**ANNEX 2**

# ASC Futures Workshop Horizon Scan Slide Pack

29th July 2021

The content of these horizon scans has been submitted by stakeholders and does not represent the view of the ASC or ASRU.

Submitted scans have been summarised and collated to generate a slide deck for distribution to all workshop participants. Scans on similar topics were reconciled to form single scans where appropriate.

# Preclinical/toxicological regulatory issues

# Second Species Testing

## Summary


- *Second species testing is the testing of pharmaceuticals or chemicals in at least two mammalian species, one of which is usually a rodent and the second must be a non-rodent species, such as non- human primates, dogs, rabbits or pigs.*
- *The Animal Procedures Committee (APC, now the ASC) and The Association of the British Pharmaceutical Industry (ABPI) discussed the requirement for second species testing, with an APC report published on regulatory toxicity asking that the Home Office "keep under review the scientific criteria for the selection and use of a second species, and in particular dogs and non-human primates".*
- *During this time, numerous scientific publications have reviewed the scientific integrity of using second species testing to make decisions about toxicity, in terms of their added value, including a joint paper from representatives of the UK NC3Rs and of the ABPI.*
- *One of the main factors to move away from second species testing in toxicology is 'species differences'. Each species reacts differently to substances, making animal tests an unreliable way to predict effects in humans.*


## Opportunities

- *The emergence of non-animal technologies (such as in silico modelling and in vitro human 3D-tissue models) could provide more relevant and predictive data and thus replace the need for data in a second species in the future.*
- *Reduction to a single species for longer-term toxicity studies directly contributes to the 3Rs.*

## Threats and Challenges

- *A key challenge is regulatory requirements and guidance. Further evidence is needed in order to shape robust recommendations for regulatory change.*
- *As pharma operates on a global stage, these changes would need to be adopted by international regulators.*
- *Another challenge is widespread adoption of these techniques. Organisations such as NC3Rs can publish on new methodologies, however institutes, organisations and companies need to feel confident in adopting these new methodologies in order for the shift from two species to one species to occur at scale.*

## Implications for ASC

- *To ensure robust scientific evidence is the driving force for regulatory decision making on the use of animals in science, it is vital that the ASRU policy can demonstrate it is adaptive to the progressing regulatory scientific landscape, as opposed to maintaining the status quo.*
- *There will be a need to ensure UK legislation and regulations can support the research and development of these products, whilst maintaining animal welfare standards and the UK's commitment to the 3Rs.*

**Certainty:** ★★★★☆

**Timescale:**

# Increase in Household Product Testing

## Summary


- *In March 2015, the Home Office Minister announced a ban to "end testing of household products on animals". The ban would cover all finished products as well as chemical ingredients, with exemptions. Subsequently ASRU published an advice note detailing the scope of the ban.*
- *The exemptions cover where proposed testing is a regulatory requirement e.g. under REACH or where no other method for obtaining the results sought that doesn't entail the use of a live animal is recognised under EU legislation. The policy also permits range-finding testing in advance of regulatory tests being performed.*
- *Practically, the policy means that companies wishing to test ingredients of household products on animals where there is no regulatory requirement, can still prospectively apply for a Home Office licence, with the justification being strong "for the proposed testing" and "sufficiently detailed to be assessed in a thorough harm benefit analysis".*
- *In the decade leading up to 2015, there were 372 procedures for the purpose of testing household products or their ingredients. In the four years since, there have been 2,614 procedures for this purpose. This is potentially a threat to the policy objective, and not supported by UK public opinion polls.*


## Opportunities

## Threats and Challenges

- *Recorded procedures for household ingredient testing have increased since the introduction of the policy ban. This is a threat to the policy objective.*
- *Detailed analysis of the testing on animals of ingredients primarily intended to be used in household products has not been published.*

## Implications for ASC

- *Given the lack of public and political support for the use animals to test household product ingredients, it is highly likely that an increase in animal use for this purpose will be unacceptable to the public.*
- *The lack of clarity indicates a failure of the original intention of the policy to support the dive for the development of non-animal alternatives, and is an issue which requires further investigation by the ASRU with the help of the ASC.*

**Certainty:** ★★★★☆

**Timescale:**

# Project Licences for e-cigarettes as medicinal products

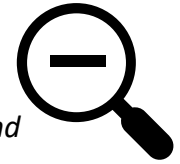
## Summary


- *In the UK there has been a ban on the testing of tobacco products on animals since 1997. However, producers of e-cigarettes and refills are required to submit information about their products to the MHRA. As these novel products may be licensed under current requirements for new medicines, the MHRA may require toxicity information, which could lead to animal testing to fulfil regulatory requirements. For submitting pre-clinical data requirements the MHRA advise that if no or limited, non-clinical or clinical data exists in the public domain, applicants should consider conducting appropriate studies in line with the ICH guideline on non-clinical safety studies for the conduct of human clinical trials and marketing authorisation for pharmaceuticals. Specifically, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines require animal toxicity studies to be conducted in two mammalian species, including one non-rodent, for repeated dose toxicity and some chronic and acute toxicity studies.*
- *There is currently a lack of information about whether animals have been used for this purpose in the UK.*
- *While no projects containing the phrase "e- cigarettes" have been identified in the Non-Technical Summaries, it is not clear that the end use of a tested substance would be specifically outlined In those documents. E-cigarette substance testing is also not specifically recorded in the annual statistics.*


## Opportunities

- *The current policy which does not allow project licenses to be granted for "developing or testing alcohol or tobacco products" can very simply be amended with the inclusion of e-cigarette products.*
- *Non-animal methods exist that can replace animal use to gain toxicity data on e-cigarettes and their constituent components*

## Threats and Challenges



- *Outside of the UK, studies on animals to test e-cigarettes have involved rats and mice. There are also indications that primates could be used for inhalation testing. Testing of e-cigarettes and their ingredients on animals is unreliable and unnecessary, and it is vital that these kinds of procedures are prevented from occurring in the UK.*

## Implications for ASC

- *In 2018 the ASC reported that the House of Commons Science and Technology Committee were currently undertaking an inquiry into the topic of E-cigarettes and that ASRU's future work would be informed by the outcome of that inquiry.*
- *Prioritising the use of non-animal methods for the testing of e-cigarettes and their ingredients presents a potential opportunity for achieving one of the long-term objectives of the ASPA, the requirement for replacement as the first of the 3Rs.*

**Certainty:** 

**Timescale:**

# Pre-Clinical Testing of Novel Medical Devices using Large Animals

## Summary


- *Increasingly UKRI funded projects are encouraging the development of innovative medical devices and spin-off companies that exploit the technology.*
- *Medical devices must be tested in a relevant animal model before being used in humans.*
- *Often the easiest and cheapest animal models are used. Pigs are the ideal animal model, in most cases, where novel medical devices are to be kept. However, few facilities exist in the UK to do this work.*
- *The infrastructure and the expert animal care required is expensive, which can consequently make funding an issue.*
- *There needs to be some consideration of places that can do such work, in a high-welfare environment as most are in the UK. The alternative is that the work goes abroad to less high-welfare countries.*


## Opportunities

- *Encouraging work to stay in the UK would strengthen the UK research base.*

## Threats and Challenges

- *Work can often be done more cheaply abroad, and as a consequence CROs or other universities may take their research abroad, creating a 'brain drain' in the UK.*
- *Animal welfare standards may be lower abroad, leading to more animal suffering.*

## Implications for ASC

**Certainty:** ★★★★★

**Timescale:**

# NAMS

# Neural Organoids

## Summary


- *Research into neural processes frequently uses human brain surrogates (model systems that can "stand in" for a conscious human brain) in order to collect data without the need for using human subjects. Neural organoids are an important recent breakthrough in this area. Organoids are in essence miniature, simplified organs built from stem cells.*
- *Neural organoids are grown to structure themselves to resemble parts of the human brain, such as the cerebrum or hippocampus. Although still small in comparison with a full human brain (at only around 5mm in diameter), the largest contain up to six million neurons. They can grow and develop over their lifetimes, forming new connections.*
- *Use of in vitro human brain tissue has been common for decades, but organoids have only been in use since 2013. As techniques improve for their production, neural organoids are becoming more complex and more closely matched to the brain segments they represent.*


## Opportunities

- *Neural organoids allow research to be conducted without the need for human (or animal) research subjects.*
- *They can be more accurate than animal models and allow for targeted research on the cell-types, or brain areas of interest.*

## Threats and Challenges

- *If sufficiently complex, organoids could possess basic sentience, or consciousness.*
- *Understanding of the processes creating consciousness is limited, and current best indicators are behavioural markers, which are not applicable to organoids.*
- *There are still some questions about how accurate and effective neural organoids are as models of the human brain.*
- *There is a risk of the science outpacing regulation, potentially leading to a scenario in which sentient organoids are created long before they are recognised as being sentient.*

## Implications for ASC

- *Neural organoids are already in use, and there is push for their continued development, as a way of improving research and reducing the numbers of animals used in experiments. However, this should not be considered as a 'free' exchange of a morally salient test subject for an inert model.*
- *A way of systematically determining which organoids are likely to be conscious and thus protected is required. If organoids are themselves sentient, then they should also be the subject of moral concern and steps taken to regulate their use. Proportionate response in this case would be to bring organoids under the same protections currently extended to sentient animals under the UK's Animals (Scientific Procedures) Act 1986.*

**Certainty:** ★★★★☆

**Timescale:**

# NAMS for Safety Decisions on Chemicals

## Summary


- *Several frameworks and case studies have been published regarding the use of New Approach Methodologies (NAMs) to allow safety decisions without the need for toxicology testing in animals (Next Generation Risk Assessment, NGRA). These frameworks and case studies have been driven largely by the Cosmetics Industry following the implementation of the animal testing bans for cosmetic products and their ingredients in the EU Cosmetics Regulation.*
- *The use of NAMs to allow safety decision-making without the need for toxicology testing in animals has been championed by the US since the National Academy of Sciences' publication in 2007 'Toxicity Testing in the 21st Century – A vision and a Strategy'. The scientific principles outlined in the US EPA's road map to eliminate toxicology testing in animals by 2035 and those used by Industry in NGRA are applicable to wider aspects of regulatory safety decision-making about chemicals within the EU and the UK.*


