



Key elements of a strategy to transition to non-animal science

Position Paper
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A clear statement that transitioning to non-animal science is a desirable and achievable goal, along with a strong commitment to work to get there

Background and rationale

Recital 10 of Directive 2010/63/EU [states](#) that “While it is desirable to replace the use of live animals in procedures by other methods not entailing the use of live animals, the use of live animals continues to be necessary to protect human and animal health and the environment. However, this Directive represents an important step towards achieving the final goal of full replacement of procedures on live animals for scientific and educational purposes as soon as it is scientifically possible to do so. To that end, it seeks to facilitate and promote the advancement of alternative approaches.”

Separately, the European Commission has also [stated](#) that “the EU shares the (...) conviction that animal testing should be phased out” and that “this is the ultimate goal of EU legislation”.

Transitioning to non-animal science has also been recognised as an important step to improve health and environmental protection, and find effective disease treatments. The Commission acknowledged in its [Chemicals Strategy for Sustainability](#) that “Safety testing and chemical risk assessment need to innovate in order to reduce dependency on animal testing but also to improve the quality, efficiency and speed of chemical hazard and risk assessments”. The reviews of EURL ECVAM of [non-animal models](#) in biomedicine also provide examples of where animal-based research has not been delivering the advances to the understanding and treatment of human diseases that society needs.

The EC and all Member States should openly **endorse the desirability of 'transitioning to non-animal science' and state their belief that this is achievable.**

Member States should also encourage research establishments within their jurisdictions to similarly publicly endorse this sentiment and goal.

And the EC should recommit to accelerating the transition to non-animal science as a **priority goal** and **produce a strategy**, based on the remaining points in this paper, to further stimulate actions to achieve this.

To further illustrate the EC's commitment, the goal of 'phasing out animal use in science' should be identified as a potential '[Mission](#)' under the next Framework Programme.

This goal is transversal to every mission, action or project that intersects with life sciences and, therefore, prioritising a transition to non-animal approaches should be an integral part of all research, innovation and education initiatives.

Clear milestones

Background and rationale

In other areas of societal concern (e.g. climate emergency, healthcare, education) governments have set out specific aims and goals. For example, signatories to the [Paris Agreement](#) agreed to aim to keep a global temperature rise well below 2 degrees Celsius above pre-industrial levels, during this century; the UK government has announced a ban on the sale of new cars and vans powered wholly by petrol and diesel from 2030; Estonia has committed to cover 40% of its electricity consumption from renewable energy sources by 2030; the Dutch government has decided to ban the use of coal to generate electricity from 2030; Ireland has pledged to carbon-proof all its governmental decisions and major investments by 2030; one of the targets in the [United Nations Sustainable Development Goals](#) is, 'by 2030, to halve per capita global food waste at the retail and consumer levels and reduce food losses along production and supply chains, including post-harvest losses'. Individual companies also set themselves targets as part of their Corporate Social Responsibility plans, for example, UK supermarket ASDA has announced plans to make all its branded packaging recyclable by the mid-2020s; European retailer Ahold Delhaize has decided to reduce absolute emissions from its operations by 50 % by 2030; the Volkswagen group has pledged to decrease the production-related environmental externalities by 45% by 2025; the leading steel company, ArcelorMittal, has committed to a net zero CO₂ investment portfolio by 2050.

Also, the European Commission sets out roadmaps with clear milestones whenever it is committed to achieving a concrete (long term) goal. For example, the EU aims to be climate-neutral by 2050. To achieve this goal, the European Commission put forward a

[roadmap](#) outlining milestones towards the target, policy challenges, investment needs and opportunities in different sectors.

Such milestones, even if not legally binding, help to focus minds and motivate and drive activities towards the desired goal. The goals should be ambitious, challenging and stretching but also realistically achievable.

For example, after achieving a [45% reduction](#) of the use of animals from 2013 to 2020, in June 2022, the French pharmaceutical company [Sanofi announced](#) it had set itself the goal of reducing its use of animals in research and testing by 50% by 2030, compared with 2020.

Action required

Objectives set in the area of animal research could, for example, be: to end the harmful use of animals for the primary purpose of education and training by 2025; 'to end severe suffering in animals by 2030'; to end the use of animals in regulatory testing by 2035; to increase funding for the development and exploitation of new non-animal technologies to the same level as that spent on animal research; to harmonise education and training in non-animal approaches in life sciences.

The achievement of developing, testing and authorising a range of new vaccines and treatments for Covid-19 within a year - when most people said it simply was not realistic - has illustrated just what is possible when people's **minds are focussed** on a goal, and where the necessary **funding and coordination** is provided and there is unprecedented pooling and **sharing of cross-disciplinary knowledge and expertise**.

