Netherlands National Committee
for the protection of animals
used for scientific purposes

From niche to norm

Transition Policy Advice: working together towards a society without animal experiments

The NCad and its methods

The Netherlands National Committee for the protection of animals used for scientific purposes (NCad) is an independent advisory body dedicated to protecting the welfare of animals used for scientific purposes. The NCad is legally mandated to perform its advisory duties under the Dutch Experiments on Animals Act (Wod). The NCad provides solicited and unsolicited policy advice to the Minister of Agriculture, Fisheries, Food Security and Nature (LVVN), the Central Authority for Scientific Procedures on Animals (CCD) and the Animal Welfare Bodies Platform (IvD Platform). Its policy advice covers the acquisition, breeding, housing, care and use of animals in experiments. The NCad also advises on promoting alternatives to experiments using animals. In this way, it advances the replacement, reduction and refinement of animal experiments, known as the 3Rs.

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1.

Foreword

Making sound choices requires more than the ability to build systems that work. It also requires the willingness to change them before they become an obstacle to progress. That takes the courage to respect what has been achieved in the past without allowing it to determine the future.

That invitation is central to this policy advice. The transition towards a society without animal experiments calls for care, collaboration, and the ability both to build on existing scientific knowledge and to make the most of new possibilities. New scientific insights, technological innovations and a growing understanding of animals and their welfare are making further change not only increasingly possible, but also increasingly necessary. Therefore, the question is how we can shape this transition together to ensure it is morally and scientifically sound, socially supported, politically feasible and strategically effective.

The transition towards a society without animal experiments involves more than technological innovation. It calls for an ongoing dialogue about the public values that come together in this transition: health, safety, scientific quality, animal welfare, capacity for innovation, sustainable development and public trust. That judgement cannot and should not be made by a single party on its own. Researchers, administrators, politicians, businesses, civil society organisations and citizens each have their own role and responsibility. Together, they contribute to the choices we make today for the science, the society and the international standing of tomorrow.

Guided by this conviction, the Netherlands National Committee for the protection of animals used for scientific purposes (NCad) adopts a transition approach in this policy advice. Not because transitions can be planned or predicted, but because a transition perspective helps us understand how innovation can grow from promising initiatives into widely embraced practice. Therefore, the success of the transition depends not only on new insights, but above all on our willingness to adapt our institutions, ways of working and collaborative practices accordingly.

Through this Transition Policy Advice, the NCad seeks not only to give direction to the further development of animal-free innovations, but above all to encourage concerted action. The recommendations strengthen the conditions under which science, policy and society can contribute to a research and innovation ecosystem that is agile enough to respond to the future. This will better protect animals, strengthen the quality of science and public trust, and increase the Netherlands' international strategic relevance as a knowledge and innovation nation.

The true significance of this Transition Policy Advice is not determined by whether each individual recommendation is adopted, but by the extent to which they take effect in an integrated way.

The title of this Transition Policy Advice, From Niche to Norm, captures the essence of our recommendations. Innovation emerges when new knowledge, insights and ways of working are given the space to develop and take root. However, a society without animal experiments will not come about by itself. A transition is required in which scientific, social, cultural, governance and technological innovations reinforce one another. This transition requires the contribution of government, science, industry, funders, civil society organisations and other involved actors, each playing their part in a shared movement. It is precisely this diversity that makes it possible to embed innovation sustainably and enable new practices to develop into the norm. This Transition Policy Advice therefore calls for national and international collaboration towards a society without animal experiments: an appeal to everyone who can contribute to this transition to help shape, together, a future in which animal-free innovation becomes an integral part of a future-agile research and innovation system.

I am calling on you not only to read this Transition Policy Advice, but also to put it into practice. Use it as inspiration to reconsider your existing convictions, as an invitation to collaborate across disciplines, organisations and interests, and most importantly, as encouragement to contribute to this joint transition from your own position of responsibility. Ultimately, the value of this policy advice will be determined not by the words it contains, but by our collective willingness to act on its recommendations.

Prof. dr. Nico L.U. van Meeteren
Chair of the NCad

2.

Reader's guide

How should this policy advice be understood?

This Transition Policy Advice is addressed primarily to the Minister for Food Security, Fisheries and Horticulture. It focuses first and foremost on the public responsibility to organise direction, coherence and coordination in the transition towards a society without animal experiments. This Transiton Policy Advice should therefore not be read as a practical manual for individual researchers, institutions or sectors, but as a strategic Transition Policy Advice on the conditions under which science, policy and society can jointly take the next step.

Above all, it also recognises the need to further develop a historically grown system on the basis of current scientific and societal insights. Scientific knowledge is developing on two fronts at the same time: on what animals are and what they experience, and on the possibilities and limits of different research models and approaches. At the same time, societal expectations are also changing. Together, this makes it necessary to reconsider how research strategies are developed, how research questions are framed, how methods are selected, how their evidential value is assessed, and which values inform these choices. The transition therefore requires more than individual commitment or technological innovation alone. It also requires changes to the conditions and structures within which research is conducted.

The recommendations in this Transition Policy Advice should be read as interconnected building blocks for a *future-agile* research and innovation ecosystem, not as isolated measures or a menu of options. Their strength lies precisely in their combined and mutually reinforcing impact within and across policy, regulation, research, education, funding, innovation practices and societal decision-making. The coherence within the research and innovation ecosystem is also reflected in the structure of the policy advice. Key concepts and analyses recur throughout this policy advice, each time considered from a different perspective, so that the chapters can also be read and understood independently. The ultimate goal set out in Chapter 4 informs the governance recommendations in Chapter 5. The transition-science insights presented in Chapter 3 provide the foundation for the ethical reassessment, innovation policy and international strategy. The five pillars under which the recommendations are organized are closely interlinked and continually reinforce

one another. In this way, the reader can recognise the textual reflection of the systemic coherence advocated throughout this policy advice:

- **Chapter 3 Introduction and remit:** Sets out the remit and rational for the advice, the analytical framework drawn from transition studies, its ethical positioning, and the evaluation of the 2016 Transition Policy Advice. This chapter should be read as the foundation on which Chapters 4 and 5 build; the concepts and findings introduced here are applied in the chapters that follow.
- **Chapter 4 Strategic ambition and societal challenge:** Elaborates the ultimate goal and situates it in its societal, political and scientific context. This chapter should be read as the rational for the direction that is translated into recommendations in Chapter 5.
- **Chapter 5 Recommendations and their rationale:** Translates the framework set out in Chapter 3 and the ambition articulated in Chapter 4 into five pillars with concrete recommendations. This chapter explains not only what needs to be done, but also why the sequencing and interdependence of the pillars matter. It should therefore be read with close attention to their coherence, rather than as a list of separate measures.
- **Chapter 6 Follow through on the Transition Policy Advice:** Describes how this policy advice will be taken forward and how the NCad will fulfil its role following publication.

The NCad invites readers to look beyond their own position, discipline or institutional responsibility and to consider the system as a whole. The central question is which collective choices are needed to make animal-free innovation more self-evident, more firmly embedded and more broadly supported by society.

Terminology used

Research category: the classification used in Dutch and European reporting for animal experiments, based on the purpose for which the experiment is carried out. There are nine categories, including fundamental research, translational and applied research, regulatory research and research for the preservation of species (reference 1).

Research domain: a defined subject area of research with its own research questions, methods and bodies of knowledge, such as oncology, neurology or immunology.

Policy domain: a coherent policy area spanning one or more ministries, with its own objectives, responsibilities and instruments.

3.

Introduction and remit

The Netherlands National Committee for the protection of animals used for scientific purposes (NCad) issues this Transition Policy Advice on its own initiative, in line with its statutory remit to provide both solicited and unsolicited advice on policies relating to the use of animals in research. This policy advice builds on the evaluation of the 2016 Transition Policy Advice (2) and an in-depth analysis of recent insights from transition studies (3).

The reason for this Transition Policy Advice is that the further phase out of animal experiments does not automatically follow from the increasing availability and application of animal-free innovations. Although the evaluation shows that animal-free innovations have gained a more prominent position both nationally and internationally, and that researchers and institutions are increasingly investing in their development and application, the NCad observes that this development is not yet sufficiently embedded within the broader system context in which animal use in research take place.

In the report 'Animal Procedures in the Netherlands 2015-2024', the NCad concludes that the number of animal experiments has decreased compared with 2015 in several research categories, but that further reduction cannot be assumed to occur automatically (1). Achieving further reduction requires a proactive and targeted acceleration of the transition. Such acceleration not only gives effect to societal and ethical ambitions but also aligns with the growing scientific opportunities offered by animal-free methods. The evaluation shows that some important drivers of system change have not been sufficiently leveraged, to this date. The continuation of the transition is not just about technological innovation but must be complemented by attention to the broader system context in which animal experiments take place. The NCad uses the term 'system context' to refer to the interdependence of and interaction among legislation, scientific practices, institutional cultures, animal welfare and assessment frameworks, societal expectations, ethical values and economic incentives. When this policy advice refers to system change, it means change in this interconnected system as a whole.

The transition is a shared societal responsibility and cannot be placed on the shoulders of individual researchers. After all, it extends beyond scientific innovation

alone. For this reason, the NCad deliberately refers in this policy advice to the pursuit of a society without animal experiments. This ultimate goal gives direction to the recommendations in this policy advice. A transition at system level requires an ambitious and clearly formulated ultimate goal, while the NCad is mindful that some of those involved do not consider this goal realistic. The NCad therefore does not attach a fixed end date to this goal. The ultimate goal serves as a guiding compass, not a prediction. The ultimate goal and its substantiation are explained in the NCad paper entitled 'What does the NCad mean by a society without animal experiments?[1]

The NCad believes that this pursuit calls for a restructuring of the transition approach, with respect for the individual role and responsibility of all parties involved (2).

Input from different perspectives and areas of expertise
To inform this Transition Policy Advice, the NCad conducted an extensive process of gathering information, exploring a range of perspectives and drawing on additional expertise. This process began in 2023 with the interviews for the evaluation referred to above, and continued after the evaluation was published, until April 2026.[2]

The NCad carried out an open survey[3], organised four thematic stakeholder meetings and held a closing meeting. At these meetings, participants exchanged perspectives, dilemmas and conditions for next steps. Participants from the Netherlands and abroad came from science, industry, government, civil society organisations and international expert networks.

In addition, the NCad held focussed discussions with experts and representatives who approach this subject from a complementary or less commonly represented perspective, including experts in transition monitoring and patient representatives. These discussions surfaced perspectives and considerations that do not typically come up in the organised debate on animal experiments. An overview of participants and interlocutors can be found in Appendix 1.

3.1 Transition Studies: Concepts and Terminology

The transition towards a society without animal experiments concerns a fundamental reorientation of the knowledge ecosystem. It is not just a matter of different methods, but of a research practice that actively allows questions, methods and societal context to evolve alongside new scientific and ethical insights. It touches on:

- the governance mechanisms in scientific research, such as how research is funded, assessed and valued;
- the ethical basis for research involving animals, including the way in which this research is justified;
- the societal expectations that are also subject to debate within the transition towards a society without animal experiments.

None of these elements is static. They must therefore be continually reassessed, both individually and in relation to one another. Transition studies provide a descriptive and analytical framework for understanding system change and identifying where it can be influenced.

Dutch knowledge base for system change
Transition studies as an academic field has to a significant extent been developed in the Netherlands, including through Erasmus University spin-off DRIFT and the Copernicus Institute for Sustainable Development at Utrecht University. This knowledge has been applied for years to specific societal challenges such as the energy transition, the agricultural transition and the government-wide mission-driven innovation policy. This experience shows that the transition framework offers useful insights for understanding system change, without providing a blueprint for it. Its application differs from one challenge to another, and transitions do not follow a predictable path; the dynamics shift along with the context. Transition studies offers a descriptive and analytical lens that can make bottlenecks and points of leverage visible, and potentially open to influence.

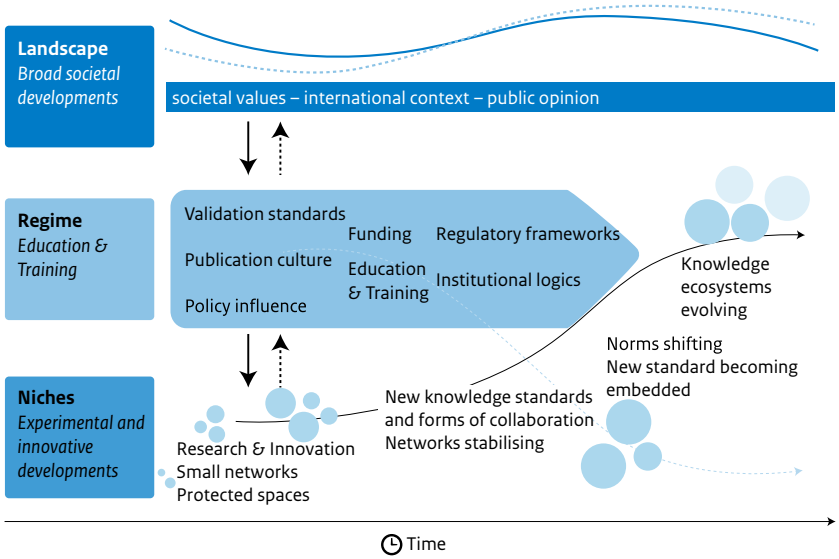
[1] Netherlands National Committee for the Protection of Animals Used for Scientific Purposes (NCad), 'What Does the NCad Mean by a Society Without Animal Experiments?', news item, 22 September 2025.
[2] Netherlands National Committee for the Protection of Animals Used for Scientific Purposes (NCad), 'Reports of NCad Stakeholder Meetings for the Transition policy advice Published', news item, 2 March 2026.
[3] Netherlands National Committee for the Protection of Animals Used for Scientific Purposes (NCad), 'Report of Open Survey Published', news item, 15 September 2025.

This political, administrative and scientific experience gives the application of this approach to the transition towards a society without animal experiments a solid foundation, and makes it possible to connect with knowledge and networks that have already been built up.

Transition studies helps to distinguish what needs to be preserved within a system, what can change, and which mechanisms promote or hinder change. These patterns are context-dependent and are experienced differently by those involved. Transition studies is not a blueprint for the desired outcome, nor does it lend legitimacy to any one position in the debate. It does not determine which methods are superior, and it does not itself set timeframes.

Within transition studies, the Multi-Level Perspective (MLP) offers a framework for understanding how fundamental, long-term changes (transitions) take place in complex socio-technical systems (Figure 1). A key observation is that change can progress rapidly within protected experimental initiatives at the niche level whereas change that challenges or alters the existing system itself tends to proceed much more slowly.

Figure 1. Levels of the Multi-Level Perspective



In figure 1 the Multi-Level Perspective is applied to the transition towards a society without animal experiments. The framework distinguishes between niches, regime and landscape. New methods, knowledge practices, norms and forms of collaboration emerge and mature within niches. The regime comprises the existing norms, rules, funding flows, infrastructure and assessment practices. The landscape encompasses broader societal, political, economic and international developments. System change occurs when developments at these levels reinforce one another and regime actors create room for scaling up, institutionalisation and, where necessary, the phase-out of existing practices.

The 2016 Transition Policy Advice relied primarily on the MLP framework. Since then, thinking on transitions has continued to evolve. Commissioned by the NCad, Prof. Dr J. Hoekman and Prof. Dr E. Moors have drawn up a systematic overview of these developments (3). They identify a number of insights relevant to this transition:

- **Insight 1: transitions take place through the interplay between innovation and the existing system.** Niches remain essential as sheltered spaces in which new methods, practices and forms of collaboration can mature. However, the speed

and direction of a transition are determined not only by the growth of niches, but also by their relationship to the existing system. Until now, the emphasis has been strongly on stimulating animal-free innovations. Stimulating niches remains essential, but must be supplemented with targeted policy through which regime actors recognise, support and institutionalise promising innovation, and adjust or phase out regime elements that hold it back.

- **Insight 2: alongside technological progress, the social and cultural dimension is also decisive for the transition's progress.** What counts as good science, how researchers are assessed and rewarded, which methods are accepted in science and regulation, how markets form around innovations, and which values are dominant in a given research category, all largely determine whether innovation is directed towards solutions within existing structures or towards reshaping those structures themselves. This dynamic differs from one research category to another.
- **Insight 3: This transition does not take place in isolation and cannot be driven by scientists and policymakers alone.** It touches on broader societal issues concerning the health of humans, animals and the environment, safety, sustainability and animal welfare. This creates opportunities for synergy, but can equally lead to conflicting goals. The involvement of citizens, patients, market parties and civil society organisations, including animal welfare organisations, is not only important for public support. It also brings in values and perspectives that enrich and broaden thinking about the transition. In doing so, the transition also becomes a political undertaking. Decisions about which innovations to support, which practices to phase out and which interests to take into account are inherently political questions.

These insights describe the conditions under which the transition unfolds. Additional perspectives are also relevant here. Governance in this context does not mean control, but rather influencing direction and pace by setting goals, assigning responsibilities and actively facilitating the interplay between innovators and the existing system. This calls for leadership from various positions, with a specific responsibility for the government that goes beyond mere facilitation (4, 5). It also requires attention to the contexts in which researchers, assessors and policymakers operate. Behaviour does not change primarily through individual conviction, but through the norms, incentives and institutions that shape what is possible and what is considered normal (6).

Terminology: definitions and choices

Words are not neutral in this debate. A definition not only determines what a term means, but also reflects the perspective from which the issue is viewed. Where a term has an established formal meaning, this policy advice follows that meaning and separately identifies the conclusions it draws from it. Where a term is contested or open to more than one interpretation, this policy advice makes an explicit choice and explains the reasoning behind it. For each concept, a clear distinction is therefore made between its generally accepted meaning and the position adopted in this advice.

- **Transition:** in transition studies, a transition is a structural system change that unfolds over a longer period, through the involvement of many actors, with an outcome that cannot be fully determined in advance. In public debate, the word sometimes takes on political overtones, suggesting a linear path towards a predetermined outcome, or implying a condemnation of existing practices. This policy advice uses the term in the first, analytical sense. It assumes that optimising the existing system is not sufficient to achieve the desired system change (see also the evaluation of the 2016 Transition Policy Advice) (2).
- **Animal experiment:** The term has a defined legal meaning under European Directive 2010/63/EU (7). This meaning is broader than is often assumed: in addition to medical and pharmaceutical research, it also covers research for the preservation of species, environmental safety and animal welfare. This policy advice uses the term in accordance with the Directive. It also emphasises that 'animal experiments' do not constitute a homogeneous category, as the ethical and societal considerations differ between research categories. An assessment that applies to one category cannot simply be transferred to another.
- **Non-animal research:** There is no established formal definition of this term. This policy advice uses non-animal research to direct attention towards methodological innovation as such, without taking current practice as its starting point. The commonly used term 'alternatives' implies secondary or derivative methods, with animal experiments as the implicit norm. The term 'Human-relevant models' also does not fully capture the intended meaning as research involving animals can also be relevant to humans. Moreover, research is also conducted for the benefit of animals.

