Cruelty Free EUROPE

Building Back Better

A Roadmap to Human Relevant Research in a Post COVID-19 World

Report on a Cruelty Free Europe workshop held virtually on 10 September 2020

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1. Introduction

Ten years since the adoption of European Union (EU) Directive 2020/63 on the use of animals for scientific procedures, the use of animals in European research remains unacceptably high. With the EU decades away from achieving the replacement of experiments on animals, there is an urgent need for an effective strategy to achieve Europe's stated goal of ultimately ending animal testing.

There is growing awareness of the limitations of animal research and its inability to make reliable predictions for humans. In recent years, the US has come to dominate the cell-based and in-vitro toxicology markets.
The EU's recovery plans to build back better after the COVID-19 crisis include ambitious proposals to reinforce research and innovation and kick-start the economy. Next Generation EU, alongside the EU Green Deal, represents an opportunity for Europe to once again become the global game-changer in replacing animal research with new approach methodologies (NAMs) and to be the world's powerhouse in humane and human-relevant science. **To do this will require a coordinated and ambitious proactive strategy across and within the institutions of the EU, member states, industry and academia.**

To this end, a workshop was organised by Cruelty Free Europe to bring together a broad range of stakeholders from the EU and the US, including regulatory decision-makers, academics, scientists, campaigners and industry representatives. The aim was to discuss the contribution new approach methodologies can make to delivering the EU Green Deal and to building back better all over the world after the COVID-19 crisis.
This report summarises the discussions that took place at the online conference on "Building Back Better – A Roadmap to Human Relevant Research in a Post COVID-19 World", held on 10 September 2020.

2. Keynote: What Europe needs to do to build back better with humane, human-relevant science

Professor Michael Balls, Emeritus Professor at the University of Nottingham, opened the event with an outline of William Russell and Rex Burch's 'The Principles of Humane Experimental Technique', which includes the well-known Three Rs (Reduction, Refinement, Replacement) concept in relation to the ethical and scientific issues in animal experimentation. It has now been over 60 years since this publication, and while the Three Rs concept is widely accepted across the world and is the basis of most national and international legislation, Professor Balls argued that there is insufficient understanding of what was actually said in the book and why it was said. This has led to lip service to the Three Rs and little genuine commitment to implement them. Indeed, *"Russell and Burch did not see the Three Rs as an end, but as a beginning."*

The book contains three main warnings, which Professor Balls argued are as relevant now as they were in 1959. First, there is the question of the nature and use of models. Current knowledge of mechanisms of toxicity and the basis of human disease is inadequate, so it cannot be known whether or when data from animal tests can be reliably used to predict effects in humans. As Professor Balls explained, *"Looking into one black box to determine what is likely to happen in another black box is irrational and unscientific, and it's time we stopped doing it"*. Secondly, there is the problem of species differences. Despite general similarities between humans and other mammals, there are major structural and physiological differences between them, which mean that data from animal tests cannot be a reliable basis for predicting the likelihood of specific effects in humans. The third warning concerns the need to take full account of human variation. One human sub-population cannot be a reliable model for all human sub-populations, and the focus in medicine, both in terms of understanding disease and treating it, is therefore shifting towards the individual patient. Professor Balls stressed the need for an honest reappraisal of the use of animal experiments and warned against the continued and naïve reliance on animals to

provide relevant data for humans.

Professor Balls suggested that it is time to abandon the Three Rs concept in the way that it was originally put forward, since the issue is no longer just about animal welfare and inhumanity to animals but also about human suffering; *"It is not a question of making choices between the interests of animals and of humans – a modern, more scientific approach would also have many social and economic benefits – there would be many winners."*

3. Opening plenary: Ten years on from Directive 2010/63/EU – time for action

The opening plenary session was chaired by **Tilly Metz**, MEP and Chair of the European Parliament's animals in science working group. Ms Metz explained that it has been ten years since the adoption of Directive 2010/63/EU, which has within it the final goal of total replacement of the use of animals in science. However, despite the many scientific developments in non-animal methods, the number of animals being used for scientific purposes remains extremely high. The current crisis and the hunt for a vaccine and treatments for COVID-19 has demonstrated how far we still have to come in the acceptance and use of non-animal methods. However, Ms Metz pointed out that *"crises are also opportunities – they allow us to reassess where we stand as a society and to build back better"*. The main goal of the Intergroup for Animal Welfare and Conservation's animals in science working group, which was established in June 2020, is to convince the European Parliament to call for the adoption of an effective strategy with concrete milestones and deadlines to transition to non-animal science. Coherence between the European Parliament, the European Commission and all European agencies is key. Ms Metz stressed that this transition *"needs to be recognised as a bigger priority than it is now" and that "any new research investment and any new scientific policy needs to be aligned with the Three Rs principles"*.