## Opportunities

- *There is an opportunity for the UK to follow the lead of the US and to champion the use of NAMs for making safety decisions on chemicals.*
- *NAMS can help reduce the number of animal tests.*
- *Traditional toxicology testing approaches are offset by high costs and lengthy test durations when compared to the use of NAMs.*
- *In some areas, modern, human-based, tiered approaches to safety assessment can produce more relevant information for the protection of humans than the information generated in traditional toxicology studies.*

## Threats and Challenges

- *Many regulations relating to the safe use of chemicals currently list traditional toxicology studies in animals amongst their requirements, with little consideration of the newer NAM approaches. This is currently resulting in requests for animal studies to be conducted where NAM approaches could equally be used.*
- *Chemical regulators have a long history and familiar with animal methods and may be resistant to change.*

## Implications for ASC

- *A key driver for the uptake of NAMs for safety decision-making by the Consumer Goods Industry was the 7th Amendment to the EU Cosmetics Directive in 2003 which laid out the timetable for animal testing bans on cosmetic products and ingredients. This led to an industry-wide upskilling in the use of NAMs. At present, there is no similar driver for upskilling in NAMs within the area of chemicals registration and regulation.*
- *NAMs are increasingly used to make decisions on chemical safety in some areas. Whilst many initiatives on 'alternatives to animal testing' for toxicology focus primarily on the scientific/technical tools, there is additional work needed to bring together the output from these technologies in the context of different safety decisions that are made by regulators and industry to gain confidence in their use for robust decision-making.*

**Certainty:** ★★★★☆

**Timescale:**

# Use of data, digital and computational models

## Summary


- *There is a general increase and plethora of data and digital technologies, many unique to the specific scientific area or broader application of Artificial Intelligence and Machine Learning that may offer for example greater search mechanisms/ability and reuse of published data.*
- *Additionally, computational and mathematical modelling is advancing rapidly with greater potential for in silico prediction either instead of or prior to animal research. Other areas include quantitative systems pharmacology and quantitative systems toxicology.*
- *Within the animal research area specifically, increased use of smart caging offers continuous and remote monitoring of animals, with potential for early indicators of adverse effects or physiological changes resulting in identification of earlier humane endpoints. The available data per individual research animal is also increased and some systems offer automated analysis e.g. activity, behaviour.*


## Opportunities

- *Maximal information gained from individual animals and experiments, supporting overall 3Rs replacement interests.*
- *Smart-caging may offer improved animal welfare /husbandry.*

## Threats and Challenges

- *Challenges with data security and breaches e.g. cloud access to data.*
- *Challenge to ensure appropriate ontologies exist to maximise data opportunities.*
- *Ensure animal welfare e.g. group vs single housing of animals is recognised and included in new technology specifications.*
- *Longer term potential for less reliance or even loss of traditional skillsets related to animal behavioural observations, welfare and husbandry.*

## Implications for ASC

- *Awareness of plethora of activity in this area.*
- *Understanding merits and weaknesses of new technologies to ensure animal welfare is maintained.*

**Certainty:** ★★★★☆

**Timescale:**

# Innovative new Therapies and Modalities

## Summary


- *Advanced Therapy Medicinal Products (ATMPs) are medicinal products which are either: a gene therapy medicinal product, a somatic cell therapy medicinal product or a tissue engineered product. They offer potential treatment opportunities for diseases that currently have limited or no effective therapeutic options.*
- *In disease areas such as cancer and rare disease, ATMPs provide an opportunity to tailor therapies to stratified patient groups and individual patients.*
- *Due to their complexity, the Committee for Medicinal Products for Human Use at the EMA recognized that conventional nonclinical animal safety testing was not always feasible for ATMPs. In a few cases, it was advised that if a hazard had already been identified (e.g., based on in silico or in vitro testing) and it could be scientifically and ethically determined that animal testing would not further substantiate the risk, animal testing was deemed unnecessary. It was then recommended to take appropriate measures clinically in order to mitigate the risk.*
- *A key driver is the shift towards precision medicine, with treatments and therapies tailored to stratified patient groups and individual patients.*


## Opportunities

- *The use of new modalities may drive further innovation in the use of animals and non- animal technologies, which could lead to reduction, replacement or refinement.*

## Threats and Challenges

- *New modalities such as cell therapies are based on the patient's biology, hence may complicate efficacy and safety studies in animal models which may not necessarily accurately mimic the human condition. This could lead to the inefficient use of animals in research and challenges with safety testing.*

## Implications for ASC

- *With over 2,000 ATMPs in development (PharmaIntelligence Informa, 2021), there is a growing need to ensure UK legislation and regulations can support the research and development of these products, whilst maintaining animal welfare standards and the UK's commitment to the 3Rs.*
- *As safety testing for new modalities and the regulations around that evolves, transparency of decision-making and methodologies are needed to help educate the research community and society, particularly patients who may be concerned that these new modalities have not been appropriately safety tested.*

**Certainty:** ★★★★★

**Timescale:**

# Artificial Intelligence/Increasing Digitised World

## Summary


- *Digital technologies, such as AI and the use of real-world data, have the potential to generate more realistic and human-relevant evidence regarding the safety and efficacy of medicines and/or the impact of exposure to environmental chemicals, which could lead to the replacement of animals in regulatory decision-making.*
- *More investment in the development and implementation of sophisticated digital technologies such as high-throughput screening, omics technologies, high-content imaging, curated legacy data and artificial intelligence (which has been shown to outperform animal testing in terms of reproducibility) as well as in personalised medicine could help streamline drug development/chemical safety assessment and provide better and safer solutions for patients and consumers.*
- *The introduction of Cosmetics Regulation 1224/2009, which includes bans on animal testing for cosmetics, and the implementation of Directive 2010/63/EU, which includes the requirement to use alternatives, have led to an increase in the development of computer-based approaches and other non-animal test methods.*


## Opportunities

- *The UK is well positioned to encourage the use of digital technologies to replace animals and invest heavily in their development to advance its reputation as a world leader in human-based research.*

## Threats and Challenges

- *Many of these technologies are highly sophisticated and are not well understood or appreciated by all members of the scientific community.*
- *There is likely to be a lack of trust and confidence in the use of computer-based approaches to inform regulatory decision making or make predictions about human health.*
- *The lack of implementation and availability of these novel technologies is also a challenge – timely updates to legislation and clear guidance are needed to allow for increased flexibility and application of these new approaches.*

## Implications for ASC

- *Education and training are key to changing scientific mindset and unlocking the potential of sophisticated digital technologies. There may be a role for the ASC in raising awareness of these technologies.*
- *Increased funding is also necessary to allow for further development and exploration of these methods.*

**Certainty:** ★★★☆☆

**Timescale:**

# Public Health and Economic Benefits of Accelerating Progress Towards Uptake of NAMS

## Summary


- *Across the world, regulatory agencies, governments and funding bodies have been encouraging a shift towards NAMs in biomedical research and testing, recognising their health benefits and economic potential over traditional animal methods.*
- *The continued development, advancement and uptake of NAMs will directly impact the use of animals in science, particularly in areas where they are a validated replacement for animal methods. NAMs present a potential opportunity for achieving one of the obligations under ASPA to require replacement as the first of the 3Rs.*
- *In seeking a shift away from animal methods towards NAMs, it needs to be acknowledged that replacement might not be straightforward. Due to the sophisticated and complex nature of non-animal technologies, one-to-one replacement of animal tests with a single 'alternative' may not be possible or even desirable. In the US, the new roadmap by the EPA acknowledges that "[r]ather than try to replace each existing animal test with an alternative method, the road map encourages government agencies to think about what information they need to make a decision."*


## Opportunities

- *NAMS have the capability to enable more rapid discovery and development of medicines.*
- *NAMs can bring safer and more effective treatments to the market compared to traditional animal methods.*
- *NAMs have the potential to offer improved translatability over animal models.*
- *NAMs can help reduce animal use.*
- *NAMS may be lower cost and higher throughput than traditional methods.*

## Threats and Challenges

- *The UK regulatory system is at risk of falling behind on global developments by requiring data from traditional models rather than adopting data generated from NAMs into regulatory guidelines.*
- *One-to-one replacements of animal tests with a single 'alternative' may not be possible or even desirable.*
- *The view that traditional animal models are the 'gold standard' against which all new technologies should be compared threatens to impede NAMs from being validated and adopted in the UK.*
- *It can be challenging to build confidence and change perceptions in NAMS. Entrenchment may extend to regulators and funders creating a barrier to funding and publishing.*

## Implications for ASC

- *To ensure that the ASRU policy is resilient and adaptive to the progressing scientific landscape, the ASC should provide guidance to the ASRU on how to incorporate developments in NAMs into policy development and regulatory decision making on the use of animals in science in the UK.*
- *By working with the ASRU, the ASC can help to educate the scientific community about the opportunities of working with NAMs.*
- *NAMs will directly impact the use of animals in science, particularly in areas where it is "possible" for NAMs to be used as a replacement for animals. It is the responsibility of the ASC to "have regard … to the protection of animals against … unnecessary use in scientific procedures".*

**Certainty:** ★★★★★

**Timescale:**

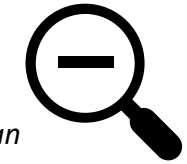
# Validation of NAMS for use in Medical Research

## Summary


- *The recent acceleration in the development of new approach methodologies (NAMs), has led to a significant increase in the availability of robust non-animal technologies which yield highly human-relevant and mechanistic data. While the benefits of transitioning to NAMs are increasingly being recognised, validation plays a vital role in demonstrating that these novel methods are fit for purpose before they can be used in any regulatory safety testing regime.*
- *Validation of NAMs involves extensive scientific studies to assess the reliability and relevance of a test method for its intended purpose. With the current high attrition rates in drug discovery, and the subsequent persistent unmet therapeutic needs for many diseases, there may be an increasing drive to extend the focus on the validation of NAMs to include their use in medical research, particularly in drug safety testing.*


## Opportunities

- *Formal validation of NAMs for use in biomedical research would help to address legislative requirements by ensuring that only test methods which produce high quality data are accepted. This would likely result in a huge increase in the uptake and acceptance of NAMs which, in turn, would bring many potential benefits beyond the reduction and replacement of animal tests.*
- *Other benefits include reducing drug attrition and incidences of adverse drug reactions, increasing throughout, cutting development time and costs and providing mechanistic insights that are not possible with in vivo research.*



