MODERNISING MEDICAL RESEARCH:

How **Britain** can become a global leader in **animal free science**

INTRODUCTION

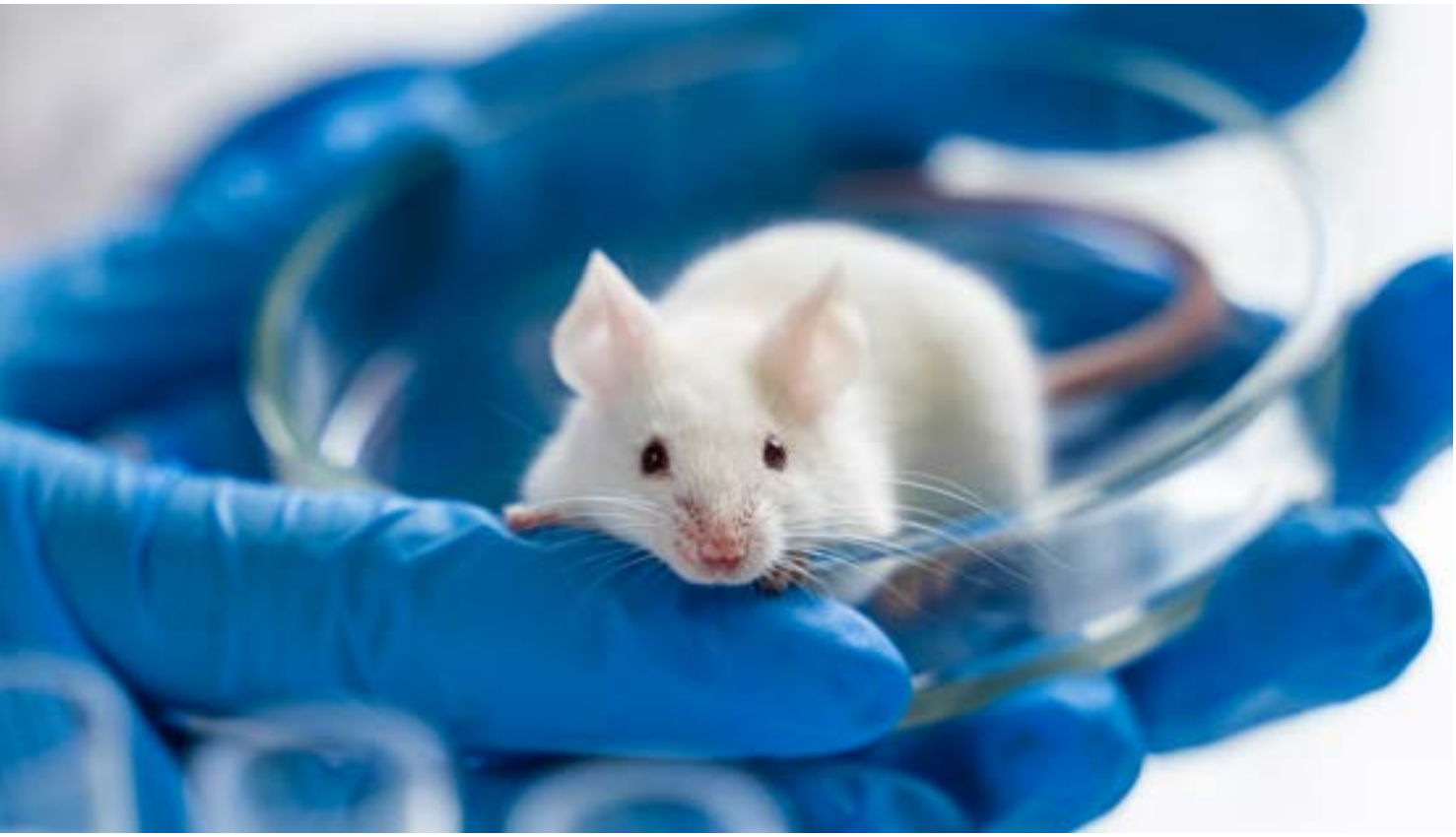
ACROSS THE WORLD, medical research is at a pivotal moment. On the one hand, it has never been more valued or high-profile, given the swift development of the Covid-19 vaccines. However, progress in other areas of research is much slower, with patients and their families still waiting for effective treatments for major diseases. Medical research currently relies heavily on animal experiments, and problems with translating this data to people play a major role in holding back progress, as well as causing suffering to millions of animals.

In several countries, policy makers are recognising the need to replace animal experiments with cutting-edge, human relevant technologies. From the US Environmental Protection Agency's ambitious goals to phase out experiments on mammals to the Netherlands' collaborative approach to developing animal free strategies, foundations are being laid for a fundamental shift in focus.

