

# Animal Aid's roadmap - phasing out animal testing



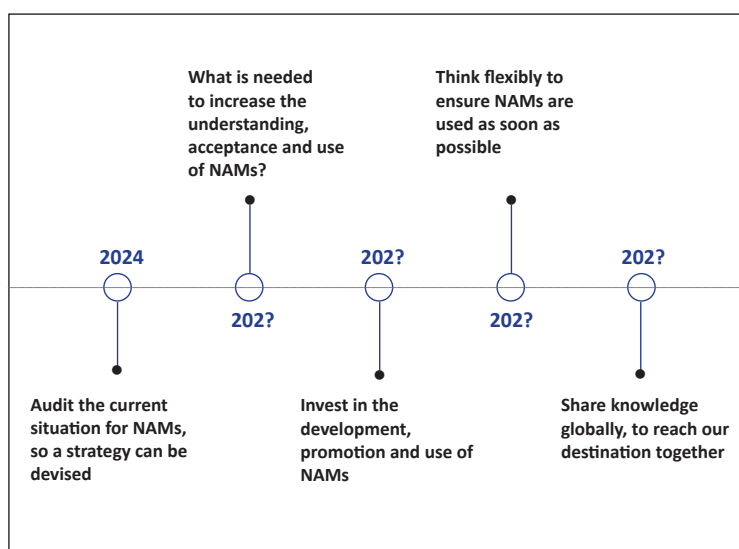
'we will partner with scientists, industry, and civil society as we work towards the phasing out of animal testing.'  
UK Government pledge - July 2024

Today, Animal Aid presents our ambitious 'roadmap to phase out animal testing' – to see an end to all animal experiments – a plan that is both forward-thinking and truly groundbreaking. Once adopted by all stakeholders, this roadmap will not only drive cutting-edge research and industrial strategy, but will also position the UK as a global leader in science and innovation.

This roadmap specifically focuses on 'animal testing', defined here as the use of animals in scientific procedures conducted for regulatory purposes.<sup>a</sup> We are initially focussing on regulatory tests as these, due to being a legal requirement, may take longer to phase out than other areas of animal use.

According to 2023 figures for Great Britain, of the 2.68 million 'scientific procedures' which were conducted on animals, 305,385 were for regulatory toxicology. These are the experiments upon which this roadmap focuses. Shockingly, it is not possible to determine exactly how many animals are 'used' globally for regulatory toxicology, due to different recording methods (or none) in different countries. The latest, and best estimate, from 2019, is that 192 million animals were used globally<sup>1</sup> in one year for all types of animal experiments.

Achieving a complete phase-out of all animal testing is both possible and within reach, with wise redirection of investment (of money and expertise) to emerging technologies, comprehensive stakeholder engagement (many of whom are already invested in NAMs as the way forward) and the determined support of government. Securing this widespread support will also encourage investment – industry stakeholders will be more confident about adopting new methodologies if regulators are receptive to them. Scientifically prudent, financially astute and ethically desirable, the move to New Approach Methodologies (NAMs) also has the support of a majority of the public.



*Animal Aid's roadmap illustrating the steps required to transition to a phase-out of animal testing and replace the use of animals with cutting edge, innovative and effective non-animal new approach methodologies (NAMs).*

<sup>a</sup> Our roadmap on the use of animals for other scientific purposes, including those animals used for basic or translational research, breeding animals for use in research and testing, or to create and maintain genetically altered animals, which we call 'animal experiments', will follow in due course but we will begin with 'animal testing' to capitalise on the shift in the political landscape and that within 'industry' that facilitate this move.

## **What are New Approach Methodologies (NAMs)?**

Not all NAMs are created equal. Some contain animal by-products, while others are entirely human-based, making them more predictive and often faster than using animals. To remove the barrier of species differences between animal and human cells, or media containing animal by-products compared to chemically defined media, no animal ingredients should be used in NAMs.

It is important to clarify that Animal Aid defines NAMs as **Non-animal new approach methodologies including any *in vitro*, *in chemico* or *in silico* methods that when used alone, or in combination with others, enable improved chemical safety assessment, toxicological assessment of human drugs and safety testing of medical devices and other products. This is achieved by using more relevant, more predictive and so more protective models which will contribute to the replacement of animals.** Any NAM may also incorporate use of appropriate existing or new data, for example from clinical trials, observational or biomonitoring studies.