## Threats and Challenges

- *The current validation process can be expensive and time-consuming and can reach a bottleneck at ECVAM and other CVAMs due to their limited capacities..*
- *NAMs are invariably assessed on how well they can predict the 'gold standard' animal data, despite animal tests never themselves being subject to this test.*
- *As reliance on animals is entrenched and institutionalised, the validation of NAMs may be perceived as a threat amongst regulators and some subsections of the scientific community, as this would drive a significant shift from the current system.*

## Implications for ASC

- *Formal validation of NAMs for use in biomedical research may result in the gradual reduction and eventual replacement of animals in medical research.*

**Certainty:** ★★★☆☆

**Timescale:**

# Animal-free antibody production

## Summary


- *Antibodies/affinity reagents are crucial tools for research diagnostics, therapeutic and regulatory applications. Both animal-based and non-animal based technologies are used to produce them.*
- *EURL ECVAM mandated ESAG to review and deliver opinion on the scientific validity of antibodies and affinity reagents produced using animal free technologies. This review concluded that 'non-animal derived antibodies are able to replace animal derived antibodies in the vast majority of applications. Moreover, well-characterised, recombinant affinity reagents will improve the reproducibility and positively impact society.' In the EU directive 2010/63 animal use is prohibited where a non-animal alternative exists. ASPA also applies this principle.*
- *UK researchers continue to generate/source/ use animal derived antibodies.*


## Opportunities

- *Non animal antibodies may have higher reproducibility than animal-derived and can be produced in unlimited supply.*
- *The uptake of non-animal derived antibodies presents a potential opportunity for achieving one of the obligations under ASPA, to require replacement as the first of the 3Rs.*
- *There are economic benefits associated with the adoption of on-animal derived antibodies.*
- *improved quality of scientific research, contributing to the advancement of public health.*

## Threats and Challenges

- *Lack of awareness, inertia, logistics, and cost.*
- *Researchers will need to be trained in discovery and production of animal-free antibodies.*
- *The development of a library to produce animal-free antibodies requires a substantial time investment.*
- *The initial production of rAbs is expensive as they are not available in catalogues yet, so must be custom made.*
- *There is no specific ASRU guidance on where use of animal derived antibodies is acceptable and presumably this relies on the HOI performing the HBA on individual PPL applications, leading potentially to inconsistencies.*

## Implications for ASC

- *The publication of the EURL ECVAM report should directly impact the work of the ASRU, particularly the licencing of new research and the assessment of existing licences where animals are used for antibody production. The uptake of non-animal derived antibodies presents a potential opportunity for achieving one of the obligations under ASPA, to require replacement as the first of the 3Rs.*
- *The implication for the ASC is that licence applications for animal antibody production are unlikely to meet the cost/benefit test and a change in practice is required in the immediate term.*
- *If non animal methods are available, then should PPLb be endorsed.*
- *Consistency across inspectors - is there a need for guidance in this area?*

**Certainty:** ★★★★★

**Timescale:**

# Personalised Medicine

## Summary


- *'Personalised medicine' is a patient-focused medical approach which uses a patient's individual genetic or other molecular profile to guide treatment and intervention decisions with regard to the prevention, diagnosis and treatment of illnesses. Genetic factors play a role in most human diseases, with gene variations contributing to their incidence or response to treatments.*
- *With the development of, for example, the 100,000 genomes project and the advent of molecular profiling technologies, such as in cancer, it is becoming easier to tailor treatments to each patient.*
- *The delivery of 'personalised medicine' has the potential to impact animal research as the scientific and medical communities develop the tools required to facilitate this powerful transition.*
- *There are Government initiatives to drive the development of tools, processes and systems that embed a culture of innovation in the development of personalised medicines.*


## Opportunities

- *Each patient is provided with the best treatments and treatment routines to overcome their disease. This could lead to an increased understanding and acceptance of new modern technologies and processes amongst the public, with increased support for new approach methodologies (NAMs) and other human relevant research that directly applies to human diseases.*

## Threats and Challenges

- *The biggest challenge in the delivery of personalised medicine is selecting the right models and systems to accurately predict what treatments and treatment routines will be most effective for a patient.*
- *By developing a personalised medicine care pathway that relies on animal research methodologies such as Patient-Derived Xenograft Models, there is the possibility that the use of animals will increase for translational/applied studies research.*

## Implications for ASC

- *Delivery of a consistent, cohesive and world class genomic healthcare or personalised medical care pathway for patients in the UK, with a focus on developing NAMs and other human relevant technologies, will drive the development of treatments that 'better reflect' the varied human disease states for individual patients, and drive down the number of animals used in research.*

**Certainty:** ★★★★☆

**Timescale:**

# Next Generation Risk Assessment

## Summary


- *Next Generation Risk Assessment (NGRA) refers to a novel chemical risk assessment approach designed to be flexible and able to integrate data from one or more New Approach Methodologies (NAMs) – in silico, in chemico, and in vitro – without the need to generate new animal data.*
- *The customized nature of each NGRA means that the development of a prescriptive list of tests to assure safety is not possible, or appropriate.*
- *A working group of the International Cooperation on Cosmetics Regulation (ICCR) define that NGRA must be: human- relevant, exposure-led, hypothesis-driven and designed to prevent harm, while additional five principles set out how NGRA should be conducted and documented. NGRA does not attempt to replicate the results of the animal tests historically used in safety assessment and instead works with a hypothesis that if there is no bioactivity observed at consumer-relevant concentrations, there can be no adverse health effects.*
- *The NGRA approach is fully compatible with the Adverse Outcomes Pathway (AOP) framework. Various NAMs may be selected to represent the molecular initiating event (MIE) and relevant key events (KEs) of a particular AOP, and the resulting data can be integrated to derive at values suitable to a regulatory conclusion.*


## Opportunities

- *Flexibility: by using all available data, and only data necessary to come to a conclusion on safety assessment, by design saving on resources.*
- *The methods are being developed in view of a higher relevance for humans, compared to tests in animals, and thus to ensure a better protection of human health.*
- *Efficiency: NGRA, being by definition human-centric, relies on integrative systems toxicology-based approaches.*

## Threats and Challenges

- *Ensuring that all relevant biological endpoints are covered (in in vitro assays/assay panels), and future research is needed to identify which additional molecular targets or cell models would increase our confidence of no bioactivity at relevant exposures.*
- *Because NGRA is exposure-driven, the quality of assessment depends on the level of quality of exposure data. NGRA is best suited to scenarios with very well defined exposure – e.g. cosmetics.*
- *As a downside to its flexibility, NGRA is likely to use customized, non-standard experimental designs, and may as a result need expert judgement in its use.*

## Implications for ASC

- *Reduced animal use – cosmetics, pesticides, consumer products.*
- *NGRA is being used in cosmetics safety assessment in the EU, and possibilities are being explored by the industry for e.g. consumer products and pesticides.*
- *A robust regulatory guidance on how to integrate data from variety of sources to support safety decisions will enable its wider acceptance and use.*

**Certainty:** ★★★★★

**Timescale:**

Short (0-5yrs) | medium (5-10rs) | Long (+10 yrs)

# Drug Development Crisis

## Summary


- *Currently 90% of drugs fail in human clinical trials even though they passed preclinical tests (including animal tests). The discovery and development of new drugs typically takes an average of 10-15 years to complete at a cost of ~$2.6 billion per drug. As a result, only a handful (approximately 20) of novel medicines are released onto the market every year.*
- *The scientific literature is now replete with concerns over the current animal testing paradigm, on which drug development remains largely based, as well as calls to transition to more predictive and more human-relevant approaches.*
- *While animal tests are increasingly being replaced with quicker, cheaper and more reliable non-animal methods, often referred to as new-approach methodologies (NAMs), progress is slow. For example, drug companies often employ a suite of cell-based tests and computer models, as well as their understanding of a drug's pharmacology, to screen drugs for efficacy and safety. However, they remain as tools to be used in the early stages of drug development and are not yet seen as full replacements for the tests required at regulatory stages.*


## Opportunities

- *Wider use of NAMS will lead to a reduction in animal use.*
- *NAMs may be able to offer increased predictability.*
- *Wider use of NAMs may reduce the time and cost required to bring a drug to market, allowing patients to access effective therapies more quickly.*

## Threats and Challenges

- *One of the key challenges is the lack of a clear scientific strategy to demonstrate how the different NAMs can be pieced together to replace all the various animal tests that are currently required to test a single new drug.*
- *Other challenges include the lack of dedicated funding for the development of NAMs, the lack of enforcement and availability of accepted NAMs and the lack of clear guidance from regulators about how data from NAMs can be used to satisfy specific requirements.*

## Implications for ASC

- *Other countries and regulatory agencies are currently leading the way with strategies to replace animal testing to help bring about real change, for example the EPA, FDA and ICCVAM strategies in the US.*
- *There may be a role for the ASC in incentivising the development and use of NAMs.*

**Certainty:** ★★★★★

**Timescale:**

# Sentience

# Sentience

## Summary


- *There is increasing interest and debate as to which non human animals should be considered to be sentient, and new studies being undertaken with the aim of providing evidence for this.*
- *Whenever evidence becomes available and accepted that a species is sentient, this has implications for how society views, considers and treats them as well as implications for animal welfare legislation. In particular, knowledge of the complexity of animal minds raises the possibility that animals are harmed by their use in science in previously unrecognised ways.*
- *The scope of UK and EU legislation relating to animal research and testing, currently includes all non-human vertebrate species, plus one group of invertebrates, the cephalopods (octopus, squid, cuttlefish and nautilus).*
- *A number of UK Animal Welfare and Ethical Review Bodies (AWERBs) already choose to additionally consider - using a 'lighter' system of oversight - projects that do not fall under ASPA but that can still raise ethical issues e.g. observation studies, the use of invertebrate species etc.*


## Opportunities

- *Inclusion within the scope of legislation of all the animals capable of experiencing pain, suffering, distress or lasting harm would increase animal welfare protections.*
- *As animals' perceived moral status increases, the same amount of harm will weigh heavier, meaning that greater benefit will be required for a procedure to be justified. This may lead to a reduction in the use of animals in science.*

