to conclusions; work is underway and due attention is being paid to animal testing.

The key takeaway, he felt, was that everyone needed to have more courage and greater determination in bringing our ambition to a successful conclusion. It's a complex challenge, but we should not hide behind that complexity.

He concluded by thanking the organisers and moderator for their efforts, but particularly singled out the work of his fellow co-chair, Rob Roggeband, in interpreting the industry needs and interests. His work had been invaluable, and he would be sorely missed as co-chair. In closing, Mr Mattinò promised a widespread dissemination of today's discussions.