Dr Katy Taylor, Cruelty Free Europe's Director of Science and Regulatory Affairs, presented some key statistics on the use of animals for scientific purposes across Europe and opened the discussion about whether the Directive is really fit for purpose. One of its main benefits is the requirement that all EU member states must authorise projects involving the use of animals based on a harm benefit assessment. This includes ensuring that wherever possible, if a non-animal alternative is available, animal tests should not be conducted. It is clear the intention of the Directive is to fully replace the use of animals for scientific purposes. However, the statistics over the last ten years do not paint an encouraging picture. While there has been some progression downwards, official EU statistics show that the number of animal experiments has only dropped by 20% in the past twenty years, a drop of just 1% per year. If you consider all animals in laboratories, the total number more than doubles from 10.9 million procedures reported in 2017 to 23.5 million. Dr Taylor stated that *"the scale of animal use in Europe is unacceptable both morally and scientifically and should be a concern to everybody"*. Several opinion polls conducted across EU member states certainly confirm that this is a big concern to the public, the majority (66%) of whom, according to a poll conducted for Cruelty Free Europe in 2020, wish to see an immediate end to animal experiments across Europe. In response to an EU Citizens Initiative petition calling for the immediate end to animal experiments, the Commission responded to say that they agreed that animal testing should be phased out, which is the ultimate goal of EU legislation.

Despite the apparent desire to eventually replace all animal experiments, Dr Taylor pointed out that the actual way in which experiments are authorised by member states is too passive. The vast majority of animal experiments, including basic medical research, are conducted entirely voluntarily; only 20% are required for regulatory purposes. Indeed, there is no limit under the Directive on how many experiments can be conducted, which partially explains the static picture of animal use across Europe over the past ten years. Furthermore, Dr Taylor pointed out that the Directive is not doing its job properly even by its own standards, which is evidenced in

the fact that so many animal tests are still being conducted in the EU where validated accepted alternatives are already available. Rabbits are still used in skin and eye irritation tests and pyrogen tests; guinea pigs are used in skin sensitisation tests; and mice are used in Botulinum toxin batch tests. Dr Katy Taylor warned that *"following the current trajectory, we will not reach zero animal experiments for nearly another 100 years, during which, an estimated 450 million more animals would have been used. Is that what we wanted to see when we revised the Directive on animal experiments?"*

Professor Thomas Hartung, head of the Center for Alternatives to Animal Testing (CAAT) at Johns Hopkins University, reiterated that while the implementation of the Directive was a step forward in terms of improving some animal welfare aspects of the legislation, there are many shortcomings that must be overcome. He gave the example of pyrogen testing to highlight the fact that, while the rabbit test has decreased significantly over the past several years, approximately 35,000 rabbit tests were still conducted in 2017 when there is no clear reason for the tests to be conducted at all. The replacement, which is based on human cells, was validated in the late 1990s and can now be used to test all types of products. According to Hartung, the reason that the rabbit tests are still being conducted is simply due to the lack of enforcement. Similarly, the REACH legislation, which included the promotion of alternative methods as one of its main goals, has failed to live up to its expectations. The only alternative method that it really promotes is read-across (RA) and even then, due to increasing requirements and unrealistic expectations of the RA assessment framework, most RA data is rejected and data from animal tests is preferred. One way to overcome these barriers is to improve confidence in these new methodologies. While the EU has been making slow but steady progress over the past few decades, the US has recently begun to take over by investing heavily in these new technologies. In 2016, Dr Francis Collins, NIH Director, predicted that in ten years the safety testing of drugs and chemicals would be largely carried out using human biochips, which would provide more accurate and relevant data than animal tests. In 2019, the US EPA committed to the phasing out of animal testing by 2035. These are bold statements with clear deadlines, the kind of progressive steps that have not been seen in Europe since the cosmetics testing bans. Dr Hartung concluded by stressing the importance of deadlines to promote change; *"the issue is not only about animals but about overcoming animal tests and their shortcomings in order to improve patient and consumer safety"*.

In the Q&A session, the scale of funding for non-animal methods compared to that allocated for animal-based research was raised as a concern. Would an increase in funding of non-animal methods promote further use and development of these methods, in other words will research follow the money? There was unanimous agreement that if a concrete strategy were put in place to prioritise non-animal methods and de-prioritise animal tests in the funding stream, this would stimulate interest from scientific researchers and help build momentum for real progress to be made. Dr Taylor stressed *"it's important to realise that this is where the innovation is, this is where the exciting science is, it's not in animal research, it's in non-animal research"*. There was also unanimous support for the need for a roadmap with concrete goals and clear targets and deadlines for animal reduction similar to what we see written into other pieces of EU policy such as climate change emissions. Dr Taylor said that one way to start would be to root out specific areas of animal testing that are completely redundant and could be ended immediately with no impact on human health. The European Centre for the Validation of Alternative Methods (ECVAM) recently issued a strong statement to support the use of phage display, an in vitro method used to produce antibodies without using live animals. If the European Commission and European Parliament were to act fast in support for this, hundreds of thousands of animals could be saved almost immediately. Tilly Metz concluded that it is not enough to express a desire to change; a written commitment and concrete strategy with set targets is needed. European legislators also need to work together with all of the key players, including regulatory agencies across different sectors, to develop coherent and unified policies that will bring about real change at all of the different levels.