## Threats and Challenges

- *There is a lack of current oversight and understanding of whether, how, where and in what numbers the animals potentially affected by any changes in legislative protection, are currently being used in research, testing and education within the UK.*
- *There is a lack of experience and expertise within ASRU of regulating the use of animals that don't currently fall under ASPA.*
- *Our current understanding of the behaviour and key welfare needs of invertebrate species is incomplete.*
- *It is likely that the more cognitively complex an animal, the more existing laboratory housing and husbandry systems fail to meet their needs.*

## Implications for ASC

- *The ASC may choose to keep abreast to developments within other regulatory jurisdictions with regard to the scope of animal welfare legislation and inclusions of a wider range of species.*
- *Both ASRU and ASC would have to consider how 'harms' to these species can be objectively considered in order to ensure a robust Harm-Benefit Analysis of project applications proposing their use.*
- *The ASC may be asked by ASRU to provide advice relating to appropriate standards for housing, care, humane killing etc of these species and the regulatory challenges outlined above.*
- *Deeper understanding of the minds of animals will elevate the moral status of animals in society. This could require a higher bar of justification for enacting harms on animals and could lead to a reduction or the end of their use in science.*

**Certainty:** ★★★★☆

**Timescale:**

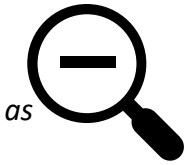
# Decapods

## Summary


- *Decapod crustaceans are an order of invertebrates, consisting of a diverse range of around 15,000 species, including crabs, lobsters and shrimps. Historically, research on these animals has been unregulated, and they fall outside the scope of the UK's Animals (Scientific Procedures) Act 1986 (ASPA). However, the current weight of evidence suggests that they are sentient – capable of experiencing pleasure and suffering - and can thus have a welfare that can be harmed by poor treatment. Such evidence includes presence of nociceptors, complex integrative brain regions and ability to make motivational trade-offs.*
- *The issue has been given prominence by the UK government's commitment to bring in new laws relating to animal sentience and welfare. Defra has consulted on the question of whether decapods should be included in the scope of these laws. If decapods are protected in other contexts, the pressure to protect them in scientific contexts may be strong.*


## Opportunities

## Threats and Challenges



- *Often, invertebrates have been used as replacement for vertebrate animals as part of the 'replacement' within the 3Rs framework; ostensibly replacing a sentient animal with a non-sentient one. However, if decapods are also sentient, then they are equally at risk of harm from use in research, such as through painful procedures and poor housing and handling.*

## Implications for ASC

- *If decapods are sentient (as current research suggests they are), then their use in research should be regulated through the ASPA. Bringing decapods within the scope of ASPA would entail that scientific work using decapods is subject to ethical review, including weighing harms and benefits and application of the 3Rs principles.*
- *This regulation would include ensuring high-welfare handling and transport for wild-caught specimens, appropriate housing and husbandry while in the lab, use of analgesia and anaesthesia for painful procedures, and use of humane methods of euthanasia. Such regulation can also improve public perception of research and increase social licence to operate. A large challenge here is that there has been (so far) relatively little research into the best methods of anaesthesia, analgesia and euthanasia in decapods.*

**Certainty:** ★★★★★

**Timescale:**

# Societal Concerns and Issues

# Mental Health

## Summary


- *Mental health is a growing area of concern, and there has been a change in attitude over the last few years which has seen a push for better treatment for people with mental health disorders.*
- *Treatment for mental health disorders falls into two broad areas – psychological (mindfulness, counselling, Cognitive Behavioural Therapy and other 'talking cures') and pharmacological (antidepressants, antipsychotics etc).*
- *Animal research has helped to develop both psychological and pharmacological treatments for mental health disorders and will be important to any ongoing and new research into novel and improved treatments. Basic research continues to discover more about how the brain functions – and what is not functioning properly in mental illness. Animals are important for both translational research and backtranslation (when treatments found to be helpful in humans are then researched in animals to find out what mechanisms are involved). In many cases, non-human primates are used for neuroscientific research aiming to identify the mechanisms of mental illness.*


## Opportunities

## Threats and Challenges

- *Push for better treatment and management of mental illness is likely to result in a demand for more animal research in this area. Public opinion may not yet have shifted sufficiently to accept that mental health problems are 'worth' the sacrifice of animals. Campaigners could argue that pharmacological treatments should not be pursued because 'talking therapies' are available.*
- *There is also concern over misuse of drug treatments for mental health problems. Misuse of benzodiazepines has been recognized for many years and recently drugs intended for mental illnesses such as ADHD have been used as 'study aids' by students. New pharmacological treatments for mental illnesses could encourage further misuse of medication.*

## Implications for ASC

- *Neuroscience research involving non-human primates requires ASC consideration before a licence is granted. Will the ASC start to see more licence applications for research into mental health disorders?*
- *How will it consider the Harm/Benefit analysis for mental health disorders as opposed to physical health disorders?*
- *Will there be greater public scrutiny of animal research for mental illness?*
- *Will the potential for drugs that enhance cognition for people who do not have a mental illness lead to applications for licences for such research?*
- *How will the ASC view such applications?*

**Certainty:** ★★★★☆

**Timescale:**

# Increasing Public Concern about the Use of Animals in Research

## Summary


- *There is increasing public interest in ethical issues involving animals. A 2018 Ipsos MORI poll on Public Attitudes to Animal Research commissioned by the Government identified increasing public regard for animal welfare, with the proportion of the public who were not at all concerned about the use of animals in research falling to just 15%.*
- *There is increasing public awareness of the poor translational value of animal research and its lack of ability to provide results that can be reliably translated to people. The 2018 Ipsos MORI poll also identified a decline in the proportion of people who thought that animal research was important for research into human health (41% agreed this was true compared to 46% in 2016).*
- *Drivers include the recent rise in veganism motivating people to find out about ethical issues involving animals, widespread use of the internet/social media and the covid-19 pandemic which has drawn attention to how medicines are developed.*


## Opportunities

- *Increased public interest in these issues is leading to growing political interest in human relevant animal-free science.*
- *Increased public interest in these issues should lead to greater openness and transparency about animal research, which would help to increase the accountability of researchers and regulators.*

## Threats and Challenges

- *Challenges are posed by issues such as personal data and intellectual property, appropriate redactions and making good use of technology could facilitate much greater transparency about the regulation of animal research.*

## Implications for ASC

- *Increased public interest in animal protection issues should encourage the ASC to advise the Home Office to promote greater transparency about the way in which animal research is regulated and to ensure that the legal obligation to seek alternatives to animal experiments is being complied with.*

**Certainty:** ★★★☆☆

**Timescale:**

# From Societal Concerns to Societal Contributions

## Summary


- *Discussions of the social aspects of animal research tend to present public opinion as a problem that needs to be monitored and managed in order to secure public trust and support.*
- *This framing of the public as only having concerns reflects the polarised nature of much past public debate around animal research. However, it may miss and make harder opportunities for building different conversations that draw on the ways patients and the public are already contributing to animal research.*
- *Members of the public are already involved in grant and ethical review, participating in clinical trials and biobanks, and taking part in other forms of public engagement based on dialogue or creative exchange where they have the potential to make a positive contribution to shaping the future priorities and practices of animal research.*


## Opportunities

- *Creative public engagements (such as the Nexus Mouse Exchange and the Research Nexus 'Vector' project) enable the public to occupy active positions through which to explore their ideas about animal research, rather than as passive witnesses. This allows participants to explore more complex, nuanced and empowering conversations in which they learn about their own views and the views of others.*

## Threats and Challenges

- *Viewing the public as a potential risk due to information deficits can lead to expert-led, top-down efforts at persuasion and education, which may not address basic issues around trust, and overlooks opportunities for public collaboration.*
- *Viewing the public in this way can increase alienation and accentuate concern and overlook the potential for societal contributions to UK animal research.*

## Implications for ASC

- *The ASC has been asked on several occasions to do further work to incorporate societal concerns in commissioning letters.*
- *There is an opportunity to balance emphasis on societal concerns with the value of incorporating societal contributions in the regulation of animal research. There would be value in reviewing the different ways in which societal views are being engaged in the different elements of the governance of animal research at present, considering whether these focus only on societal concerns or are open to the potential for societal contributions.*

**Certainty:** ★★★☆☆

**Timescale:**

# Public and Political Interest in a "Phase Out" Programme

## Summary


- *There is growing interest in committing to a "phase out" programme, to eradicate the use of animals in research. This is partly driven by the veganism movement, ongoing animal welfare concerns, loss of confidence in the reproducibility and translation of in vivo methodologies and the public perception of animal research.*
- *Examples include: The commitment in the Netherlands to phase out regulatory animal testing by 2025 and the UK Government's interest in redefining animal sentience including the Animal Welfare (Service Animals) Bill.*
- *Public perception around the use of animals in research is variable. A recent report published in May 2019 by Ipsos Mori presented findings of the 2018 survey into public acceptance, awareness and attitudes towards the use of animals in scientific research in the UK found that: two thirds of the public do not feel well-informed about the use of animals in research, while interest in finding out more about work to find alternatives and improve the welfare of animals in research is high and has risen. The report also found that public trust in the regulation of animal research in the UK remains at levels recorded in previous years and public awareness of government work on the 3Rs of animal research remains low.*


## Opportunities

## Threats and Challenges

- *Increasing reference to "human-relevant" science may fuel an incorrect belief that animal data is not relevant to humans and animal products cannot have therapeutic value.*
- *Increasing public movements with political visibility may drive decision-making around UK and international regulations on the use of animals in scientific research.*

## Implications for ASC

- *As public and political agendas flux, the sector must work collaboratively to articulate transparently the high animal welfare standards in the UK and the efforts around 3Rs. Education is clearly needed around the 3Rs and the role of ASRU.*

**Certainty:** ★★★☆☆

**Timescale:**

# Ethical Consumerism

## Summary


- *Ethical consumerism involves preferentially purchasing products that are [or are viewed as] produced in a way that is not harmful to people, the environment, or animals. Historically, purchasing cosmetics not tested on animals has been one of the most popular ethical shopping practices.*
- *A growing public awareness of the sentience of animals (especially companion animals) is contributing to an increase in the number of people concerned about how products they use impact animals including animal testing. This concern is growing beyond cosmetics to encompass household, DIY, food, investment products and is leading to a greater divergence between government and science policy and public opinion on the use of animals for testing.*


## Opportunities

- *The biggest economic argument for avoiding animal testing for household cosmetics and household products is that it is what consumers increasingly demand.*

