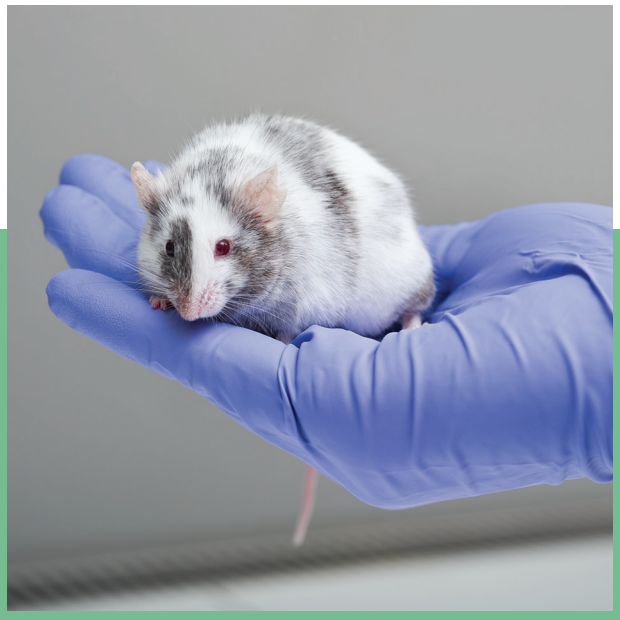
Home Office

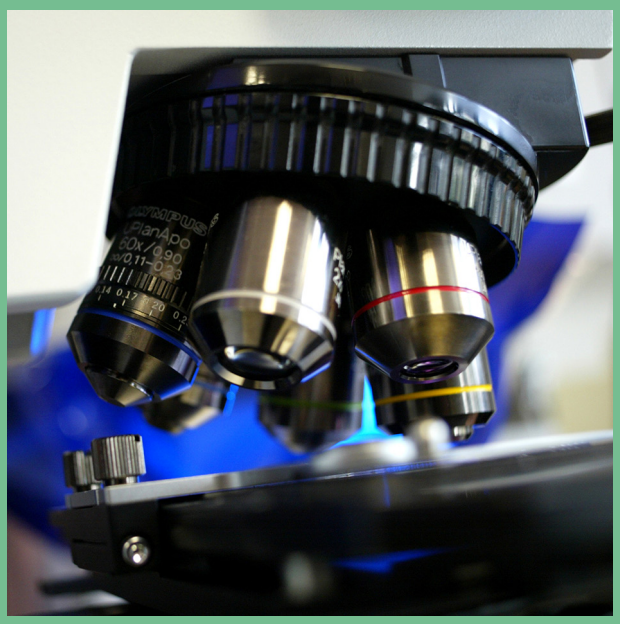
Department for Business Innovation & Skills

Department of Health

Working to reduce the use of animals in scientific research

Delivery Report





Acknowledgements

This Delivery Report describes the progress made on actions set out in the Delivery Plan published on 7 February 2014. The Report has been prepared by the Home Office (HO), the Department for Business, Innovation and Skills (BIS) and the Department of Health (DH). It includes substantial contributions from other government departments including the Department for Environment, Food and Rural Affairs (Defra), the Foreign & Commonwealth Office (FCO) and the Food Standards Agency (FSA), and from government agencies including Public Health England (PHE), the Medicines and Healthcare Products Regulatory Agency (MHRA), the Veterinary Medicines Directorate (VMD), the Animal & Plant Health Agency (APHA), the Food and Environment Research Agency (Fera), the Centre for Environment, Fisheries and Aquaculture Science (Cefas) and the Health and Safety Executive (HSE). The Research Councils have also contributed significantly to this work.

We recognise in particular the major contribution made to the implementation of the Delivery Plan by the National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs).

ISBN: 978-1-78246-731-1

Foreword

In February 2014, the Government published its Delivery Plan 'Working to reduce the use of animals in scientific research'[1]. In this Delivery Report we summarise progress since that publication.

The Delivery Plan brought together new and existing initiatives, through a science-led approach, for promoting the widespread adoption of scientific and technological advances which present significant opportunities to **replace** animal use, to **reduce** the number of animals used and to **refine** the procedures involved so as to find additional ways to minimise suffering of animals used in scientific research – the **3Rs**. The Plan also proposed ways in which the UK would increase openness and transparency.

Since the Plan was published, a wealth of significant new research and knowledge dissemination on the 3Rs has been completed. It includes the launch of the first products from the NC3Rs open innovation programme CRACK IT, a £4m competition run by Innovate UK and the NC3Rs to fund the commercialisation of non-animal technologies, and the publication of important new studies on veterinary and human vaccine testing by Defra and Public Health England which have identified scope to reduce the numbers of animals used in developing vaccines. New joint working by the RSPCA and the Home Office has additionally produced refined testing models to reduce animal suffering.