If the UK is to achieve its ambition of becoming a science superpower, it is vital that we play a leading role in this research revolution. With world-class universities and research facilities, we are in a strong position to lead the way in developing high-tech alternatives to animal tests. As well as benefitting patients and protecting animals, modernising medical research has huge economic potential. But if this initiative is to succeed, then bold policy action will be required, with strong attention from the heart of government.

The following report examines the scientific, ethical and economic case for modernising medical research; looks at how this can help the UK become a science superpower; provides examples of progress happening around the world; and recommends policy action that the UK Government can take to become a global leader in human relevant life sciences. As Britain establishes its place in the world post-Brexit, and looks to build a strong, future-proof economy, there has never been a better time to lead the way in modernising medical research.

The case for modernising medical research



EVERY MINUTE OF EVERY DAY, SIX ANIMALS ARE USED IN RESEARCH IN THE UK.

IN 2019, 3.4 million animal experiments were carried out in Great Britain, on animals including mice, rats, dogs, cats, primates and horses.[1] While animal experiments take place on an industrial scale, they represent an outdated approach. Fundamental differences between species mean that the results from animal experiments cannot be reliably translated to people. Looking at a few everyday items shows how differently people and animals can react. Chocolate, for example, is poisonous to dogs[2], while paracetamol is poisonous to cats.[3] These crucial differences have a significant impact in holding back the development of new medicines. 90 per cent of drugs that show promise in animal tests go on to fail in human clinical trials.[4] A new medicine can take 10-15 years to develop and costs are estimated to be as high as $1.8 billion.[5] Only 5 in 5,000 new drugs progress into clinical trials, with only 1 in 5,000 eventually gaining approval.[6] This crisis in pharmaceutical Research and Development has a devastating impact for patients. There are several thousand diseases that affect people, yet only around 500 of them have treatments available.[7]

As well as these scientific issues, the suffering caused to animals in laboratories presents a powerful ethical argument for change. The Animals in Science Regulation Unit (ASRU) publishes non-technical summaries of licences granted for experiments to be carried out on animals. The latest batch of these, summarising licences granted during the first half of 2020, provides a sobering reminder of what animals in laboratories can endure. Examples include deliberately inflicting wounds on

pigs and pain experiments on rats and mice, such as having their tails dipped into hot water.[8] The welfare of the millions of animals used in experiments is monitored by a small team of inspectors. At the end of 2018, there were just 22 inspectors (20.8 full time equivalents).[9] This means that in 2019, there would have been one inspector for every 159,890 animals used in experiments.[10] This lack of regulatory oversight, combined with the sheer number of animals held in laboratories, means that shocking welfare violations occur. ASRU's 2018 annual report (the latest available), describes chilling incidents such as mice dying due to inadequate food and water provision and a cage of mice being accidentally placed into an autoclave, where they died.[11]

Using animals in experiments is not the only option. There are a range of cutting-edge, animal free techniques which are human relevant, and provide results that are directly applicable to human patients. These New Approach Methodologies (NAMs) include artificial intelligence; the use of human cells or tissues; organ-on-a-chip technology and stem cell technology. Such techniques have been used by researchers to speed up the development of treatments and vaccines for Covid-19. For example, lung-on-a-chip technology was used to identify drugs that could potentially be repurposed to treat the viral infection.[12]

There is strong public support for modernising medical research in this way. A YouGov poll commissioned by Animal Free Research UK and carried out in February 2021 found that:

- **68%** of respondents would support a policy ending animal experiments in medical research in the UK and replacing them with non-animal alternatives (e.g. artificial intelligence and using human cells or tissue).
- **70%** of respondents would support animal experiments in medical research being phased out by 2040.[13]

The 2018 Ipsos MORI survey on public attitudes to animal research, which was commissioned by the Government, identified increasing public regard for animal welfare. The proportion of the public that was not at all concerned about the use of animals in research fell to just 15%.[14] In addition, 75% of respondents felt that more work should be done to find alternatives to animal experiments.[15] Britain is often described as being a 'nation of animal lovers', and this concern for animal welfare is likely to increase in future. There is currently a huge growth in interest in veganism, with the number of people taking part in Veganuary doubling between 2019 and 2021.[16] Veganism is defined as 'a philosophy and way of living which seeks to exclude—as far as is possible and practicable—all forms of exploitation of, and cruelty to, animals for food, clothing or any other purpose; and by extension, promotes the development and use of animal-free alternatives for the benefit of animals, humans and the environment.'[17] If veganism continues to grow, public demand for animal free research is likely to follow suit.

How modernising medical research

can help the UK become a global science superpower

THE COVID-19 PANDEMIC has underlined the vital importance of medical research, and of making sure that no time is wasted in bringing vaccines and treatments from bench to bedside. At the same time, this global crisis has shed light on the shortcomings of the current system. This is acknowledged by the Government's *Research and Development Roadmap*, which states:

> 'the pandemic has also brought long-standing issues in our R&D system into sharp relief. We will seize the moment to harness the ingenuity, creativity and agility shown by the R&D system over the last few months, in turn making the system faster and more responsive, resilient and sustainable, driving up confidence and securing rapid and long-lasting benefits for people and businesses right across the UK. We will take a whole systems approach to ensure that we make the bold changes needed to ensure our system is fit for purpose now and for the future.'[18]

Taking decisive policy action to facilitate the transition to human relevant research would be a prime example of the 'bold changes' that the Roadmap pledges.