- **Validation:** This is the process of demonstrating the reliability and relevance of a method for a particular purpose. In regulatory contexts, it is a formal recognition procedure based on internationally agreed criteria, for example in toxicology. This policy advice points out that validation is not only a technical issue, but also a systemic one. In current practice, animal-free methods are often validated by assessing whether they produce the same outcomes as animal experiments. However, an animal-free method is fundamentally different from an animal experiment. Similarity to the animal model is therefore not an appropriate measure of its value. This policy advice states that validation should be tailored to the intended purpose and context of use of the method. Where research is focused on humans, relevance and predictive value for humans should be central; where research concerns animals or ecosystems, the relevant target system should serve as the reference. Agreement with an animal experiment is not, in itself, a measure of scientific value.
- **Valorisation:** This is the translation of knowledge into societal and economic value. This policy advice regards valorisation as a prerequisite for the sustained adoption of animal-free methods. Without this step from knowledge to practice, new methods remain confined to the research stage.

3.2 Ethical position

The NCad states that the transition towards a society without animal experiments requires a fundamental shift in the research paradigm. In practice, methodological choices are also shaped by historically established research programmes, accumulated knowledge within existing model systems, publication standards, and the available material and institutional infrastructure. This context also shapes the conditions under which alternative approaches can be recognised as an equivalent. The choice of research methods is not merely a technical consideration, but is embedded in the way scientific research is organised and accorded legitimacy. The paradigm shift advocated here is therefore not only methodological, but also institutional, epistemic and ethical.

Kramer and Bovenkerk show how ethical considerations concerning the use of animals in scientific procedures are shaped and which normative assumptions are implicit in them. A reassessment of human-animal relations is a core component of the ethical positioning advocated by the NCad. Animals are no longer regarded solely as instruments for scientific purposes, but as sentient beings with intrinsic value, and are also recognised as such in law. However, growing knowledge about animals also reveals complex cognitive and social capacities. The current application of ethical frameworks, including the harms-benefit analysis and the 3Rs, provides insufficient guidance for weighing these broader interests of animals explicitly, consistently and transparently (8).

New knowledge about animals and new insights in animal ethics therefore call for critical and explicit reflection on, and ethical justification of, every use of every animal in scientific research.[4] The interests of animals must be given due consideration in this assessment.

The ethical reassessment advocated by the NCad has two dimensions. On the one hand, it calls for greater recognition of the importance of animals' interests. On the other, it requires critical reflection on the intended purpose and relevance of the research itself, considered from a broad perspective. This must include a critical and explicit assessment of the societal relevance of the research, as well as the likelihood, nature and time frame of the intended benefits (8).

This calls for a framework in which:

- the shift in perspectives on animals, their relationship with humans, their interests, and the ethical justification for their use is explicitly recognised, supported and acted upon in research practice;
- guidance is provided for the reassessment of human-animal relationships and implications of these relationships for research;
- researchers and other actors directly and indirectly involved are provided with practical tools to operationalise ethical considerations;
- ethical considerations are linked to policy instruments and transition indicators.

[4] The phrase 'every use of every animal' extends beyond animal experiments. Many animal-free methods still use animal-derived products, such as foetal bovine serum or basement membrane extracts known by brand names including Matrigel, Geltrex and Cultrex. The same ethical questions that apply to the use of laboratory animals must therefore also be asked in relation to the use of these products. The NCad recognises that, in the short term, the growth of in vitro methods resulting from the transition is likely to increase the use of animal-derived products. This is an undesirable unintended consequence and warrants consideration in future policy advice (see Chapter 6).

3.3 Evaluation

The conclusions and implications arising from the evaluation of the 2016 Transition Policy Advice are set out below (2).

3.3.1 Reflection on the 2016 Transition Policy Advice

Reception and uptake of the Transition Policy Advice
The 2016 Transition Policy Advice was received as ambitious and providing clear direction. The evaluation shows how stakeholders viewed and interpreted this ambition and how they connected it to practice. Across stakeholder groups, there was unanimous support for the development of animal-free innovations. At the same time, stakeholders differed in their views on the need for system change and on the pace, feasibility and scope of the transition. Stakeholders referred to the knowledge and insights gained through research involving animals, but also highlighted the fundamental limitations of translating findings from animals to humans as a reason why an increasing number of researchers are turning to animal-free methods. These differing positions shaped how the Transition Policy Advice was received. Some stakeholder groups perceived the advice as support for innovations that were already underway, whereas others viewed it as a calling for far-reaching changes to existing research practices. In particular, the proposed timeline and the implications for regulatory research were considered unrealistic.

The NCad takes the criticism of the 2016 Transition Policy Advice seriously. This criticism is also one of the reasons why this Transition Policy Advice does not set an end date. However, it does not alter the ultimate goal, which applies to all research categories. The pathway towards that goal will differ between research categories, each requiring tailored interim goals. Sharing experiences and breakthroughs across research categories will accelerate the transition.

The evaluation shows that, from the outset, there was a tension between the ambition of the Transition Policy Advice and what could and would actually be implemented, also in light of the international context. The policy advice was valued for its nuanced approach and its recognition of differences between research categories. At the same time, following its launch, it received insufficient follow-up support from the NCad and lacked a clear governance structure and implementation and communication strategy. This created a gap between the intention of the policy advice and the way in which it was received and interpreted by some stakeholder groups.

Progress and persistent barriers
The evaluation shows that the period since 2016 has seen both successes and persistent barriers. The capacity to develop and advance animal-free innovation has grown. The Dutch government launched the Transition Programme for animal-free Innovation (TPI) [5], which brings together government, civil society, industry and academia. At the same time, the range of new approaches has expanded, including organ-on-chip technology, 3D cell models, in silico models and integrated assessment strategies. Programmes and initiatives such as More Knowledge with Fewer Animals [6], Human relevant models [7], the Virtual Human Platform for safety assessment [8], PARC [9], hDMT [10] and the Ombion Centre for Animal-Free Biomedical Translation[11] help build networks, advance knowledge and translate animal-free methods into practice.[12]
The development of *target images*[13] and the increased attention paid by regulators and end users to validation, acceptance and implementation also show that greater emphasis is being placed on establishing a shared direction and promoting practical application. Taken together, these developments show that the Life Sciences & Health (LSH) sector is expanding and that the transition to non-animal research is producing tangible results through complementary bottom-up and top-down efforts, with researchers, public and private institutions and government working together.

The period since 2016 shows that technological development does not automatically lead to application, scaling up and structural change. From the outset, the transition to non-animal research has been characterised as a complex and normatively charged issue, involving divergent interests, uncertainties and interconnected causes.

[5] https://www.animalfreeinnovationtpi.nl/
[6] https://www.zonmw.nl/en/program/more-knowledge-fewer-animals
[7] https://www.gezondheidsfondsen.nl/themas/humane-meetmodellen/ (website in Dutch)
[8] https://platform.vhp4safety.nl/
[9] https://www.eu-parc.eu/
[10] https://www.hdmt.technology/
[11] https://site.ombion-cpbt.nl/
[12] Ministry of Agriculture, Fisheries, Food Security and Nature, Progress Letter on the Transition to Animal-Free Innovation (website in Dutch), 18 november 2024, reference DGA-DAD/89569323
[13] https://english.ncadierproevenbeleid.nl/target-images-on-animal-free-research

The nature of this complexity differs at each system level. Within niches, specific methods and practices can be developed and tested in a relatively focused manner. At regime level, the main sources of resistance lie in the interconnectedness of funding, infrastructure, assessment criteria, regulation, professional routines and established knowledge practices. At landscape level, broader societal values, political choices, international developments and economic relationships come into play. It is precisely the interaction between these levels that makes system-level coordination necessary.

In competitive research funding, proposals are in principle assessed in a method-neutral manner on the basis of scientific quality and relevance. The limitations of NAMs must be acknowledged and contextualised: they are partly methodological and partly attributable to a system that is currently not sufficiently adapted to their use. In many cases, animal experiments remain the most familiar option because of established protocols, existing expertise, available reference data and existing infrastructure. This mechanism is most clearly visible in the validation of animal-free innovations. In practice, the animal model often serves as the reference point, whereas validation should ultimately be based on reference to the human, animals or ecosystem for which the method is intended. As a result, experiments using animal continue, inadvertently, to shape the very innovation that are intended to move beyond them. At the same time, this established pathway is gradually losing its self-evident status, as animal-free methods steadily develop their own knowledge base and foundation for practical application. Pressure on the regime is also increasing from the landscape level, driven by changing societal values, growing knowledge about animals, and the resulting shifts in perspectives within animal ethics, as well as developments in international regulatory frameworks.

Many niche innovations fail to progress from development to practical application. Initiatives such as the safe harbour concept have seen only limited use, and it proved impossible to establish a national system for monitoring the transition. The evaluation therefore highlight an important issue: how the transition can be monitored and meaningfully measured. The Transition Policy Advice provided direction and ambition, but did not set out a coherent vision for the governance tools and indicators needed to track progress systematically. In practice, it proved difficult both to establish and to quantify the relationship between the measures introduced and changes in the use of experiments using animal. This is because the development and application of animal-free innovations do not automatically result in a reduction in the number of animal experiments at an aggregated, system-wide level. As a result, there has been limited insight into the effectiveness of policy interventions and the contribution of individual initiatives to the broader transition.

These barriers illustrate that technological development leads to system change only when the conditions for application, acceptance and long-term embedding evolve alongside it. This conclusion is consistent with lessons learned from other transitions. The energy transition did not accelerate through the availability of renewable technologies alone, but because standards and regulation, funding, infrastructure, market development and sustained policy began to reinforce one another. The same applies to the transition towards a society without animal experiments: technological innovation will only achieve system-level impact when institutional and regulatory conditions evolve alongside it. Unlike in the energy sector, however, animal-free methods do not automatically displace existing practices through price and market mechanisms. Reducing dependence on animal experiments therefore also requires explicit normative, regulatory and institutional choices.

3.3.2 Relationship to the 3Rs (Replacement, Reduction and Refinement)

The core principles of the 3Rs, formulated by Russell and Burch in 1959, are widely endorsed by the scientific community, in both the public and private sectors, and by legislators (9). The 3Rs demonstrably improve practice and remain important for as long as animals continue to be used in research. At the same time, they do not in themselves provide mechanisms for systematically phasing out the use of animals in experiments. The 3Rs are usually applied within a research strategy in which the use of animals has already been included as a possible approach. Within this approach, an ethical assessment is made in which the benefits of the research are weighed against the harms to the animals. Efforts are made to minimise those harms by applying refinement, reduction and replacement wherever possible. This often leaves the more fundamental question of whether the research question and research strategy justify the use of animals at all to be addressed only at a late stage or not addressed explicitly enough.

Müller argues that many policymakers and researchers implicitly assume that successful application of the 3Rs will automatically lead to fewer animal experiments. According to Müller, this is a fundamental misconception. The 3Rs were designed as an ethical framework for the responsible use of laboratory animals, not as a strategy for ending such use. Successful measures based on the 3Rs can therefore coincide with stable or even rising numbers of animal experiments (10). This is consistent with the transition studies literature and the animal ethics publications by Kramer and Bovenkerk (3, 8, 11, 12).

This distinction is relevant to the transition. Transition thinking moves beyond the perspective of the 3Rs by shifting the starting point: rather than focusing on improving individual animal experiments, it seeks to shape the context and research practice so that non-animal methods become the default rather than animal experiments. The ethical and scientific questions must therefore be raised early in the process, when defining the problem, the research question and the evidence strategy, rather than only at the licence application stage, when fundamental choices have usually already been made. A transition perspective thus extends the application of the 3Rs to the design of the research system as a whole.

With regard to Replacement, Russell and Burch regarded absolute replacement as the most humane outcome and emphasised that their concern was not merely to reduce the use of animals in research, but to develop fundamentally different research methods. This focus is also enshrined in law: Article 4 of Directive 2010/63/EU stipulates that an animal experiment may not be carried out if the intended result can also be achieved using a method that does not involve live animals (7). The Directive defines replacement not as replacing an existing animal experiment, but as research that achieves the intended result without using live animals. The ultimate objective of this legislation is to phase out animal experiments as soon as this is scientifically achievable. This objective is also being translated into concrete policy, as demonstrated by the European Commission's 'Roadmap towards phasing out animal testing for chemical safety assessments'.[14]

[14] European Commission, Roadmap towards phasing out animal testing for chemical safety assessments, announcement C(2026) 3497, 1 June 2026.

With regard to Reduction, reducing the number of animals used at the level of individual experiments does not necessarily result in fewer animals being used at system level. For example, technology can lead to a reduction in animal use at the project level, while at the macro level it may actually result in increased animal use by opening up new research questions and making this technology accessible to a larger number of researchers. Müller shows that making experiments cheaper, faster or easier can enable researchers to conduct more of them. This is an example of a rebound effect, a phenomenon also recognised in energy and environmental policy. Reduction therefore remains an important principle, but does not in itself lead to a structural phase out (10).

With regard to Refinement, reducing distress remains highly important for as long as animals continue to be used. Refinement concerns more than distress alone. It also encompasses questions relating to positive welfare, integrity, agency, instrumentalisation and telos. These concepts are explained in more detail in Appendix 2 (8). Questions of Refinement however only arise once the decision to use an animal has already been made. At that point, conducting the animal experiment is already taken as a given. A transition perspective raises more fundamental questions and does so at an earlier stage, before any decision is made to use an animal. Under this approach, the interests of animals are weighed a priori against the interests that humans, the environment or animals may have in the research, already at the early stages of research design.

3.4 International positioning

The Netherlands is positioning itself as an international catalyst for innovation aimed at reducing reliance on animal experiments.[5] This ambition is both symbolic and strategic: acting as a model in the development and implementation of animal-free innovations goes hand in hand with strengthening the positioning of research institutes and companies as partners in international innovation. This front-runner role requires a delicate balance. Moving too far ahead risks becoming isolated, while those who hang back risk losing their leading position.

At landscape level, the scope for Dutch policy is shaped to a significant extent by international laws and regulations, trade relations, multilateral institutions, societal values and economic competition. These factors shape the scope for the national policy, but also provide opportunities to influence the international arena. A consistent national approach can, in turn, help shape that international arena. Active participation in international harmonisation processes offers opportunities to strengthen the Netherlands' position and its connections with international networks, and to secure broad acceptance of animal-free methods.

At regime level, international standards, regulations and recognition procedures, for example, are key determants of whether and how animal-free methods are applied. Without regulatory harmonisation and recognition of animal-free methods by multilateral institutions, the effect of national initiatives will remain limited. Poor coordination also increases the risk of duplicate or conflicting requirements, delaying innovation and placing additional burdens on research institutions and companies.

Market dynamics are also part of this regime. High investment costs, despite potentially substantial benefits, infrastructure constraints and the risks associated with new technologies can impede adoption. Industry interests and economic competition also often favour technologies that generate rapid returns. International trade obligations and export requirements may also require animal experiments for markets outside Europe, even where animal-free methods are available. Dutch choices therefore cannot be considered in isolation from the trade relationships and access to international markets on which companies depend.

At niche level, the Netherlands has a strong starting position. Thanks to the international reputation of its biomedical knowledge and innovation ecosystem, its high-quality academic centres and infrastructure, and its experience in providing policy support for the development of animal-free methods. Trade opportunities and regulation must therefore be treated as integral parts of the transition strategy. International cooperation is not only a prerequisite for the national transition, but also a strategic instrument for influencing global standards and firmly embedding the national ambition.

International developments

Non-animal research is high on the international agenda. In 2025, the United Kingdom published a national strategy setting out concrete phase-out deadlines for specific tests and investment in validation infrastructure.[15] In the United States, the Food and Drug Administration (FDA)[16] and the National Institutes of Health (NIH)[17] are reforming their frameworks and actively promoting non-animal methods for regulatory research. The European Commission has published its Roadmap towards phasing out animal testing for chemical safety assessments, and the European Medicines Agency (EMA)[18] actively promotes the regulatory acceptance of non-animal methods for medicines development through its 3Rs Working Party.

This momentum is real, but progress is uneven. While Europe and several other jurisdictions are developing policies to reduce or phase out animal experiments, the number of animal experiments remains high in other countries and sectors and is increasing in some cases. This uneven progress calls for a strategy in which national ambition and international developments reinforce one another. The Netherlands can build on the international momentum while drawing on its own expertise in managing transitions to connect technological innovation with genuine system change.

[15] Department for Science, Innovation and Technology, Home Office en Department for Environment, Food & Rural Affairs, Replacing Animals in Science: A Strategy to Support the Development, Validation and Uptake of Alternative Methods, CP 1429, 11 november 2025.

[16] U.S. Food and Drug Administration, 'FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs', press release, 10 april 2025.

[17] National Institutes of Health, 'NIH to Prioritize Human-Based Research Technologies', press release, 29 april 2025.

[18] https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp/3rs-working-party

4.

Strategic ambition and societal challenge

The strategic ambition of this Transition Policy Advice is to contribute to achieving a society without animal experiments, with scientific, legislative and societal engagement forming an integral part of the transition. This ambition follows from the evaluation of the 2016 Transition Policy Advice, which identified the absence of a shared understanding of the ultimate goal (2). The word 'society' has been chosen deliberately. The use of animals in research, safety testing and education concerns not only animal welfare and science, but also legislation, the economy, education and societal values, both nationally and internationally. Reaching the ultimate goal therefore requires system change that extends beyond the scientific domain.

The ultimate goal serves as a strategic reference point. Its value does not lie in the certainty that it will be fully achieved within a specified timeframe, but in the direction it provides for the choices made along the way. Views differ on whether it is fully achievable, and the NCad has deliberately not attached a timeframe to it. Nevertheless, a clearly and ambitiously formulated ultimate goal is essential, even without such certainty. The NCad previously set out what it means by a society without animal experiments in a note.[1] The essence of that note is presented below and supplemented with its implications for governance and the management of the transition.

4.1 Definition and scope of a society without animal experiments

A society without animal experiments is one in which animals are no longer used for publicly or privately funded scientific research or education. The ultimate goal also includes ending the use of animal-derived products produced specifically for research purposes, such as foetal bovine serum and basement membrane extracts known by brand names including Matrigel, Geltrex and Cultrex.

The ultimate goal is ethically grounded and strategic in nature. It provides direction for societal, scientific, policy and investment decisions. The NCad recognises that

the transition is unfolding along different pathways across research categories and research domains. It is therefore not appropriate to attach a single fixed enddate to the ultimate goal. The absence of a specific timeframe does not, however, imply a lack of commitment. This is precisely why the ultimate goal is essential as a compass: it prevents necessary choices from being postponed and makes visible which structures and developments support or hinder progress in the desired direction.

The ultimate goal is an ambition that requires support across niches, the regime and the landscape. It cuts across science, policy, regulation, industry and society as a whole, and requires active engagement of all these actors. Science and education drive the development of knowledge and train new generations of professionals. Industry partners co-develop methods, invest in infrastructure and decide whether new methods are incorporated into industrial pipelines. Public-sector bodies set frameworks, fund development and determine which methods gain regulatory acceptance. Civil society organisations contribute values and perspectives that enrich and broaden thinking about the transition.

Although careful treatment of animals and the refinement of procedures remain essential, and must be fully supported for as long as animals continue to be used, optimising existing practice does not in itself constitute a transition. System change does not passively await technological maturity, but actively creates the conditions in which responsible innovations can mature, be assessed and achieve broad implementation. This also involves addressing fundamental questions, such as how relevant the research actually is and whether it remains tenable to assume that human interests should take precedence over those of animals.