We have taken major steps to encourage greater international adoption of 3Rs techniques, including a ground-breaking programme of knowledge-sharing with regulators and life science associations in China led by the Animals in Science Regulation Unit. In addition, we have published collaborative research across the global life sciences sector led by the NC3Rs and the UK's Medicines and Healthcare Products Regulatory Agency to minimise the use of recovery animals in pharmaceutical development.

The use of animals in scientific research rightly attracts considerable attention and scrutiny. The public is entitled to know why such research is carried out, how animal welfare needs are addressed and what steps are being taken to reduce dependence on animal-based research. We are therefore delivering on our commitments to increase openness in the use of animals for research in the UK. In particular, we have consulted on options to reform section 24 of the Animals (Scientific Procedures) Act 1986 to allow greater access to animal research information. Greater openness brings increased opportunities to explain why the carefully regulated use of animals in scientific research remains of vital importance in improving our understanding of human and animal disease, and in ensuring the safety of new medicines.

The UK is a global leader in the 3Rs and the concerted efforts underpinning the Delivery Plan have provided a new platform and new tools to accelerate the domestic and international uptake of scientifically valid alternatives in research and safety testing. Ongoing scientific and technological advances will provide many further opportunities to reduce our dependence on animal-based testing. We will build on the momentum generated and cross-sector relationships developed through this Plan's implementation to ensure that the UK stays at the forefront of global efforts to find and use alternatives to animal testing, while continuing to make clear the important benefits that animal research brings to society.

The Rt Hon Lynne Featherstone MP
Minister for Crime Prevention
Home Office

George Freeman MP
Minister for Life Sciences
Dept for Business, Innovation & Skills,
& Dept of Health

1 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/277942/bis-14-589-working-to-reduce-the-use-of_animals-in-research.pdf

Contents

Introduction

The Government is clear that science has a major role to play in developing new technologies and approaches that wherever possible replace, reduce and refine the use of animals in scientific research (the '3Rs'). Breakthroughs in areas such as tissue engineering, stem cells and computer modelling have opened up significant opportunities to reduce our reliance on animal research models. Government departments, agencies and other publicly funded bodies with a role in life sciences research have an important part to play in helping find and seize these new opportunities, and to share knowledge in this area both in the UK and internationally.

The Government is also committed to increasing openness and transparency in animal research, by giving the public new tools and opportunities to understand how and why such research is carried out, and to scrutinise the steps being taken to minimise suffering and find alternatives.

The Delivery Plan, published on 7 February 2014, set out three strategic priorities in meeting the Coalition Government's commitment to work to reduce the use of animals in scientific research:

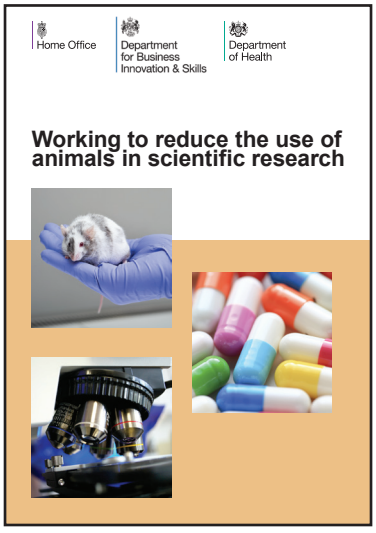
- advance the use of the 3Rs within the UK;
- use international leadership to influence the uptake and adoption of 3Rs approaches globally; and
- promote an understanding and awareness of animals where no alternatives exist.

In Sections 1, 2 and 3 of this report, we describe the progress that has been achieved in pursuing these three core objectives, including new initiatives that have been launched since the original Plan was published. In the tables at the end of the report we provide updates on each specific action.

The Plan has been implemented through a partnership comprising:

- relevant central government departments and non-ministerial departments including the Home Office, BIS, Defra, the Department of Health, the Foreign Office and the Food Standards Agency;
- the National Centre for the 3Rs (NC3Rs); and its main funders, the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBSRC); and
- agencies, including Public Health England (PHE), the Medicines and Healthcare Products Regulation Agency (MHRA), the Health and Safety Executive (HSE), the Food and Environment Research Agency (Fera), the Animal & Plant Health Association (APHA), the Centre for Environment, Fisheries and Aquaculture Science (Cefas), the Veterinary Medicines Directorate (VMD) and Innovate UK (formerly the Technology Strategy Board).