4. Workshop one: Change in action – initiatives to prioritise non-animal research around the world

Dr Warren Casey, Acting Chief of the Biomolecular Screening Branch at the US National Institute of Environmental Health Sciences (NIEHS) and Executive Director of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), attributed the US's recent successes in the advancement of non-animal technologies over the past few years to the publication of ICCVAM's roadmap, which lays out some basic steps to develop more human-relevant approaches and move away from animal testing. While the roadmap was inspired by efforts in the EU (particularly the UK and the Netherlands), the US took a different and arguably more successful approach by inviting regulatory agencies to help with the development of the roadmap. Dr Casey stressed that the key to moving away from animal testing is to get end-users and regulators involved from the very beginning and to shift the focus from validation to development. History has shown that validation is often the bottleneck – it could take a decade to validate a very simple method and, in the end, either the regulators still would not accept it, or industry would not use it. Another roadblock is caused by agencies who either claim that they do not require animal testing or that they accept all alternative methods but then go on to reject non-animal data. According to Dr Casey, these issues can be solved if agencies are willing to engage and be transparent about what they want and what they will accept; *"when you begin having agencies involved at the very start, the validation becomes easy and fast."* Other major roadblocks include the continued use of animal data to validate human-relevant methods, lack of international harmonisation and the need for improved access to high quality, computationally friendly data. Dr Casey believes that, if we could solve these problems, we would be 80% of the way to eliminating animal testing.

During the Q&A session, which was chaired by **Michelle Thew**, CEO of Cruelty Free International, Dr Casey was asked to elaborate on the issue of international harmonisation and provide some suggestions on what could be done to overcome this roadblock. Dr Casey explained that while the US has the advantage of being able to work directly with regulators, this is more difficult to accomplish in the EU due to barriers put in place to protect conflicts of interest. Therefore, the continued reliance on and support for international organisations, such as the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) and the Organisation for Economic Cooperation and Development (OECD), is necessary to bring about change. However, Dr Casey warned that progress is slow; OECD policy operates on a 100% consensus basis so if one country objects to a particular method, the process can be delayed for another year. He encouraged people to become more active and engaged in their country's stance at the OECD to push for a faster process. Finally, Dr Casey was asked to provide some examples of animal tests that are prime for elimination to which he responded by describing the gross inaccuracy and unreliability of the notorious Draize eye irritation in rabbits. Dr Casey also explained that many tests can be eliminated simply by doing a retrospective analysis of the data, helping agencies to understand what data they really need and what they are using the data for. This could help to eliminate superfluous animal tests as well as highlight specific areas where new methods are needed.

To describe similar efforts being made in the Netherlands, **Tanja Timmermans**, Programme Manager for the Netherlands Transition Program for Innovative Animal Free Research (TPI), presented a brief history and description of the inception and goals of TPI. In 2016, the Dutch government announced an ambitious plan to phase out animal experimentation by 2025. However, it was later decided that this goal was unattainable due to difficulties in engaging all stakeholders, which led to a polarisation of the debate on how research should be conducted in the Netherlands and how quickly certain areas of animal research could be replaced. In 2018, it was decided that instead of focusing on the reduction of animals per se, it would be more constructive to focus on accelerating the development and funding of non-animal methods. The hope was that by shifting the focus towards animal free innovation, those researchers still working in animal research would feel less ostracised and the end-goal of

making animal use redundant would be realised in a more constructive and sustainable way. Ms Timmermans also stressed the importance of education and collaboration and described some recent efforts by TPI to get more people involved in knowledge sharing. The launch of TPI TV – an online video platform for exchange where people can congregate to discuss animal-free research – has encouraged the creation of joint research groups and funding to achieve common goals. Ms Timmermans concluded that *"it could take 20-30 years to replace all current research with animal free alternatives. To move forward, this must be a joint effort between all parties. We must strengthen international ties and cooperation and harness the creative power of animal free researchers to really drive change"*.