UK-based XCellR8 *in vitro* testing laboratory, are experts in this field. Their [website](#) states: *‘an increasing body of evidence shows the importance of having a system that models human physiology as closely as possible, rather than relying on the use of animal-based culture systems.’*

They continue, *‘At XCellR8, we’ve invested years of research into developing adaptations of existing safety tests, where all animal components have been eliminated. In their place, we use human-derived serum and antibodies from approved sources as well as chemically defined products. This approach maximises both the human relevance and reproducibility of the test results.’*

To accelerate the complete replacement of regulatory procedures on animals with NAMs, there are essential elements which must be initiated, or actioned with urgency. These elements do not necessarily follow in a linear, chronological order; instead, different elements will take precedence, or receive more investment or attention at different times.

Crucial to this process is an urgent shift of emphasis and investment away from the traditional use of animals and towards more human-relevant science. Resources currently allocated to animal-based methods should be redirected to advance the development, application and adoption of NAMs. This financial shift must be accompanied by a change in mindset which is embraced and embedded by all stakeholders, encouraging innovation and the pursuit of better solutions to current scientific challenges.

Achieving the goals of this ambitious roadmap will require collaboration of the brightest academic minds, the most progressive global leaders and stakeholders across all sectors and career levels. Together, we can - and we must - urgently make this vision become reality.

The five steps of our roadmap are explained in brief below, and thereafter in more detail.

### **1. Audit the current situation for NAMs, so a strategy can be devised**

No one entity is currently aware of all the NAMs that are in use or under development. A collaborative audit, involving regulators, NAMs developers, producers, industry and academics should begin immediately to gain a comprehensive understanding of the current NAMs landscape – those in use, those under development and those which only exist as concepts. The UK can, and should, lead on this initiative globally.

Immediately establish a NAMs audit body, consisting of experts from all stakeholder groups, to identify NAMs already in use and requiring development.

### **2. What is needed to increase the understanding, acceptance and use of NAMs?**

Maximising the understanding of the scientific and commercial need to accept and use existing NAMs through training and education is crucial for regulators, industries and individuals. The requirements of different stakeholders will vary – regulators may require training and awareness, industry might seek assurance that NAMs data will be accepted while students will expect to see a significant focus on NAMs in syllabuses to ensure their careers are ‘future-proofed.’ These shifts in knowledge and attitude will also be relevant to the ‘developing NAMs’ as they progress to ‘market’. Additionally, once NAMs are ubiquitous, widely accepted and used globally, our newly gained knowledge will facilitate making ‘conceptual’ NAMs a reality.

Remove real and perceived barriers to NAMs use through training and education for all stakeholders to maximise knowledge and use of NAMs.

### 3. **Invest in the development, promotion and use of NAMs**

Investment in NAMs must be increased to expedite the introduction to market of human-relevant methods that represent superior science. This should be a three-pronged approach based on the current status of the NAM in question:

- **Existing NAMs** – Knowledge of these should be disseminated amongst all stakeholders, their production scaled up and training in their use provided.
- **NAMs in development** – These may need front-loaded investment and a collaborative approach to acquire the knowledge needed to progress them, akin to a '[helpathon](#)'
- **'Concept-only' NAMs** – This will depend on emerging knowledge and the need to address 'known unknowns' to become a reality. However, as knowledge improves, and investment increases alongside [exponential technological change](#), these NAMs can be developed.

Funding to be diverted from animal testing to developing, promoting and implementing NAMs. Ensure all stakeholders are clear on legislative and other changes in order to plan, invest and adjust outputs accordingly.

### 4. **Think flexibly to ensure NAMs are used as soon as possible**

NAMs do not need to be formally validated to be used. Many methods are already used 'in-house' by companies without methods undergoing validation. There are certain ways ('weight of evidence' (WoE) and integrated approaches to testing and assessment (IATA)) whereby different types of evidence are considered to provide a full picture of, and answer, the scientific question at hand. WoE and IATA are explained in more detail below and should be integral to training for all stakeholders, ensuring NAMs are used at the earliest opportunity to create the most scientifically robust testing methods.

Regulators should be supported with a revised framework to drive a progressive approach to NAMs to maximise the submission of NAMs methods, their acceptance and use. An environment must be established to allow industry stakeholders to submit NAMs as the rule instead of the exception.