The partnership has brought together expertise, knowledge and data-sharing around a common set of priorities and provides a strong platform to identify further opportunities to implement the 3Rs in the UK and overseas. It has also helped drive a more proactive and consistent approach in communicating with the public about the use of animals in scientific research.



PROGRESS ON THE THREE STRATEGIC OBJECTIVES

Strategic Priority 1

Advancing the use of the 3Rs in the UK

Overview and summary progress on actions (for a detailed breakdown see Tables, Strategic Priority 1)

The UK has strength and depth to support the delivery of 3Rs approaches through the NC3Rs, other funders and the regulatory framework but also strongly supported by researchers and organisations in the life sciences sector.

The NC3Rs' mission is to replace, refine and reduce the use of animals in research. Building on their ten-year history, they not only lead the UK science community in developing and sharing 3Rs techniques and practice here but show strong international leadership in the field. The various programmes and initiatives funded by the NC3Rs have both identified problems and found innovative solutions to shape changes in policy, practice and regulations through science-led approaches. The recent publication of the NC3Rs' vision for the next ten years is a holistic approach focusing on five inter-related areas: Practice, Procedures, People, Places and Policy[2].

It is not only the 3Rs that are important. The Government recognises that innovative approaches to research can open up new fields of study in areas where animal methods have limits, and in doing so find improved methods for answering scientific questions that could lead to a real reduction in the use of animals in the longer term. Such innovation is being backed by Innovate UK, working with the NC3Rs and the Research Councils, through the funding (£3m committed) last year of business-led feasibility studies into Non-Animal Technologies (NATs). Innovate UK has now announced a new £6m funding competition in this area which opens on 23 March[3] and is working in parallel with partners, including the NC3Rs and Research Councils, to produce a NATs Roadmap for the UK. The Roadmap will provide a focus for supporting and increasing the scale and impact of NATs activities in the UK research and industry base, and develop routes to commercialisation and adoption of the NATs products and services generated.

The Home Office Animals in Science Regulation Unit (ASRU – the regulator) has delivered new Guidance and a Code of Practice with increased emphasis on the 3Rs during 2014. ASRU continues to engage across the spectrum of stakeholders, through proactive stakeholder

2 http://www.nc3rs.org.uk/our-vision

3 https://interact.innovateuk.org/-/developing-non-animal-technologies

meetings, consultation and presentations at a range of national fora, to disseminate the 3Rs and promote leading practice to improve animal welfare within the regulatory framework.

Case study examples from the Delivery Plan

Action 1.1 (1) Publication of the review of the NC3Rs' pharmaceutical industry collaborations

The NC3Rs published its ten-year review of working with more than 40 pharmaceutical and biotechnology companies and regulatory agencies from the UK, elsewhere in Europe and the USA, fostering a cross-company approach to the 3Rs. The NC3Rs is a trusted partner for data-sharing with companies providing extensive non-clinical and clinical data-sets from historic compounds and those currently in development. The NC3Rs works with companies to interrogate and analyse data and rationalise the requirement for *in vivo* studies to deliver 3Rs impacts. Through its collaborations the NC3Rs has sought to build evidence bases that could not be achieved by any one company alone.

Action 1.8 Updated requirements for applications which include animal research

The Medical Research Council and the Biotechnology and Biological Sciences Research Council (MRC and BBSRC) have produced updated guidance on their expectations for applicants and reviewers in relation to the use of animals in bioscience research. The emphasis is on improving the information on experimental design and the 3Rs. As part of the process of implementing this, a workshop was held jointly with NC3Rs in September 2014 to promote the importance of improved scrutiny of experimental design in the peer review process, including representatives from charitable funders.

Further actions supplementing the Delivery Plan

Frozen Embryo and Sperm Archive

There has been a steady increase in usage of the Frozen Embryo and Sperm Archive (FESA) at MRC Harwell, part of the European Mutant Mouse Archive, both for archiving stocks and in requests for distribution. Improved techniques have led to a shift from freezing embryos towards freezing sperm, which reduces the numbers of mice necessary per strain for archiving and recovery.

Strategic Priority 2

Influencing the uptake and adoption of 3Rs approaches globally

Overview and summary progress on actions (for a detailed breakdown see Tables, Strategic Priority 2)

The UK's commitment and development of 3Rs approaches places it in a strong position to spread best practice and influence overseas. Our vision for the continued development of non-animal technologies provides a bright future for predictive test systems that supports both the drive for animal welfare and a thriving life sciences community that uses animals only where there are no validated alternatives. Furthermore, the UK seeks to give companies with high ethical standards greater opportunities to trade in growing markets that currently require the use of questionable animal tests in order to market their products. The UK also continues to support the UK life sciences industry through working to harmonise international regulatory testing requirements.