## Threats and Challenges

## Implications for ASC

- *The implication is that the public will be increasingly sceptical and critical of the use of animals in testing for consumer products and they will continue to use their consumer power to avoid products that involve animal testing across a growing number of product sectors and to preferentially purchase products that do not involve animal testing. This may go beyond the rejection of animal-tested cosmetic products to also include household, DIY, food and investment products that have been tested animals.*
- *The ASC should be mindful of the public's attitude towards animal testing and encourage a move away from its use in product testing beyond cosmetic and household products.*

**Certainty:** ★★★★★

**Timescale:**

# Culture of Care

## Summary


- *The term Culture of Care is used in the laboratory animal community to indicate a commitment to improving animal welfare, scientific quality, care of the staff and transparency for the stakeholder.* (norecopa 2021)
- *The culture of care has been identified within the animal research community as a key area of shared interest and concern, with key questions emerging around how cultures of care are defined, practiced and shared and what the institutional and other barriers may be to realising these. In particular, existing infrastructures and training provision within animal research facilities, while sensitive to the need to promote a good culture of care, are currently struggling to meet the gap between formal mechanisms of delivery and the more open, deliberative, cross-cutting conversations needed to really articulate shared meanings, values and experiences of care.*


## Opportunities

- *A good culture of care is widely recognised as being key to the welfare of both staff and animals in animal research facilities, and to the quality of the science produced.*

## Threats and Challenges

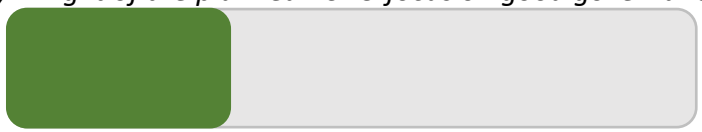
- *Culture of care is a complex and multifaceted phenomenon and hard to teach in conventional, standardised ways.*
- *Animal research regulation emphasises care for the animal, sometimes at the expense of care for the staff.*
- *It can be difficult for people to talk openly and in depth about questions such as what constitutes good care and how this can be put into practice. Restrictions on face-to-face meeting during the Covid-19 pandemic have further limited opportunities for the kinds of informal interactions which facilitate the building of shared cultures, understandings and values.*
- *How can we continue to build, sustain and evidence a culture of care for animal research, without reducing this to a 'tick-box' exercise?*

## Implications for ASC

- *A good culture of care is promoted by regulators of animal research in the UK (Home Office Animals in Science Regulation Unit Compliance Policy, December 2017) as key to delivering compliance with A(SP)A. It is also the focus of sustained efforts and concern within the animal research community in the UK and beyond, evidenced in a number of publications and meetings focusing on understanding and benchmarking a culture of care.*
- *The question of how to build, sustain and evidence a culture of care remains an ongoing concern for the ASC, especially in light of the planned ASRU focus on good governance over the coming year.*

**Certainty:** ★★★★★

**Timescale:**



Short (0-5yrs) | medium (5-10rs) | Long (+10 yrs)

# Unsustainable use of Primates and Dogs

## Summary


- *One of the impacts of the COVID-19 lockdown period has been even more households in the UK with companion animals, especially dogs, at home. The public does not support the use of dogs or primates in experiments. According to an Ipsos MORI poll on 'Public attitudes to animal research in 2018', 86% of the UK public are against testing on dogs while 86% are against testing on large primates such as macaques and 84% are against testing on smaller primates such as marmosets.*
- *Under UK legislation, greater restrictions are placed on the use of primates and dogs compared to other species, but they are still used. In addition, whilst there is a ban on the use of great apes in the UK, no such ban exists for other primates, despite their substantial similarity to great apes.*
- *Dogs and primates are routinely used for second species toxicity tests following experiments on mice and rats. There are questions about how predictive this is of toxicity in humans.*


## Opportunities

- *Phasing out the use of dogs and primates would led to a reduction in animal suffering and use.*
- *The public may support phasing out the use of dogs and primates, which would benefit the reputation of the UK as a centre for humane and human-relevant science.*

## Threats and Challenges

- *There is some reluctance to move away from the use of dogs and primates and these tests are often required by regulators.*

## Implications for ASC

- *The ASC could set up a working group dedicated to this issue and advise the Home Office to adopt stricter criteria when assessing project licence applications.*
- *A working group dedicated to the issue of dogs and primates in two species toxicity testing could also be set up to take a close look at the available evidence and evaluate whether stricter guidance could be developed to reduce requirements for these tests and advise on non-animal methods to replace their use.*

**Certainty:** ★★★★★

**Timescale:**

# Thematic Review

## Summary


- *Article 58 of Directive 2010/63/EU states: "The Commission shall, where appropriate, and in consultation with the Member States and stakeholders, conduct periodic thematic reviews of the replacement, reduction and refinement of the use of animals in procedures, paying specific attention to non-human primates, technological developments, and new scientific and animal-welfare knowledge".*
- *The UK has now left the EU but a clear commitment to conduct thematic reviews is set out in the Guidance: "Although the obligation to carry out reviews is on the Commission, and does not require transposition, we believe that similar reviews can play an important part in ensuring the effective operation of the ASPA. We therefore propose to carry out our own thematic reviews and to consult the Animals in Science Committee, practitioners and other interest groups, including animal welfare and patient advocacy groups, in determining suitable topics as well as on the reviews themselves". Following the consultation on the transposition of Directive 2010/63, the UK government also expressed its "strong support for periodic thematic reviews".*


### Opportunities

- *Thematic review is a realistic mechanism for replacing the use of animals in research. If systematically implemented it can provide an open and transparent method for critical examination of scientific justifications for specific uses of animals in experiments, and result in actions and roadmaps to phase out that animal use.*

### Threats and Challenges

- *As thematic review is yet to be formally implemented in the UK, there is a threat of the concept not being applied systematically, and potential loss of opportunity for robust and realistic actions for phasing out the use of animals in certain areas.*
- *If thematic review is not suitably implemented, the UK risk being left behind as developments in review and assessment of specific areas of animal use are advanced in the EU.*

### Implications for ASC

- *Thematic review provides a mechanism for systematic replacement of animal use in specific areas of research. This makes it an important tool to consider for mapping potential animal uses which can be reviewed for ways to phase out, especially where deemed of little scientific value, and where advanced non-animal methods, more relevant to humans, are available. The Guidance to the ASPA already states that the Government will consult the Animals in Science Committee on proposals for thematic review, so it is an issue directly relevant to the Committees work.*

**Certainty:** ★★★★☆

**Timescale:**

# Section 24 and Transparency

## Summary


- *When the Animals (Scientific Procedures) Act 1986 (ASPA) was passed, bars to public access of the details of animal experiments were strengthened.*
- *Section 24 of the ASPA places a blanket ban on the release of any information from animal laboratories by regulators. Section 24 is now widely acknowledged to be redundant, since equivalent protection is enshrined in the Freedom of Information Act.*
- *For many years there have been calls from animal protection organisations, Parliament, government advisors, experts and the public, for the removal of Section 24. The Animal Procedures Committee (APC) noted that "Section 24 of the ASPA should be abolished" as major changes to the ability of the public to access information since it was created in 1986 - FOIA and the internet – "In our view, this renders Section 24 obsolete".*
- *In mid-2014 the Government published a public consultation on Section 24, in which it was noted that "Section 24 is incompatible with the Government's policies on openness and transparency and the central principles of the Freedom of Information Act (2000)".*


## Opportunities

- *If the evaluation process of project applications were more open, it would allow access by experts to propose up-to-date developments in advanced non-animal methods that could replace animal use. There would be benefits for the progression of the 3Rs.*
- *The removal of Section 24 would provide the opportunity to provide information that would allow a more free, open and constructive debate amongst the public.*

## Threats and Challenges

- *Section 24 is a threat to transparency because it prevents open public debate and wider scientific scrutiny of the use of animals in research. It may be a barrier to producing a strategy to replace the use of animals in research.*
- *Some consider that Section 24, causes public mistrust and a lack of transparency in a public body which is responsible for authorising animal experiments, an issue which is of high societal concern.*
- *Without a robust review and disclosure process, there are also substantial risks to the quality of the science itself.*

## Implications for ASC

- *This issue of the secrecy around animal research, which has been created by Section 24, causes public mistrust and a lack of transparency in a public body which is responsible for authorising animal experiments, an issue which is of high societal concern.*
- *As the public's expectations of transparency by public authorities increase, there may be growing dissatisfaction with the non-availability of information about the specific outcomes of investigations into poor practice, and as to the sanctions then imposed on individual establishments and personal licence holders.*
- *Having been addressed a decade ago by the APC, but with no change in the issue since, the Section 24 topic will continue to be negative for regulators, animal researchers and animals in research for as long as it remains unresolved.*

**Certainty:** ★★★☆☆

**Timescale:**

# Review of Membership Profile of the ASC

## Summary


- *The Animal in Science Committee (ASC) performs the essential function of advising the government on the operation of ASPA in terms of its scientific, ethical, legal and operational currency.*
- *The ASC performs a vital function in a constantly changing environment and its membership profile should be periodically reviewed to ensure it reflects this.*
- *Although there is limited lay or academic membership, the overall balance is currently weighted towards scientific and pro-animal experimentation representation and does not reflect the wide-ranging base of public and expert opinion in the area.*
- *A review of the ASC membership profile has synergies with calls for greater transparency, addresses questions of wider public involvement and calls for oversight to be more equal in terms of opinions on animal experimentation. It answers calls for greater accountability regarding the link between science, public morality and the law in this area.*


### Opportunities

- *A broader membership base might provide enhanced public confidence in the continued review, development, implementation and oversight of regulation of animal experiments.*
- *An enhanced membership profile provides the opportunity to ensure that oversight reflects the views of diverse voices and the breadth of extant knowledge.*
- *Review provides the potential to draw on expertise that can help to develop alternative approaches to conducting animal experiments, through, for example, enhanced representation of expertise in alternative methods and statistics.*

### Threats and Challenges

- *There is a possibility of encountering resistance from within the scientific community/current membership who might fear change in itself, or the nature and form of new conversations and scrutiny around scientific experimentation.*
- *Another potential challenge is the push-back from the scientific community which currently has 'ownership' of the area in terms of fearing of outside interference in scientific development, time consuming delays and unnecessary hindrance of scientific development.*
- *The scientific and development community has cited threats to commercial interests through enhanced openness and external involvement.*