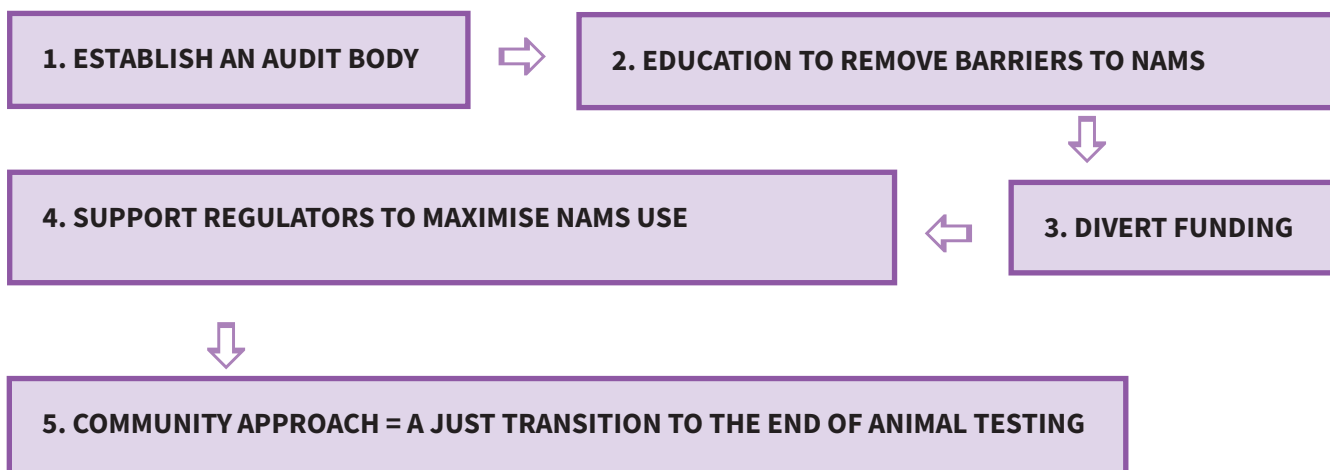
### 5. **Sharing knowledge, globally, to reach our destination together**

The roadmap must be actively promoted, to showcase the progress which is being achieved, being led by the UK, and ensure global co-operation and harmonisation.

Develop a community approach where all stakeholders are heard to enable an efficient and just transition.

## Our asks

- Immediately establish a NAMs audit body, consisting of experts from all stakeholder groups, to identify NAMs already in use and requiring development.
- Remove real and perceived barriers to NAMs use through training and education for all stakeholders to maximise knowledge and use of NAMs.
- Funding to be diverted from animal testing to developing, promoting and implementing NAMs. Ensure all stakeholders are clear on legislative and other changes in order to plan, invest and adjust outputs accordingly.
- Regulators should be supported with a revised framework to drive forward-thinking in their approaches to NAMs to maximise the submission of NAMs methods, their acceptance and use. An environment must be established to allow industry stakeholders to submit NAMs as the rule instead of the exception.
- Developing a community approach where all stakeholders are heard to enable an efficient and just transition.



## 1 Audit the current situation for NAMs, so a strategy can be devised

Some NAMs are currently in widespread use, others are still in development and certain ‘potential NAMs’ are only at the stage where there is an awareness of a specific use of animals, which is unscientific and unreliable and which needs to be replaced by a NAM. There will be both unknown unknowns and known unknowns that over time will become known knowns. The status of each NAM will determine what steps are needed to advance their development, to bring them to market, to scale up their production and to disseminate knowledge of them to the relevant stakeholders to maximise their use.

No one entity – regulator, animal protection group, industry sector – is currently aware of all the NAMs that are being used, developed or conceptualised. Nor will they be aware of the myriad ways in which animals are being used for testing chemicals, pharmaceuticals, medical devices, batch testing and batch safety testing of vaccines, etc. Furthermore there is inconsistency across different global regulations and test guidelines which either mandate animal use or do not explicitly forbid it, instead leaving it to the discretion of the scientist.

Collaboration among industry, SMEs, universities, animal protection groups and anyone with an interest in this area is essential to ensure a thorough understanding of which NAMs are required across different sectors. Each stakeholder group will have a distinct focus to their enquiries and a specific emphasis to their communications: regulators should be transparent about which NAMs they have already accepted and the context of their use, industry should communicate which NAMs they are using and in what scenario, while animal protection groups might be concerned with which areas of animal use should be replaced first.

The UK is uniquely positioned to be a global leader in this field. We boast [some of the world’s top universities](#), English has been [recognised](#) ‘as the universal form of communication in science, in fact, the language of both science and technology’. Furthermore we have the [infrastructure to facilitate](#) an increase in financial investment and expertise in NAMs. While the UK will be leading this paradigm shift, it is imperative that global harmonisation is built in from the outset.