Through the Delivery Plan we have made significant progress against our objectives, in particular by:

- supporting the NC3Rs' international initiatives;
- engaging with other countries to promote harmonisation of global regulatory standards which use alternatives wherever possible;
- providing an evidence base for where changes would be beneficial to international regulations which require animal use; and
- working to end unnecessary animal testing for cosmetics globally.

Case study examples from the Delivery Plan

Actions under 2.1 Joint international leadership by the NC3Rs and MHRA

In addition to engagement with specific countries on the 3Rs, the UK has helped lead discussions in OECD and other international fora to secure agreement to new validated alternatives to animal testing. The tables with this report describe joint international leadership by the NC3Rs and the MHRA to identify opportunities to reduce the use of animals in safety pharmacology studies and to minimise the use of recovery animals in pharmaceutical studies. The UK also played a key part in discussions that led to the OECD publishing two new Test Guidelines on human health hazard endpoint skin sensitisation that are expected to replace gradually animal tests required in this area.

The Government and its partner agencies have taken new action to promote the 3Rs within Europe. For example, the NC3Rs carried out a detailed programme of knowledge-sharing with the Italian Ministry of Health and the Lombardy Regional Government. This is helping lead to the creation of a panel of scientists that can advocate the use of the 3Rs in Italy.

Action 2.4 Cosmetics alternatives and Action 2.5 Developing Delivery Plan priorities into an effective international communication and influencing strategy

The UK and EU have banned animal testing of cosmetics. However, 80% of other countries have not. There is therefore significant scope to reduce global testing on animals through the UK showing global leadership and influence. This will, in turn, deliver economic benefits for the UK by opening up foreign cosmetics markets to ethically produced UK cosmetic products.

This priority has a particular focus on China where animal testing is mandated for cosmetics imported from the EU and elsewhere. Through this work we support a drive to further incorporate 3Rs techniques into frameworks, thus encouraging the move towards greater acceptance of non-animal data and the opening up of markets to trade.

China has relaxed the requirements for animal data on domestically produced cosmetics so that there is no longer a mandate to provide such data as long as an adequate risk assessment can be made based on other data. However, there is still work to be done both to apply this to cosmetics produced outside China (e.g. in the UK) and to up-skill Chinese regulators and cosmetics producers to be able to perform such risk assessments. We are supporting China in this endeavour alongside our partners in the EU Commission and the European trade association, Cosmetics Europe.

The Home Office Animals in Science Regulation Unit, and BIS have hosted a visit to the UK by a senior delegation of officials from the China Food & Drug Administration (CFDA) to discuss ways in which human safety of cosmetics and medicines can be assured through rigorous risk assessments which do not include unnecessary animal data. Their programme included visits to: the NC3Rs; Huntingdon Life Sciences; the Association of the British Pharmaceutical Industry (ABPI); Unilever; Walgreens Boots Alliance; and meetings with the EU Commission and Cosmetics Europe as well as UK government teams. The visits demonstrated best practice in cosmetic and pharmaceutical safety testing and showcased UK expertise in the 3Rs with a particular focus on non-animal testing methods.

UK government officials, in partnership with the Chinese Association for Laboratory Animal Sciences (CALAS), held a scene-setting seminar in Beijing to explore opportunities for UK–China cooperation in the development of standards for the welfare of research animals and their ethical use in China. This is important to create an ethical framework within which UK scientists can collaborate with partners in China on a compatible basis. A further UK–China Seminar is planned for 2015 to support the further development of current voluntary standards for research animal care, welfare and ethical use to become mandatory national standards in China.

We have also engaged with other countries that mandate testing for cosmetics, including Brazil, where we are encouraging a new domestic political initiative to legislate against the unnecessary use of animals in testing cosmetics and also the acceptance of safety data which has been produced overseas, such as in the UK. As the third largest consumer of cosmetics in the world, Brazil has the potential to deliver the great reductions in animal testing.

Strategic priority 3

Promoting an understanding and awareness about the use of animals where no alternatives exist

Overview and summary progress on actions (for a detailed breakdown see Tables, Strategic Priority 3)

The Government is committed to promoting a culture of openness and transparency around the use of animals in scientific research. Openness is crucial to help people understand, and challenge if they wish, the reasons for animal research where no validated alternatives exist, and to demonstrate more widely the many safeguards in place to minimise suffering. Public trust in the regulatory system depends in large part on people feeling that they have the ability to get answers to their questions and to explore any concerns. Being able and willing to talk openly about the use of animals also helps signal to global industry and academia that the UK remains one of the best places for high quality life sciences research.