The importance of collaboration was also emphasized by **Franz Lamplmair**, Advisor for Alternative Approaches to Animal Testing at the European Commission and co-chair of the European Partnership for Alternative Approaches to Animal Testing (EPAA). The EPAA is a public-private partnership between the Commission and industry to promote the development, validation and acceptance of 3Rs approaches in regulatory testing in Europe and around the world. The EPAA is currently working on ten scientific projects that are focused on key areas where animal tests are ripe for replacement such as acute toxicity, rabies and clostridial vaccines and skin sensitisation. They also provide funding to support the research and training of young scientists and produce, as well as disseminate, training videos and scientific publications following all major workshops and projects. According to Mr Lamplmair, *"our biggest asset is the collaborative cross-sector structure of the partnership. There is a strong commitment from all partners, who bring along their expertise and knowledge in this very technical field, to identify gaps and develop cross sectoral approaches with mutual benefits"*. The upcoming EU Green Deal and Chemical Strategy for Sustainability are also key policy areas which Lamplmair suggested could increase attention and funding for non-animal alternatives. However, he warned that while MEPs recently expressed their commitment to adopt alternatives and minimise animal testing in their resolution on chemicals, they also highlighted some areas where more protection for citizens, animals and the environment is needed (endocrine disruptors, polymers, cocktails of chemicals), which could lead to an increase in animal testing in the short-term, or at least until non-animal technologies are more advanced and widely available.

Dr Hermes Sanctorum, Consultant and former member of the Flemish Parliament and Belgian Senator, presented the case of the Brussels capital region to answer the question of whether proactive strategies at the national/regional level are compatible with the EU Directive. In Belgium, animal welfare is not a federal matter but rather each of the three regions is responsible for the use of animals within its own territory. According to Dr Sanctorum, this has created an interesting dynamic for each region to try and do better than the other in terms of animal welfare. In October 2017, the government of the Brussels capital region announced a new policy proposal that included a reduction target in animal testing of 30% by 2025 as well as the phasing out of experiments on primates, dogs and cats by 2020. Clear target and reduction paths are common for other policy areas (for example, climate change, traffic-related deaths) so it seemed logical to also set targets in animal experimentation. Unfortunately, however, the Belgian state council ruled that the proposal was not compliant with the EU Directive on the use of animals in scientific research, specifically with Article 2, which prevents member states from adopting stricter measures at a national/regional level than the rest of the EU, and the proposal was abandoned. Dr Sanctorum stated, *"the harsh reality is that, unlike any other policy area, the Directive makes it difficult for member states to be proactive and become true frontrunners with clear targets and reduction paths for animal experiments"*. Therefore, a unified EU-wide approach appears to be the only clear way forward.

To conclude workshop one, all the panellists were asked to sum up what they think is key to bringing about a faster reduction to animal testing:

- Collaboration between all different parties involved including regulators, researchers, businesses, government funders and NGOs.

- Increased attention from high-level decision-makers – while non-animal alternatives are becoming increasingly available, it will remain difficult for them to become accepted into EU guidelines until they are seen as a political priority.
- The desire to set reduction targets, if not at the national level then at the EU level.
- Legislation with some teeth – Dr Casey pointed out that *"people don't change when they see the light, they change when they feel the heat"* – in other words, in the absence of legislation and real incentives, people are not going to change.

5. Workshop two: Kickstarting economic recovery through European investment in non-animal research and innovation

Maria Spyraki MEP opened the second workshop of the day with a summary of some key opinion polls as a reminder of how important the issue of animal testing is to EU voters and why Parliament must take these concerns seriously. She said, *"animal tests are costly, they are misleading, and they are unacceptable. While it is important to have the proper legislative instruments to achieve the goal of replacement, it is also important to put pressure on governments to implement the legislation"*. As an author of the Parliament's recently adopted resolution on the Chemical Strategy for Sustainability, Ms Spyraki highlighted its call to minimise and replace animal testing through the expanded funding and use of NAMs and animal-free approaches to chemical safety assessment. A key proposal included in the strategy is the demand for the European Chemical's Agency (ECHA) to facilitate a new data platform for chemicals that will be widely accessible to all parties and can be used to develop NAMs, particularly computational models, to replace animals. When asked how to convince politicians that animal testing is a mainstream issue, Spyraki said that the business aspect of animal testing is an important motivating factor: *"To test a single pesticide it currently takes about a decade, costs 71 million dollars and kills up to 8,000 animals. Animal tests are costly and simply not affordable in terms of business"*.

Elisabet Berggren, Deputy Head of the Chemicals Safety & Alternative Methods Unit at the European Commission's Joint Research Centre (JRC), described the purpose and mandate of European Union Reference Laboratory for alternatives to animal testing (ECVAM) established under the Directive to provide scientific advice on the validity and use of NAMs. ECVAM is traditionally focused on regulatory testing and works in this context on three key levels to help achieve the final aim of the Directive – the full replacement of animals. The first is the scientific level to develop and evaluate more efficient approaches to testing and assessment and replace the use of animals; the second is the regulatory level to develop a framework that is not based on information from animal studies and the third is the policy level to prioritise animal protection and understand its importance across all sectors and pieces of EU legislation. In addition, ECVAM investigates and promotes alternative methods applied in biomedical research where most animals are used and is actively involved in the education at high school, university, and professional levels. When asked what ECVAM needs from politicians to move forward more efficiently with its agenda, Ms Berggren said: *"we need support, an open debate about animal use and also, a realistic discussion about what we don't have today – there are a lot of chemicals on the market that we still don't know anything about. We need to acknowledge that animal models are not the gold standard and more human relevant tests are needed to fill these gaps"*. She also highlighted the importance of collaboration; "*we need to work together to get more information, to understand better, to avoid doing the same thing twice and to learn from each other*".