## 2 What is needed to increase the understanding, acceptance and use of NAMs?

Ensuring that those NAMs being developed align with actual regulatory needs is an obvious step and one stated by van der Zalm et al<sup>2</sup>: ‘Ideally, NAM developers should communicate with stakeholders such as regulators and industry to identify the question(s), and specified purpose that the NAM is intended to address, and the context in which it will be used.’ Collaboration at the outset of this process will maximise the likelihood of this.

We must concentrate our energies and expertise on ensuring we have the right tools to determine human and environmental safety. We have some data for chemicals, but not all and a significant proportion of data after decades of the current testing strategy raises concerns over limited or [poor quality](#). However, our understanding of human biology and hazard assessment is continually advancing. This knowledge enables us to mitigate risks associated with highly toxic chemicals by limiting exposure, using comprehensive labelling, restricting use to trained operators, and using PPE (personal protective equipment) as we did during the Covid-19 pandemic.

Not only is UK-wide collaboration vital, but so too is global horizon-scanning for emerging trends in animal use (be these increases or phasing-out). We cannot predict all potential future challenges, such as another pandemic, just as we have yet to fully understand the risks associated with vaping despite years of animal testing. New NAM-based approaches, for example to investigate inhalation toxicity testing are proving more predictive for assessing the risk

to human health than traditional animal-based methods. Therefore fostering a strong and supportive environment for the funding, development and application of NAMs will serve us better for any future challenges.

Global collaboration, coupled with open dialogue and a realistic appreciation of the strengths and weaknesses of different stakeholders, should avoid unnecessary duplication of the development of NAMs. This approach will enable the UK to position itself at the forefront of NAMs development, streamlining the process in terms of time and money. If we seize this opportunity, the UK has the potential to become a global scientific powerhouse, with unlimited business opportunities and UK competitive advantage.

To maximise global harmonisation, it is essential to ensure, once NAMs begin to enter the market, that key stakeholders and decision makers are familiar and confident in how they work. As described by PETA<sup>3</sup>, there is a need to ‘*Educate and train researchers and regulators on the benefits of and how to use non-animal testing approaches.*’ In an assertion which is echoed by Innovate UK<sup>4</sup>, referring to ‘non-animal technologies’ (NATs), they recommend ‘*Support capacity building in multidisciplinary science and technology development to ensure that the UK has the right skills base to drive NATs for company decision-making and risk assessments.*’ The RSPCA echoes this sentiment too, urging ‘*Better training for life scientists in searching for NATs and using new techniques. For those working in regulatory toxicology, training and encouragement to challenging [sic] regulatory requirements for data from animal tests.*’

### **3 Invest in the development, promotion and use of NAMs**

As stated previously, some ‘new approach methodologies’ contain animal by-products, while others are entirely human-based, making them more predictive and often faster than using animal testing. These gold standard, wholly human NAMs must be prioritised along with comprehensive training in their use. The importance, in order to ensure human relevance, of developing and utilising methods for human health and risk assessment which are based on human data or using human materials cannot be overstated.

Comparing NAMs data to ‘traditional’ animal data, comes with risk as: ‘*the predictive capacity has usually been determined through comparison to results from traditional animal test methods, for which reproducibility and human biological relevance were often assumed rather than empirically demonstrated*’<sup>2</sup>. The primacy of human data is also emphasised by Marshall et al<sup>5</sup>: ‘*“Promoting innovative science with human biology as the gold standard” encompasses the scientific and technological advances underpinning the development and use of advanced, human-based non-animal NAMs.*’

Globally, there are different regulations and test guidelines that either prescribe animal use or do not explicitly forbid it, instead leaving it to the discretion of the scientist. As stated by Archibald et al,<sup>6</sup> ‘*although regulators may be willing to accept non-animal approaches in place of particular animal tests, nowhere is this explicitly stated in their guidelines.*’ Sewell et al<sup>7</sup> clarify how this reticence can be ‘circular’: ‘*This creates a “chicken and egg” conundrum where, because NAM approaches are not submitted, regulatory agencies do not have the opportunity to review and become familiar with/build confidence in new approaches, and without the precedent and encouragement to apply a new approach registrants may not conduct or submit them, and so opportunities to use NAMs are not taken up.*’

A bold and ambitious approach to this issue is essential. The UK must lead in this area, not only because it is better science, but also because there is huge political appetite for this which is [mirrored in public opinion](#) and within industry. As UK regulators gain confidence with the NAMs which have been developed and used domestically, ongoing dialogue and a commitment to global harmonisation will enhance acceptance of these methods by regulators in the EU, US and globally. Indeed the 2015 Innovate UK roadmap recommends this for the UK, regarding non-animal technologies (NATs): ‘*Ensure early engagement of regulators in the development and use of NATs to expedite a path to regulatory acceptance*’<sup>4</sup> Our strategy must be embraced with enthusiasm and a genuine desire to see real change.