To understand public opinion in this area and gauge the success of new approaches on openness, the Government continues to commission an independent opinion poll on public attitudes to animal research. Results from the latest poll in March 2014 indicate that around two-thirds of the public continue to accept the use of animals in medical research where there are no alternatives. At the same time, the poll suggested that more could be done to increase public understanding around animal research. For example, only three in ten respondents said that they felt “well informed” about the use of animals in research, while a similar proportion still believed that animal testing is allowed for cosmetics, despite this having been banned in the UK for over a decade. The poll clearly indicates the need for openness and transparency to place public understanding on a firm footing to inform well-evidenced public debate on the issues. Since that poll was carried out, a number of new initiatives on openness and transparency have been launched, as summarised below.

Action 3.3 Concordat on openness and transparency

In May 2014, the life sciences sector launched a landmark ‘Concordat on openness and transparency in UK animal research’[4]. The Concordat has been signed by 86 organisations working across the UK life sciences sector, including major pharmaceutical companies and contract research organisations, UK universities engaged in animal research and the UK’s medical research charities. It commits each organisation to the following four pledges.

- To be clear about when, how and why they use animals in research.
- To enhance their communications with the media and the public about their research using animals.
- To be proactive in providing opportunities for the public to find out about research using animals.
- To report on progress annually.

4 http://www.understandinganimalresearch.org.uk/policy/concordat-openness-animal-research/

The Concordat puts the UK life sciences sector at the head of global efforts to increase openness and transparency in animal research. Every signatory organisation has given a clear commitment both to facilitate greater scrutiny of their animal research and to be visibly accountable by reporting annually on their progress towards implementing the Concordat.

Its publication has already led directly to a number of new initiatives on public engagement, including the development of new websites[5] and outreach activities by, among others, University College London, the University of Cambridge, the University of Bristol and Cardiff University. Signatories are also taking steps to engage directly with the public and the media, to explain why they use animals in research and the measures in place to ensure animal care and welfare. This more accountable approach to the use of research animals is intended to give members of the public a clearer idea of the work carried out in animal research facilities, as well as stimulate discussion and challenge. A progress report on implementation of the Concordat is due to be published in June 2015, and will include measures taken to promote greater public dialogue about the use of animals in research, as well as to invite greater accountability.

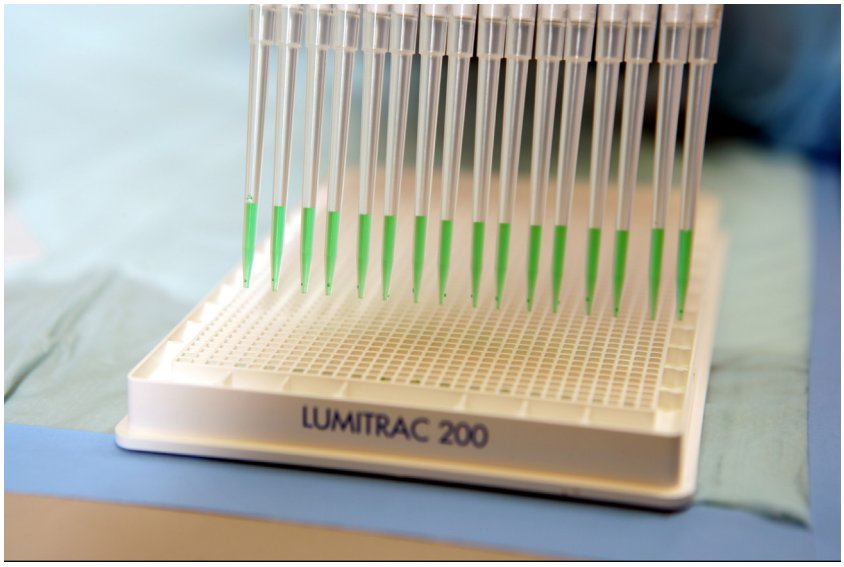
Action 3.4: Review of section 24 of the Animals (Scientific Procedures) Act 1986

As we committed to in the Delivery Plan, the Government has held a full public consultation on options to reform section 24 of the Animals (Scientific Procedures) Act 1986 (ASPA). Section 24 currently places a blanket ban on the disclosure of any information provided to the regulator or those involved in animal research in confidence. The Government recognises that this is out of step with wider policy on openness and transparency. Last year's consultation document set out a preferred government option of moving to more open disclosure of information while retaining statutory prohibitions on the disclosure of sensitive information, including that which could prejudice intellectual property rights or compromise personal safety.