### Implications for ASC

- *The potential of a broader and more representative membership for the ASC is to gain greater public and agency support in terms of greater democratic, operational and ethical scrutiny. The ASC would gain greater democratic authority.*

**Certainty:** ★★★★☆

**Timescale:**

# UK Policy in an International Context

# Brexit and FTAs

## Summary


- *Currently, animal research is regulated across the EU under Directive 2010/63/EU. The purpose of the Directive is to harmonise standards across the EU and promote the 3Rs. The UK implemented the Directive in the Animals (Scientific Procedures) Act 1986. This Act will remain in force after Brexit; however, the cooperation between the UK and other Member States will no longer be regulated under EU law. It is possible that the final UK-EU free trade agreement will include some provision in this area (currently the draft provides "each party should establish rules to avoid duplicative testing on vertebrate animals" in article IP.45). However, whether (and how) research animal welfare features in any such agreement is uncertain.*
- *The main driver in this area is the UK's departure from the EU, which has led to the ability and necessity to negotiate trade agreements with third countries and the implications that come with this.*


## Opportunities

- *Whether there is a final agreement or whether any such provision is included, this is a desirable policy goal both in terms of efficiency in testing and in view of public perception.*
- *Whether this is included in the agreement or in any other trade instrument, there is scope for the UK, in its future international relations, to encourage engagement with and support of the 3Rs*

## Threats and Challenges

- *In view of animal welfare as an area for negotiation in any free trade agreement, the UK may also experience pressure to weaken protections.*
- *These agreements may restrict or limit funding of certain procedures considered unethical in one country but not another, or insist on allowing procedures previously prohibited in the UK.*

## Implications for ASC

- *Any international obligations imposed upon research in a free trade agreement could have implications for the work of the ASC because such obligations may change the regulatory environment. Future scoping could consider how these matters have been dealt with in existing agreements between third countries and between third countries and the UK. Engaging fully with this subject would enable the ASC to provide relevant information and advice to the Home Office.*

**Certainty:** ★★★★★

**Timescale:**

# Post Brexit Challenges and Opportunities

## Summary


- *Throughout the UK's European Union Membership, the UK and European Union ("EU") collaborated to successfully implement progressive animal research legislation and regulation. Whilst part of the EU, the UK and the EU have both influenced each other to improve animal welfare standards for animals used in research and largely benefitted from each other in this area.*
- *The British public will want reassurance that leaving the EU will not result in a drop in standards or increased use of animals for research. There are opportunities to demonstrate leadership in the reduction and replacement of animal testing. Chemical regulation and avoidance of duplicate testing is a priority area.*
- *Many of the positive elements of EU Directive 2010/63/EU ("The Directive") still remain enshrined in Animals (Scientific Procedures) Act 1986.*


### Opportunities

- *The UK now has an opportunity to review and improve the statutory framework under which animal experiments are conducted, since it is no longer subject to Article 2 of the Directive.*
- *The UK has an opportunity to lead the way in strengthening legislation on the 3Rs.*

### Threats and Challenges

- *The UK will lose access to EU funding for scientific research, including both animals and non-animal research.*
- *Lack of EU mechanisms for accountability could lead to a fall in UK animal testing standards and reduced public confidence.*
- *Animal testing bans and welfare standards may be comprised as the UK seeks new trade deals.*
- *The UK no longer participates in EU REACH system which aims to avoid duplicate animal testing for chemicals. The UK has developed a UK REACH system to mirror this, but lack of access to EU REACH system may still lead to duplication.*

### Implications for ASC

- *The ASC will have to grapple with the issues that flow from Britain's departure from the EU and will face the challenge of maintaining (as a minimum) and ideally, improving, animal protection and reducing animal use.*
- *The Home Office may also wish to consider how it can encourage improvements in animal welfare standards outside the UK. Given the UK's desire to maintain its leading position in biotechnology and other life sciences and in pharmaceuticals, the UK needs to ensure that its regulation of scientific procedures using animals does not lead to such procedures being 'offshored' to countries with lower standards.*

**Certainty:** ★★★★★

**Timescale:**

Short (0-5yrs) | medium (5-10rs) | Long (+10 yrs)

# UK Duplication Issues

## Summary


- *The legislation which sets out chemical testing requirements in the EU, Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), contains provisions to reduce the duplication of animal testing, such as mandatory data sharing between companies within the EU and encouraging companies to use other means before conducting (vertebrate) animal tests.*
- *Data sharing is essential to reduce the use of animals involved and avoid duplication of these chemical tests.*
- *Regulations were passed in 2019 to create a UK regulatory system for chemicals, which will be "similar" to the current EU system following the UK's exit from the EU.*
- *The exit of the UK from the EU is the driver for this loss of mandatory data sharing. The switch is currently being made to the REACH UK system, there has been concerns over the cost of this move, stemming from duplication of efforts in the EU.*


## Opportunities

## Threats and Challenges

- *Mandatory data sharing agreements between the UK and EU, which reduce the duplicative testing for chemical safety tests have been lost. UK companies with no access to chemical safety data from EU companies, may have to do animal testing themselves, potentially repeating tests already conducted in Europe.*
- *The generation of a UK REACH system will require huge amounts of money from the chemicals industry. This will be a main factor in attempts to reduce animal testing which will be part of efforts to reduce the costs associated with duplication.*

## Implications for ASC

- *The Home Office and ASRU have a role to play in the evaluation of animal tests which may have already been carried out in the EU. The ASRU is responsible for ensuring "that REACH compliance is taken into account when projects are agreed for the conduct of animal tests needed under or for REACH". While it has been suggested that licences may "be amended to ensure REACH compliance is taken into account when projects are agreed for the conduct of animal tests, and appropriate conditions added to licences so that meaningful and informative records of these tests are maintained and made available for inspection" , the potential block in access to data which could lead to duplicate animal testing must now be taken into account.*

**Certainty:** ★★★★★

**Timescale:**

# Rapid Progress in the Netherlands on Reducing Animal Experiments

## Summary


- *In 2016, the Dutch Agriculture Minister 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.*
- *NCad produced a series of recommendations, concluding 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, such as vaccines. For fundamental research, applied scientific research and education, NCad committed to facilitating the development of 10-year 'visions for animal free innovations'. Other recommendations included incentives to promote the development and application of animal free methods, a specific fund for such technologies and ensuring that animal free innovation is included in the Netherlands' Science Agenda.*
- *The Dutch Government has also set up the Transition Programme for Innovation without the use of animals, which is a network organisation with partners who are active in government, academia and industry.*


## Opportunities

- *NCad recommends that the Netherlands undertakes international, collaborative work to reform the guidelines that currently result in animal testing for regulatory purposes. This could make it easier for UK researchers to use animal free methods for regulatory tests.*
- *Ncad recommends the creation of a "data warehouse" on the 3Rss and animal experiments. If this UK were to access this in the future, it could be a valuable resource for UK researchers and ASRU inspectors.*

## Threats and Challenges

- *The incentives recommended by NCad to encourage companies to develop NAMs. This could result in UK companies working on human relevant techniques relocating to the Netherlands. This would result in a 'brain drain' in the human relevant life sciences sector and the UK falling further behind in replacing the use of animals in research.*

## Implications for ASC

- *British regulators often view the UK as a centre of excellence for animal welfare, but ambitious initiatives being undertaken by other countries mean that we risk being left behind in the drive to replace animals with human relevant techniques. If Britain is to become a 'science superpower', as well as maintaining our reputation for high standards of animal welfare, it is vital that politicians and regulators take bolder action to replace animal experiments.*
- *The ASC should carefully follow developments in the Netherlands and seek out opportunities for learning and collaboration and the implementation of similar initiatives.*

**Certainty:** ★★★☆☆

**Timescale:**

# Climate Change

# Sustainability

## Summary


- *Extinction Rebellion and Greta Thunberg have highlighted the climate emergency, emphasizing that the world is at a tipping point. Research in 2019 (before the coronavirus pandemic) showed that the public cited climate change as the biggest global threat.*
- *David Attenborough's Blue Plant II focused on the issue of single-use plastics contaminating seas and oceans, which in turn increased the British public's opposition to single-use plastics.*
- *Big companies have announced changes in practice to help tackle climate change, from moving to renewable energy sources to cutting the amount of plastic packaging they use.*
- *The UK is in the process of setting its own chemicals for sustainability policy and it is highly likely to mirror efforts in the EU towards a toxic free environment.*


## Opportunities

- *Using innovative modern human-relevant testing methods to produce consumer products to do no harm to people, animals, and the planet, fits within broader sustainable development goals.*

## Threats and Challenges

- *Animal research laboratories do not currently score highly on sustainability. Many use single-use PPE (overalls, masks, shoe covers, hair nets, gloves). Those that use washable scrubs still require daily laundering. Cages are sterilized and supplies autoclaved at high temperatures and facilities are required to maintain certain temperatures for animal welfare.*
- *Oxford University states that laboratory buildings (not just animal research laboratories) are responsible for over 60% of total energy consumption and carbon emissions across the University .*

## Implications for ASC

- *Will animal research become the focus of campaigns against unsustainable practices?*
- *Should the contribution to climate change be included in harm/benefit analyses and other ethical considerations around animal research?*
- *Should animal facilities be encouraged to improve their environmental impact in the short term, before environmental campaigns position such laboratories as environmental pariahs?*
- *The ASC could play an active role in the development of the UK's own chemical strategy for sustainability.*

**Certainty:** ★★★★☆

**Timescale:**

# De-Extinction

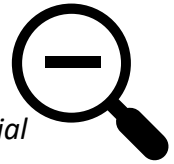
## Summary


- *De-extinction, sometimes called resurrection biology, is the replacement of an extinct species by adapting a living organism to replace the extinct species. This can be achieved by various breeding techniques, including artificial selection, back-breeding and precise hybridization facilitated by genome editing. One goal of de-extinction is to restore vital ecological functions that sustain dynamic processes producing resilient ecosystems and increasing biodiversity and bioabundance.*
- *The rapid advances in genome editing using CRISPR-Cas9 technology make de-extinction of many species more likely to be achieved.*
- *For recently extinct species, 'standard' cloning technology could be used such as the nuclear transfer used to generate 'Dolly the Sheep'.*
- *De-extinction by generating proxies is limited by the half-life of the DNA of the extinct animal and the technological ability to synthesize its DNA. However, advances in synthetic biology and genome editing should allow longer sequences of 'extinct' DNA to be synthesised.*