According to **Anna Lönnroth Sjödén**, Head of Healthy Lives Unit, DG Research and Innovation in the Commission, the EU has funded 200 research projects on non-animal methods over the past 20 years, at a cost of 700 million euros. While spending has remained stable and significant during the last decade with roughly 45 million euros a year, the Commission will increase funding in the near future and is currently evaluating project proposals on

the safety of chemicals without the use of animal testing, to which it has allocated 60 million euros, and on the development of next-generation organs-on-chips with a budget of 24 million euros. The COVID-19 pandemic has recently risen to the top of the funding agenda with emergency calls issued to scientists to submit proposals to develop new therapies, drugs, vaccines and diagnostics. According to Ms Lönnroth Sjödén, only 0.2% of this funding has gone towards animal experiments. Together with ECVAM, the Commission is conducting a study to retrospectively assess the value of animal models and alternatives in EU funded projects and is expected to publish the results early in 2021. Ms Lönnroth Sjödén stressed that while we should see a slight increase in funding for alternatives, no significant progress will be made unless more efforts are made to work more closely with member states to coordinate funding and to also collaborate more with other EU agencies including ECHA and the European Medicines Agency (EMA), particularly in the area of data-sharing; *"it's about dialogue, coordination and collaboration"*. Ms Lönnroth Sjödén also highlighted implementation, the uptake of existing non-animal methods by scientists and regulators, as a key area where more work needs to be done.

The importance of funding, collaboration and education was once again brought into focus by **Debby Weijers**, Director of Stichting Proefdiervrij (Dutch Society for the Replacement of Animal Testing), who provided some examples of how even the work of a small Netherlands-based NGO can make a real impact. The aim of Stichting Proefdiervrij is to replace all animal testing by stimulating the development and application of animal-free innovation. Over the past ten years, they have been able to support 50 projects worth approximately five million euros, which may not sound like a significant amount, but when considering that the funds came solely from local citizens, demonstrates how important this issue is to the public. The NGO now looks to move beyond funding the development of non-animal technologies but to also focus on providing support for the application and implementation of these methods. The importance of building public confidence that products and pharmaceuticals tested using non-animal methods will be safe was is an important aspect that can be addressed by increased education. Ms Weijers stated that *"while communication and dissemination within the scientific community is key, societal pressure is also an important tool"*. Her final point was that *"the best scientist is usually not the best entrepreneur, and vice versa, so it is important to find a way to bring these two together to bridge the knowledge gap"*. To address this, Stichting Proefdiervrij is launching a venture challenge in 2021 – a ten-week program from which a scientific breakthrough will be converted into a solid business case.

To conclude workshop two, which was chaired by **John Howarth**, Director of Politics Without Borders, all the panellists were asked to sum up what they think is key to progressing the research and development of non-animal methods and bringing about a faster reduction to animal testing. The following were suggested:

- Engagement and dialogue – engage with all the relevant actors in research and innovation and ensure that there is dialogue between them.
- Widespread implementation and use of available non-animal alternatives.
- Continued funding for the development of new non-animal alternatives.
- Communication and dissemination – it is important to share information that is already available, which will in turn highlight areas where increased knowledge, and funding, is needed.
- Collaboration – international collaboration, collaboration with industry, with NGOs, between the Commission, between member states and between regions.

6. Workshop three: Promoting cruelty free cosmetics – are the EU's cosmetics testing and marketing prohibitions working?

The final workshop of the day was chaired and introduced by **Sirpa Pietikainen** MEP who stated that the focus of the session would be on how to better promote cruelty free cosmetics and to discuss whether the current testing and marketing prohibitions of animal-tested cosmetic products are working. According to Ms Pietikainen, *"We*

already have processes in place that do not rely on animals and it is not necessary to subject them to such cruelty for the purpose of cosmetics testing". She also called on society, including the institutions of the European Union, to push for a global ban on the use of animals in cosmetics testing.