A further theme within the Roadmap is reducing unnecessary bureaucracy, and the Government has now launched an independent review on this subject.[19] The Roadmap comments that 'This is

also an opportunity to shift the research sector to more modern methods of research, which will help cut red tape too.'[20] Replacing animals with human relevant techniques is exactly the kind of shift to more modern methods that will help to reduce bureaucracy. Whilst we feel strongly that animal research is not tightly regulated enough, it nonetheless requires a significant amount of administration, such as submitting licence applications for each project that uses animals. Using NAMs can allow researchers to spend more time on science and less time on administration.

Making medical research more human relevant will help to safeguard patients, supporting the focus on patient safety in the Medicines and Medical Devices Act 2021.[21] The current reliance on animal data can leave people at risk from side effects that animal experiments have not predicted. This can result in disasters such as the TGN1412 trial, where six volunteers were left in a life-threatening condition. The volunteers had been given a dose of the drug 500 times smaller than that which appeared safe in animal tests.[22]

Facilitating a transition to more human relevant research would help the Government achieve its ambition of making the UK a leading hub for life sciences, following its departure from the European Union. The UK is well placed to become a global leader in the development of NAMs. This point is emphasised by *A non-animal technologies roadmap for the UK* which was drawn up by a number of research councils, the NC3Rs and Innovate UK, and states that 'the UK has the necessary academic and industrial strengths to develop, exploit and deploy new non-animal technologies, positioning it as a global powerhouse in this area.'[23] The UK is home to four out of the top 10 universities in the world[24] and two major pharmaceutical companies – GlaxoSmithKline and AstraZeneca. There has never been a more opportune moment for the UK to become a world leader in the field of NAMs. 2021 will see the UK host the UN Climate Change Conference (COP26), hold the G7 presidency and establish its global post-Brexit position – it is time for decisive action to ensure that Britain remains at the forefront of science.

How modernising medical research
can strengthen the UK economy

THE LIFE SCIENCES INDUSTRY has vital importance for the UK economy. For example, UK exports of pharmaceutical products had a value of $31 billion in 2018, and the UK was the eighth largest exporter of these products amongst the comparator group, which included the USA, China and Switzerland.[25] The life sciences attracted £2.8 billion of investment in 2019.[26] However, the economic value of the pharmaceutical industry is threatened by the current productivity crisis in Research and Development.

It has also been recognised that an area of weakness for the UK is translating discoveries into products with commercial value. This is extremely relevant to the life sciences sector, where discoveries should ultimately result in new medicines and treatments for patients. The *Research and Development Roadmap* describes innovation as 'the process by which ideas are turned into economic growth – where discoveries are translated into new products, services and jobs, creating positive change in businesses, public services, government and wider society.' It comments that the UK underperforms in this area, compared to research.[27] This same theme appears in evidence recently submitted to the House of Commons

Science and Technology Committee. For example, written evidence from the UCL Institute for Innovation and Public Purpose, stated that 'the UK's national system of innovation is particularly strong in universities but weak compared to international competitors in translational or applied research, typically conducted in applied research centres and national laboratories.'[28]

Placing greater emphasis on NAMs would help bridge this gap from discovery to translation, by ensuring that the results of preclinical research are more relevant to people. The global market for NAMs has enormous potential, as illustrated by the following figures:

- In 2018 the global market for cell-based assays was estimated to be worth **$20.1 billion**. It is predicted to rise to **$32.7 billion** by 2023, with a compound annual growth rate of **10.2%** from 2018-2023.[29]
- In 2016 the global 3D cell culture market was worth **$1 billion**. In 2017 it was estimated that the market would be worth **$3.9 billion** by 2021.[30] However, these predictions have turned out to be underestimates. The global 3D cell culture market was estimated to be worth **$10.3 billion** in 2020, rising to **$14.8 billion** by 2025, at a compound annual growth rate of **7.5%**.[31]
- Analysis of the global market for organ-on-chips in 2019 showed that it reached a value of almost **$41.6 million** that year, after growing at **70.5%** since 2015.[32]

GLOBAL EFFORTS
to modernise medical research

IF THE UK IS TO BECOME A GLOBAL LEADER in human relevant research, it must be well-informed about initiatives taking place around the world, willing to learn from these, and ready to seek out opportunities to collaborate with international partners.