## Opportunities

- *Potentially substantial benefits for biodiversity, world ecology, and an opportunity to rectify past harms inflicted by humans on other species.*

## Threats and Challenges



- *Challenges include cost, technical difficulties, ethical implications and the controversial nature of reversing extinction itself.*
- *Threats include public outrage, ecological disaster, and the potential to alter the course of natural history.*
- *Many species have become extinct due to habitat loss and such habitats may not be replaceable. Resurrected species would be considered endangered and would therefore require conservation, using already limited resources.*
- *De-extinction could have the unintended consequence of condoning extinction (since species could be brought back later) and could give impetus to endeavours that threaten biodiversity.*

## Implications for ASC

- *Protected animals will be used as surrogates for the birth of genetically modified species that currently do not exist. Research will be carried out with extant species to determine ecological niche requirements etc.*
- *The legal status of 'resurrected' species will need to be determined. How would a de-extinct species be classified?*

**Certainty:** ★★★★☆

**Timescale:**

# Pollution and Health

## Summary


- *Pollutants in the environment are described as the largest cause of disease and early death globally. Anthropogenic chemicals extensively pollute water, air and soil and it has been estimated that since the 1950s, >140,000 new chemicals have been released into the environment.*
- *Many of the contaminants exhibit bioaccumulation, biomagnification and are lipohilic and thus stored in fat. Anthropogenic environmental chemicals are considered a "significant global public health concern". The story is complex, because humans/animals are exposed to mixtures of chemicals, which may also interact, making it difficult to extrapolate the effects to a single chemical. Given the complexity of pollutant impacts on humans, the study of mechanisms that underlie chemical induced disease in humans is often hampered by both ethical and logistical constraints.*
- *Animal and non-animal models can be used to study the effects. Such studies include: chemical mixture effective reflective on human exposure, effects persisting across generations, sentinel species for human exposure, toxicity testing and in vitro mechanistic studies.*


## Opportunities

- *Animal studies can be used to inform regulators, politicians, industry and science itself. A recent example of this is the UK parliamentary audit on Toxic chemicals in Everyday Life and selected animal models are integral to this process.*
- *Non-animal models can also be used.*

## Threats and Challenges

- *Extrapolating from animal studies to the human comes with the caveat that human effects might differ.*

## Implications for ASC

- *Awareness of pollution related disease and dysfunction is increasing and the negative impacts of pollutants on human and animal health and well-being, requires the application of combined methodologies inclusive of justified animal exposure systems combined with sentinel studies, human biomonitoring and in vitro studies.*

**Certainty:** ★★★★☆

**Timescale:**

# Global Food Sustainability

## Summary


- *Feeding the world sustainably is a pressing challenge, now and in the future. It is estimated that 26.4 % of the global population are subject to moderate or severe levels of food insecurity.*
- *There is currently a drive to apply genome editing (GE) techniques to address health and welfare problems in farmed animals, increase yields and improve nutritional value. This involves the use of regulated procedures to create new lines, and there are pressures to release the maintenance of these animals from regulations controlling animal use in scientific procedures.*
- *Laboratory animals are used to develop and test treatments and vaccines against diseases of farmed animals, which may become more prevalent if farming is intensified without concomitant precautions against disease spread.*
- *Laboratory animals will also be used to develop and test treatments and vaccines against zoonoses and epi/pandemics that may be created by more widespread farming and destruction of habitats to create more agricultural land for grazing or feed production.*


## Opportunities

- *The benefits of affordable, nutritious food are clear, in preventing both undernourishment and obesity.*
- *The use of GE is often suggested to help address increasing human demands for animal protein, meats of specific qualities and animals resistant or resilient to infectious disease. GE has also been suggested to help respond to animal welfare concerns and to global heating (e.g. by creating 'hornless cattle' and heat tolerant animals).*

## Threats and Challenges

- *GE techniques can cause unpredictable and unintended changes to the genome.*
- *There are ethical and animal welfare concerns about the application of these technologies to farmed animals.*
- *Publics have expressed concerns about genetically modified animals in food in the UK and EU.*
- *It can be argued that the environmental and animal welfare impacts of these practices, and the potential human cost of future pandemics, warrants serious scrutiny of proposals to apply biotechnologies or develop medicines to facilitate suboptimal husbandry*.

## Implications for ASC

- *As a body that is responsible for advising the Secretary of State and AWERBs, the ASC will likely be involved in monitoring the drivers, harms, benefits and wider ethical issues associated with research that aims to increase the yields and availability of animal-based foods.*
- *The many wider ethical issues and societal concerns would need to be considered when making judgements about animal use in scientific procedures to create new GE farm animals, or to develop and test vaccines and treatments for farmed animals.*
- *There will likely be cross-over with other committees such as the Animal Welfare Committee, Food Standards Agency NDPBs, Advisory Committee on Novel Foods and Processes, Regulatory Horizons Council and Advisory Committee on Releases to the Environment.*

**Certainty:** ★★★★★

**Timescale:**

# Can Anaesthesia Go Green?

## Summary


- *Modern halogenated inhalation anaesthetics undergo little metabolization during clinical application and evaporate almost completely to the atmosphere.*
- *Atmospheric concentrations of anaesthetic gases have been determined, and the most damaging agent, desflurane, is rapidly increasing.*
- *The damage caused by the release of anaesthetic gases has been comprehensively described; nevertheless, the barriers to sustainable practice changes in anaesthesia have not been sufficiently addressed.*
- *Inhalational agents are widely used in biomedical research settings as they allow easier control of the depth of anaesthesia, and the rate of induction and recovery is rapid.*


## Opportunities

- *Biomedical research anaesthetists have a considerable opportunity to drive sustainability within their organisations through modification of their practice, research and education.*

## Threats and Challenges

- *The scope of change would have to extend far beyond the UK, since climate change is a global phenomenon, and global practices vary widely between countries.*
- *Welfare implications if alternatives do not sufficiently manage pain. In some cases, such as NO2, alternatives do not yet exist.*
- *Whilst TIVA eliminates the greenhouse gas emissions associated with volatile agents, the drugs still exert an environmental impact because of their manufacture, transport and syringe driver delivery.*
- *Increased cost factors (funding implications).*

## Implications for ASC

- *Impact on science.*
- *Impact on the planet / climate crisis.*
- *Animal welfare considerations when using alternatives such as injectable agents which may have a lower safety margin and longer recovery times.*
- *Impact on the 3Rs e.g. refinement options becoming not available for light sedation or restraints of animals in science.*
- *Better education and recommendations for the bioscience sector.*
- *Lobbying for reduction in price costs for more environmentally friendly options and techniques.*

**Certainty:** ★★★☆☆

**Timescale:**

# Issues Affecting Establishments

# Use of gene altering technology

## Summary


- *Genetically modified (GM) is a term used to describe animals that have had their DNA altered, for example by adding, removing, or modifying specific genes., including adding genetic material from other species.*
- *In scientific research this is normally a deliberate change to model a disease or investigate the function of a biological process.*
- *This technology has opened the door to the ever-expanding potential uses of genetically altered animals in the study of human disease.*
- *The advent of modern gene editing technologies such as CRISPR/Cas 9, has further increased the ability to carry out specific genome edits in animals, and create strains of mice for many different disorders on demand.*
- *Of the 3.4 million regulated procedures carried out on animals in 2019 nearly half, 1.67 million, were for the creation and breeding of GA animals, mainly mice.*


## Opportunities

- *Increased knowledge of the function of various genes in animals and humans has helped us understand aspects of some human conditions and disorders.*
- *Increased validity that comes from reducing variation in a sample, leading to more conclusive results.*
- *Gene editing technology can be used directly on human tissue to establish the role of certain genes directly in human cells without the need to use animals.*

## Threats and Challenges

- *Modelling the genetics of a varied human population would potentially require multiple GA animal lines with different genetic backgrounds, leading to more animals and more expense.*
- *The value of producing more complex GA animal models of human diseases must be considered not only ethically and financially, but also weighed against the scientific relevance of the model and the number of animals required to create it.*
- *Gene manipulating technology can lead to 'off-target' effects where other genes are mutated as well as the target gene.*
- *This technology is increasingly complex and sufficient training in breeding, genotyping and phenotyping of GA animals is required.*

## Implications for ASC

- *There are opportunities to review current systems and incorporate resources to enable researchers to assess the value of GA animal lines in certain areas and the availability of alternatives.*
- *Quality controlling genetic research.*
- *GA NHP.*
- *Genome editing can be applied to all species including NHP. There are no current genetically altered NHPs in the UK, but this could be a future development.*

**Certainty:** ★★☆☆☆

**Timescale:**

# Complexities of GA / GE creation and subsequent incorrect/overbreeding

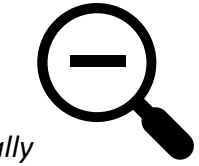
## Summary


- *GA mice and fish are the most widely used animal models and account for 1.67 million of the 2019 HO return figures.*
- *Genetically altered animal 'models' are becoming increasingly complex, using many new genes and species. Poor practices can lead to the incorrect genotypes and excessive animal breeding.*
- *This breeding presents a complex problem in laboratory zebrafish who have lost part of the sex-determining gene.*
- *Reports that large numbers of mice and fish were culled at the start of the Covid-19 pandemic, primarily seems due to interruption of research projects and the lack of available animal care staff to maintain breeding colonies.*
- *Animal Facilities need permanent staff that are trained in this area to ensure minimum wastage and correct breeding strategies. There are issues surrounding research staff undertaking the breeding programmes, a lack of basic understanding and that the positions are usually temporary.*


## Opportunities

- *This would have a positive impact on rodent animal welfare and a reduction in waste numbers of animals produced from overbreeding and tick over colonies.*
- *There are good cryopreservation programmes for zebrafish – which could be opened up to anyone using the species. This could reduce the numbers of animals required.*

## Threats and Challenges



- *There are issues surrounding research staff undertaking the breeding programmes, a lack of basic understanding and that the positions are usually temporary.*
- *Poor practices can lead to the incorrect genotypes and excessive animal breeding.*
- *If incorrect animals are produced this leads to science which is unreproducible and incorrect.*