Funding, validation frameworks, career incentives and regulatory frameworks must be actively aligned with the ultimate goal. The same applies to society as a whole. Societal choices about what constitutes valuable research and which interests are taken into account shape the direction of the transition. Maintaining direction towards the ultimate goal and protecting the animals currently being used are equally important and must proceed in parallel. Neither should come at the expense of the other.

4.2 Strategic policy context

The transition towards a society without animal experiments does not take place in isolation, but is closely intertwined with broader restructuring of innovation ecosystems in health, biotechnology and strategic innovation. Animal-free innovations are part of the wider Life Sciences & Health ecosystem, in which government, science and industry work together to develop knowledge, infrastructure, regulatory applications and markets. Illustrative examples include the 2025 European Life Sciences Strategy, the EU Biotech Act, the Netherlands' National Technology Strategy 2035 and the Government-wide Vision on Biotechnology (13-16). These policy frameworks aim to overcome fragmentation, strengthen the links between science and application, and enhance societal and economic capacity. The 2026 Interministerial Biotechnology Implementation Agenda explicitly includes replacing animal experiments with animal-free test methods as part of strategic biotechnology policy, thereby confirming that this transition is an interministerial innovation challenge.[19] The Wennink Report (2025) places this in a more forceful perspective: only by making targeted investments in strategic innovation domains, including life sciences and biotechnology, can the Netherlands safeguard its future earning capacity, public services and international strategic relevance (17). An important prerequisite is an agile research toolkit in which new research methods and evidence strategies are developed, combined and applied alongside, and as replacements for existing approaches. Animal-free innovations strengthen this toolkit and create new opportunities to address scientific and societal research questions.

The innovation potential that the Netherlands has built and continues to invest in is a strategic asset. Through the National Growth Fund, investments are being made in several large-scale life sciences and biotechnology initiatives, including Biotech Booster, Health-RI, Ombion, Oncode Accelerator and PharmaNL.[20] In 2025, eight National Growth Fund organisations, including these five, formalised their collaboration to build an integrated, internationally competitive Life Sciences & Health ecosystem, with a

[19] Parliamentary Papers II 2025/26, 27 428, no. 413, Interdepartementale Uitvoeringsagenda Biotechnologie 2026 [Interministerial Biotechnology Implementation Agenda 2026], 23 June 2026, (website in Dutch).

[20] National Growth Fund, 'Thema Gezondheid en Zorg', (website in Dutch).

focus on societal impact in the Netherlands.[21] This illustrates how initiatives that often emerge from niches become embedded in the broader research and innovation system. Moreover, the context in which this development is taking place is rooted not only in science and policy, but also in political and administrative decision-making. The Ministerial Task Force on Future Prosperity and the Business Climate (2026) designated life sciences and biotechnology as a strategic domain within Dutch industrial policy.[22]

4.3 Societal and political context

The transition towards a society without animal experiments touches on widely shared values concerning animal welfare, health, safety and innovation. These values do not automatically point in the same direction. The societal and political context of the transition raises the question of how these values relate to one another when they come into tension.

Advancing scientific understanding of animals' emotions, cognitive capacities and consciousness gives this context added weight. This knowledge provides greater insight into what matters to animals. As a result, we gain a deeper understanding of their interests and must give them greater weight in our ethical considerations. This also calls into question the underlying assumptions of the ethical foundation on which the use of animals in science is based.

Such pressure is not new. Objections to animal experiments have a long history, ranging from individual moral unease to organised anti-vivisection societies in the nineteenth century and present-day campaigns. The desire to reduce the suffering of animals used in science and to end or drastically limit animal experiments has been a recurring theme throughout history (18). The desire to reduce the suffering of animals used in science led to the emergence of laboratory animal science, the formulation of the 3Rs and the introduction of legislation such as the Dutch Experiments on Animals Act (1977) and European Directive 2010/63/EU and the subsequent amendment to the Dutch Experiments on Animals Act in 2014 (7, 9, 19, 20). The recognition that animals are sentient beings with intrinsic value is an essential normative guiding principle. In the Netherlands, the use of animals in experiments is therefore governed by a 'no, unless' principle, meaning that animal experiments are, in principle, prohibited. The desire to end animal experiments, or at least to limit them drastically, is reflected in sustained societal and political calls for further action. This can be seen, for example, in a European Citizens' Initiative[23] urging the European Commission to act, and in repeated parliamentary motions and questions[24] calling for faster progress. At the same time, societal views are not unequivocal, as is also demonstrated by various surveys (21-23). The fact that different measurement methods can lead to different representations of societal views is not unique to the debate on animal experiments. In its State of Central Government Accounts 2025, the Netherlands Court of Audit observes that this issue applies more broadly across government policy (24). It underscores the importance of ensuring the structural involvement of diverse societal perspectives in decisions and deliberations made on behalf of society as a whole.

Alongside calls for faster progress, there are concerns about the feasibility of the transition and its potential consequences for research and innovation. These concerns are shared by parts of the scientific community and industry, as well as by societal, governmental and political actors. A key tension is that new methods need to demonstrate their value in practice, while they can only mature through application, investment and the building of trust.

[21] PharmaNL, 'National Growth Fund Initiatives Join Forces to Strengthen the Dutch Life Sciences & Health Ecosystem', news item, 4 december 2025, (website in Dutch).

[22] Ministry of General Affairs, Aanbiedingsbrief bij opdrachtbrieven Ministeriële Taskforces ['Cover Letter Accompanying the Letters of Assignment for the Ministerial Task Forces'], parliamentary document, 6 March 2026, (website in Dutch).

[23] European Commission, 'Save Cruelty Free Cosmetics – Commit to a Europe Without Animal Testing', European Citizens' Initiative, 25 January 2023.

[24] See, for example, the motion by Kostić on the Netherlands' leading role in animal-free innovation, Parliamentary Papers II 2024/25, 32 336, no. 158; the motion by Kostić and Graus on animal testing for substances used in cosmetics, Parliamentary Papers II 2024/25, 32 336, no. 159; the motion by Graus et al. on animal-free models and testing methods, Parliamentary Papers II 2024/25, 32 336, no. 163; the motion by Graus and Kostić on appointing a national coordinator for the transition to animal-free innovation, Parliamentary Papers II 2025/26, 28 286, no. 1425; and the written questions submitted by Kostić on government communication concerning animal testing and innovative animal-free research methods, Parliamentary Papers II 2025/26, 2026Z12041.

Such plurality of perspectives is characteristic of transitions. Major transitions typically unfold within a system of differing values, interests and perspectives, whose interaction helps shape the transition. Legislation, regulation and scientific practice alone are therefore insufficient when developing policy and making decisions. As these issues concern public values, shared responsibilities and acceptable uncertainties, societal co-ownership is crucial. This need is also recognised in biotechnology policy: the government has made its further implementation conditional on structured citizen consultation, societal input and the development of an ethical assessment framework.[19]

4.4 Scientific context

The transition towards a society without animal experiments is taking place within a research system that is itself undergoing change. Meta-research empirically examines the reliability and reproducibility of science and has exposed shortcomings in areas including research design, publication practices and incentive structures (25, 26). Initiatives such as Science in Transition and Open Science therefore emphasise the importance of quality, transparency, collaboration and societal relevance (27, 28). This broader movement provides an important opportunity to rethink research strategies and model choices.

At the same time, new methods and technologies have become available across a wide range of research fields. Their scientific significance lies not only in their individual capabilities, but above all in their increasing integration. Integrated approaches are emerging in which innovative methods are used together to understand biological mechanisms and answer research questions. Science is therefore gradually shifting from a model-centred to an evidence-integrative approach, in which different types of evidence are considered in conjunction. The rise of personalised and precision medicine is reinforcing this shift. Where individual biological variation is central, human data and models offer opportunities that animal models are inherently limited in providing.

Many of these developments emerge in scientific niches, such as public-private innovation programmes, validation consortia, living labs, data and modelling platforms, and international partnerships. These niches not only develop and validate technological innovations, but also give rise to new forms of collaboration, knowledge sharing, education, assessment and regulatory interaction. Responsibility for their wider uptake does not lie primarily with the niches themselves. System actors, in particular, have a responsibility to identify promising developments at an early stage, create the conditions for their further development and application, remove barriers and ensure that successful practices become firmly embedded. This Transition Policy Advice addresses precisely the challenge of turning promising developments into broader change at regime and landscape level.

5.

Recommendations and their rationale

The recommendations in this chapter build on the evaluation of the 2016 Transition Policy Advice (2), recent insights from transition studies (3), the open survey[3], stakeholder meetings[2] and the in-depth interviews. The NCad analysed these sources of knowledge in an integrated manner, examining where insights converged and where they diverged. Where relevant, additional sources were used. This provided a clear picture of where genuine change is needed. Specific references are included where an observation or claim can be directly attributed to a single source.

Foundations of this policy advice

These recommendations rest on two strong foundations: transition studies, also referred to as transition thinking, and a Theory of Change.[25] Transition thinking helps us understand what kind of change is needed. A Theory of Change makes explicit how that change is expected to occur: which interventions are required, through which steps, involving which actors, under which assumptions, and how progress can be recognised. A Theory of Change is not a linear planning tool; rather it makes explicit the pathways through which change can unfold within a broader system transition.

The transition requires coherent change across five pillars. Together, these form a pathway of change in which innovations can emerge and mature, be scaled up and institutionally embedded, and ultimately contribute to a society without animal experiments.

[25] A Theory of Change describes how and why interventions are expected to contribute to societal change. It makes the causal links between activities, the actors involved, intermediate outcomes and long-term impact explicit, including the assumptions and dependencies underpinning this reasoning. See Appendix 3 for a more detailed explanation.

Pillar	Function and relationship to the other pillars
I. Governance & ownership	Assigns responsibility, coordination and strategic direction, and public accountability. This pillar therefore provides the conditions for the other pillars to have an effect: ethical reassessment, innovation policy, international strategy and monitoring.
II. Reassessment of the ethical framework	Reassesses the normative basis of the system. In doing so, this pillar guides which research choices are regarded as standard practice across innovation and ecosystem policy, from governance, funding and education to assessment practices.
III. Innovation and ecosystem policy	Creates the conditions for targeted funding, validation, acceptance and scaling up of animal-free innovations. This pillar translates the updated ethical framework into practical application and thereby strengthens the international position.
IV. International strategy	Directs Dutch efforts towards actively shaping international frameworks, including regulatory, scientific and normative frameworks. This pillar is decisive for the policy space available to the Netherlands and for the scalability of innovations emerging from innovation and ecosystem policy, as both depend in part on what is internationally recognised as valid evidence and established practice.
V. Monitoring	Monitoring makes progress, stagnation and coherence between the pillars visible. This pillar provides the governance information needed to make adjustments and to assess whether the updated ethical framework, innovation policy and international strategy are translating into meaningful change across the system.

The pillars are interdependent. Governance is the foundation on which the other pillars rest. Without clearly assigned responsibility and coordination and strategic direction, the other pillars remain fragmented rather than developing into a coherent, mutually reinforcing approach. An updated ethical framework will only have an impact when funding and education evolve alongside it. If this connection is not established, the updated framework will have limited effect beyond the formal licensing process for animal experiments. Innovation policy that is not linked to international acceptance will result in methods whose application remains limited. And monitoring that is not connected to governance with a mandate to act on its findings will record developments, but cannot steer them.

The recommendations are structured around these pillars. The government provides direction, organises shared conditions and assigns responsibility. System actors, including governments, funders, regulators, knowledge institutions, professional associations and international organisations, are responsible for recognising niche innovations at an early stage, giving them room to develop, removing barriers, learning from them and embedding successful innovations in established practice. This broadens the role of regime actors: in addition to safeguarding quality, safety and public values, they must actively enable, assess and institutionalise responsible system renewal.

The mechanisms of adoption, diffusion and institutionalisation therefore form an integral part of the recommendations. The distinction between a successful innovation and successful system change does not lie in the method itself, but in the institutional environment. An animal-free method may be scientifically established, validated and available, yet still fail to become standard practice if funding conditions, guidelines, accreditation, grant assessment, economic incentives and education do not support its routine use. Responsibility for these mechanisms lies partly with government and partly with the other system actors. Institutionalisation therefore requires movement from both sides at the same time.

5.1 Governance & ownership

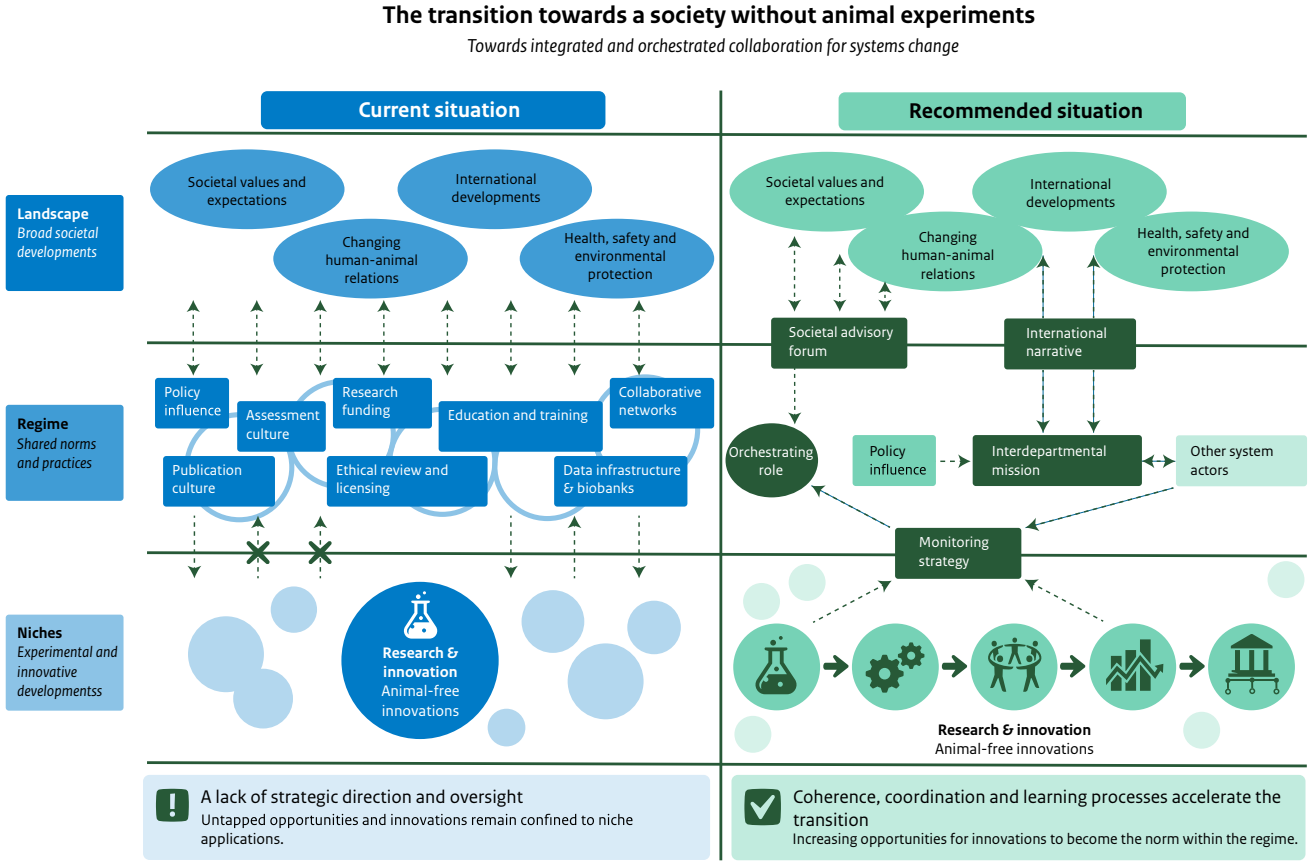
Recommendation I. Embed the transition towards a society without animal experiments as an interministerial mission, with shared ownership and clear responsibilities.

The transition towards a society without animal experiments is now widely recognised, but is not yet sufficiently embedded at governance level. The integrated analysis shows that direction, ownership and responsibility have not been assigned structurally enough to allow the transition to feed systematically into knowledge development, regulation, funding, education and professional training, innovation policy, societal considerations and international strategy.

In 2016, the NCad highlighted the need for clear transition goals, a transition strategy and coordination and strategic direction, while allowing for reflection, learning and course correction. Since then, efforts by the field, supported by enabling government policy, have led to greater agenda-setting, network-building and visibility of animal-free innovation. The next phase requires embedding the transition within governance structures, linking the foundation that has been built to clear responsibilities, coherence across policy domains and public accountability for progress (see Figure 2).

In figure 2, the left-hand side illustrates how the actors and conditions within the regime are insufficiently connected. As a result, innovations emerging from niches face difficulties in scaling up into mainstream practice. The right-hand side shows the recommended situation: an interministerial mission and a shared international narrative provide direction, the orchestrating role connects and monitors, the societal sounding board contributes normative and societal input, and policy agendas specific to each domain translate this shared ambition into implementation. In this way, successful innovations are incorporated into policy, research, education and practice.

Figure 2. From fragmented initiatives to coordinated system governance



I.1 Interministerial mission and allocation of responsibilities

An increasing number of animal-free methods are becoming available, and international attention is growing. Nevertheless, the overall picture for the number of animal experiments in the longer term remains uncertain. If policies remain unchanged, stabilisation or an increase in the medium term is more likely than a further decline (1). This shows that the transition towards a society without animal experiments is not solely a matter of technological innovation or animal welfare policy. The analysis in the NCad-report Animal Procedures in the Netherlands 2015-2024 shows that, in 2024, more than half of all animal experiments conducted in the Netherlands were directly driven by European legislation and national policy choices (1). Examples include safety requirements for chemical substances, obligations relating to nature restoration and zoonotic disease surveillance. This means that several ministries effectively co-determine the number of animal experiments, while responsibility for this has not been structurally assigned.

The existing interministerial coordination mechanism is not designed to fulfil this role. It is primarily project-based and portfolio-oriented. It does not provide a structure capable of addressing an objective spanning multiple decades and multiple policy domains. A government-wide mission addresses this governance gap by linking a shared goal to ministerial responsibility within each policy domain.

Recommendation I.1 The NCad recommends the Minister for Food Security, Fisheries and Horticulture to establish the transition towards a society without animal experiments as an interministerial mission of central government, within formal and preferably existing structures bringing together the responsible ministers of the Ministry of Defence, Ministry of Economic Affairs and Climate, Ministry of Infrastructure and Water Management, Ministry of Education, Culture and Science, Ministry of Social Affairs and Employment, Ministry of Health, Welfare and Sport. For each policy domain, the responsible minister should establish a dedicated transition policy agenda setting out:

- which specific interim goals are to be pursued in each policy domain and the timeframe for achieving them;
- the policy instruments to be deployed;
- the route and moments through which the minister will report on progress;
- the public and private actors responsible for, and/or accountable for, specific aspects of the transition.

The interim goals are adaptive reference points that are periodically reassessed on the basis of progress and new insights. Each transition policy agenda should specify which financial resources are available or will become available. The responsible minister is accountable for implementing the agenda and for progress within their respective policy domain. The Minister for Food Security, Fisheries and Horticulture, with overall system responsibility, safeguards coherence between the transition policy agendas, coordinates their collective progress and reports periodically to the House of Representatives.