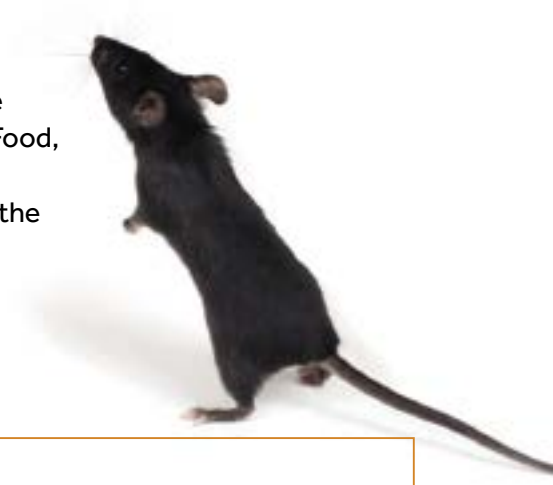
While the Government emphasises its commitment to high standards of animal welfare, the 2020 Animal Protection Index gives the UK a 'C' rating within the category of 'protecting animals used in scientific research'.[33] The Index assesses 50 countries against a range of animal protection criteria, giving a ranking of A-G for overall animal protection, and ratings for specific areas.[34] Countries that received an 'A' rating for protecting animals used in research were Austria, Denmark, France, Germany, the Netherlands, Poland, Sweden and Switzerland.[35]

As members of the European Union, Denmark and the Netherlands are both covered by European Directive 2010/63 on the protection of animals used for scientific purposes.[36] The Directive has the ultimate aim of replacing the use of animals in experiments.[37] Looking beyond the provisions of Directive 2010/63, both Denmark and the Netherlands have undertaken valuable initiatives which could provide inspiration for the UK Government.

Denmark

DENMARK HAS MADE STRONG PROGRESS in giving animal welfare professionals a voice in regulating animal experiments. The Animal Experimentation Council is responsible for assessing applications to carry out animal experiments, and its members also take part in laboratory inspections. While the Council members are appointed by the Minister of Environment and Food, this is done after consultation with diverse stakeholders. Of the eleven Council members, one is appointed after consulting with the Danish Animal Ethics Council, and four after consulting with Danish animal welfare organisations. As a result, the current membership of the Council includes Bente Lakjer, Director of the Danish Society for the Protection of Laboratory Animals.[38]

In addition, the Danish 3R-Center was established in 2013 and describes itself as 'a unique collaboration with both the pharmaceutical industry and animal welfare organizations.'[39] The Center's Collaborators include the Ministry of Environment and Food, the Danish Animal Welfare Society and LEO Pharma.[40] Its tasks include limiting the use of animals in laboratories and promoting the development of alternative methods.[41]



Learning for the UK

WHAT STANDS OUT from Denmark's approach is its strong emphasis on giving animal protection organisations a meaningful voice within the regulation of animal research. UK animal protection organisations are currently invited to regular meetings with ASRU, which is a welcome form of dialogue, but results in no meaningful influence on regulation. Whilst the UK's Animals in Science Committee (ASC) currently has one member from an animal welfare organisation,[42] the Committee is only involved in advising on applications to conduct certain animal experiments, such as those involving inflicting severe suffering on cats, dogs, monkeys and equines.[43] While the UK's National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs) does valuable work, it is not constructed in the collaborative, cross-sector manner of the Danish 3R-Center.

The UK Government should take proactive steps to involve the animal protection sector in the regulation of animal research and efforts to phase it out. For example, redacted and fully anonymised versions of selected project licence applications could be shared with stakeholders who have expertise in replacement methods, such as Animal Free Research UK. They could then suggest techniques that could be used to replace animals, helping to ensure that the legal requirement to use non-animal methods wherever possible is being properly enforced.

The Netherlands

THE NETHERLANDS has made strong progress in preparing for a transition towards animal free research.

In 2016, the Dutch Agriculture Minister Martijn van Dam asked the Netherlands National Committee for the protection of animals used for scientific purposes (NCad) to produce a schedule for phasing out animal experiments. He requested that the Netherlands should become a leader in 'innovations without laboratory animals' by 2025.[44]

The NCad sought input from a range of stakeholders and experts, including people carrying out animal research and animal protection organisations, before producing a series of recommendations. NCad concluded that certain categories of animal experiment could be phased out by 2025. These were: the regulatory safety testing of chemicals, food ingredients, pesticides and (veterinary) medicines and the release of biological products. For fundamental research, applied scientific research and education, NCad committed to facilitating the development of 10-year 'visions for animal free innovations' which were to include clear objectives.[45]

When the subsequent administration took office, Rutte III, the approach moved away from mentioning specific dates, but maintained a strong commitment to the transition to animal free research.[46] In 2018, Carola Schouten, Minister of Agriculture, Nature and Food Quality, set up the Transition Programme for Innovation without the use of animals (TPI). This aims to accelerate the transition to animal free research by 'encouraging alternatives and innovations'.[47] It includes partners from government, academia, industry and the third sector.[48] The vision of Minister Schouten and the TPI became one of 'the Netherlands as a frontrunner in the international transition of innovation without the use of animals.'[49]