Dr Katy Taylor, Director of Science and Regulatory Affairs at Cruelty Free Europe, gave a brief history of the EU Cosmetics and REACH Regulations and discussed how the two pieces of legislation overlap and what impact that has had on the cosmetics animal testing ban in Europe. The final 2013 ban sent a signal to rest of the world that the EU did not consider it was ethical to test cosmetics products on animals and that there were strong scientific reasons why it did not need to be done. It also encouraged other countries to put their own national bans in place. The EU's chemicals safety legislation (REACH) was adopted in 2006 and required the registration of new chemicals as well as 30,000 existing chemicals. Despite the inclusion of important clauses in the legislation, – articles 1 and 25, which state that REACH must promote the use of non-animal alternative methods and that animal testing must be a last resort, respectively – an estimated 2.6 million animals have been used to date to satisfy REACH requirements. In 2013, the European Commission and ECHA ruled that even with the cosmetics ban in place, cosmetics ingredients were not exempt from REACH registration and could be tested on animals if they are also used in other products or if there is likely to be worker exposure. Dr Taylor said that this left very little now where the testing bans under the cosmetics regulation bite. The impact of this erosion of the cosmetics ban has already been significant, and many cosmetics ingredients (including UV filters used in sunscreens, foundations and moisturisers, preservatives, tea tree oil and foaming agents) have been recently tested on animals for REACH. Dr Taylor concluded that *"sadly, there are very few cosmetics that are safe from this interpretation, is this what parliamentarians and EU citizens really expected to see?"*.

Dr Dani Loughran, Managing Director at Aston Chemicals Ltd., provided an overview of the effects of the animal testing ban from an industry perspective and echoed some of the issues experienced with the conflict between of the Cosmetics Directive and REACH legislations. She said that overall, the outcome of the EU cosmetics ban has been positive as it has forced people to think harder about the issue of animal testing and has changed a lot of behaviours, both at the consumer and manufacturer level. Many consumers now actively seek out non-animal tested personal care products and ask questions about the animal testing status of ingredients. This has in turn encouraged manufacturers to become more stringent on what ingredients they are willing to purchase from suppliers. They have to check that each chemical substance that will form the ingredients of their products has not recently been tested on animals. Dr Loughran said that *"from the European cosmetic industry perspective, we really don't want to perform animal tests, our customers [personal care product manufacturers] don't like them and they don't think they're necessary. But ultimately, we are businesses, so we have to do whatever the regulations tell us to do"*. She said that manufacturers can face the difficult choice to either conduct the animal tests and accept that many customers may refuse to use their products, or to stop marketing the product entirely. Dr Loughran stressed that *"for both ethical and commercial reasons, manufacturers really want to avoid this kind of situation, and we'd really like to eradicate all animal testing for REACH through the use of non-animal alternative methods, pragmatic risk assessments, read across where possible and data-sharing."*. She concluded her presentation with a summary of the implications of Brexit on REACH and the possibility that substances may require duplicative testing for UK and EU markets and emphasised the importance of achieving regulatory alignment and data-sharing between the UK and EU chemical legislations.

David Thomas, solicitor and co-founder of Advocates for Animals, discussed the legal aspects of the cosmetics testing ban. In a 2016 case, the European Federation of Cosmetics Ingredients (EFCI) originally argued for a very narrow interpretation of the cosmetics testing ban i.e. the ban would only apply if the testing was done specifically for the Cosmetics Regulation and not for REACH or third country testing. That argument failed in the High Court in London and the Court of Justice, looking at the effect of animal testing in third countries, later ruled that cosmetics products could not be sold in the EU if it were necessary to 'rely on' data from animal testing to do so.

On this basis, Thomas explained the nominal purpose of the test, where the test was carried out or whether the ingredient is sole-use or multi-use should be irrelevant. This became known as the 'reliance test', and while it is not an ideal interpretation of the cosmetics legislation from the point of view of animal protection organisations, it at least provided some clarity. However, ECHA and the European Commission still maintained that their previous, restrictive interpretation of the legislation was justified. In a more recent case, ECHA's Board of Appeal (BoA) upheld a decision by ECHA to require German chemical company Symrise to carry out several animal tests on two of its cosmetic ingredients under REACH. In August 2020, the BoA decided that new animal tests are not banned under REACH even if the substance is used exclusively as an ingredient in cosmetics and instructed Symrise to carry out the tests. It was hoped Symrise would appeal to the General Court [and has now done so] but, according to Mr Thomas, if there is no successful legal resolution of the issue then it should fall on MEPs to consider amendments to both REACH and the Cosmetic Regulation to clarify the wording and take into account the complications in regards to overlapping legislations; *"Parliamentarians need to ask themselves if this very narrow scope for the cosmetics ban is really what was intended. When legislation is interpreted by the courts in a way which the legislator did not intend, the legislator simply has to try again"*.

The key conclusions of the workshop were:

- The erosion of the cosmetics testing ban in the EU has had a serious impact on animals and is not what was intended by legislators at the time.
- Parliamentarians should consider seeking amendments to both REACH and the Cosmetics Regulation to prevent conflict between the two pieces of legislation in a way that rules out animal testing.
- Collaboration and data-sharing between the UK and EU is necessary to prevent duplicative animal testing for chemicals.
- Industry is generally supportive of the desire to move away from animal testing, mainly due to the increased popularity of cruelty free products among consumers.