Identification and prioritisation of key research areas where resources and efforts need to be targeted

Background and rationale

Article 58 of the Directive lays down a requirement for the Commission to conduct '*periodic thematic reviews of the replacement, reduction and refinement of the use of animals in procedures, paying specific attention to non-human primates, technological developments, and new scientific and animal-welfare knowledge*'. More than ten years have now passed since the Directive came into force, yet no thematic reviews have so far been carried out. Nor is there a transparent process in place for decision making as to the priority areas for these reviews (which might be based on a combination of factors, including: number of animals involved; severity of animal suffering involved; scope for replacing/avoiding animal use, etc.), nor is there any published timetable for delivering them.

The reviews of EURL ECVAM of non-animal models in biomedicine explore ways to study specific disease/therapeutic areas without the use of animals, but do not analyse the continued use of animals in these areas or how to replace them. Understanding the potential for the reduction and replacement of animals in the disease/therapeutic areas covered by the reviews of EURL ECVAM could be part of the first Thematic Reviews under the Directive.

The lack of translational value and/or reproducibility of much of the animal research currently carried out is well publicised. But funding continues to flow for the use of such models and tests, and projects involving them continue to be authorised and published. This should stop.

The Commission should establish a panel of experts with representation from all stakeholders and Member States, to help **identify key areas appropriate for Thematic Reviews** and to advise on a **clear mechanism and timetable** for delivering these, starting with those considered to be the clearest priority areas. For example, 'batch potency testing' currently accounts for approximately 22% (over 215 000 uses of animals) of the animals who experience 'severe' suffering in the EU. Mechanisms for directing focus and funding to promote replacement activities in these areas should then be identified as part of clear roadmaps aimed at achieving transformative change. Any outcomes aimed at improving the uptake of alternative approaches or discouraging specific uses of animals should subsequently be reflected in project authorisation processes.

All research funders (including the European Commission and national research councils, among others) should commit to undertake **regular and comprehensive reviews of the outcomes and impact of research that they fund** which involves animals, with the results made publicly available. This should include further critical and **systematic reviews of the validity and translatability** of specific animal-based methods and tests; and all funders should review and assess the 'value' of the animal research they have funded (including 'basic or fundamental research') - and where this cannot be established, no further authorisations should be given for animal use.

An appropriate level of funding to support the development and uptake of new, advanced non-animal technologies

Background and rationale

Article 47 includes the commitment that *'The Commission and the Member States shall contribute to the development and validation of alternative approaches which could provide the same or higher levels of information as those obtained in procedures using animals, but which do not involve the use of animals or use fewer animals or which entail less painful procedures, and they shall take such other steps as they consider appropriate to encourage research in this field.'*

The word 'contribute' is open to interpretation (what, how much) and there is no firm requirement for Member States to actually take any further steps themselves.

Much of the responsibility for delivering progress in this area seems to have been deflected to EURL-ECVAM and the network of national reference laboratories involved in the validation of new approaches. Whilst they are undertaking important and productive work, given the huge range of research areas that animals are currently used in the EU, across basic research, applied research, and regulatory testing for example, this activity alone will not be sufficient, or achieve the rate of transformative change required.

Whilst the provision of additional funding in itself will not provide the solution, it is nevertheless a significant limiting factor in the ability to attract wider activity in this area and make faster progress. The amount of money provided in this area has increased in recent years, but it is still dwarfed by the amount provided for research involving the use of animals. In Horizon 2020, more than 45 million euros were committed each year to research projects on the development of non-animal alternative methods, but this

accounts for only 0.5% of the total annual budget for this Framework Programme.

Furthermore, projects that use or develop methods that do not rely on the use of live animals (e.g. in vitro methods) may still use [animal-derived components](#).

Funders of animal research have a huge responsibility to help facilitate progress, this includes the European Commission. If every grant given prioritised funding to allow better development, implementation and/or dissemination of replacement activities, and included this as a requirement of, and work package within, the grant this would not only directly contribute to the undertaking of more humane science, but would also help to promulgate 3Rs aspects of a good 'culture of care'.

Action required

Too much emphasis is currently placed on EURL-ECVAM to deliver the results that everyone wishes to see. Whilst EURL-ECVAM does excellent work, several other Directorates-General of the European Commission and all Member States must step up their activity, coordination and own support in this area.

The imbalance between the funding of research involving animals, and that targeted towards aiding the development of new, advanced non-animal technologies needs to be urgently addressed. The strategy should include clear targets for Member States to **increase the percentage of their science funding for the development of new, advanced Non-Animal Technologies**. Funders, including the EC and national science and research agencies, should **ensure that 3Rs elements - with a focus on replacement - are a compulsory deliverable of every research grant** that uses animals and that funding would be denied for researchers that fail to meet minimum criteria for implementing and advancing the 3Rs as part of their research (i.e. the replacement of animals, and actively improving refinement).

There should also be **incentives** to encourage scientists to promote non-animal technologies and approaches, e.g. a fund that covers the cost of paying for open access publications of new, advanced non-animal methods, or of acquiring or establishing non-animal models and technologies in research infrastructures. Furthermore, the use of animal-free components in laboratory materials and reagents should be demanded when using and developing non-animal technologies.