The Ministry of Agriculture, Fisheries, Food Security and Nature is the natural choice as coordinating ministry for the interministerial mission, since it holds system responsibility for animal experiments policy. The levers for change within each research domain also lie with other ministries, including in the fields of medicines policy and public health, science and education policy, chemical safety and environmental policy, innovation and industry policy, and defence research. Transition policy agendas per policy domain are therefore needed. The interministerial mission builds on the foundation that researchers, businesses, civil society organisations and other innovators have developed bottom-up across a range of niches.

Because these foundations have largely developed in a decentralised way, formal governance arrangements are essential in the next phase. The Netherlands Court of Audit notes that, across central government policy, many long-term objectives are at risk of not being achieved when they are insufficiently embedded and implementation capacity does not mach the level of ambition (24). For the transition towards a society without animal experiments, the absence of shared governance creates a genuine risk that initiatives will continue to exist alongside one another, lessons will not be shared sufficiently, and dependencies on experiments using animals will not be challenged enough. The evaluation of the 2016 Transition Policy Advice shows that decentralised efforts without shared direction and clear ownership for follow-upremain dependent on voluntary commitment (2).

A government steering role should not be confused with a uniform top-down steering approach. Stakeholders emphasise that there must be room along the way for improvements that are directly needed and feasible, such as the reduction and refinement of animal experiments. Experiences from other transitions also shows that change progresses furthest when system actors themselves take ownership of their goals. The transition policy agendas must therefore provide a shared direction while ensuring that those responsible for delivering the transition in practice have the ownership to do so.

Different research categories, interconnected transition challenges
The recommendation calls for transition agendas for each policy domain because the substantive levers for change differ fundamentally between research categories. *Target images* can provide further direction for differences within research categories. At the same time, differentiation must not lead to siloed approaches: transition pathways may differ, but they remain part of a single coherent transition challenge.

In **fundamental research and translational and applied research**, the logic of change centres on the relationship between the societal or scientific problem and the formulation of the research question or questions, the choice of model or combination of models, scientific assessment and funding opportunities. Stakeholders emphasise that, for some research questions concerning complexity, system interactions, behaviour or disease processes, an animal model is still considered necessary. At the same time, model choice is also shaped by historical datasets, publication culture, peer review, funding criteria and international expectations. The question is therefore not only whether animal models can be replaced, but also how the frameworks shaping the formulation of research questions, model choices and evidence pathways need to change, and how this change can be enabled.

In **regulatory research**, change depends on building confidence in new forms of evidence within complex scientific and regulatory frameworks. Methods must generate relevant and reliable evidence about interactions within organisms or between biological systems in order to answer questions about efficacy and toxicity. The existence of established guidelines and testing frameworks does not, in itself, make the transition in this category easier (29, 30).

The pathway to change lies in industry, assessors and regulatory authorities working together on concrete cases and taking responsibility for the development, evaluation and acceptance of non-animal evidence. Standardisation can accelerate this process, but it can also reinforce existing practices involving animal experiments as long as guidelines continue to rely primarily on animal data.

In **education and training**, the logic of change centres on shaping norms. What we teach determines what future researchers, assessors, biotechnicians and professionals come to regard as self-evidently good research.[26] This is not only about the importance of technical training in animal-free methods, but also about systematically teaching critical model selection, ethical reflection and an understanding of uncertainty.

Research for the preservation of species includes research into populations and habitats, migration and tracking, the assessment of fisheries and catch management, and research for water management and infrastructure. In this category, the logic of change is centred on the extent to which societal developments directly drive the research. The system change emphasised in this policy advice also calls for critical reflection on these societal developments. The same applies to the category of **research for protection of the environment**, which includes research in ecotoxicology, bird research and population dynamics, fish research, aquatic ecology, infectious diseases and surveillance.

[26] Ambition Statement on Innovation in Higher Education Using Fewer Laboratory Animals, 25 January 2024.

I.2 National orchestrating role for a society without animal experiments

The interministerial arrangements set out in I.1 establish the governance structure. However, they do not provide the system-level coordination and strategic direction needed to create coherence between policy domains, knowledge institutions, industry and civil society organisations. Existing initiatives mainly connect parties that are already involved in the transition. Those outside these networks remain beyond the reach of this system-level coordination, even though their links with the rest of the system are equally important for advancing the transition. Information on progress, bottlenecks and lessons learned is currently fragmented across annual reports, programme reports, monitoring data and ad hoc evaluations. It is not brought together anywhere into a coherent overview that can inform policy, science and societal debate.

The need for a system-wide orchestrating role was raised emphatically and repeatedly in both the meetings and the expert interviews. Parties occupying different positions within the system pointed to the lack of national coordination, a coherent picture of progress, and independent interpretation of bottlenecks. The convergence of these signals shows that this is a system-wide coordination problem. This is also evident from this policy advice. Experience across central government with cross-domain challenges also shows that an orchestrating role embedded within existing ministerial structures is insufficiently to overcome the siloed approaches it is intended to address (24).

No existing system actor currently fulfils this system-level coordination and strategic direction role, including organisations with a broader reach across the system. An organisation that is itself involved in implementation and in driving the transition cannot, without additional safeguards, also provide independent system-wide monitoring and interpretation. Within its statutory remit, the NCad provides independent policy advice across all policy areas relating to the use of animals for scientific purposes, but it is not resourced or organised to provide continuous monitoring across central government covering all such policy areas. The Transition Programme for animal-free Innovation (TPI) combines a partner programme in which public and private parties jointly drive the transition with a policy support role for the Ministry of Agriculture, Fisheries, Food Security and Nature. TPI therefore plays a valuable role in connecting parties and setting the agenda, but its close involvement in policy and implementation precludes it from taking on a different role.

Recommendation I.2 The NCad recommends the Minister for Food Security, Fisheries and Horticulture, together with the ministers responsible for the relevant domains, to assign and structurally embed an orchestrating role for the transition towards a society without animal experiments, supported by a small, structurally funded team. This orchestrating role:

- monitors and interprets progress in the transition from an independent position, and identifies deviations from the transition policy agendas;
- identifies and brings to the agenda bottlenecks that transcend policy domains, research categories and actors, framing them as system-level challenges;
- connects learning processes across policy domains, research categories and actors, enabling the system as a whole to learn.

Based on the three tasks outlined above, the body performing this orchestrating role reports periodically and publicly on progress in the transition. This role should preferably be organisationally embedded within an existing executive agency, with close links to substantive expertise in transition studies, thereby building on existing infrastructure. Its mandate, interministerial scope, access to information and authority to report independently and publicly should be formalised through an establishment decision.

The five pillars on which this Transition Policy Advice is structured are interdependent rather than cumulative. The orchestrating role is responsible for determining whether this interdependence is also evident in practice: whether rfeassessment of the ethical framework, innovation policy and international strategy are reinforcing and shaping one another, or whether progress in one pillar fails to translate into progress in the others.

The orchestrating role needs a broad and continually informed view of how the transition is developing. This is provided by the wider monitoring framework set out in Recommendation V, which looks beyond the number of animal experiments, and by the systematic inclusion of signals from society and practice under Recommendation I.3. Together, these inform the assessment of progress, stagnation and the need for adjustment in the transition.

These signals do not always point in the same direction. The task of the orchestrating role is to weigh them, identify contradictions and distil from them where the transition is progressing and where it is stalling. What the orchestrating role puts on the agenda cannot simply be disregarded, but decisions on what action to take in response remain with the ministers.

What the orchestrating role does in practice
A comparable function exists, for example, in the form of the Delta Commissioner within the water domain. It is an independent, long-term role focused on safeguarding the overall direction, identifying bottlenecks that transcend individual organisations, and periodically reporting on progress. The role is not to implement policy, but to provide an integrated overview, make interdependencies visible and support government decision-making. The orchestrating role for the transition towards a society without animal experiments fulfils the same function: it is the point where information, signals and progress come together, are interpreted and translated into courses of action for policymakers and practice.

The expertise required is fundamentally transition-oriented and analytical: the ability to assess how choices in one part of the system affect another, and how scientific, societal and governance factors accelerate or slow the transition. An understanding of the relationship between public-private collaboration and between science and society is essential. Societal expectations, trust and legitimacy all influence whether the transition as a whole makes progress. Expertise specific to particular research categories is brought in where needed through staff or experts from government ministeries, knowledge institutions or the wider field, while ensuring independence is safeguarded.

This role requires structural safeguards. Without an interministerial mandate, the orchestrating role can operate only within the Ministry of Agriculture, Fisheries, Food Security and Nature ‘s portfolio and loses the system-wide overview that defines its purpose. Experience from other transitions shows that temporary programmes and project funding are insufficient to safeguard institutional memory, continuity and timely adjustment (31).

The orchestrating role and its supporting team should therefore be established as a compact but permanent function. A stakeholder power analysis can reveal which actors actually shape the transition, where responsibility is disconnected from the capacity to act, and where mandates are insufficient to overcome interdependencies between policy domains.

I.3 Structural societal involvement

The governance structure set out in Recommendations I.1 and I.2 provides direction, ownership and transition capacity. That structure lacks sufficient rigour as long as societal and normative signals do not have an established place in monitoring, agenda-setting and public accountability. The transition involves normative choices about which research is considered socially valuable, which uncertainties are acceptable, how the interests of animals are weighed, and how trust in new methods is established. These choices cannot be made solely by scientific, regulatory, public and private parties.

Without structured societal input, fundamentally normative choices about direction and priorities risk being treated as if they were merely technical matters. A permanent societal advisory forum therefore gives societal perspectives an established place in the governance of the transition and provides the orchestrating role with perspectives that the professional field does not automatically bring to the table.

Recommendation I.3 The NCad recommends the Minister for Food Security, Fisheries and Horticulture to establish a permanent societal advisory forum that provides the orchestrating role with societal signals and priorities. The forum should ensure structured participation by organisations representing perspectives on normative questions in the transition that are otherwise not structurally represented in governance, including patient organisations, animal interest organisations, nature and environmental organisations, and consumer organisations.

The forum should have a clear mandate: it should independently determine which societal priorities, bottlenecks, conflicts of values and concerns about

societal support it brings forward, and should raise these issues both upon request and proactively. In its public reports, the orchestrating role must account for how the signals raised have been weighed and what action has been taken in response.

The stakeholder meetings show that the debate on a society without animal experiments cannot be reduced to a simple division between supporters and opponents. Arguments span science, ethics, legitimacy and strategy. They reflect a wide range of concerns regarding feasibility, terminology, timelines, public expectations and progress achieved. Which arguments become dominant also depends on who is represented at the table. Plurality of perspectives must therefore be actively organised.

The dialogue should be structured in such a way that concerns, values and underlying interests are made explicit, without further entrenching positions. Citizen participation helps to make broader public values visible, but it is not a substitute for the continuous input of organised societal perspectives. The structural embedding of societal input, rather than its only on an occasional collection, is consistent with broader policy research (see box 'From societal involvement to responsive governance').

How the dialogue is structured matters. Insights from research on participation, transitions and conflict show that complex societal issues benefit more from processes aimed at mutual understanding and joint exploration of the problem than from attempts to persuade others. Making underlying values, interests and concerns explicit has also been shown to be important in building trust and legitimacy.
The literature emphasises that concerns should not be seen solely as resistance to change, but also as expressions of engagement, professional identity, institutional responsibility or societal values. From this perspective, emotions are not merely barriers to change, but can also provide important signals of what those involved perceive to be at stake.

From societal involvement to responsive governance
Across various policy fields, there is growing recognition that societal involvement can be more than consultation at predefined moments. The key question is not only whether policy is explained adequately, but whether policymaking learns in a timely manner from societal values, expectations, trust, practical bottlenecks and new forms of knowledge.

In its guidance on transformation-oriented policy, the Advisory Council for Science, Technology and Innovation (AWTI) emphasises that transformations emerge through interaction between government, research organisations, companies, funders and civil society organisations (32). The role of government is in mobilising, stimulating and, where necessary, slowing down developments. This broad coordination is needed to avoid the 'technology trap': the tendency to approach transitions primarily as a matter of science and technology development.

The Rathenau Institute links this to responsive policymaking. Signals from society should be gathered, weighed and fed back. Societal involvement thereby shifts from occasional consultation towards a form of learning governance. Signals become part of monitoring, priority-setting and policy agenda-setting (33).

The perspective of the Netherlands Court of Audit is also relevant (24). Where public goals are pursued over longer periods of time, across multiple organisations and at different levels of government, clear responsibilities, information on progress and public accountability are essential. Societal involvement only becomes meaningful when it is connected to such accountability structures.

For the transition towards a society without animal experiments, this means that societal signals must have an established place in monitoring, agenda-setting and policy preparation. A societal advisory forum can fulfil this function.

A solid foundation for this already exists in the field. Various initiatives bring together research, industry, patient organisations and public-sector parties. Some funders incorporate societal perspectives into research decisions, for example through funding criteria or patient panels that help determine which outcomes are genuinely valuable in everyday life. However, these examples do not resolve the governance question. The analysis shows that societal parties are not always involved at an early enough stage and that it is not always clear how their input is weighed and followed up. Their involvement remains dependent on individual initiatives, available capacity and the willingness of professional actors in the field to actively incorporate societal perspectives.

A permanent societal advisory forum could reduce this fragmentation. Three issues need to be considered in establishing such a forum.

The first issue is **representation**. Patient, consumer, nature, environmental and animal interest organisations are not interchangeable. Different perspectives also exist within these groups. An individual patient, a patient organisation or an expert by experience may, for example, place emphasis on different aspects.

A particular challenge concerns the position of animals. Animals cannot directly articulate their own interests. How those interests should be interpreted and represented is therefore a matter of ongoing ethical and societal debate. The Netherlands has various bodies that oversee animal welfare. However, these parties fulfil different roles and do not necessarily represent a single, clearly defined animal interest. Their responsibilities range from licensing and supervision to policy advice and advocacy, with animal welfare always considered in relation to other societal, scientific or governance considerations.[27] The transition is driven in part by changing societal views on human-animal relations. It is therefore important that perspectives on animal welfare, animal behaviour and animal ethics are visibly taken into account when reflecting on direction, priorities and progress. This is not about designating a single actor to speak on behalf of animals, but about ensuring structured and explicit representation of this perspective in decision-making processes.

The plurality of societal actors requires a flexible governance arrangement. Permanent participants can provide continuity, while additional participants can be invited when their perspective is relevant to the issue under discussion. This allows the forum to remain broad enough to capture societal signals, while sufficiently focused to provide meaningful input to governance.

The second issue concerns the **knowledge gap and the power imbalance**. Parties that work with animal experiment policy on a daily basis generally have more technical knowledge, policy experience and capacity than patient and societal organisations. Without accessible information, timely agenda-setting, preparation and support where needed, a broadly constituted forum may still leave the greatest influence with those who have a knowledge advantage in that case, there is no level playing field. The forum therefore requires practical support in terms of information provision and preparation, enabling societal organisations to participate as equal partners in the dialogue.

The third issue is defining the **boundaries** of the forum's role. Its function is to identify signals, put issues on the agenda and provide reflection. It does not take decisions on the transition and does not replace governmental responsibility. The orchestrating role incorporates these signals into the broader analysis and explains in its public reports how they have been addressed. The forum brings societal priorities, concerns about the pace and direction of the transition, underrepresented interests and ethical tensions into view. The forum is not a one-way process. Through participation, societal actors also gain insight into the considerations, uncertainties and consequences associated that underpin decision-making.

In this way, the forum completes the chain established in I.1 and I.2: the interministerial mission assigns governmental responsibility, the orchestrating role provides an overview of coherence and progress, and the societal advisory forum ensures that normative and societal signals become a structural part of monitoring, agenda-setting and public accountability.

[27] Examples include the Central Authority for Scientific Procedures on Animals (CCD), supported in this role by Animal Ethics Committees (DECs), the Netherlands Food and Consumer Product Safety Authority (NVWA), Animal Welfare Bodies (IvDs), the Council on Animal Affairs (RDA) and civil society organisations concerned with animal welfare.

5.II Reassessment of the ethical framework

Recommendation II. Reassess the ethical basis of research involving animals.

The harms-benefit analysis forms the institutional basis for the ethical justification of research involving animals. Animal Ethics Committees (DECs) and the Central Authority for Scientific Procedures on Animals (CCD) base their assessments on this analysis. Researchers, Animal Welfare Bodies (IvDs) and funders apply comparable considerations in their decision-making.

Revision of the ethical assessment framework is necessary because its current application is insufficiently aligned with current scientific knowledge about animals, developments in animal ethics and research practice. On the harms side, there is a strong emphasis on distress, while other relevant animal interests are not always explicitly and consistently weighed. On the benefits side, uncertainties regarding the nature, scale, timeframe, likelihood and translatability of expected benefits often remain too implicit.

Moreover, the formal emphasis currently lies on the licensing stage, whereas fundamental ethical choices are made earlier in the process, when defining the problem, determining the research strategy, selecting the model and allocating funding. The key questions of the updated framework should therefore be embedded throughout the research chain and recognisably reflected at every stage. A further challenge lies in implementation. In practice, the current framework has been developed primarily around distress. As soon as the assessment concerns broader concepts of welfare or uncertainties on the benefits side, a grey area often emerges in which the framework provides insufficient guidance. Discussions with those involved show that even people who deal with these questions on a daily basis struggle to resolve them without a structured approach. Greater conceptual clarity does not solve this problem unless the practical conditions for applying them change as well.

The current ethical assessment framework warrants updating in its own right. The fact that updating the framework is also a prerequisite for broader system change increases its urgency, but is not the basis on which it rests. When the framework provides insufficient guidance in practice for identifying the interests of animals on the harms side and uncertainties on the benefits side, the assessment remains too implicit and incomplete. What remains implicit is not weighed consistently and may prevent the assessment from being sufficiently rigorous. As long as this mechanism is not addressed, the other pillars of this policy advice will not function optimally either. Accordingly, the recommendation does not focus on introducing new ethical concepts as an end in itself, but on applying ethical considerations more explicitly, consistently and transparently throughout the entire research chain.

Recommendation II.1 The NCad recommends the Minister for Food Security, Fisheries and Horticulture to take the lead in updating the ethical assessment framework for research involving animals and to ensure that the outcomes are embedded throughout the research chain: in research strategies, model selection, funding decisions, Animal Welfare Bodies advice, Animal Ethics Committees advice and Central Authority for Scientific Procedures on Animals decision-making.

Establish an independent working group for this purpose, with a strong and independent foundation of ethical expertise, including expertise in animal ethics, animal behaviour and animal welfare. In addition, involve practical knowledge and societal perspectives to determine which research, assessment and funding practices need to change to enable the framework to take effect throughout the research chain. The working group should be tasked with delivering, within a specified timeframe, a concrete proposal for an updated framework and an implementation plan for embedding it in existing formats and assessment practices.

The update should focus on four areas that are insufficiently developed in the current framework:

- Operationalising broader welfare concepts and other ethically relevant concepts, ensuring that the interests of animals extend beyond distress alone and can be weighed in a transparent and traceable way as part of the proportionality assessment.

- Giving uncertainty on the benefits side an explicit place in the assessment, so that uncertainty about the nature, scale, timeframe and translatability of expected benefits is made visible rather than being subsumed under general references to scientific, societal or economic relevance.
- Including an explicit forward-oriented question as an integral part of the assessment: what changes in research strategy, knowledge, funding, collaboration or infrastructure are needed to answer the relevant research question without animals in the future?
- Establishing the practical conditions required to ensure that the framework to have an effect throughout the research chain.