Currently the investment in NAMs is dwarfed by the funding for ‘other’ scientific research.

- Analysis in 2020/21 revealed that NAMs receive only 0.2-0.6% of the UK’s biomedical research funding according to the All-Party Parliamentary Group for Human Relevant Science in their report, ‘Bringing back the human: Transitioning from animal research to human relevant science in the UK’ (March 2022)<sup>8</sup>
- Historically, the National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs) has received around £10 million per year<sup>9</sup>. However, it is important to note that this funding does not solely support projects to replace the use of animals. Refinement and reduction projects are funded which do not aim to increase the human-relevance of the science.



- In contrast, the Medical Research Council reported gross research expenditure for 2017/18 of over £800 million. This stark disparity in funding highlights the urgent need to realign financial resources toward NAMs to advance human-relevant science.<sup>10</sup>

It is imperative to swiftly reverse the current funding imbalance, in order to achieve our ambitious goals within a defined timeframe. This shift is crucial not only for bringing as many NAMs as possible to the market, but also to scale up their production, to ensure widespread availability. Redirection of current funding away from animal ‘testing’ and towards the development of NAMs would provide an effective and forward thinking strategy. Collaboration among funders, industry and other bodies is essential, many of whom would embrace diversion of funds towards the NAMS they are interested in.

#### **4 Think flexibly to ensure NAMs are used as soon as possible**

Formal validation of NAMs is not essential to their being in use. There are ways to consider the scientific evidence which is available now, and different NAMs, to avoid animal tests – these include Weight of Evidence (WoE) and integrated approaches to testing and assessment (IATA).

The [European Chemicals Agency](#) explains that the ‘*Weight of Evidence approach can be generally described as a stepwise process/approach of collecting evidence, assessing, integrating and weighing them to reach a conclusion on a particular problem formulation with (pre)defined degree of confidence.*’ AcutoX for example, described below, is ‘*considered to be suitable for inclusion in a weight of evidence approach.*’

Regarding the ‘integrated approaches to testing and assessment’, [the OECD](#) explains that: ‘*Advances in testing methods, biotechnology and computational models are paving the way for major improvements in how scientists evaluate the risks posed by potentially toxic chemicals. **These advances enable toxicity testing that is faster, less expensive and more relevant to human responses than traditional toxicity testing methods.** These new methods also rely on in silico, in chemico and in vitro approaches that reduce the need for animal testing.*’ (our emphasis added)

The OECD continues: ‘*IATA combine multiple sources of information to conclude on the toxicity of chemicals. IATAs may include existing information from the scientific literature or other resources, along with newly generated data resulting from new or traditional toxicity testing methods to fill data gaps. These approaches are developed to address a specific regulatory scenario or decision context.*’

The Innovate, 2015, roadmap states: ‘*Widen engagement in the development of NATs [non-animal technologies] to include disciplines, expertise and individuals not previously involved in toxicology and efficacy testing.*’<sup>4</sup> This widespread engagement, and the ability to have many ‘voices at the table’ should increase the flow of information between parties and so increase confidence in the NAMs being developed, ensuring that these methods are fit for purpose and will encourage efficient regulatory uptake. Again, the 2015 roadmap makes the recommendation to ‘*Build capacity and confidence in NATs and accelerate the path to market by supporting the development of NATs with powerful predictive ability and bridging the gap between development, proof of concept and scale-up.*’

To illustrate how methods not using live animals might be combined, two such methods are explained below. These were developed specifically to eliminate the oral LD50 test – a horrific Lethal Dose test which was initially devised almost 100 years ago, in 1927. The aim of this test is to feed increasing doses of a substance to groups of animals until 50% of them are dead. Despite the advance of science, in 2023, more than 11,000 animals were used in LD50-type tests in Great Britain alone (across the world this is likely to be hundreds of thousands of animals if not more).