Since its formation, the TPI has placed a strong emphasis on collaborative discussion amongst diverse stakeholders, including an international conference and 'helpathons.' Helpathons are described as 'intensive brainstorming sessions about specific cases, guided by the auxiliary question: Assuming you are not allowed to carry out animal procedures, how could this research still be done?'[50]

In addition, NCad is currently running an initiative to encourage different stakeholders to collaborate in setting timelines and goals for replacing the use of animals in different fields of work, drawing up strategies known as 'target images on animal-free research'.[51] A short film featuring members of NCad notes that stakeholders in various fields of research have embraced the idea, with strategies now being developed for reducing the use of animals in higher education, as well as in cardiovascular research.[52]

In a review of its work, the TPI comments that 'the most striking difference with other countries is the role the Dutch government has taken on in this transition. As far as we are aware, in no other country has the government explicitly positioned itself as a transition director and actively brought together many different parties in this capacity.'[53]

Learning for the UK

THE DUTCH GOVERNMENT has embraced the need to transition to animal free research and has actively brought together stakeholders to begin a dialogue and take practical steps to facilitate progress.

The UK Government should make a clear commitment to modernising medical research by moving away from animal experiments. It should proactively organise collaborative discussions and problem-solving sessions involving regulators, industry and the third sector. Such discussions should result in tangible outputs such as strategy maps for reducing animal use in particular areas. These could be used to inform strategic funding decisions with a view to ensuring that any gaps in animal free methods are addressed.

Outside the European Union

STRONG PROGRESS is also being made outside the European Union, which is particularly relevant to the Government's vision of post-Brexit Britain as a global leader in the life sciences.

Switzerland

IN EARLY 2021 Switzerland's Federal Council announced a National Research Programme to advance the 3Rs. The purposes of this programme are to reduce the number of animal experiments, refine animal experiments and develop ethical and societal principles. The priority areas for the programme are:

- **'Innovation':** Developing, improving or validating methods that could advance the 3Rs in either specific areas or in general terms.
- **'Implementation: opportunities and barriers':** Focusing on transferring the 3Rs from principle to practice, as well as identifying barriers and developing strategies to overcome them.
- **'Ethics and society':** Focusing on the ethics of using animals in experiments and the development of human-animal relationships.[54]

The programme will take place for five years and has a budget of 20 million Swiss Francs (around £15.6 million).[55] Information about the programme is still limited at this stage, but a call for projects will be published in Spring 2021.[56]

While the budget for this programme is relatively modest, it is more than 50% greater than that of the UK's NC3Rs.[57] In addition, this project represents a significant step in acknowledging the importance of transitioning to human relevant research. National Research Programmes are described as 'research projects that can contribute to solving current questions and challenges of national importance'.[58]

Learning for the UK

THE LAUNCH of Switzerland's programme recognises the need to modernise medical research as a pressing issue of national importance. The UK Government should also acknowledge the importance of this issue and prioritise the transition to animal free research. As the Government works to implement the *Research and Development Roadmap*, it should make sure that replacing animals in medical research is given the same prominence and consideration as other government priorities.

USA

US GOVERNMENT AGENCIES are making significant progress in replacing animals in toxicity testing, which could provide valuable insight for the UK Government.

In 2007, the National Research Council (NRC) of the U.S. National Academy of Sciences, published a landmark report: *Toxicity Testing in the 21st Century: A Vision and a Strategy (Tox21).* The report was later summarised by the Food and Drug Administration (FDA) in the following terms: 'the Tox21 report outlined a new vision for the future of toxicity testing, advocating a shift away from traditional animal studies, which can be expensive and time consuming and have drawbacks, toward a focus on alternative methods that evaluate the effects of chemicals on biological processes.' [59] In 2017, the National Academies of Sciences, Engineering, and Medicine produced a follow-up to the Tox21 report, *Using 21st Century Science to Improve Risk-Related Evaluations.*[60]

In 2011, the FDA published its *Advancing Regulatory Science at FDA* plan, which identified 'modernize toxicology to enhance product safety' as a priority area. The plan includes commitments to human relevant research such as to 'evaluate and promote the use of cell- and tissue-based assays that more accurately represent human susceptibility to adverse reactions.' [61]

In 2017, the FDA published its *Predictive Toxicology Roadmap*. The goal of the Roadmap was to 'invigorate and strengthen FDA's long commitment

to promoting the development and use of new technologies to better predict human, animal, and environmental responses to a wide range of substances relevant to FDA's regulatory mission.' [62] It articulates a series of steps to be taken, including educational events, research programmes to identify data gaps and fostering collaboration.