The Minister for Food Security, Fisheries and Horticulture should designate a responsible party for the further development, implementation and periodic updating of the ethical framework. Following its implementation, an evaluation should assess whether the framework is in fact being applied throughout the entire chain, from the development and support of research through to assessment, licensing and funding of research involving animals, and whether this results in more rigorous and transparent ethical assessments.

Many elements of this recommendation are already part of current practice. The challenge is therefore not primarily to introduce entirely new assessment questions, but to ensure that existing questions on both the harms and benefits sides are applied more explicitly, consistently and transparently throughout the research chain. Scientific knowledge of animals' cognitive, social and emotional capacities has changed over recent decades and continues to develop. Thinking about animal welfare has shifted from preventing negative experiences towards a broader understanding that also encompasses positive experiences, opportunities to engage in behaviour and freedom of choice.

This provides a different perspective on animals' interests and on the ways in which those interests can be compromised. A further challenge is how to ensure that the interests of animals are adequately represented in decision-making in which animals themselves cannot participate. A further question is whether the fact that animals used for scientific purposes are generally killed at the end of the experiment is given sufficiently ethical weight in current assessment practice. At the same time, views are changing on what can justify the use of animals in the first place.

On the harms side, distress, pain, suffering, fear and lasting harm dominates in practice. This is relatively concrete insofar as it can be observed, categorised and compared. providing a degree of clarity. However, it also means that forms of harm not expressed in these terms, such as psychological suffering, are insufficiently weighed systematically. Concepts such as integrity are included in legislation and in the Animal Ethics Committee's format, but have not been operationalised for use in proportionality assessments: what does a moderate impairment of integrity mean in the practice of an Animal Ethics Committee, and how should it be weighed against expected benefits? Concepts such as agency and telos (see Appendix 2 for an explanation) add other dimensions that are not present in the current framework. The issue is not only what an animal experiences, but also what an animal is able to do and pursue, and whether it is able to behave in ways that, for example, make a mouse a mouse or a pig a pig. This is relevant both to the way animals are currently kept and used in research and to the transition towards a society without animal experiments.

It is important to recognise that deciding what evidence is sufficient to acknowledge animal's capacities is itself a normative choice. History shows that these capacities have repeatedly been underestimated. Such underestimation preserves a degree of freedom in how people may treat and use animals that becomes less self-evident once those capacities are recognised. People may therefore have an interest in maintaining that underestimation (11). This observation calls for an update to the way the interests of animals are described and weighed in the assessment of harms and benefits. This is not about abandoning existing legal requirements, but about strengthening the way in which they are interpreted and applied in practice.

With regard to the benefits side of the assessment, it has become increasingly clear how complex and multifaceted the uncertainty surrounding the benefits and their weighting really is. The current framework provides insufficient structure for systematically identifying and weighing these multiple forms of uncertainty. As a result, uncertainty remains implicit behind references to scientific or societal relevance, and it is not made visible which considerations ultimately determine the outcome. Particularly in fundamental research, the nature, likelihood, timeframe and magnitude of potential benefits are often uncertain. This uncertainty is multi-

dimensionalfaceted and concerns not only the likelihood that the intended societal benefits will actually be achieved, but also which benefits may arise, precisely because fundamental research can sometimes lead to unexpected insights. It is also often unclear who may benefit, over what timeframe, and what weight those potential benefits should carry in the assessment. Regulatory research on chemical substances involves a different but equally real tension. The ethical assessment focuses on the experiment itself, while in practice it can be difficult to include the more fundamental question of whether the societal or economic need for the substance justifies the animal suffering caused by testing it. The regulatory requirement therefore functions as an implicit justification for the use of animals, without that justification itself being subject to systematic ethical assessment. In both cases, there is no self-evident basis for weighing benefits to humans against animal suffering. Kramer and Bovenkerk show that the two are qualitatively different: even when both are expressed in terms of welfare, deciding how human and animal welfare should be weighted agains each other remains a normative choice that cannot be resolved by the analysis itself. A harms-benefit analysis that leaves this choice implicit therefore omits an essential part of the ethical reasoning (8). A detailed description of the forms of uncertainty on the benefits side is provided in Appendix 2.

The multiple uncertainties surrounding the benefits do not make careful assessment impossible, but they do require the underlying considerations to be made more explicit. The translatability to the intended application, the expected gain in knowledge in relation to existing knowledge, and the likelihood of meaningful benefits need to be assessed in a transparent and traceable way. Expected knowledge gain should be regarded as a potential addition to existing knowledge, rather than assuming that not carrying out a particular animal experiment would in itself constitute a loss of knowledge. The absence of a complete alternative is not, in itself, a justification for the use of animals. The assessment must also extend to the research question itself and to the research strategy chosen to address it.

The approach outlined above builds on the NCad's earlier policy advice on an assessment framework for prioritising animal experiments for replacement (34), which links ethical assessment, scientific relevance and the prioritisation of replacement.

A shared approach to assessment ensures that the same core questions are asked at different points throughout the research chain. For researchers and licence holders, this concerns the formulation of the problem, research questions and research strategies. For Animal Welfare Bodies, it concerns early advice on model selection and feasibility. For funders, it concerns the assessment of proposals at a stage when the research strategy is often still open to change. For the Animal Ethics Committees and the Central Authority for Scientific Procedures on Animals, it concerns the formal proportionality assessment and the justification for the use of animals. This is not about replacing existing formats, but about refining and better aligning existing application, advisory, assessment and funding instruments.

Expertise plays a crucial role in this. Building knowledge of new methods takes time and requires collaboration. A lack of such knowledge can influence model selection independently of the scientific question. Moral deliberation can provide support at an early stage, particularly by making explicit and critically examining assumptions, uncertainties and normative choices that might otherwise remain implicit in the choice of research strategy.[28] Its value does not lie in delivering a judgement, but in making explicit what is at stake before decisions become fixed.

Finally, the ethical assessment of research involving animals cannot be considered separately from the broader societal context in which that research takes place. The transition towards a society without animal experiments is intertwined with developments in health, agriculture, food production and the climate. Some health and safety challenges for which research involving animals is used are themselves connected with broader patterns in human-animal relations, intensive production systems, consumption and land use. This is the case with, for example, zoonoses and antimicrobial resistance, although through different mechanisms. Taking these interconnections into account helps to ensure that the benefits of research involving animals are not assessed in isolation. It also makes clear that health and safety benefits depend on broader societal conditions, policy choices and system developments. This wider context may therefore be relevant when assessing the necessity, proportionality and societal significance of research involving animals.

[28] Moral deliberation refers to a facilitated form of dialogue in which those involved explore underlying values, moral questions and considerations on the basis of a specific case. Its primary purpose is not to reach a decision, but to deepen understanding of one's own position and those of others. It is characterised by an exploratory dialogue that allows room for doubt, uncertainty and different perspectives.

5.III Innovation and ecosystem policy

Recommendation III. Create the conditions within the research and innovation ecosystem that enable animal-free innovations to scale up from niche applications to mainstream practice.

The Netherlands has a strong foundation for the transition towards a society without animal experiments. It has relevant knowledge and infrastructure and participates in public-private partnerships. The Netherlands is also among the international frontrunners in rapidly developing fields such as organoids, organ-on-chip technologies, human-based measurement models, advanced in silico approaches, FAIR data infrastructures, data visiting and applications of artificial intelligence. These areas of technology and expertise are strategically important for health, economic potential and technological leadership, and align with national and European innovation agendas (14-17).[29]

However, this strong foundation does not automatically translate into widespread application of knowledge, technologies and expertise. Promising methods often stall after the scientific development stage. Further development, standardisation, validation, funding, infrastructure and intellectual property arrangements are crucial. The fact that many organ-on-chip systems remain commercially confined to niche applications demonstrates that scientific promise alone does not automatically lead to further development, adoption and scaling up.

The transition therefore requires an ecosystem policy. The normative shift set out in the preceding recommendations will only have a lasting effect if it changes how actors, incentives and enabling conditions shape research practice. Universities, knowledge institutions, the pharmaceutical and chemical industries, CROs, biotech companies, suppliers, funders, regulators, professional groups and educational institutions all influence whether animal-free innovations are developed, scaled up and adopted on a structural basis. A substantial proportion of research involving animals is conducted by private-sector organisations; industrial adoption therefore also helps determine the scale and pace of the transition. Companies are already investing in animal-free innovations, but uncertainty about regulatory acceptance, commercially sensitive knowledge and the absence of shared standards can impede broad implementation. The gap lies in the conditions needed for broad implementation: pre-competitive collaboration, regulatory learning environments, scale-up, valorisation and the development of shared standards.

This is not a coincidental pattern, but a systemic problem. The transition literature shows that niches only bring about system change when they are linked to changes in the regime: standards, funding, infrastructure, skills, market access and regulatory acceptance must change as well (3, 31, 32). The challenge is twofold: to strengthen promising methods and to remove the barriers that prevent them from scaling up into mainstream practice.

III.1 Positioning within science and innovation policy

The transition is not yet sufficiently embedded in science and innovation policy as a strategic innovation challenge. As long as animal-free innovation is approached primarily as an ethical challenge or as a separate issue, funding, infrastructure, education and international engagement will remain insufficiently connected to the transition goal. As a result, animal-free innovation is not sufficiently recognised within the science system as a scientific, economic and societal challenge in its own right.

The transition is relevant to the Netherlands' economic potential and international position in the life sciences, biotechnology and data-driven research. For example in 2009,Hans Clevers and Toshiro Sato developed a robust method for culturing adult stem cell-derived organoids (35). This scientific breakthrough was widely adopted internationally and created new opportunities for research and application. At the same time, it illustrates that a strong knowledge base does not automatically lead to large-scale implementation. This requires sustained funding, accessible infrastructure, standardisation, entrepreneurship, user involvement and regulatory acceptance.

[29] Knowledge and Innovation Agenda for Key Technologies (KIA ST), 'RECAP: Official Presentation of Action Agendas'.

Recommendation III.1 The NCad recommends the Minister for Food Security, Fisheries and Horticulture, together with the ministers responsible for the relevant domains, to embed the transition in broader science and innovation policy as part of *future-agile* science. Animal-free innovation must be aligned with the transition goal in policy agendas and funding programmes.

Use *target images* as a tool to provide direction and ensure implementation within each research domain. The interministerial working group, informed in part by signals from the orchestrating role, determines which domains require new or updated *target images* and how their implementation can be strengthened. The NCad safeguards coherence and quality across the *target images* and ensures that lessons learned are carried across from one *target images* to another.

The National Technology Strategy has identified biomolecular and cell technologies, biosystems, organoids, bioinformatics, data science, data spaces and AI as interconnected key technologies (16). These technologies underpin many animal-free innovations. Investing in this transition therefore also means investing in strategic technology areas in which the Netherlands has scientific strengths and where international competition is increasing. At European level, this aligns with the EU Life Sciences Strategy, which links the life sciences to health, innovation and competitiveness, and with the announced Biotech Act, which supports a more innovation-friendly framework and faster routes to application. In this context, animal-free innovation brings together new models, biotechnology, data-driven analysis, automation and regulatory science (14, 15).

The transition involves more than one-to-one replacement or the exclusively use of human-relevant modelling. It encompasses the full breadth of agile science: the choice of research strategy and the resulting model selection, methodological innovation, data-driven research, biotechnology, AI, research infrastructure, valorisation and ethical reflection. This aligns with mission-driven innovation policy, in which societal challenges are addressed across ministerial boundaries. The ministries involved should therefore make explicit how their own instruments, including funding, infrastructure, regulation, education and international engagement, contribute to the transition.

Authoritative institutions within the science system can strengthen this movement by placing animal-free innovation on the agenda as an opportunity to advance scientific quality, innovation and valorisation, as well as an ethical challenge. These include organisations such as Royal Netherlands Academy of Arts and Sciences (KNAW), Dutch Research Council (NWO) and the Netherlands Organisation for Health Research and Development (ZonMw), as well as the European Commission, universities and university medical centres, and private organisations including pharmaceutical companies and CROs. This also fits within the remit of 3Rs Centres. One example is the Suppo3Rt programme of the 3Rs Centre Utrecht.[30]

Reflection on *target images* as an instrument for achieving impact[31]
Conversations with stakeholders show that *target images* are a valuable instrument. They stimulate debate, awareness and movement within research domains. At the same time, it is clear that the instrument could be used more effectively to provide direction, coherence and impact within the transition.

The existing *target images* were developed under different circumstances, with variations in commissioning, working group composition, process and final output. This variation allowed for tailored approaches, but limits the recognisability, comparability and impact of the instrument. An improved quality framework could help to set clearer expectations for the process, content and follow-up in advance, without losing scope for domain-specific tailoring.

This includes, among other things, a balanced composition of working groups, concrete and time-bound goals, involvement of relevant societal parties, and a role for the NCad in safeguarding coherence and quality across *target images* and promoting learning between them. Societal input requires a workable format, for example through an advisory group, interviews or consultation, to ensure that scientific ambition, societal relevance and the interests of animals are considered together from the outset.

[30] Utrecht University, 'Suppo3Rt facilitates the integration of NAMs in basic science: a success story', nieuwsbericht, 1 oktober 2025.
[31] https://english.ncadierproevenbeleid.nl/advice/target-images-on-animal-free-research

A consistent message emerging from the discussions is that *target images* gain greater significance when they are linked to ownership, implementation plans and monitoring. Their role in future funding policy could be strengthened, but for both existing and new *target images* this first requires a joined reflection on quality, value for the transition, and scientific and societal relevance. For new *target images* in particular, there is considerable potential in establishing ownership and follow-up from the outset, allowing the *target image* to develop into an instrument for achieving genuine change.

III.2 Funding

Structural funding is essential to move animal-free innovation from scientific promise to broad implementation, but it currently falls short of a structural basis. The National Technology Strategy emphasises that funding, scale-up facilities and market creation are necessary conditions for bringing key technologies into the application stage (16). For animal-free innovation, this means that funding must not stop at method development, but should also support further development, standardisation, validation, scale-up and valorisation.

Important steps have been taken through initiatives such as the Virtual Human Platform (VHP4Safety)[8] and the National Growth Fund project Ombion[11]. At the same time, these initiatives do not remove the need for continued and sustained attention to the broader funding challenge. Such programmes often have a defined duration and thematic focus, whereas the transition requires structural funding across different research categories and for ecosystem functions that are not automatically covered by existing funding models.

This challenge calls for a coherent funding landscape in which public, private and public-private investments complement one another. Public funding remains essential for activities with substantial societal value for which there is no obvious business model, such as validation research, data and tissue infrastructure, reference materials, standardisation, innovation in education and pre-competitive collaboration. Private-sector parties play a crucial role in the further development, application, scale-up and dissemination of new methods. Public-private partnerships are often needed to bring together knowledge, practical experience, data, infrastructure and investment.

Recommendation III.2 The NCad recommends the Minister for Food Security, Fisheries and Horticulture to establish long-term, ecosystem-oriented funding streams for animal-free innovation, in which public, private and public-private investment complement one another and support the full pathway from method development to structural use. Funding programmes should explicitly set out the steps expected to lead to application.

Focus support on structured engagement with end users and market actors from the early development phase, without prematurely forcing new evidence pathways into existing assessment paradigms. This should follow a technology-readiness model and a phased approach in which scientific, technical, regulatory, user and market readiness are assessed together. Funding should be linked to *target images* and phase-out pathways once these have been sufficiently developed, assessed and assigned to responsible parties.

The phase between scientific development and widespread implementation is critical for achieving societal impact, yet often falls in a funding gap between fundamental research funding and application-oriented or market based funding: the so-called *valley of death*. This gap is caused not only by technological immaturity, but also by the incentive structure. Work at this stage is often considered less attractive academically and does not yet fit naturally within commercial funding models. As a result, it remains structurally underfunded.

Ecosystem-oriented funding should specifically support the steps needed to make methods reliable, usable, accepted and scalable. Validation requires particular attention, as it is not an automatic by-product of method development, but a distinct phase with its own expertise, costs, data requirements and need for international coordination. Validation should also not be narrowed down to the question of whether a method reproduces the outcomes of animal experiments. The relevant question is whether a method is fit for answering the research question and, where applicable, improves predictive value for humans.

Part of the challenge is technical. The reproducibility, quality and scalability of human cells, tissues and materials remain genuine challenges. These technical limitations are closely linked to funding: targeted investment in areas including quality control, standardisation and shared production and testing facilities can accelerate their resolution.

Funding needs differ by research category. In fundamental and exploratory research, the emphasis is on methodological innovation, model development, data reuse and creating scope to formulate research questions differently. In translational and applied research, the focus is more often on building evidence, reproducibility, comparison between models and alignment with clinical or human data. In regulatory research, funding is needed for standardisation, validation, acceptance and international coordination. Veterinary, ecological and agricultural research involve different considerations: predictive value for humans is not always central; instead the key issues are quality of model selection, the availability of relevant data and the development of research strategies tailored to the specific research questions.

The role of government is not to replace private investments, but to create the conditions in which public and private efforts reinforce one another. This can be done through long-term programme-based funding, shared standards, pre-competitive collaboration, safe environments for experimentation, support for shared infrastructure, and the removal of institutional or regulatory barriers to implementation.

Public and/or private funding streams should therefore, from the outset, require applicants to set out the intended pathway to scaling-up and valorisation, including the further steps, partners, infrastructure and evidence-building required. This requirement should be applied proportionately. Fundamental research does not need to be immediately market-ready, but it can make explicit which knowledge, infrastructure, partners or evidence-building steps may be needed at a later stage. In this way, funding becomes not only a means of developing new methods, but also an instrument for strengthening the innovation ecosystem.

From safe harbour to regulatory readiness

In 2016, the NCad advised establishing a safe harbour, drawing on the example of the US FDA: a protected setting in which innovative methods could be explored without the resulting data affecting regulatory decision-making. A similar principle can be found in the EMA's Innovation Task Force, where companies can confidentially submit data generated through innovative methods, with the assurance that these data will not be used in regulatory decision-making.

Conversations with stakeholders show broad support for such safe spaces, sandboxes and learning-by-doing environments. At the same time, regulatory safe harbours of this kind are rarely used in practice. The apparent tension between broad support and limited uptake becomes easier to understand when different forms of regulatory experimentation are distinguished.

A safe harbour in which exploratory data have no formal role in regulatory decision-making has an inherent limitation. For companies, the incentive to participate may be limited: the route towards clinical studies is tightly regulated, investments are substantial, and an unexpected signal emerging from an exploratory process may still raise questions later on. Regulatory authorities face the opposite difficulty. A significant safety finding cannot simply be disregarded on ethical grounds, even where it was agreed in advance that the finding would fall outside the formal assessment. The assurance that such data will remain outside consideration therefore becomes difficult to maintain once they prove genuinely relevant.

Two other approaches appear more promising. The first is a pre-competitive space for dialogue, in which researchers, regulatory authorities and industry share data, bottlenecks and vulnerabilities without an immediate formal assessment being at stake. The second is to explore innovative approaches in parallel with a conventional regulatory dossier. The Scientific Committee on Consumer Safety (SCCS), for example, assessed a UV filter for which a dossier based on a Next Generation Risk Assessment approach was submitted alongside the standard dossier. This made it possible to examine the innovative approach while maintaining the required level of protection (36).