The first example is CATMoS which is a computational model that uses historical data from pesticide toxicity tests instead of poisoning groups of rats until half of them were dead. A paper describing this model reports how the computer predictions were compared to animal data, spanning more than two decades. The predictions were so accurate that the authors state: ‘*Our evaluation supports the potential use of CATMoS predictions of TGAI [pesticide] acute oral toxicity in place of animal studies.*’<sup>11</sup>

The second example, called AcutoX, uses donated human skin cells instead of animals. Developed by XCellR8, a UK-based laboratory, this totally animal-free test involves the human cells being exposed to increasing doses of a substance. The health of the cells is monitored and the poorer the cell health and their metabolism, the more toxic the chemical to which they were exposed. This test is already being used by two multinational companies and AcutoX’s developers stated in a recent paper: ‘*Over 60 chemicals of varying degrees of known toxicity were run through the AcutoX test and the results were compared to widely available toxicity data that was obtained in animal*

models. The data comparisons revealed that the AcutoX test could correctly predict the safety of a significant number of chemicals.<sup>12</sup> AcutoX can be used alongside *in silico* approaches such as CATMoS.

The examples of acute toxicity testing, outlined above are relevant for chemical safety testing. In addition, there are opportunities for replacing animals used in drug testing. One is described in the paper by Ewart et al<sup>13</sup>, which notes that ‘Drug development is lengthy and costly, as it relies on laboratory models that fail to predict human reactions to potential drugs...toxic drugs sometimes go on to harm humans when they reach clinical trials or once they are in the marketplace. Organ-on-a-Chip technology involves growing cells on small devices to mimic organs of the body, such as the liver...we analyzed 870 Liver-Chips to determine how well they predict drug-induced liver injury, a common cause of drug failure, and found that Liver-Chips outperformed conventional models. These results suggest that widespread acceptance of Organ-Chips could decrease drug attrition, help minimize harm to patients, and generate billions in revenue for the pharmaceutical industry.’ The financial implications are significant ‘routine adoption of the Liver-Chip into preclinical workflows would generate an **additional \$3 billion annually** for the pharmaceutical industry.’(our emphasis added)

With the UK leading on these processes, the additional income can only make the UK science sector stronger – leading to more jobs, increased investment and further income – placing the UK as the global scientific leader.

## 5 Share knowledge globally, to reach our destination together

Maintaining disparate testing requirements globally hinders trade and raises both scientific and ethical concerns. One historical example of the often glacial pace of global harmonisation is the ‘one-year dog toxicity study’, which was required by certain pesticide regulatory jurisdictions. A 2010 paper stated: ‘the routine inclusion of a 1-year dog study as a mandated regulatory requirement for the safety assessment of pesticides is no longer justifiable and a globally harmonized approach should be taken to match the latest legislation of the European Union and the US EPA.’ However, it was 2018 when Japan was [reported to be considering dropping the same test](#), late 2018 when South Korea [dropped the requirement for this test](#) and it took until mid-2019 before Brazil agreed to waive the requirement for data from dogs. Building global harmonisation in from the outset could help to prevent these painful delays.

Once a roadmap is in place, it is imperative that all parties involved in its creation, and those who weren’t but who work in science, technology and further afield, embrace its vision and actively promote its aims and objectives. Effective communication, not only of the timescale, but of all elements of the roadmap, will be key to success, enabling stakeholders to act promptly and cohesively.

## Concluding remarks

The Government has pledged to: ‘publish a roadmap to end the use of animals in the scientific testing of products.’ We would hope they will adopt Animal Aid’s roadmap and support this with sufficient expertise and financial investment to position the UK at the forefront of NAMs development and utilisation, thereby making the UK a global scientific leader. Anything less than our comprehensive and achievable roadmap would compromise progressive human-relevant science, undermine public health improvements and perpetuate the use of animals in unreliable tests for decades to come.

A roadmap to a brighter future is not a simple thing – but it is essential. This is not only vital to develop the better science that we need and deserve, but is also crucial to maximise public health and environmental safety, increase the economic prosperity of the UK and also to fulfil the demands of millions of members of the public, MPs, policymakers, industry leaders and academics: an end to animal testing.

We now have the political will to turn this vision into a reality. It’s imperative that all stakeholders begin to communicate effectively, share knowledge, embrace change and invest time and money into making this happen. We share this roadmap with you in the hope that you will be inspired, recognise the possibilities and commit to do everything in your power to achieve the goal of an end to animal testing.

For more information, please contact: [jessamy@animalaid.org.uk](mailto:jessamy@animalaid.org.uk)

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