Further actions supplementing the Delivery Plan objectives on openness

Publication of investigation reports

Further to the Delivery Plan, the Home Office has, in 2014, started publishing anonymised summaries of reports where there has been a substantial investigation by the regulator[6]. The Home Office has routinely reported high-level summaries of all cases of non-compliance in the ASRU Annual Report for several years. However, these reports are in addition to the usual reporting to help ensure that all stakeholders can learn from the outcomes of these investigations as early as possible and enable them to address any potential weaknesses. In addition, the reports provide



5 http://www.ucl.ac.uk/animal-research
http://www.cam.ac.uk/research/research-at-cambridge/animal-research
http://www.cardiff.ac.uk/research/our-research-environment/integrity-and-ethics/animal-research
http://www.bristol.ac.uk/university/governance/policies/animal-policy.html

6 https://www.gov.uk/government/publications/compliance-investigations-by-the-animals-in-science-regulation-unit

the public with an insight into this work. In determining which investigation reports to publish, the Home Office have applied a public interest test. In the interests of transparency, we expect that a decision to not publish an investigation report to be the exception.

Publication of actual severity data pilot[7]

The recently transposed EU Directive (2010/63/EU) requires the collection of data on the actual severity of procedures. Each animal that undergoes scientific procedures must be allocated a severity classification indicating the level of harm actually suffered due to those procedures. As an aid to ensuring a smooth implementation of the new requirement for reporting actual severity, a pilot study was carried out over a two-month period in August and September 2013. The data collected were a sample and not intended to be entirely representative of the distribution of procedures performed in the UK; however, it provided a preliminary snapshot of the distribution of actual severity.

A prospective classification that predicts the likely harms is assessed by inspectors and is used as part of the harm–benefit analysis of a proposed project. The intention behind introducing recording actual rather than just prospective harm is primarily to increase transparency on the real harms of animal use. Collecting these data will also have the potential to aid in the targeting of refinement initiatives by identifying areas of high severity.

The results showed that 5% of the 35,409 procedures reported were determined to be sub-threshold, 81.5% were reported as mild, 11% were reported as moderate and only 2% were reported as severe. Just over 1% were non-recovery procedures. The severe procedures involved mainly mice, rats and fish. Severe outcomes were reported for both basic and applied research procedures, and also for routine production, but not for regulatory testing.

This information is now formally collected in the UK, and in the rest of the EU for the first time for procedures completed from January 2014 onwards. It will be published for the first time later in 2015.

7 https://www.gov.uk/government/publications/animals-in-science-regulation-unit-annual-report-2013

Tables

In this section we describe each of the actions set out in the Delivery Plan and provide a detailed report on progress.

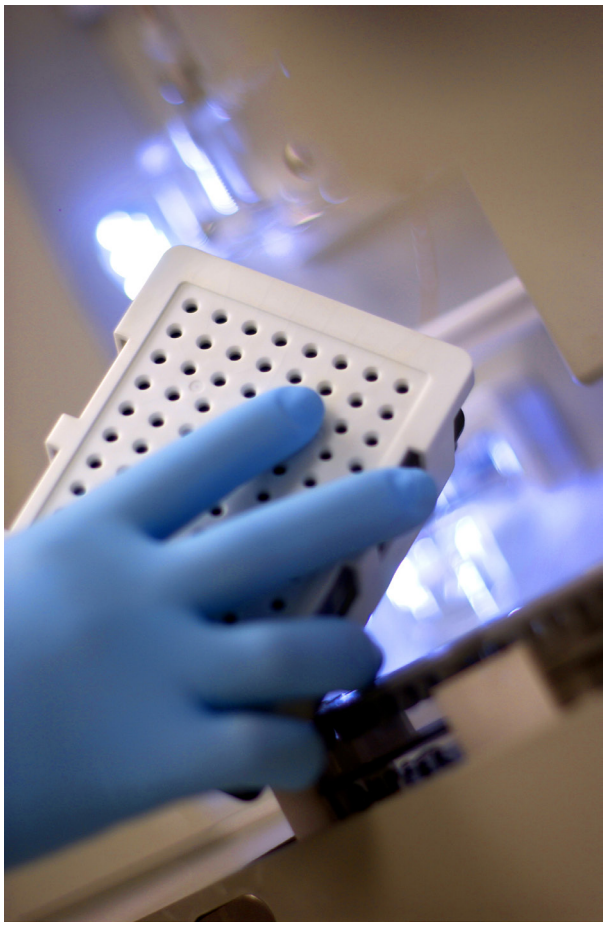
In the Delivery Plan we described a wide range of measures to promote the 3Rs, both within the UK and internationally. The Plan also provided opportunities for researchers and industry to address the 3Rs in their work. The actions included existing programmes and also sought to foster new, specifically targeted, programmes.