7. Closing plenary: Implementing a roadmap to animal-free research in the EU

The closing plenary session, which focused on how the EU would implement a roadmap to end experiments and promote the use of animal-free research in Europe, was chaired and introduced by **Dr Katy Taylor**. She reiterated that if the EU continues its current trajectory, animal experiments would remain for another 80 years or more and suggested that the implementation of a clear strategy for reducing animal tests would be one way to help speed up this process. Indeed, a recent EU-wide poll found that 72% of the public agrees that the EU should set targets and deadlines to phase out animal testing similar to the target-based approach in place for a number of other areas in the EU (for example, carbon emissions and recycling). While these strategies exist in other parts of the world, notably in the US where there are several sector-specific roadmaps in place to reduce animal testing, an EU-wide strategy is lacking. Dr Taylor suggested some obvious areas of testing in the EU that could be prioritised in the short-term, including the use of animals in tests where there are alternatives already in place (for example pyrogen tests, antibody production etc.), primate neuroscience research, the production of genetically modified mice, the use of animals in education and training and the testing of other superfluous products such as food and household products. Dr Taylor concluded that, *"if the EU sets a target for the reduction of animal experiments, it will lead to increased investments in technology as well a shift in the mindset of the research industry."*

Eleonora Evi MEP provided some suggestions as to what policymakers can do to achieve full replacement of animals more quickly in the EU and expressed support for the implementation of an EU-wide roadmap as an important step. She began by stating that, in her opinion, *"over the past few years, Europe has not done enough to achieve the goal it set itself to phase out the use of animals in science"*, which is evidenced by the staggering

number of animals that are still used every year for scientific purposes in the EU, often in redundant areas or in areas where non-animal alternatives are available. While some promising initiatives have taken place in recent years (including SEURAT and EU ToxRisk, the establishment of EURL ECVAM, the increase in public petitions to end animal testing and the launch of an animals in science working group in the European Parliament), progress remains slow and, according to Ms Evi, the time is right for the EU to develop an effective strategy with concrete milestones and precise timelines to accelerate the necessary transition to animal science; *"I believe that the way forward is an EU-wide roadmap that is built on three key words – milestones, money and mindset"*. She echoed the suggestion made throughout the workshop that the adoption of binding targets is key as well as the identification of areas of testing where tests on animals can be banned immediately. For example, Italy adopted a ban on the use of animals in recreational drug research. However, bearing in mind what happened in the case of the Brussels capital region, it is important that the EU also makes progress in these areas to avoid infringement procedures for countries that have adopted rules on animal testing that are stricter than what the EU Directive stipulates. Increased funding is also imperative to progress, particularly at this moment where a budget is being set for the post-COVID-19 recovery in the EU. Ms Evi pointed out that only 0.1% of the 80-billion-euro budget of Horizon 2020 was allocated for non-animal research in the period of 2014-2020. Finally, there needs to be a change in the mindset of researchers, regulators and the general public where non-animal methods should be seen as the default. Education should play a central role in reframing the issue to not only be considered an ethical one, but also a necessary one for medical advancement particularly in areas like cancer and Alzheimer's disease where animal models have failed; Ms Evi stressed that *"non-animal methods have a huge potential that needs to explored"*.

The need for a common strategy and coordination between the European Commission and EU member states was echoed again by **Dr Luisa Bastos**, Programme Leader at Eurogroup for Animals. She began her presentation by highlighting the fact that *"the current scientific culture, infrastructures and education do not enable a scientific practice that uses animals only as a last resort, and the EU legislation in place is not helping to improve this scenario"*. She expressed the urgent need to overcome some of the key barriers that are deeply rooted in today's scientific culture. For example, EU laboratory animal scientists have claimed that they lack the necessary equipment or knowledge to use non-animal methods and, maybe as a consequence, they still lack trust in these methods. Dr Bastos reminded the audience that although animal welfare is one of the major concerns of EU citizens, the EU continues to invest very little in non-animal science, comparing to the investments in animal-based science, and mentioned opportunities that are coming up to shift investments towards NAMs. For example, concerted actions between the Commission and Member States will be essential for the success of Horizon Europe's Mission on Cancer, as well as for the resolution of the current pandemic and other diseases. She highlighted that a transition to human-based health science can help overcome the colossal failure rates of clinical trials to move towards better, safer and more humane science. Dr Bastos stressed that if the EU is committed to phasing-out the use of animals in science, it is imperative that it works to ensure the continuous revision of educational programmes to disseminate and promote knowledge on NAMs, while at the same time, building the infrastructure necessary to guarantee access to these new methods that can replace the use of animals. She concluded that the EU *"must have an open and constructive goal-oriented dialogue with all key players to develop a strategy with defined milestones and necessary systemic actions to make progress together. Nobody can be left out"*.