In 2020 the FDA formed the Alternative Methods Working Group. The Group's development was part of efforts to support the Toxicology Working Group in advancing the objectives of the FDA's *Predictive Toxicology Roadmap*.[63] The Group's work includes a webinar series on alternative methods in which developers are invited to demonstrate their techniques to FDA scientists.[64]

In January 2021, the FDA published *Advancing New Alternative Methodologies at FDA*.[65] This reports on progress across the FDA on the integration of alternative methods into regulatory programmes. It includes details of progress across numerous organisational bodies within the FDA including the Office of the Chief Scientist, the National Center for Toxicological Research, and all six product centres.[66] For example, the Center for Biologics Evaluation and Research (CBER) took part in a workshop to find a replacement for the potency testing of the rabies vaccine. This resulted in identifying an alternative test that should be taken forward to validation.[67] In addition, the National Center for Toxicological research is exploring the potential of patient-derived stem cells to provide personalised predictions of whether anti-cancer drugs could damage the heart.[68]

The USA has also made significant progress in reducing the use of animals in chemical testing. In 2016, the Frank R. Lautenberg Chemical Safety for the 21st Century Act [69] gave new directions to the Environmental Protection Agency (EPA). The EPA summarises these requirements in the following terms:

> 'Reduce and replace, to the extent practicable and scientifically justified, the use of vertebrate animals in the testing of chemical substances or mixtures'

> 'promote the development and timely incorporation of alternative test methods or strategies that do not require new vertebrate animal testing'

> 'develop a strategic plan on this topic and provide a progress report on the implementation of the plan to Congress every five years since the date of the enactment of the Lautenberg Chemical Safety Act, i.e. beginning in 2021'.[70]

Taking this agenda further, in September 2019 the EPA Administrator Andrew Wheeler issued a memo directing the Agency to 'aggressively pursue a reduction in animal testing'.[71] [72] The memo set out the following EPA goals: 'the EPA will reduce its requests for, and our funding of, mammal studies by 30 per cent by 2025 and eliminate all mammal study requests and funding by 2035.' [73] In June 2020, EPA published its *New Approach Methods Work Plan*.[74] The work plan set out how the agency will go about achieving the objectives set out in the memo. This includes undertaking a thorough analysis of the legislation and regulations that currently require tests on mammals; developing a framework to assess the quality of NAMs; creating a central website to host information about NAMs and the EPA's progress in this field; and organising training sessions on the use of NAMs.[75]

In October 2020, the Humane Research and Testing Act was introduced as a draft bill.[76] This sought to establish a National Center for Alternatives to Animals in Research and Testing, under the National Institutes of Health (NIH). The new Center was to provide funding for the development of animal free methods, offer education and training to scientists and establish collaborations. Importantly, the bill would have obliged federally funded research agencies to release statistics of the number of animals used in experiments, and to develop plans for reducing these. The 'Findings' section of the bill strongly condemns the current reliance on animal experiments, stating 'there is widespread agreement among scientists and regulatory agencies that animal models are poor predictors of the human response, with over 90 percent of new candidate drugs never making it to market.' [77] While the bill was not able to move forward in October 2020, it has now been re-introduced.[78]

Learning for the UK

US FEDERAL AGENCIES are making significant progress in replacing the use of animals in toxicity testing. The UK should follow the EPA's lead in setting ambitious, time-bound goals to replace animals with human relevant methods and producing detailed plans to ensure the implementation of these.

Practical policy recommendations

to modernise medical research

MODERNISING MEDICAL RESEARCH and becoming a global leader in the field of NAMs will require bold and decisive policy action. It is important that the machinery of central government is structured in a way that will accelerate this vital transition.

At present, no department is leading the way in transitioning to animal free research, although this area of work is relevant to the Home Office, the Department for Business, Energy and Industrial Strategy (BEIS) and the Department of Health and Social Care (DHSC). As part of its regulation of animal research, the Home Office is responsible for enforcing the provisions of the Animals (Scientific Procedures) Act 1986, which state that 'scientifically satisfactory' non-animal methods must be used wherever possible, instead of an animal experiment.[79] However, the non-technical summaries of licences issued during the first half of 2020 suggest that this requirement is sometimes being treated by researchers as a tick-box exercise,[80] and the small team of inspectors tasked with assessing licence applications do not have the resources to rigorously enforce this. With this in mind, it is hardly surprising that in 2020, no applications to conduct experiments on animals were refused permission.[81]

BEIS has overall responsibility for scientific research, which includes the development of NAMs. While the department provides funding for the NC3Rs via UK Research and Innovation (UKRI), there is little information available about further funding for NAMs. The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive agency of DHSC and has responsibility for approving medicines for use in humans. At present, international regulatory guidelines on the safety of medicines generate an expectation that these must be tested on animals.[82] While the MHRA appears open to dialogue about animal free approaches, information about this process is difficult to access in practice.