For policymakers, this means that regulatory readiness cannot be organised as an optional or retrospective process, while at the same time new methods should not be forced from the outset to conform to existing assessment paradigms. Regulatory expertise should be available from an early stage, while sufficient room remains to develop new pathways to evidence. The technology-readiness framework being developed by Ombion and Oncode reflects this approach by identifying, at each stage, when regulatory or commercial alignment becomes relevant. The FDA example points in the same direction: progress was driven not by observing innovation from a distance, but by the regulator actively requesting human data in areas where animal models were considered insufficient.

The core of this recommendation is therefore not a general shift in funding, but better alignment of funding instruments with the different stages and functions of the innovation system. The funding landscape as a whole should ensure that promising methods do not stall between scientific publication and actual use. Wherever possible, funding should be linked to concrete phase-out objectives for research involving animals and should support initiatives that offer an animal-free pathway for activities associated with stable or increasing levels of animal use.

Target images can play an important role in guiding funding, but only where their status and follow-up arrangements are clear. Existing *target images* were not developed with this purpose in mind. Linking individual or interconnected *target images* to funding therefore first requires an assessment of their quality, transition value, and scientific and societal relevance. For new *target images*, the format should be designed from the outset in such a way that it can support connections with appropriate funding instruments.

III.3 Infrastructure: data, biobanks and core facilities

Animal-free innovation relies on high-quality data, human-derived material and shared facilities. Promising innovations will only gain broad credibility when the underlying evidence is findable, interpretable, interoperable, reusable and reproducible. Conversations with stakeholders show that the absence of such an evidence base is itself a barrier to the acceptance of new methods.

The necessary infrastructure is partly already in place, but it is not yet sufficiently aligned with the needs of the transition. Existing data infrastructures, biobanks and facilities are often organised around specific research domains, poorly connected to one another and not systematically accessible for animal-free innovation. The challenge is therefore not to build an entirely new infrastructure, but to adapt existing facilities explicitly to support the transition and supplement them where necessary.

Recommendation III.3 The NCad recommends the Minister for Food Security, Fisheries and Horticulture, together with the responsible members of the government and relevant infrastructure stakeholders, to explicitly adapt existing data, material and research infrastructures to support animal-free innovation. This should include safeguarding quality standards, interoperability, sustainable access to human-derived material, the reuse of both human data and historical animal data, shared core facilities, and secure forms of data visiting.

The orchestrating role, in collaboration with relevant infrastructure stakeholders, funders and subject-matter experts, should develop a proposal for the infrastructure required, both nationally and at European level. This proposal should identify which components require public-private partnerships. It should then be used to inform the design and adjustment of policy and funding programmes.

The earlier NCad policy advice on human tissue remains relevant in this context. The challenges identified there, concerning availability, accessibility, professionalisation, harmonisation and connectivity between systems, directly affect the practical feasibility of animal-free innovation.

The infrastructure challenge is also a ecosystem challenge. Universities, university medical centres, knowledge institutions, companies, CROs, biobanks, data platforms, funders, assessors and societal parties all have a role to play in ensuring that data, human-derived material, standards, shared facilities and assessment pathways are organised in a way that makes them usable and reliable. This is consistent with the

broader innovation logic of national and European policy agendas: key technologies only reach application when knowledge development is connected to facilities, funding, users, implementation capacity and pathways to application (15-17).

The issue is not only one of availability, but also of quality and interoperability. Human datasets, human-derived material, testing facilities and reference materials need to be shareable, comparable and reusable under appropriate conditions. Standards for data quality, metadata, provenance, consent, reproducibility and model description are needed to enable results to be interpreted across institutions, domains and applications. Without such standards, new methods remain difficult to compare and the evidence base lacks sufficient credibility. Data visiting offers a relevant approach in this respect (see text box).

The infrastructure challenge operates at three levels. At national level, the focus is on making existing facilities accessible and interoperable. At European level, harmonisation of standards and interoperability are needed to ensure that Dutch infrastructure connects with and contributes to broader European infrastructures. Public-private partnerships are needed for shared facilities that no individual organisation would be expected to fund or manage alone. Together, these three levels should ensure that knowledge, data, materials and expertise become available to support robust and practically implementable animal-free research strategies.

Data infrastructure and data visiting as drivers of animal-free innovation
The primary challenge is not to build new centralised databases, but to make existing infrastructures FAIR, semantically interoperable and suitable for responsible querying. With data visiting, data remain at source wherever possible, while analyses, algorithms or research questions are brought to the data. This enables the use of human data, historical animal data, experimental data and other sources of knowledge while preserving control over the data, privacy, security and data provenance.

The Netherlands already has important building blocks in place, several of which are highlighted here. Health-RI is developing an integrated data infrastructure for data-driven research, policy and innovation, with a focus on the reuse of health and life sciences data. This directly addresses a key need in animal-free innovation: human data, biomedical data, human-derived material and research data need to become more findable, interoperable and reusable.[32]

Relevant building blocks also exist for viable human tissue. VitalTissue[33] makes residual human tissue from healthcare available for scientific research. This is important for animal-free innovation because human-based models depend on suitable, well-documented human-derived material being available when needed (37).

Within this broader approach to infrastructure, data visiting is particularly relevant. Its central principle is that data do not always need to be stored centrally in order to be used. Instead, algorithms and analyses are brought to the data within trusted infrastructures. This combines privacy, control over the data, security and scientific usability. LIFES demonstrates how this principle can be put into practice. LIFES is working to connect experimental data, clinical information and existing scientific knowledge, including through knowledge graphs. This is relevant to animal-free innovation because new models and data-driven methods can only develop further if dispersed datasets and existing knowledge can be systematically combined and interpreted.[34]

Data-driven breakthroughs such as AlphaFold show how new models can build on many years of carefully collected and standardised research data.[35] Animal-free innovation faces a similar challenge: historical animal data, human data and experimental data need to become more findable, interpretable, interoperable and reusable, enabling their use in the development of new models, method comparison and animal-free research strategies.

[32] Health-RI, 'Data-Driven Health: Connecting, Sharing and Reusing'.
[33] VitalTissue, 'Together for Better Healthcare and Fewer Laboratory Animals'.
[34] LIFES, 'FAIR, Equitable and Sustainable Data Reuse', LIFES Association.
[35] Google DeepMind and EMBL-EBI, AlphaFold Protein Structure Database.

III.4 Education and professional development

The transition ultimately depends on the people: students, doctoral candidates, analysts, researchers, assessors, regulatory professionals, entrepreneurs and other professionals. New methods will only become established in routine practice if current and future professionals learn to work with them, are able to assess them critically and consider them as a matter of course when choosing a research strategy.

Education is not simply about transferring knowledge; it also shapes professional culture. Degree programmes, doctoral training, lifelong learning programmes and professional practices influence which research strategies and methods come to be regarded as standard, authoritative or necessary. Model selection is therefore not purely an individual decision. It is also shaped by education and training, available expertise, methodological traditions, publication practices and assessment criteria within scientific and professional communities.

This development is not starting from scratch. Education, continuing professional development and research practice already include attention to animal-free methods, critical model selection and ethical reflection. For academic education, the field has also articulated this direction in a *target image* for educational innovation (UNL/NFU), which calls, among other things, for wider use of available animal-free teaching methods (38).

The task is to build on this foundation and structurally embed these developments across education, training and research practice. Stakeholder meetings highlighted that existing education and training structures are still largely organised around the animal model as the conventional standard. As a result, students are primarily taught to work within that norm rather than also learning to question it. Several specific bottlenecks were identified, including certification requirements that emphasise competence in working with animals used for scientific purposes, a growing international influx of researchers with widely varying prior knowledge, and the absence of a shared language between researchers who work with animal models and those developing animal-free methods. These signals point to a broader pattern: progress is being made, but structural embedding has not yet been achieved.

This challenge aligns with the Netherlands National Technology Strategy and the European Life Sciences Strategy, both of which place strong emphasis on talent development and on ecosystems that connect research, innovation, skills and application. For animal-free innovation, this means that professionals need to be able to work at the intersection of fundamental and translational biomedical science, data science, ethics, engineering, clinical relevance and industrial application (15, 16).

Education and professional development can therefore serve as a positive lever for *future-agile science*. Life sciences curricula can prepare students for the science of tomorrow by equipping them with knowledge of the full range of methods, skills in critical model selection, familiarity with ethical reflection, and an understanding of human-based, data-driven and animal-free approaches.

Recommendation III.4 The NCad recommends the Minister for Food Security, Fisheries and Horticulture, together with the Minister of Education, Culture and Science (OCW), to structurally orient education, vocational education and professional development in the life sciences are structurally towards *future-agile* science. Curricula and lifelong learning programmes should embed knowledge of the full range of available methods, critical assessment of research strategies and model selection, ethical reflection, data science, regulatory science, and the development and application of animal-free approaches. Attention should also be given to internationally trained researchers with diverse prior knowledge and established ways of working.

5.IV International strategy

Recommendation IV. Coordinate Dutch efforts through a coherent international strategy for multilateral and bilateral cooperation.

The transition is taking place within an international system of scientific practices, market authorisation requirements, validation standards, publication cultures, funding criteria and trade obligations. National investment will therefore only have broad impact when animal-free innovations are also recognised, accepted and applied internationally. The Netherlands has strong scientific expertise, innovative research infrastructure, public-private networks and experience with transition-oriented policy. However, this position only gains strategic significance when Dutch efforts are brought together in a coherent and recognisable way.

Stakeholders in the field point to fragmentation between initiatives, differences between sectors and varying expectations about what is needed for broad implementation, all of which limit the effectiveness of national efforts. Effective multilateral engagement requires authorities, knowledge institutions, funders, companies and societal actors to align their approach at a national level in advance. This should establish which priorities the Netherlands seeks to advance, through which forums, and which European and international developments are most relevant.

Dutch efforts should focus not only on accelerating progress nationally, but also on shaping international norms around research involving animals. This requires coherence between multilateral engagement, bilateral cooperation and participation in international research and innovation networks. It is not only about formal regulation and validation, but also about quality criteria, data infrastructure, education, exchange of expertise, scientific assessment practices and building confidence through case studies, parallel studies and regulatory learning environments.

An international strategy serves two purposes. It increases the likelihood that national investments and research findings contribute to international recognition and implementation. It also enables Dutch expertise to be strategically deployed in the forums where international frameworks are shaped. Together with other countries, the Netherlands can work towards shared pathways for phasing out the use of animals in scientific research and education, including shared objectives, with attention to knowledge development, implementation and differences between research domains.

IV.1 International narrative

An international strategy requires a consistent narrative. The way animal-free innovation is presented influences how it is perceived internationally. Framing such methods as ‘alternatives’ can easily preserve animal experiments as the implicit norm, placing animal-free methods in a derivative position. Animal-free methods should be assessed on their own scientific merits and not solely by comparison with animal models, particularly where the animal model itself is not an inherently appropriate benchmark.

Recommendation IV.1 The NCad recommends the Minister for Food Security, Fisheries and Horticulture, together with the other responsible ministers, to consistently communicate a single shared core narrative: animal-free innovation achieves replacement not primarily by reproducing existing animal experiments one-to-one, but by transforming research questions, evidence strategies and science itself. Methods should be assessed on their relevance, reliability, societal significance and ethical justification, rather than against the animal model as an assumed standard.

The 3Rs provide the internationally shared framework for this policy. The transition builds on this framework. It gives effect to replacement at the level of the research system and therefore goes beyond replacing an existing animal experiment on a one-to-one basis. It is part of *future-agile* science and encompasses model selection, more meaningful research, data-driven science, new biotechnological possibilities and ethical justification. This requires precision: uncertainties and limitations of

animal-free methods must be clearly communicated, as overselling undermines trust. The distinctions between regulatory research, fundamental research, and translational and applied research must also remain explicit, as pathways towards implementation and acceptance differ between research categories.

A constructive narrative does not frame the transition as a choice between maintaining or abolishing animal procedures, but starts from the question of what makes research scientifically sound, ethically justified and societally valuable. This encompasses not only the scientific quality and relevance, but also the care with which animals and their interests are treated. The central questions are: which research questions are asked, which models are selected, which assumptions remain implicit, and how are ethical considerations justified? This shifts the focus away from general positions on animal experiments towards the conditions that enable animal-free innovation to become embedded in research, assessment and implementation.

The core narrative should be reflected consistently in ministerial communications, international presentations, funding calls, educational modules, regulatory processes and progress reporting. This prevents the Netherlands from sending mixed messages internationally: being ambitious in animal welfare and innovation policies, while being less clearly aligned in regulatory and scientific assessment practices.

IV.2 Priorities for multilateral engagement

Multilateral engagement is essential because many of the conditions that determine whether animal-free innovation can progress are shaped internationally. The Netherlands should therefore engage across a range of international forums, not only those concerned with the formal validation or acceptance of methods, but also those that influence research funding, the usability of data, which models are regarded as authoritative, and what kinds of evidence are considered persuasive.

The key question is not how widely the Netherlands can be represented, but where Dutch expertise and national priorities are best placed to contribute to and benefit from international developments. This may be in areas where Dutch knowledge institutions and companies are already leading, in international initiatives in which the Netherlands is already involved, or in standards and assessment practices that do not yet adequately accommodate the broad use of animal-free innovation.

Recommendation IV.2 The NCad recommends the Minister for Food Security, Fisheries and Horticulture, together with fellow ministers, to formulate a coherent international strategy that translates the core narrative on the transition towards a society without animal experiments set out in IV.1 into clear priorities for Dutch action in multilateral forums, bilateral partnerships, and international research and innovation collaboration. The strategy should make explicit what changes the Netherlands seeks to achieve in international norms, frameworks and assessment practices, and where Dutch expertise and international developments can most effectively reinforce one another.

This prioritisation is urgent because several international developments are now converging, including the European roadmap[14], the ERA4NAMs initiative[36], in which the Netherlands plays a leading role, and national strategies outside the European Union, such as those of the United Kingdom[15], the USA[16] and Canada[37]. Without clearly defined priorities, there is the risk that the Netherlands participates in relevant international initiatives but does not clearly demonstrate which objectives it seeks to advance through them.

Setting clear priorities would align multilateral engagement with the national transition strategy. International cooperation supports national objectives within specific research domains, while national priorities guide Dutch engagement in European and global forums.

[36] European Commission, Directorate-General Research and Innovation, 'Accelerating New Approach Methodologies (NAMs) to Advance Biomedical Research and Testing of Medicinal Products and Medical Devices', in ERA Actions 2025–2027.

[37] Environment and Climate Change Canada en Health Canada, Strategy to Replace, Reduce or Refine Vertebrate Animal Testing under the Canadian Environmental Protection Act, 1999, juli 2025.

Regulatory harmonisation as an example
Regulatory harmonisation illustrates why clear international priorities are needed. Animal-free innovations are not assessed through a single, uniform system. In safety assessment, OECD Test Guidelines are among the key frameworks, whereas in the pharmaceutical domain the route more often involves qualification, standardisation and defining the context of use. The pathways to recognition and actual use therefore differ from one domain to another.

Formal acceptance of a method does not in itself mean that it will be taken up in regulatory processes or used in practice. Discussions on regulatory research have emphasised that regulation plays an important role in shaping the choices made by private-sector organisations. When international frameworks provide a scope for animal-free innovations, and that scope is applied consistently and predictably in regulatory practice, organisations have greater reason to invest in these methods and to use them in practice. Changes to legislation and terminology can help create that scope, for example by replacing explicit requirements for animal experiments with method-neutral wording. This shifts the focus away from prescribing a specific method and towards the quality and relevance of the evidence.

IV.3 Bilateral cooperation

Bilateral cooperation with like-minded countries is not a substitute for multilateral engagement, but a way of accelerating progress. While multilateral processes often progress gradually, smaller coalitions can move more quickly to build practical experience and evidence, strengthen common positions and prepare joint proposals.

Recommendation IV.3 The NCad recommends the Minister for Food Security, Fisheries and Horticulture to work with like-minded countries on targeted bilateral initiatives that build practical experience and evidence and strengthen international coalitions. These initiatives should be used to advance reforms that create a level playing field for animal-free innovations, both within regulatory frameworks and validation standards and in the criteria governing how scientific research is funded, assessed and published.

The Netherlands can use such cooperation to create practical opportunities for joint learning, including through case studies, parallel assessments, regulatory learning environments, data sharing and comparisons of assessment criteria. These initiatives make visible the conditions under which animal-free methods are considered reliable, fit for purpose and acceptable by researchers, companies, funders and assessment bodies.

Bilateral cooperation can also be pursued beyond the regulatory domain. Examples include joint funding calls, closer coordination between research funders, agreements on data sharing, the development of data visiting protocols, aligned assessment criteria for human models, and joint training for researchers and assessors. The knowledge, experience and evidence generated through these activities can subsequently inform discussions and decision-making in multilateral forums.

5.V Progress and monitoring

Recommendation V. Monitor the transition in an integrated and coherent manner.

The transition towards a society without animal experiments requires monitoring that looks beyond trends in the number of animal experiments. Those figures remain relevant, but cannot, on their own, explain how the increasing availability of animal-free innovations affects the number of animal experiments. This is evident,

among other things, from Dutch records on animal experiments since 2015: years in which the number falls alternate with years in which it rises, even as more animal-free methods become available year after year. The relationship is therefore not a straightforward one in which an increase in one automatically leads to a decrease in the other.

A decline may reflect replacement, but it may also result from research being relocated to other countries or transferred to private-sector organisations, or from a combination of these factors. An increase may indicate that change has failed to materialise, but it may equally reflect growth in research fields where animal-free methods are not yet widely used, changes in legislation and regulation, or additional research involving animals prompted by findings from animal-free methods.

In the context of a transition, monitoring has a specific purpose: it generates steering information on the basis of which the government evaluates the direction of travel and adjusts course where necessary. This cycle of monitoring, evaluation and course correction is only effective if it is assigned to an actor with the mandate and the standing to interpret findings, place bottlenecks on the agenda, and hold actors responsible for policy delivery to account for necessary adjustments. Independent monitoring should be organised as set out in Recommendation V.3. The orchestrating role described in Recommendation I.2 should use and interpret the findings to inform agenda-setting and governance-level course correction.

This is consistent with insights from transition studies. Transitions do not follow a linear path, and their effects often become visible only after considerable time.