The [Open Research Europe](#) initiative is a very welcome initiative for enabling those who receive funding under the Framework Programmes to publish their research free of charge 'open access' but this should (if not already planned) be extended to all research that is publicly funded in the EU.

Large scale support for building key infrastructure that would allow fuller exploitation of existing and new alternative methods

Background and rationale

Article 4 of the Directive states that '*Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure*' and Article 13 states that '*Without prejudice to national legislation prohibiting certain types of methods, Member States shall ensure that a procedure is not carried out if another method or testing strategy for obtaining the result sought, not entailing the use of a live animal, is recognised under the legislation of the Union*'.

Both of these statements allow plenty of flexibility for the circumventing of the principle and spirit of the provision. For example, it is only a very small subset of procedures on animals, usually related to regulatory testing, for which 'alternative' methods would currently be formally recognised 'under the legislation of the Union'. Most methods and models used in basic and applied research for example would not be likely to be captured under such a process. Also, some Member States have transposed the requirements for using alternatives (or to implement these in practice) only where this is '*practical*' - which allows for users to claim exemption on the grounds of a lack of suitable equipment, training, etc. One such example might be where researchers do not have the up front resources to invest in the setting up of a phage display library required to fully exploit the potential of non-animal methods for antibody production. Increased core infrastructure funding to allow the creation of more, and shared resources of this nature would vastly increase their likely use and uptake. Other examples would be where a single researcher in a small university cannot provide the resources to purchase major items such

as MRI, or CT scanners, 3D printers, or organ-on-a-chip technology that various other institutions already have and use, and so the scientist in place at the first institution will continue to use sub-optimal methods where animal use and suffering is not being minimised.

Action required

Strategic funding for the creation of 'hubs' where researchers from different institutions can share or rent equipment that would allow them to exploit new technologies at a far cheaper cost, would significantly increase access and thus uptake. For example, the [Centre for Predictive in vitro Methods](#) in the UK provides access for researchers to organ-on-a-chip technology.

Likewise, Member States can **facilitate the functional sharing**, within the network, of equipment across universities and other research institutions in the country and neighbouring countries. This practice is already in place through individual agreements between some universities.

The EU should also develop a scaled up version of the NC3Rs [CRACK-II](#) scheme, which could be administered via existing EU funding schemes as long as the **development of and transition to non-animal technologies** is set as a project priority.

Education and training in non-animal technologies

Background and rationale

One current obstacle to the wider uptake and use of non-animal technologies is the insufficient level of support for researchers, educators and regulators to change working practices and have the knowledge and skills to embrace new methods.

Practices that reinforce the use of animals as a gold standard can start early on in education. A recent [exploratory survey](#) has found that educators tend to use as teaching 'tools' the same type of models they use in their research. This may partially explain the findings of a recent [paper](#) showing that animals are still being used in education and training of students even where other methods are available.

A recent [study](#) from EURL ECVAM on evidence needs in chemicals policy and regulation showed that the science directly informing policy and regulatory decision-making often lags behind current science. Aspects that seem to contribute to this delay include: a lack of consensus on different methods and approaches in toxicological sciences; mistrust among stakeholders in different sectors; and no shared understanding of how data is constituted as evidence for regulatory decisions, or for current and future policy regarding chemicals.

Additional focus should be put into initiatives that reach people in all relevant roles to **help train and provide confidence** in the use of new, advanced non-animal models and approaches. This includes not only scientists and educators in academia and industry, but also all appropriate regulators (those involved in the evaluation and authorisation of projects involving animals, and also from regulatory bodies such as OECD, WHO, EMA, ECHA, etc.).

More robust project evaluation and authorisation processes, and peer review and publication policies from scientific journals

Background and rationale

Weaknesses in the design, carrying out and reporting of research involving animals are well documented, but continue to persist. Projects that are poorly designed or do not fully implement the 3Rs or which raise significant ethical concerns, or involve animal-based methods known to be of poor validity, continue to be authorised by competent authorities and accepted for publication by scientific journals.

Moreover, the mindset that at least a part of a scientist's research needs to involve animal studies to achieve the high-level publications needed to enhance their career still needs to be challenged, as does the demand from some peer reviewers that the findings of research using non-animal technologies need to also be shown in a parallel animal study before they will be accepted.

Action required

Decisive and immediate steps need to be taken to **stop poorly designed, executed, analysed and reported science involving the use of animals from being funded and licensed, getting past reviewers and being published.**

Transparency concerning the evaluation and authorization of projects is essential to harmonise the decisions of competent authorities. The decision making process for authorising or rejecting a project application should therefore be made public. Actions to harmonise project evaluations within and between Member States are still necessary by, for example, delivering training to evaluators based on common learning objectives,

setting up a common framework for the understanding and implementation of ethics and the 3Rs, with a strong focus on replacement.

NB: Many of these activities require coordinated cross-government department communication and activity, and rely on multi-disciplinary and multi-sectoral collaboration and the engagement and involvement of regulators early on and ongoing.

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