By establishing a function dedicated to replacing animals with human relevant techniques, the Government could accelerate this important transition. Recommendations for the form of this new function are discussed below, but it would need to undertake the following activities:

Accelerating modernisation

- Spearhead a government declaration about the national importance of modernising medical research. This would build on the work done in Switzerland to highlight the replacement of animals as a matter of national importance.
- Produce a roadmap for phasing out animal experiments for medical research and replacing them with human relevant methods.
- Create detailed workplans containing time-bound targets, to set out exactly how the transition to animal free research will take place. This would build on work done by US federal agencies, such as the EPA.
- Ensure that the goal of replacing animals in research is reflected in the development and implementation of other government plans and roadmaps, such as the *Research and Development Roadmap*.

Providing education

- Devise and implement an effective communications programme aimed at educating different stakeholders about the advantages of replacing animal experiments with human relevant techniques.
- Provide practical support and training for scientists to reduce or replace the use of animals. This could involve, for example, supporting SMEs that are looking for an animal free pathway for their drugs to gain approval for use in clinical trials.
- Provide support for early career researchers to pursue an animal free career pathway.

Enabling collaboration

- Facilitate collaboration between government, academia, industry and the third sector to accelerate the development and take-up of replacement methods.
- Coordinate a pilot project which involves ASRU sharing redacted and fully anonymised versions of selected project licence applications with stakeholders who have expertise in replacement methods, such as Animal Free Research UK. They could then suggest techniques that could be used instead of animals. This would build on the work done in Denmark to ensure that diverse stakeholders are involved in the regulation of animal research and efforts to replace it.
- Organise conferences and roundtable discussions that map out pathways for transitioning to animal free research in specific areas, such as toxicity testing or cancer research. The discussions could include representatives from academia, industry and the third sector. This would build on the collaborative approaches taken in the Netherlands.
- Contribute to international efforts to modernise medical research, including influencing international regulatory guidelines; raising awareness of work being done in the UK; and learning from initiatives in other countries.

Awarding strategic funding

- Provide funding for the development of replacement methods – on a scale that reflects the urgency and importance of this issue.

We understand that BEIS currently has responsibility for a large proportion of scientific research funding, via UKRI and its research councils. We would not suggest a change to this basic process but believe that any new function should be empowered to provide funding for research projects that directly support its objective of accelerating the transition to animal free science. For example, if a roundtable discussion identifies a particular area where replacement methods are lacking, the new function could issue a specific call for projects designed to address this shortfall and fund those that show most promise. This funding would focus much more narrowly on accelerating the complete replacement of animals than that currently provided by the NC3Rs.

In addition, we believe that the modernisation of medical research should become a key focus for the new Advanced Research and Invention Agency (ARIA). A March 2021 policy statement clarified that 'ARIA will exclusively focus on projects with potential to produce transformative technological change, or a paradigm-shift in an area of science.' [83] The transition from animal experiments to NAMs certainly has the potential to transform scientific research for the benefit of public health and the economy. While we understand that ARIA will have autonomy to determine its own programmes, any biomedical research should be underpinned by a focus on human relevant, animal free techniques, in order to maximise its transformative impact. Projects funded by ARIA would of course need to be those that are deemed high-risk and high-reward, in line with the agency's functions.

How the new function would work

THIS NEW FUNCTION could take a number of forms and we have described several possible approaches below.

Full government department

The most effective means of accelerating the transition to animal free science would be to set up a fully-fledged government department, including a Secretary of State with a seat at the Cabinet; additional ministers in supporting positions; a Permanent Secretary and a team of civil servants. The new Department would work closely with the Home Office, BEIS and DHSC. For example, it could ensure that developments in NAMs were brought to the attention of the Home Office and used instead of animal experiments. It could also advise the MHRA on alternative methods that could be used to generate the data required for regulatory approval.

We acknowledge that creating a new government department has a financial cost and can involve significant work and disruption. We are also aware that 'machinery of government' changes of this kind are most commonly undertaken when a Prime Minister takes office. However, we believe that taking the bold step of creating a Department for Animal Free Science would reflect the urgency of this issue and its fundamental impact on public health. The Institute for Government has estimated the direct cost of setting up a new government department as being around £15 million[84]. If the UK were to play a leading role in modernising medical research, this would have the potential to generate significant return on investment. For example, in 2018 the global market for cell-based assays was estimated to be worth $20.1 billion. It is predicted to rise to $32.7 billion by 2023.[85]

Joint office

A joint office for Animal Free Science could bring focus to this issue, driving and coordinating relevant action from the Home Office, BEIS and DHSC. This could work in a similar way to the Office for Veterans' Affairs.

Joint ministerial role

A ministerial role focusing on Animal Free Science could work across the various relevant departments and provide the opportunity to set up an office that worked closely with BEIS, DHSC and the Home Office to drive a coordinated initiative to modernise medical research. While a more informal office of this kind would not have a Secretary of State, or the capacity of a full department, it could play a valuable role in securing meaningful progress. This approach was taken in 2015, when Richard Harrington was appointed the Minister for Syrian Refugees and worked with the Home Office, Department for International Development (DfID) and Department for Communities and Local Government (DCLG).[86] More recently, Nadhim Zahawi has been appointed Minister for Business and Industry and Minister for COVID Vaccine Deployment, meaning that he is part of both BEIS and DHSC. This makes him responsible for both vaccine deployment (led by DHSC) and the Vaccine Taskforce (led by BEIS).