Dr Carol Treasure, Founder and CEO of XCellR8 – a UK-based company that develops and uses non-animal alternatives – explained how she thinks industry would react to an EU-wide roadmap for the replacement of animal tests and also provided some suggestions on how to achieve success in this area. She said that in her experience, industry is generally very supportive of the complete replacement of animal tests and often does everything possible to avoid it despite pushback from regulators, including the use of methods that may not be fully accepted by the OECD but nevertheless have a lot of scientific credibility and validation behind them.

However, there is still room for industry to be more proactive in terms of coordination, collaboration and data-sharing to avoid duplicative efforts and to help identify gaps that should be prioritised in terms of development opportunities. Dr Treasure also highlighted the importance of funding and issued a rallying cry to industry to invest more of their own funding into the development of alternatives rather than relying on external funding which is often disappointing; *"there is a massive funding gap that we are all facing and even though we talk about millions of pounds being invested in the development of alternatives, in the whole scheme of things it's still a small amount and is not enough to drive the replacement of those more complex human health endpoints"*. Her final suggestion was for industry to be more transparent and educational with their customers so that the public is more informed on what has already been achieved as well as where the challenges are; often, industry doesn't get the credit for all the positive progress that has taken place and there's a need to raise awareness about this as well as openly share where the challenges remain. Transparency builds trust. *"Real change in the EU began with the public. The public drove the changes in regulations which then put pressure on industry to come up with new tests."*. Dr Treasure concluded that overall, all stakeholders, including the public, NGOs, industry and regulators are heading in the same direction and that everyone wants products which are kinder to animals and better for humans.

Carla Matias dos Santos, Research Counsellor at the Permanent Representation of Portugal to the EU, provided an overview of some relevant priorities (still indicative at the time) of the forthcoming Portuguese presidency as it prepares to take over the presidency of the Council of the EU from January to June 2021. These priorities are framed by the Trio programme composed by Germany, Portugal and Slovenia that identified the role of R&I for growth and jobs and for contributing to a resilient Europe in terms of preparedness to future pandemic crisis through the support to R&I activities, development of skills, education and health; the potential of R&I for innovative transformative solutions to achieve the SDGs; the renewal and reconceptualization of the European Research Area (ERA); and the timely adoption of the legislative proposals under the next multiannual financial framework. As a first priority Portugal will give continuation to bringing upfront the importance of research and innovation, which includes a continuation of the work for the swift adoption of Horizon Europe, important to the scientific community, including in the context of research on the development of non-animal testing methods. The second priority is to encourage a broad discussion on research careers encompassing all the important dimensions in a holistic approach, including responsible research and ethics, which is of course relevant to animal testing. Another priority Portugal would like to pursue in its presidency is increasing the investment in research and innovation, which is relevant to the discussion on the funding gap experienced by many scientists wishing to pursue NAM development. Finally, Portugal hopes to encourage a greater level of societal engagement, which also echoes earlier comments made about the importance of public awareness and education. Santos concluded with a note on the COVID-19 crisis; *"this pandemic has shown how research and innovation is important in the context of the resilience and preparedness of Europe and that human-relevant research in a post-COVID-19 world is more important than it ever was".*

The event came to an end with a closing speech by **Vanessa Mae**, world-renowned violinist and Ambassador for Cruelty Free International, who spoke of her own passion for animals and implored the assembled representatives to work together in order to end the suffering of animals in European laboratories.

8. Conclusion

The online conference was attended by over 100 people and brought together a wide-range of stakeholders including decision-makers, scientists and industry.

The first of the day's three workshops examined examples of proactive replacement and reduction plans for

animal research. In the second workshop, participants looked at the call for the EU to take the lead in sustainable science and sustainable solutions to reduce the suffering of animals in laboratories, while the final workshop examined what the EU's bans on cosmetics animal testing have achieved since coming into final effect in 2013 and what the future of the bans looks like. Participants also discussed specific initiatives underway in Europe and North America to replace animal testing, what programs such as Horizon Europe can do to bring about a paradigm shift and how applying the logic of targets could be the important next step.

There was consensus that increased collaboration and fixed targets are needed to see an end to animal testing in Europe. The best way forward would be to develop a comprehensive EU-wide roadmap towards ending animal testing with agreed goals, milestones and deadlines.

Initiatives that could help achieve this goal included:

- An increase in dedicated funding for non-animal technologies to encourage innovation
- Increased collaboration between all relevant stakeholders – including early involvement of regulators, data sharing between companies and cross-sector collaboration
- More investment in education for young scientists but also to help change the mindset of the current scientific community
- Using public and political pressure to drive change
- Greater transparency in terms of where the gaps in knowledge are and how they can be filled
- Better enforcement and availability of accepted non-animal methods
- Continued support for global harmonisation to reduce region-specific barriers in terms of data requirements and acceptance of alternatives
- Timely updates to legislation to encourage innovation and flexibility
- More ownership of the EU's goal to end animal testing by high-level decision-makers in the EU and its member states

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