As in the Delivery Plan, the Delivery Report tables in this section consider progress on delivery against each of our three strategic priorities:

Strategic Priority 1 – a domestic programme which focuses on advancing the use of the 3Rs within the UK;

Strategic Priority 2 – an international programme aimed at influencing the uptake and adoption of 3Rs approaches globally; and

Strategic Priority 3 – a programme aimed at promoting an understanding and awareness about the use of animals where no alternatives exist.



Strategic Priority 1: Advancing the use of the 3Rs domestically by putting them at the heart of science-led programmes.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
1.1 National Centre for the Replacement, Refinement and Reduction of Animals in Research programmes **(NC3Rs)**	1) Publication of the second review of the NC3Rs research portfolio by November 2013.	- Received positively by stakeholders and sector. - Enhanced understanding by stakeholders and public of high-quality research funded by the NC3Rs and the animal welfare, scientific and societal benefits of this.	Completed.
	2) Launch of the NC3Rs Experimental Design Assistant online resource.	Early uptake and use by research community and improved understanding of the 3Rs benefits to good experimental design.	The beta testing is now complete and the system is being amended from stakeholder feedback. The Experimental Design Assistant will be launched in 2015.
	3) CRACK IT: The 2013 CRACK IT Challenges competition consists of five Challenges identified jointly by the NC3Rs and industry sponsors who provide in-kind contributions including data, access to compounds, validation studies, etc. CRACK IT Challenges is a milestone-driven funding competition from the NC3Rs which is designed to (i) minimise the use of animals in research; and (ii) support the development of marketable products and/or improved business processes. The total budget for the 2013 round of CRACK IT Challenges is approximately £7m.	Contracts awarded to address the challenges.	The 2014 Phase 1 awards for proof-of-concept studies have been made for the three CRACK IT Challenges – these focus on toxicity end-points and we have sponsors (who provide in-kind contributions) from the pharmaceutical and chemical sectors. The Phase 2 winners will be decided in July 2015.
	4) Strategic award: Imaging technology development for the 3Rs – the NC3Rs have recently announced a strategic funding call to support high-quality research proposals to address genuine technological challenges in preclinical imaging which, if solved, would advance science and the 3Rs. The total budget for this strategic call is £1m.	Awards made.	The sum of £1.5 million has been invested in five imaging projects with co-funding from the Engineering and Physical Sciences Research Council (EPSRC).
	5) Disease models – the NC3Rs are developing a programme of work, based on previous experience, focusing on disease models and efficacy testing. This includes disease areas such as asthma, epilepsy and pain, and they are working with the ABPI to secure funding to lead on this. An initial priority is cancer models.	Engaging and building relationships with the cancer research community in applying the 3Rs to their research.	A workshop was held in February 2015 covering preclinical oncology research models. The output of workshop will inform NC3Rs' future plans in oncology such as research investment.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
1.2 Improved resource sharing including outcomes of research, resources, animals and data **(NC3Rs with MRC and BBSRC)**	Examples of ongoing work include: - Recently launched NC3Rs Infrastructure for Impact (IfL) scheme. - Shared Ageing Research Models (ShARM – Biorepository of aged mouse tissues). - Availability of Non Human Primate tissue from Centre for Macaques (CFM). - Enhanced archiving of animal models in academia. - Coordinated mouse phenotyping of genetically altered animals (IMPC). - The NC3Rs and funders are considering ways to enhance data-sharing and publication of negative results.	Four Infrastructure for Impact projects awarded totalling £1.3m.	There has been a steady increase in usage of the Frozen Embryo and Sperm Archive (FESA) at MRC Harwell, part of the European Mutant Mouse Archive, both for archiving stocks and in requests for distribution. Improved techniques have led to a shift from freezing embryos towards freezing sperm, which reduces the numbers of mice necessary per strain for archiving and recovery. A workshop was held in February 2015 that brought together funders, publishers and scientists to discuss the impact of publication bias on animal research
1.3 Postgraduate 3Rs training **(NC3Rs)**	PhD studentship scheme as part of the NC3Rs strategy to embed the 3Rs in the training and development of scientists from the start of their careers. To date 37 awards in total have been made.	Improved training on project design for PhD students.	In December 2014 an award was given to a further cohort of ten PhD studentships totalling £900,000. Two of the awards are for projects to refine rodent models of stroke.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