Function within the Cabinet Office

Evidence provided to the House of Commons Science and Technology Committee indicated that moving responsibility for Science from BEIS to the Cabinet Office could be under consideration.[87] This change was presented in the context of major challenges such as achieving net zero, which require dedicated attention from the heart of government. Modernising medical research is another societal challenge that deserves major government focus. If Science moves into the Cabinet Office in future, modernising medical research should become a priority stream of work.

Tsar

The Covid-19 pandemic has resulted in a number of 'tsars' being appointed. The Institute for Government defines these as 'personal ministerial appointments charged with driving progress and bringing coherence to specific issues.' [88] This includes, for example, the appointment of Kate Bingham to chair the Vaccine Taskforce. A scientific expert in replacement science could help to drive the Government's work in transitioning to animal free research. This external expert could report directly to the Prime Minister on this issue of national importance.

Involving the Commissioner for Patient safety

The Medicines and Medical Devices Act 2021 makes provision for the appointment of a Commissioner for Patient Safety.[89] This provision reflects a key recommendation of the report of the Independent Medicines and Medical Devices Safety Review, chaired by Baroness Cumberlege.[90] One of the Commissioner's core duties will be to 'promote the safety of patients with regard to the use of medicines and medical devices'.[91] Ensuring that preclinical research is human relevant, and therefore able to predict adverse effects, is highly relevant to patient safety. If a dedicated function cannot be established, then modernising medical research could become part of the Commissioner for Patient Safety's duties. In addressing this issue, they would need to work closely with any Animal Welfare Commission that may be appointed in connection with future legislation on animal sentience.

Conclusion and summary

of recommendations

THERE IS AN URGENT NEED to modernise medical research, for the benefit of animals and people.

If the UK is to maintain its commitment to animal welfare, and to establish itself as a science superpower, then it must lead the way in transforming medical research to be animal free and human relevant.

We have seen many positive examples of action being taken around the world to accelerate this transition. This includes Denmark's efforts to involve a wide range of stakeholders in the regulation of animal research; Switzerland launching a research programme that establishes reducing animal experiments as a matter of national importance; and the FDA producing ambitious strategies to integrate NAMs into its regulatory processes in the US.

Britain is in a strong position to lead the way in this field, but dedicated attention from the heart of government will be essential. In particular, the Government should set up a function tasked with taking the lead in modernising medical research, coordinating activity with the Home Office, BEIS and DHSC.

The new function's core activities would be to:

- Spearhead a government declaration about the national importance of modernising medical research.
- Produce a roadmap for phasing out animal experiments for medical research and replacing them with human relevant methods.
- Create detailed workplans containing time-bound targets to set out exactly how the transition to animal free research will take place.
- Ensure that the goal of replacing animals in research is reflected in the development and implementation of other government plans and roadmaps, such as the *Research and Development Roadmap.*
- Work to realise the huge economic potential of NAMs and maximise return on investment on funds spent on the new function.
- Facilitate collaboration between government, academia, industry and the third sector to accelerate the development and take-up of replacement methods.
- Provide support for early career researchers to pursue an animal free career pathway.
- Coordinate a pilot project which involves ASRU sharing redacted and fully anonymised versions of selected project licence applications with stakeholders who have expertise in replacement methods.
- Organise conferences and roundtable discussions that map out pathways for transitioning to animal free research in specific areas.
- Contribute to international efforts to modernise medical research, including influencing international regulatory guidelines.
- Devise and implement an effective communications programme aimed at educating different stakeholders about the advantages of replacing animal experiments with human relevant techniques.
- Provide practical support and training for scientists to reduce or replace the use of animals.
- Provide funding for the development of replacement methods – on a scale that reflects the urgency and importance of this issue.

A full government department would have maximum impact in modernising medical research and harnessing the economic potential of NAMs. Alternative approaches that could be considered include:

- **Establishing a Joint Office**
- **Appointing a Joint Minister**
- **Developing a function within the Cabinet Office**
- **Appointing an external expert or 'tsar'**
- **Involving the Commissioner for Patient Safety**

It is vital that the Government looks to the future and takes bold steps to modernise medical research. This will benefit animal welfare, public health and the British economy, while firmly establishing the UK as a world leader in scientific research.

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About Animal Free Research UK

Animal Free Research UK is Britain's leading medical research Charity working for a world where human diseases are cured faster without animal suffering. The charity funds pioneering animal free research that saves humans and animals and is forging a future where animals are replaced with modern, human relevant techniques.

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