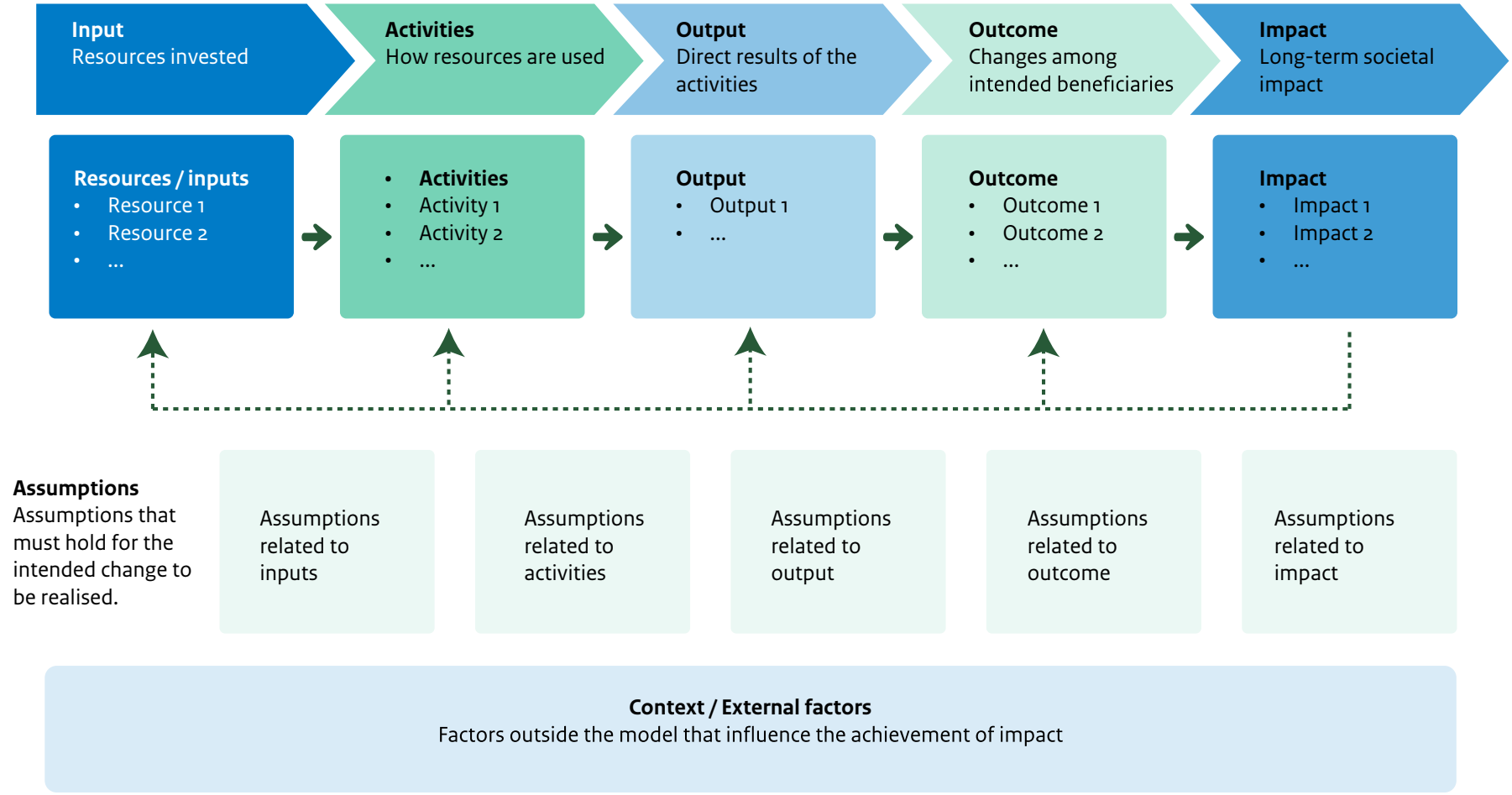
A monitoring system that only records what has already happened is, by definition, lagging behind system developments. Effective governance therefore also requires interim qualitative indicators that reveal change before it becomes visible in quantitative data: Is knowledge being shared? Are funding and infrastructure adequate? Are assessment practices changing? Are new ways of working being scaled up? And, where possible, are established routines that impede progress being redirected or phased out?

Monitoring also helps government deal with uncertainty in governance. It makes visible where stakeholders can organise change themselves and where a connecting or facilitating role is sufficient. At the same time, monitoring shows where progress is not being made, where dependencies remain unresolved, or where a more active coordination and strategic direction is required.

V.1 Monitoring framework based on a Theory of Change

Without an explicit account of how change is expected to occur, monitoring can easily end up measuring what is readily available rather than what matters. A Theory of Change (Figure 3) sets out the changes being pursued, the interventions and mechanisms through which they are expected to occur, the assumptions and dependencies involved, and the relevant time horizons. It thereby provides the link between the five pillars, the indicator framework and adaptive course correction. This Transition Policy Advice provides the change architecture and the core substantive logic for a Theory of Change (see Figure 4).

Figure 3. Generic model for a Theory of Change



A Theory of Change explicitly sets out how inputs and activities are expected to lead to outputs, outcomes and impact, and identifies the assumptions underpinning each step in this pathway of change.

Its further development, testing and periodic reassessment should take place through co-creation. The recommendations identify the key pillars: ownership, coordination and strategic direction; reassessment of the ethical framework; stronger innovation policy and policy across the research and innovation chain; education and infrastructure; and an international strategy. The Theory of Change should translate this core logic into a testable framework: what change is expected, through which levers for change, on the basis of which assumptions, in what sequence and over what timeframe?

Recommendation V.1 The NCad recommends the Minister for Food Security, Fisheries and Horticulture to commission the development of a Theory of Change for the transition towards a society without animal experiments, based on the core logic of this Transition Policy Advice.

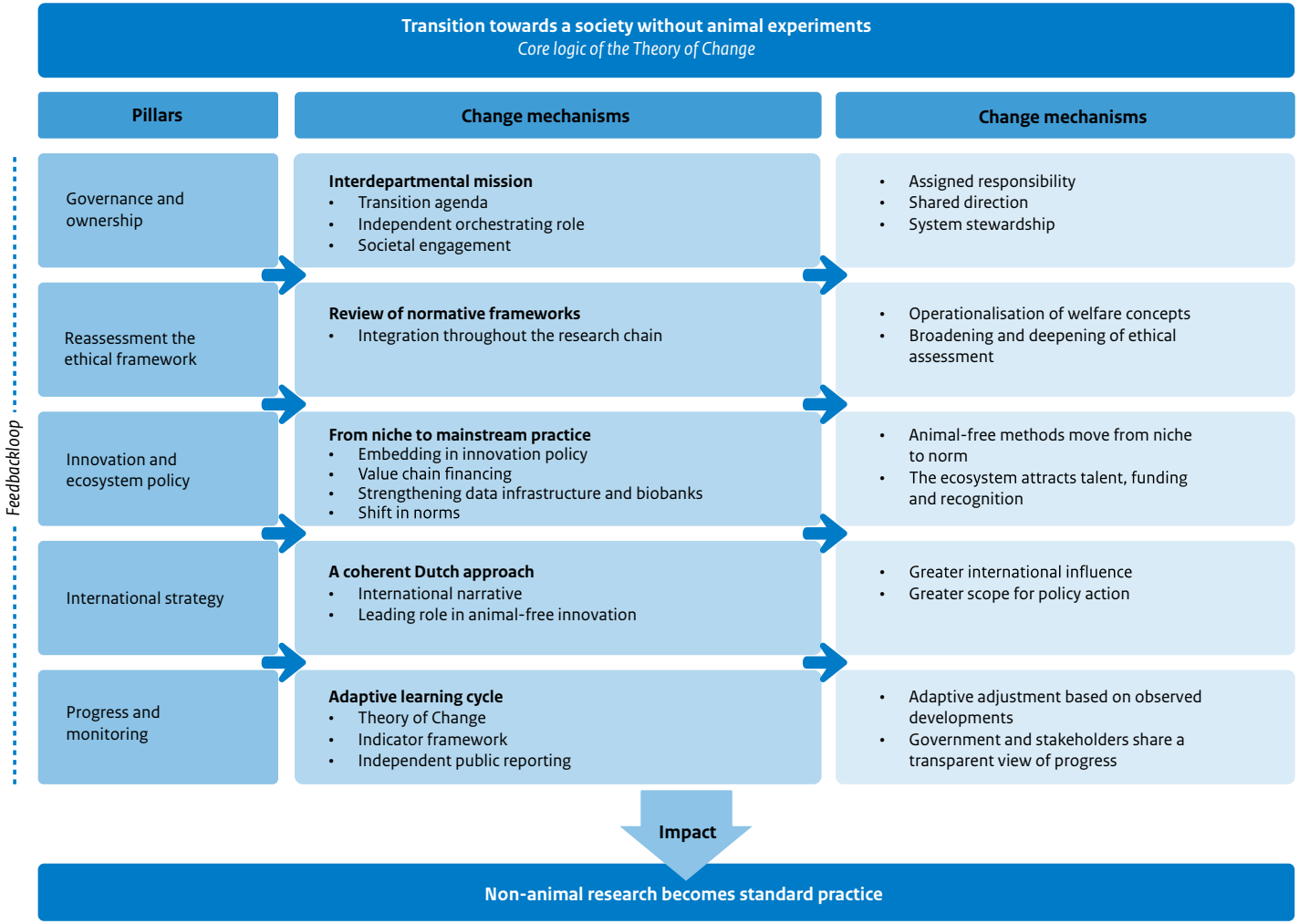
The orchestrating role should take ownership of the process of developing and periodically reassessing the Theory of Change. It should ensure that the Theory of Change is developed with independent methodological support and through co-creation with relevant actors. Adoption and any subsequent revisions should take place within the interministerial structure set out in Recommendation I, ensuring that the Theory of Change is embedded in government decision-making and serves as the foundation for monitoring, evaluation and adaptive learning.

The Theory of Change should explicitly map which combinations of interventions can create positive feedback loops and potential tipping points, which interventions are enabling conditions, and where unintended consequences or rebound effects may occur.

Because the actors operate from different roles, interests and time horizons, a useful Theory of Change must be developed through co-creation. Researchers, developers, assessors, funders, policymakers and civil society organisations should jointly construct and validate the causal links and indicators. The Theory of Change must show which changes are prerequisites for others. Without funding, training and data infrastructure, animal-free methods are unlikely to become standard practice. Without adapted assessment criteria, new methods will remain at a disadvantage in funding applications, publications and regulatory assessment. Because research domains differ in their dynamics and pace of change, the Theory of Change must also provide scope for domain-specific *target images* as a basis for outcome and system indicators.

The Theory of Change determines which indicators are relevant, which domains require priority attention and when course correction is needed. Without this shared change logic, monitoring risks becoming limited to recording what is already availabe, such as numbers of animal experiments, while the underlying levers for change that drive the transition remain out of sight.

Figure 4. Core logic for the Theory of Change of the transition towards a society without animal experiments



Together, the pillars of this Transition Policy Advice set out the core logic, or logic of change, for making non-animal research standard practice. The five pillars are shown on the left, the underlying mechanisms of change in the centre, and the intended change on the right. This core logic provides the basis for a Theory of Change to be developed through co-creation.

V.2 Indicators: two levels

Without a limited but relevant set of indicators, the Theory of Change remains a line of reasoning that cannot be tested. Not everything that can be measured merits inclusion in the monitoring framework. Indicators must inform governance and align with the pillars of this policy advice. They should show where progress is being made, where stagnation occurs, which assumptions do not hold and which actor needs to act.

The indicator framework therefore consists of two levels. Outcome indicators build on existing records, such as the number of animal experiments and available data on the use of animal-free methods. System indicators show whether the conditions under which animal-free innovation can become standard practice are changing. The distinction between the two levels is crucial: measuring outcomes alone provides information too late for effective adjustment, while measuring system conditions alone risks becoming non-committal if it remains unclear whether those changes ultimately lead to reduced use of animals in research.

Recommendation V.2. The NCad recommends the Minister for Food Security, Fisheries and Horticulture to develop, on the basis of the Theory of Change, a focused set of indicators structured around two interrelated levels. Outcome indicators should track and interpret changes in animal use and in the application of animal-free research strategies. System indicators should track whether the conditions for change are shifting, including ownership, funding, infrastructure, training, assessment practices, regulatory acceptance, market development, and whether routines that impede progress are being phased out.

Outcome indicators build on existing records, including the number of animal experiments, the number of animals used for scientific purposes, types of research, classifications of distress, licences and available data on the use of animal-free methods. These data remain relevant, but become meaningful only when interpreted together and by research domain. The recent NCad report on Animal Procedures in the Netherlands 2015–2024 shows that the overall picture comprises distinct dynamics within individual research categories, each with different underlying causes and different options for action (1). A change in the number of animal experiments is therefore not, in itself, a measure of progress or stagnation. It is necessary to establish what is driving that change: actual replacement, shifts in research questions or fields of research, changes in regulation, different implementation practices or new societal research obligations. Outcome indicators therefore always require interpretation within the context of the transition challenge, including the scope for action available to the actors involved.

System indicators show whether the conditions under which animal-free innovation can become standard practice are changing. The literature on transitions and innovation systems identifies a set of interrelated processes: developing and disseminating knowledge, creating markets, mobilising resources, experimentation by frontrunners, building legitimacy and providing direction (39-41). Together, these processes determine whether a promising method can develop into mainstream practice. Some of them can be quantified while conditions such as legitimacy and trust require qualitative and narrative interpretation.

Applied to this transition, these processes correspond to the pillars of this policy advice. The system indicators show whether the levers for change associated with those pillars are actually beginning to drive change. Stakeholders suggested a number of possible indicators during the meetings, including investment in animal-free methods, the number of methods and submissions accepted for regulatory purposes, the uptake of pre-registration and open data practices, and changes in attitudes among researchers and the public. These examples indicate the kinds of indicators that may be useful. The monitoring framework itself will be developed in greater detail on the basis of the Theory of Change. This will require clarity about the knowledge, evaluation frameworks and data needed to monitor progress, system change and the effects on animal welfare and innovation. Within this level, a category is also needed to captures the phase-out of existing practices, including the removal of animal experiments from information requirements and research routines.

The European roadmap offers useful guidance.[14] ‘Engagement indicators’ could, for example, provide insight into knowledge sharing, awareness, collaboration and public engagement. ‘Status indicators’ could track the development, validation, funding, industrial use and regulatory acceptance of animal-free innovations. ‘Counter-progress indicators’ are important for identifying

mechanisms that impede progress, such as animal-free methods triggering additional animal experiments, or funding biases that favour research involving animals. Where possible, the Netherlands should align its indicators with those being developed for the EU roadmap, without making the national framework dependent on that process.

Within the system indicators, particular attention should be paid to ownership, coordination and strategic direction. This lever of change is a prerequisite for progress under the other pillars. Assigning responsibilities, setting interim goals and ensuring government-level follow-up provide the foundation for using the indicator framework effectively to make adjustments in practice. Without this institutional embedding, changes in ethics, innovation, education and international engagement remain vulnerable.

V.3 Independent, public monitoring

Monitoring must be carried out independently and reported publicly. This is essential in a transition where scientific, economic, ethical and societal interests intersect. Independence prevents monitoring from being reduced to policy communications about progress and increases the likelihood that stagnation, blind spots and unintended consequences are also brought to light. Public reporting is necessary because the transition is not merely an internal policy challenge. It affects science, patients, animal welfare, innovation, safety, education, industry and societal legitimacy.

In this context, independence has three dimensions. Substantive independence requires the analysis to remain free from policy preferences or institutional interests. Organisational independence requires the body carrying out the monitoring to operate separately from the commissioning ministries. Independence in governance requires interpretation and agenda-setting to rest with the orchestrating role, rather than with the policy directorate responsible for the transition. Only when all three are safeguarded can monitoring fulfil its purpose: bringing uncomfortable findings to light and authoritatively placing the need for course correction on the agenda, even when this is politically or institutionally inconvenient.

Recommendation V.3 The NCad recommends the Minister for Food Security, Fisheries and Horticulture to assign responsibility for monitoring with an independent body that is institutionally separate from the commissioning ministries. Establish a fixed evaluation cycle, preferably every three years. Monitoring is effective when, in each cycle, the assumptions underpinning the Theory of Change are tested, trends and areas of stagnation are interpretted, and it is identified where course correction is required. The orchestrating role coordinates the process, interprets the findings and brings conclusions and required actions onto the agenda within the interministerial structure.

Existing records provide an important starting point, but must be interpreted in context if they are to inform the transition. The recent NCad report Animal Procedures in the Netherlands 2015–2024 shows that figures alone provide only limited insight into the developments and factors behind them (1). Linking records on the use of animals to the non-technical summaries submitted with project licence applications could help to identify patterns more clearly. In which types of research are animals being used? Which alternatives were considered? What barriers are reported, and where do these call for course correction? Existing tools can also provide data for the monitoring framework. At organisational level, the Beyond Animal Testing Index (BATI) maps the efforts made by institutions in relation to animal experiments and animal-free innovation, and can therefore contribute to outcome and organisational indicators (42). Such sources do not replace the system-wide framework, but provide data for it.

Reporting must go beyond publishing figures. It must interpret trends, breakthroughs and stagnation. It must show which developments are consistent with the Theory of Change, which assumptions prove incorrect, where research domains diverge and where indicators need to be reassessed.

Data collection and analysis should be assigned to an independent body, which reports publicly on its findings. Wherever possible, existing data collection should be used to avoid creating unnecessary new infrastructure and administrative burdens. The orchestrating role interprets the findings in conjunction with the transition policy agendas, places necessary course correction on the agenda and reports on government-level follow-up. This keeps independent analysis and policy responsibility clearly distinct.

6.

Follow-through on the Transition Policy Advice

6.1 Uptake and follow-up of the Transition Policy Advice

This policy advice advocates a system change that emerges through the interaction between niches, the regime and the landscape, and is supported by many different parties. The same logic applies to how this Transition Policy Advice takes effect. The recommendations cannot be implemented through a single decision; instead the responsible actors must translate them into their own domains and practices. A policy domain formulates specific interim goals, a funder adjusts its assessment criteria, an educator updates its curricula and a regulatory authority develops appropriate evidence pathways. This translation is necessary, but the guiding ultimate goal and the coherence between the five pillars together form an indivisible whole.

Keeping with its statutory and independent advisory role, the NCad will continue to monitor how the Transition Policy Advice is interpreted and what new questions arise in practice. It will not assess day-to-day implementation, which is the responsibility of ministers, the orchestrating role and system actors, but rather the continued validity of the normative guiding principles, the coherence of the pillar architecture and the need for additional policy advice.

In future, this may give rise to new policy advice where the field interprets the framework set out in this policy advice more narrowly or differently than intended, where it encounters limits that require separate consideration, and where the premises underpinning this policy advice warrant revision in light of what has since become apparent. The follow-up agenda in Section 6.2 is the first application of this approach. It is not a list of topics left unaddressed by this policy advice, but a set of issues that became apparent because, while this policy advice was being developed, the field was already translating it into its own practices and encountered the limits of what the framework of this Transition Policy Advice can provide.

6.2 NCad follow-up agenda

The NCad actively informs and develops its follow-up agenda. The continued validity of the ethical framework and the pillar architecture depends on up-to-date scientific, societal and practical insights. In the coming years, the NCad will therefore continue to organise meetings, expert sessions and focused discussions bringing the relevant parties together around existing and emerging questions. In this way, the NCad brings together knowledge needs and perspectives, but does not fulfil a coordinating role and is not responsible for monitoring or governance adjustments to the transition.

Policy advice on system change inevitably reaches the limits of its own scope. It is precisely by considering the transition as system change that related questions come into view which nevertheless fall outside that scope. Such questions arose repeatedly during the development of this Transition Policy Advice. The NCad presents them here as an initial outcome of the learning approach described in this chapter. They will inform the NCad's follow-up agenda and can be explored in greater depth and expanded through that approach.

Research without animal-derived materials. This Transition Policy Advice concerns the transition towards a society without animal experiments. However, many non-animal methods still use animal-derived products, such as foetal bovine serum or basement membrane extracts used in cell culture and known by brand names including Matrigel, Geltrex and Cultrex. A method that does not use laboratory animals is therefore not necessarily free from animal-derived materials. The NCad has previously drawn attention to this issue, including by providing information on the concerns surrounding foetal bovine serum and the availability of animal-free alternatives.[38] Avoiding animal-derived products, and pursuing research without animal-derived materials more broadly, raises distinct scientific questions, for example about the variability and reproducibility of animal-derived materials, and has its own dynamics in terms of development and availability. The NCad will address this in a separate policy advice.