## Implications for ASC

- *The ASC should be aware of the issues surrounding the problem and be seen to be promoting best practice.*
- *As a large proportion of the annual stats is made up of creation and breeding of genetically altered (GA) animals, this would suggest mandatory training should be developed throughout the laboratory animal science sector for delivery on the Personal licence training course.*

**Certainty:** ★★★★☆

**Timescale:**

# Animal Research at Places Other than Licensed Establishments (POLEs)

## Summary


- *There is a growing recognition that non-laboratory research at POLEs presents its own unique practical and ethical challenges compared with laboratory work, relating to: 1) supervision; 2) working under an array of regulations; 3) navigating regulatory interfaces; 4) ethics; 5) the involvement of stakeholders and publics in research; and 6) negotiating productive relationships with inspectors and NVSs.*
- *POLEs researchers, particularly those undertaking wildlife field research, often express the idea that A(SP)A was not written with their work in mind. Greater attention to laboratories in terms of guidance and support is understandable given that POLEs are quite rare, and that working at POLEs may involve researchers working alone or in small groups in remote locations*


## Opportunities

- *Further attention to the challenges of non-laboratory research in future would be appreciated by researchers working at POLEs, along with encouragement in establishing support networks and further training for researchers working at POLEs.*
- *Addressing the challenges associated with POLES presents and opportunity for improved supervision, clearer regulatory interfaces, clearer ethical considerations and more productive relationships with inspectors and NVS.*

## Threats and Challenges

- *Supervision by inspectors and named veterinary surgeons (NVSs) may be more challenging and less frequent given the remoteness of many wildlife research field sites, and the lack of permanent presence of named persons.*
- *Regulatory interfaces may be difficult to navigate for researchers based at POLEs, with certain kinds of studies which incorporate elements of both research and animal husbandry or veterinary treatment.*
- *Stakeholders and members of the public may be present at field sites and involved in research, making it challenging to navigate different perspectives on animal ethics and treatment with these groups.*

## Implications for ASC

- *The ASC could potentially have a role in clarifying the RVP/research boundary and other grey areas, and also providing options for research that falls into grey areas.*
- *Some AWERBs already look beyond the scope of A(SP)A to oversee projects that are sub-threshold, based overseas, or involving animals not covered by the Act. Furthermore, organisations that typically do not hold A(SP)A licences (e.g. zoos, agricultural colleges) may still have ethical review bodies that oversee non-A(SP)A research with animals. Such moves are broadly supported by stakeholders; the ASC may therefore wish to consider encouraging local ethical review even of non-A(SP)A work, which echoes the idea that AWERBs should be viewed as hubs for ethics and welfare discussion.*

**Certainty:** ★★★★☆

**Timescale:**

# Transport and Supply of Animals

## Summary


- *Critical to the continuing success of the biomedical sector is the timely and efficient import/export transport of purpose-bred research animals, biological samples and vaccines. Without the ability to move research animals from one country, or continent, to another, or from a breeder or supplier, to a research institution, scientific research may be disrupted.*
- *Post-Brexit there are a number of changes to the way in which products, including live animals, are imported or exported. Although major disruptions are yet to be seen, some companies have described difficulties in moving animal feed.*
- *In the UK and US, long standing restrictions imposed by cross border transport providers, have made it increasingly difficult for the biomedical community to move the research animals.*
- *EARA and other significant associations in Europe and the US, as well as a number of pharmaceutical companies and contract research organisations, are concerned about the ongoing and future impact of China's ban on the export on non-human primates.*


## Opportunities

## Threats and Challenges

- *Changes to import/export processes and requirements may cause disruption to animal supply in the short to medium term.*
- *Short-term shortage of animals for medical research could significantly impact the progress of both covid-19 and non-covid-19 research.*
- *Potential to impact the scientific competitiveness of the UK if R&D activities are impeded.*

## Implications for ASC

- *Any significant impact on the number of animals available and used for UK research may impact the UK's annual statistics on use of animals in scientific procedures, but this will likely take a number of years before such trends are visible.*

**Certainty:** ★★★☆☆

**Timescale:**

# Veterinary Retention

## Summary


- *All animal research establishments must have a Named Veterinary Surgeon (NVS) 'who accepts responsibility under ASPA to provide advice on the health, welfare and treatment of animals within these establishments'. But despite this key regulatory position, veterinarians remain under-researched in academic studies of laboratory practice. Existing publications have noted the difficult balance between welfare and science, the complexity of the professional role, and how laboratory vets talk about public views of animal research. Whilst published research specifically focussed on the NVS role is still scarce, existing research can help identify challenges facing the wider veterinary profession which may eventually impact on laboratory animal practice.*
- *The UK veterinary profession is currently facing a significant recruitment and retention challenge and at the same time, research from the Animal Research Nexus Programme on NVS suggests that many vets had a general lack of awareness of the NVS role. If this apparent low level of awareness of the potential career path of laboratory veterinary medicine continues, the retention challenge currently faced by the veterinary profession may have knock-on effects on the ability to recruit future NVSs.*


### Opportunities

- *Whilst the formal veterinary curriculum is undoubtedly under pressure, ensuring the NVS role is highlighted in university career sessions should ultimately assist those for whom veterinary clinical practice is not experienced as a good fit.*

### Threats and Challenges

- *Qualified veterinarians planning on leaving general practice due to working conditions may leave the profession entirely, due to low awareness of the existence of the Named Veterinary Surgeon role. This may result in future recruitment issues.*
- *Failure to horizon scan and plan for future NVS recruitment may thus cause problems for the animal research community.*

### Implications for ASC

- *Veterinary surgeons are a key component of the UK's animal research governance structure. Consideration could be given as to how the NVS role can be made more visible within the veterinary profession as an alternative to a career in general practice.*
- *There is minimal existing data on the extent to which the current challenge faced by the veterinary profession as a whole is reflected or experienced in the NVS community, or whether and how the recruitment squeeze will impact the availability of NVSs for laboratory work.*

**Certainty:** ★★★☆☆

**Timescale:**

# Increased Automation in the Management, Housing, Care and Welfare of Laboratory Animals

## Summary


- *Within the laboratory animal science sector, new equipment is allowing technology to take over many of the tasks previously undertaken by people.*
- *Technology can provide efficiencies in the management of animal facilities and reduce human variability in the carrying out of certain tasks.*
- *Data management systems are helping establishments manage their animal colonies (inc. complex breeding programmes for genetically altered animals) and maintain appropriate records.*
- *It is common for research establishments to have robots that wash dirty cages, and prepare new ones by adding a pre-programmed quantity of bedding for example.*
- *Animal housing systems are also becoming more advanced e.g. allowing increasing levels of monitoring and control of environmental inputs and parameters.*
- *Technologies to recognise and monitor the behaviour of individual animals in their home cages are becoming more sophisticated (e.g. see the IntelliCage) and widely used.*
- *As breeding and research programmes are becoming ever more complex, facilities are looking for opportunities to help them manage this and commercial companies are also looking to profit.*
- *Technology could allow a lot more data to be collected and analysed automatically, with potential benefits to animal welfare and science.*


## Opportunities

- *Technology could provide cost savings and time efficiencies. It could also potentially reduce the scope for or impact of 'human error'.*
- *Freeing up animal technologists and others from tasks such as cage washing or feeding could allow them to spend more time on animal-centred tasks, e.g. animal observation, care, and training etc. which could benefit both animal welfare and science.*
- *Potential to gather more data (improving experimental data sets) and also change the way some procedures are carried out*

## Threats and Challenges

- *Over-reliance on technologies to assess welfare (e.g. software that recognises predicted clinical signs) can risk animal welfare, as human observers provide an important failsafe.*
- *Some technologies, particularly behavioural recognition software, generate very large volumes of data which need to be processed, which can be resource-intensive.*

## Implications for ASC

- *It will be important for ASRU to stay up to date with technological developments within the sector to identify potential risks and benefits to animal welfare. ASC could choose to take steps to assure itself that this is happening.*
- *ASC could liaise with the Institute of Animal Technology on the topic, to see whether its members identify any risks or benefits to animal welfare and the Culture of Care.*
- *ASC will need to advise AWERBs with respect to implications for establishment culture and staff training, if use of the above technologies increases (e.g. with respect to AWERB tasks relating to supporting named persons and provision of appropriate training, establishing and reviewing processes for monitoring animal welfare).*

**Certainty:** ★★★★☆

**Timescale:**

# Heterogeneity

## Summary


- *The organisation of laboratory animal research for biomedical purposes has been highly focused around mice and rats. However, there are growing critiques around how this standardisation may have created incentives for generating statistically significant publishable results, which may also be of low reproducibility and relevance for human disease.*
- *The use of individually ventilated cages (IVCs) in these experimental systems also appears to impact animals, potentially causing many mice to exhibit abnormal behaviour, hypothermia, and stress. Individually ventilated cages may therefore only yield results that apply only to a narrow set of unusual conditions.*
- *One response to these challenges has been to increase the heterogeneity of the species, environments and experiments used in animal research. This has several different elements. There are calls for more heterogeneity in animal housing and experimental design; there are moves to introduce a greater diversity of species into animal research; there are demands for methods of statistical analysis better able to manage complex multifactorial data sets from animals and environments; and there is a rise in the use of so-called "real life" experiments in veterinary clinical settings.*


## Opportunities

- *Increasing the heterogeneity of animals and environments used in biomedical research may have benefits in opening up new avenues for understanding and treating disease and improving the reproducibility and translatability of preclinical animal research.*
- *Working with more heterogenous environments may benefit animal welfare.*

## Threats and Challenges

- *The focussed development of research systems around GM mice in standardised individually ventilated cages, means that many research facilities, methods, and skills are not currently well equipped to deal with this diversity. In addition, diversification may bring new challenges around experimental design, statistical analysis, animal welfare, and ethical review.*
- *Introducing other species to laboratories when their needs are poorly characterised may initially involve greater harms.*

## Implications for ASC

- *There is a dual challenge here, of understanding how to increase the capacity of systems of biomedical animal research to move beyond experiments on single gendered mice in standard IVCs and to do so in a way that takes full account of the potential benefits and harms associated with this shift. Making experiments more experimental increases both opportunities and uncertainties. This has implications for processes of harm-benefit analysis, but also underlines the importance of including scientific validity and research benefits as key elements in the harm benefit analysis.*
- *The ASC has been asked to assist in ASRU's new vision for a composite measure of harms.*

**Certainty:** ★★★★☆

**Timescale:**