Refinement. As long as animals continue to be used in research, refining the conditions under which they are used remains essential. Refinement concerns limiting pain, suffering and distress, not only during the procedure but throughout the animal's entire life, from breeding and transport to housing and care. Increasingly, refinement also encompasses positive welfare, opportunities to express behaviour and freedom of choice, concepts that have been placed at the heart of the updated ethical assessment. Refinement therefore operates at the level of the individual animal and the day-to-day practice of research and animal husbandry. It is relevant to every animal that continues to be used and requires a dedicated development agenda, with its own expertise and standards. The NCad will address this in a separate policy advice.

The future of *target images*. Building on the findings of this Transition Policy Advice concerning *target images*, the NCad envisages a follow-up policy advice to further develop the *target image* instrument, including a standard format and a reference framework for quality, assessment prior to publication and coherence. This should include clear arrangements for three roles that were not adequately assigned in the existing *target images*. First, a *target image* should be commissioned or endorsed by the relevant policy domain, preferably as part of the transition agenda of the responsible minister, so that it has a clear mandate and is followed up. Second, responsibility for developing and supporting a *target image* should lie with the field, preferably with the relevant professional association. Third, the NCad should safeguard the quality and coherence of the instrument as a whole. In addition, current practice requires greater attention to the implementation, facilitation and monitoring of *target images*.

'Target-species research'. Fundamental research and translational and applied research in which humans are not the 'target species', such as the use of birds to measure biodiversity loss, are not explicitly addressed in this Transition Policy Advice. The NCad considers this a distinct domain within the research categories and envisages a separate policy advice devoted to this domain.

[38] https://english.ncadierproevenbeleid.nl/documents/20/6/1/careful-use-of-fetal-calf-serum-for-reliable-research-results-and-taking-into-account

Appendix 1

Participants in the stakeholder meetings and expert contributions

The NCad gratefully drew on input from stakeholders and experts from the Netherlands and abroad. Those consulted are not co-authors of this Transition Policy Advice and may hold opinions on certain points that differ from those presented by the NCad in this Transition Policy Advice. Some participants are listed solely by their organisational affiliation.

Input was gathered through an open survey, a series of thematic stakeholder meetings, a final stakeholder meeting and in-depth interviews. Respondents to the open survey who did not take part in the stakeholder meetings or interviews are not listed individually. Participants in the final meeting are not listed individually.

The following people took part in the thematic stakeholder meetings:

Participating organisation	Participant
European Food Safety Authority (EFSA)	dr. Z. Al Harraq
Utrecht University	prof. dr. S. Arndt
Charles River Laboratories Den Bosch	dr. M. Beekhuijzen
BioDetection systems (BDS)	dr. P.A. Behnisch
European Commission - Joint Research Centre (EC - JRC)	dr. E. Berggren
PAASP (Partnership for Assessment and Accreditation of Scientific Practice)	dr. A. Bespalov
Utrecht University	prof. dr. B.J. Blaauboer
Leiden University Medical Center (LUMC)	dr. T. de Boer
Wageningen University & Research (WUR)	prof. dr. P.J. Boogaard
ZonMw	K. Bos, MSc.
Leiden Academic Centre for Drug Research (LACDR) / Leiden University	prof. dr. I. Bot
Eindhoven University of Technology	V.V. Brunsberg, MSc.
Dutch Society for the Replacement of Animal Testing	A. Burgers, MSc.

Participating organisation	Participant
VU Amsterdam	prof. dr. M.B.M. van Duursen
Humane Society International/Europe	A. Effraimidou, MSc.
Amsterdam UMC	prof. dr. T.B. Geijtenbeek
Donders Institute for Brain, Cognition, and Behaviour/ Radboud University	dr. L. Genzel
Amsterdam UMC	prof. dr. S. Gibbs
hDMT	dr. ir. J. van Ginkel
Shell Global Solutions International B.V.	dr. M. Guarin
Rathenau instituut	dr. M. Habets
The Netherlands Environmental Assessment Agency (PBL)	A. Hanemaaijer, MSc.
SAFE consortium	L. Hansell, MSc.
Danone Global Research & Innovation centre, Utrecht	dr. J. van der Harst
European Animal Research Association	dr. M. Havermans
Netherlands Institute for Neuroscience	dr. A. Heimel
Radboud UMC	dr. M. Henckens
PETA UK (REACH)	dr. J. Hochmuth
PETA UK	dr. J. Hogervorst
People for Animal Rights Germany (PARG) - The Federal Association Against Vivisection	dr. C. Hohensee
Radboud UMC	prof. dr. J. Homberg
Leiden University Medical Center (LUMC)	dr. G. van der Horst
Toxys	dr. A. Jamalpoor
EPAA mirror group / Ethisch bedrijf	dr. M.R.E. Janssens
Animal Tests Committee (DEC) Utrecht	dr. W. Jong
European Commission - DG GROW	N. Kaloferova
Radboud University	dr. T. van Kerkoerle
National Institute for Public Health and the Environment (RIVM) - Utrecht University	prof. dr. A. Kienhuis

Participating organisation	Participant
Utrecht University	dr. K. Kramer
HU University of Applied Sciences Utrecht	dr. C. Krul
VU Amsterdam	dr. C. Kunne
Amsterdam UMC	dr. D.W.D. Kuster
TNO / NVDEC	dr. T. Lagerweij
MIMETAS Leiden	dr. H. Lanz
DALAS	dr. P. van Loo
The Animal Welfare Body (AWB)	dr. J. Lorteije
The Ministry of Agriculture, Fisheries, Food Security and Nature (LVVN)	dr. J.A.K.R. van Luijk
Partnership for the Assessment of Risks from Chemicals (PARC) - WP6	prof. dr. M. Luijten
Medicines Evaluation Board (MEB)	dr. P. van Meer
HU University of Applied Sciences Utrecht, Institute for Life Sciences and Chemistry	dr. J. van Meeuwen
UMCG / DEC KNAW	L. van der Miesen, MSc.
Leiden University Medical Center (LUMC)	prof. dr. B. Mons
Leiden University Medical Center (LUMC)	dr. A.G. van Montfoort
Eindhoven University of Technology	dr. P.J. Nickel
ZonMW	dr. M. Nolte
Netherlands Institute of Ecology (NIOO-KNAW)	prof. dr. K. van Oers
PEPPER	dr. T. Österlund
Eurogroup for Animals	J. Pochat, MSc.
Safer Medicines Trust	dr. P. Pound
Leiden University Medical Center (LUMC)	prof. dr. J.B. Prins
Unilever	dr. A. Punt
Dutch Arthritis Foundation	A. van Ravestijn, MSc.
EFPIA	dr. K. Reid
PETA UK	dr. T. Renahan

Participating organisation	Participant
SAFE consortium	prof. dr. J. Ritskes-Hoitinga
Ministry of Education, Culture and Science (OCW)	R. van Roon-Pruis, MSc
Brain foundation of the Netherlands	dr. D. Saaltink
Ombion Centre for Animal-Free Biomedical Translation (Ombion)	prof. dr. D. Salvatori
Association of Collaborating Health Foundations (Samenwerkende Gezondheidsfondsen)	dr. A. Scholman-Végh
Erasmus MC	prof. dr. M. Schonewille
European Commission - DG ENV	dr. K. Schutte
Leiden University Medical Center (LUMC)	prof. dr. F.J.T. Staal
MSD Animal Health	dr. R. Stabile
J&J Innovative Medicine	dr. T. Steckler
European Commission - DG GROW	dr. G. Streck
University Medical Center Groningen (UMCG)	dr. C.M.A. Thuring
Leiden University Medical Center (LUMC)	dr. E.A. Tolner
MERLN Institute	prof. dr. R.K. Truckenmüller
YoungTPI	T. Tsikari, Msc.
TNO	dr. W.H.J. Vaes
Utrecht University	dr. A. van Veen
Leiden University Medical Center (LUMC)	dr. M.G.R. ter Veld
Radboudumc	dr. ir. N. Verhave
Netherlands Institute of Ecology (NIOO-KNAW)	prof. dr. M. Visser
HU University of Applied Sciences Utrecht	dr. R. Vlasblom
National Institute for Public Health and the Environment (RIVM), Bureau REACH	dr. J. Vriend
NVDEC DECWUR	dr. T. Vrijenhoek
The Ministry of Agriculture, Fisheries, Food Security and Nature (LVVN) - Animal Free Innovation (TPI)	M.D. van Waaij, MSc.
The Ministry of Agriculture, Fisheries, Food Security and Nature (LVVN) - Animal Free Innovation (TPI)	S.H. de Waard, Msc.
EU project RiskHunter	prof. dr. B. van de Water
Dutch Society for the Replacement of Animal Testing	D. Weijers, Msc.
Netherlands Institute for Neuroscience	dr. J. Westerberg
YoungTPI	S.A.W. van Wijk, Msc.
VU Amsterdam	dr. A. Wilmes
UMC Utrecht / WKZ	dr. L. Witter
Amsterdam UMC	dr. K. Wolthers
Radboud University	dr. M.C.J. Wolvekamp
Netherlands Cancer Institute: NKI	dr. S. Zerp
Erasmus MC	Research Technician / IvD member
Hollandbio	Program manager
uniQure	Associate Director

The following people took part in an interview:

Participating organisation	Participant
Radboud University	prof. dr. M.N.C. Aarts
Maastricht University	prof. dr. ir. W. Bijker
Utrecht University; Hubrecht Institute	prof. dr. H. Clevers
Rathenau Institute	dr. R. Edelenbosch
Amsterdam UMC	prof. dr. T. Geijtenbeek
Rathenau Institute	dr. M. Habets
PBL	drs. A. Hanemaaijer
Erasmus MC	prof. dr. R. Hendriks
Utrecht University; former NCad member	prof. dr. C. Hendriksen
ZonMW	prof. dr. A. Ikram
Utrecht University	dr. ir. M. Janssen
Ombion Centre for Animal-Free Biomedical Translation (Ombion)	dr. M.R.E. Janssens
KWF Dutch Cancer Society	dr. K. Kos
IvD-Platform	dr. J. Lorteije
Prinses Máxima Centrum; UMC Utrecht	prof. dr. R. Medema
University of Twente	prof. dr. A. van der Meer
LUMC; Leiden Initiative for FAIR and Equitable Science (LIFES)	prof. dr. B. Mons
University of Twente	prof. dr. Robert Passier
Ombion Centre for Animal-Free Biomedical Translation (Ombion)	prof. dr. D. Salvatori
Dutch Burns Foundation	dr. C. van Schie
DALAS	dr. ir. M. ter veld
IKONE	A.M. Vroom, Msc.
Raadslid AWTI	prof. dr. C. Wijmenga
Utrecht University, Copernicus Institute of Sustainable Development	prof. dr. E. Moors
Utrecht University, Copernicus Institute of Sustainable Development	prof. dr. J. Hoekman
Utrecht University	dr. K. Kramer
Wageningen University & Research (WUR)	prof. dr. B. Bovenkerk

The following individuals were commissioned by the NCad to prepare background reports on transition studies and ethics for this Transition Policy Advice. Drawing on their expertise, they subsequently remained involved in incorporating these reports and advised the NCad on this process:

Participating organisation	Participant
Radboud University	prof. dr. M.N.C. Aarts
Maastricht University	prof. dr. ir. W. Bijker
Utrecht University; Hubrecht Institute	prof. dr. H. Clevers
Rathenau Institute	dr. R. Edelenbosch

Appendix 2
Concepts and uncertainties in the ethical assessment

The revision of the ethical assessment framework requires greater precision on both sides of the harms–benefit assessment. On the harms side, this concerns concepts that enable animal interests to be described more broadly than in terms of recorded adverse effects alone. On the benefit side, it concerns forms of uncertainty that make clear why expected benefits are not always straightforward to establish or weigh.

Concepts for a broader weighing of the interests of animals

Integrity refers to an animal's species-specific wholeness and completeness, and its capacity to sustain itself independently in an environment appropriate to its species. The concept is already included in the Dutch Animals Act and the Animal Ethics Committee advisory report template. The challenge lies in operationalising it: what does a moderate impairment of integrity mean in practice when conducting an assessment, and how should it be weighed in the harms-benefit analysis? Integrity may be impaired physically through irreversible interventions, behaviourally by depriving an animal of opportunities to express natural behaviour, and mentally by suppressing behaviour or through sedation. The dependence on humans created by some forms of research involving animals, for example when an animal can no longer function independently, is therefore itself a form of impairment of integrity.

Agency can be defined in different ways. A minimal definition is the capacity for self-directed behaviour. A broader definition describes it as the ability to influence the world in ways that express an individual's wishes and will. It is important to recognise that not all animals possess the higher cognitive capacities assumed in human autonomy. Definitions that do not require sentience or subjectivity make clear that even animals without demonstrable self-awareness may have goals that can be frustrated. Agency is also a relational concept: the ability to exercise it is partly determined by the environment and is constrained when an animal has little freedom of choice or control over its situation. The concept is relevant to the transition to non-animal research, but also to the way animals are currently housed and used in research, because environments with limited stimulation and restricted freedom of choice systematically constrain animal agency. Agency also has ethical

value in its own right. It is comparable to autonomy in that both concern having choices and being able to pursue one's own goals, although the comparison is not exact because animal agency and human autonomy are not identical.

Telos refers to the set of intrinsically valuable behaviours that animals of a particular species would normally pursue and to which they are well adapted: the way of life that makes a mouse a mouse and a pig a pig. The concept makes clear that the use of animals in research can not only cause harm to their welfare, but can also interfere with what is fundamentally important to an animal, irrespective of what it experiences at a particular moment. Disruption of telos is ethically problematic not only because it causes distress, but because it interferes with the species-specific way in which an animal can lead a good life.

Instrumentalisation refers to the reduction of animals to means for human ends, whereby their intrinsic value is ignored or undervalued. Brom distinguishes three levels: viewing an animal as a means to an end, treating an animal as a means to an end, and turning an animal into a means to an end (43). These gradations show that instrumentalisation is not merely an attitude, but can also occur in varying degrees of severity. The concept makes clear that the ethical significance of animal experiments cannot be determined solely on the basis of recorded distress, but is also connected to the nature of the human-animal relations expressed through the conduct of animal experiments.

The animal's voice refers to the question of how the interests of animals can be incorporated structurally and explicitly into assessments in which animals themselves cannot participate. Unlike human research participants, animals cannot consent or refuse. Animal ethics explores whether forms of assent, proxy consent or hypothetical consent could play a role in research involving animals, by analogy with standards in human research ethics. However, this analogy is not unproblematic: animals cannot be informed in the same way as humans who lack decision-making capacity, and how assent or refusal in animals should be recognised and interpreted remains a matter of ongoing debate. The question of how the interests of animals should be represented in the assessment procedure therefore remains relevant, without there being a single clear-cut solution.

These concepts are not intended as standalone tick-box criteria, but as tools for describing the interests of animals more precisely and weighing them more consistently in the harms-benefit analysis. For a detailed discussion of these concepts and their application to animal experiments, see Kramer, Bovenkerk and Ten Cate (11).

Forms of uncertainty on the benefits side

Kramer and Bovenkerk distinguish several forms of uncertainty that complicate the harms-benefit analysis, particularly, though not exclusively, in fundamental research (8).

The first is **uncertainty about the likelihood that the intended societal benefits will be achieved**. In fundamental research, this likelihood is difficult to quantify, precisely because new research is conducted in ways that differ in relevant respects from previous research, meaning that historical success rates do not provide a reliable basis.

The second is **uncertainty about which benefits may arise**. Fundamental research sometimes produces unexpected insights that could not have been anticipated in advance. This possibility is difficult to incorporate into an assessment at project level because the direction that these unforeseen benefits may take is unknown.

The third is **uncertainty about the scale, beneficiaries and timing of potential benefits**. It is often unclear how many people may benefit from a possible application, within what timeframe and to what extent, partly because the future incidence of conditions may differ and other therapies may become available.

The fourth is **normative indeterminacy when comparing human welfare, animal welfare and scientific knowledge**. These cannot readily be reduced to a common measure and weighed against one another, even when both human and animal interests are expressed in terms of welfare. Whether human and animal welfare should be given equal weight is a normative choice that must form an explicit part of the assessment and cannot be left implicit.

The fifth point requiring attention is **the risk that alternative approaches to the harms-benefit analysis merely shift these problems rather than resolve them**. An assessment that considers only scientific benefits avoids some uncertainties but increases normative indeterminacy: scientific knowledge and animal suffering are of such fundamentally different kinds that they remain difficult to compare, even using qualitative categories.

Uncertainty is therefore not a technical detail but an essential part of the ethical assessment. Where benefits are uncertain, difficult to quantify or normatively difficult to compare with the harms to animals, attention should be paid to making the considerations and decision rules used explicit. Only when considered together can these factors provide a basis for assessing whether the use of animals is justified. For a detailed discussion of these forms of uncertainty and possible decision-making models, see Kramer and Bovenkerk (8).

Appendix 3

Theory of Change as a foundation for monitoring

A Theory of Change describes how and why interventions are expected to contribute to societal change. It makes visible the causal links between activities, the actors involved, intermediate outcomes and long-term impact, including the assumptions, dependencies, attributions and time horizons on which this reasoning is based. These links are established through an iterative process that brings together literature, data, practical knowledge and actor perspectives. Relevant causal factors are identified, tested and prioritised, and then modelled as causal pathways or system maps. Recent literature emphasises that a Theory of Change is particularly valuable when, in addition to causal pathways, it explicitly addresses feedback loops, contextual factors, uncertainties and potential unintended effects, enabling it to serve as a basis for monitoring, evaluation and adaptive learning (44-46).

For a system transition, it is also important to identify where self-reinforcing feedback loops may emerge. A Theory of Change should therefore describe not only linear causal pathways, but also potential positive tipping points, interactions between interventions, phase-out mechanisms, rebound effects and the conditions under which effects may fail to materialise.

Transitions also require a dual perspective. The multi-level perspective helps explain how the landscape, regime and niches interact, and how institutional dependencies, path dependency and system complexity influence change (47-49). At the same time, change in practice often emerges in specific niches, where new models, assessment practices, educational initiatives, research strategies and innovative enterprises are developed and tested. A Theory of Change for the transition towards a society without animal experiments must therefore connect the system level with niche practices. It should show which levers for change are enabling conditions, which have a direct effect on practice, what forms of institutionalisation are needed and where stagnation may occur.

A broadly supported Theory of Change requires co-creation by the relevant actors in the context in which the transition actually takes shape. Researchers, developers of non-animal methods, assessors, funders, policymakers, societal organisations and

users bring together scientific knowledge, practical experience, implementation expertise, policy insight and societal values. Precisely because these actors operate from different roles, interests and time horizons, causal links, assumptions and indicators must be jointly constructed and validated. In this way, a Theory of Change can develop into a shared, testable and adaptable account of how change is expected to occur.

This Transition Policy Advice provides a basis for jointly developing a Theory of Change. The relationships between levers for change, niche practices and system conditions can guide the development of a limited but meaningful monitoring framework. Outcome indicators show what is changing in records and in practice, while system indicators show whether the underlying levers for change are actually shifting. Monitoring can thus serve as a tool for evaluation, adaptive learning, public accountability and targeted adjustments to the transition (44, 50, 51).

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