1.4 Increase the impact of Home Office inspectors and other regulators in the dissemination of 3Rs advances and advise about implementation **(HO and MHRA)**	Enhanced dissemination of the 3Rs through continued development of expert knowledge networks (internal HO Inspectorate activities working with others e.g. NC3Rs) and externally with licensees through: - publication of Guidance on the operation of the Act with increased emphasis on 3Rs and harm–benefit assessment; - outreach activities attending and speaking at meetings and conferences; and - regular discussions with new and existing licensees.	i) Guidance to new regulations published including significant material on 3Rs and harm–benefit assessment. ii) Inspectorate have formalised a strategy for internal knowledge transfer. iii) Inspectorate have formalised a strategy for dissemination of 3Rs information and implementation with licensees. iv) Continuation of Continuous Professional Development activities and networking with relevant stakeholders.	i) Guidance completed. ii) Improved knowledge transfer and dissemination of 3Rs information being developed as part of a technology reset programme to be delivered late 2015. iii) A review of the inspection process has emerging findings to advance thematic inspection to develop wider engagement with specialist groups, NC3Rs and licensees to promote consistent leading practice. iv) Ongoing including attendance at NC3Rs workshops, external stakeholder meetings (LASA, LAVA, International Neurology and Immunology Conferences) and EU Commission workshops.
	Increased requirement to applicants for new Marketing Authorisations to demonstrate absence of a suitable non-animal test before an authorisation based on an animal test will be approved. Working with the Home Office, MHRA to pursue manufacturers with existing Marketing Authorisations to validate non-animal tests for their product, particularly where the animal test is severe, or where another manufacturer of a similar product has validated a non-animal test.	i) New Marketing Authorisations based on non-animal tests being approved. ii) Waiving of application fee by classifying such a change as a Type 1 variation to the Marketing Authorisation. iii) Non-animal tests for existing Marketing Authorisations being submitted.	The Medicines and Healthcare Products Regulatory Agency (MHRA) has continued to work with companies to develop animal alternatives and highlights any such possibilities when assessing dossiers.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
1.5 Refinement of models **(RSPCA with HO)** **(Cefas with NC3Rs)**	Work to refine the most severe models to avoid or reduce animal suffering. Models to be considered include: - Experimental Autoimmune Encephalomyelitis (EAE); - Seizures; - Rheumatoid arthritis; and - Sepsis.	- Reports on each of the selected topics prepared and published. - Recommendations promulgated.	Rheumatoid arthritis report completed and submitted to Arthritis Research & Therapy, currently with reviewers. Report promoted via poster at RUS-LASA-ICLAS by HOI co-author, further promotion by Royal Society for the Prevention of Cruelty to Animals (RSPCA) planned when report is in press[1]. The RSPCA also developed and published a 'Road Map' towards ending severe suffering in 2014[2]: This provides generic guidance in the form of a series of practical steps that establishments can take to identify and implement approaches to enable them to work towards ending the use of models and procedures that can cause severe suffering. RSPCA plans for work on severe suffering for 2015: • Two further EWGs will be established in 2015 with the aim to complete guidance for publication in early 2016. • The 'Road Map' approach will be developed further, including the production of a resource pack that can be implemented at establishments. • An online resource to provide practical guidance on refining and avoiding procedures that could cause severe suffering is currently at the planning stage.

1 http://journals.lww.com/shockjournal/Abstract/publishahead/Refinement_of_Animal_Models_of_Sepsis_and_Septic.98571.aspx

2 http://www.frame.org.uk/wp-content/uploads/2014/09/RSPCA-Road-Map.pdf

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
	i) Measures taken to eliminate death as an end-point in fish disease studies to reduce suffering. This represents between 76% and 94% of the fish work of the National Reference Laboratory. ii) Refinement of the Fish Sexual Development Test (FSDT) for detecting early life-stage effects and potential adverse consequences of putative endocrine disrupting compounds on sexual development (Cefas – funding from NC3Rs). The development of molecular markers for stickleback endocrine function and protocols for studying behaviour of the animals to facilitate a decrease in use of sticklebacks. iii) NC3Rs' funding to examine indicators of fish well-being.	i) Active evaluation of different ways to reduce animal suffering and animal numbers used. The new project licence for this work does not include death as an end-point. ii) Has resulted in a 25% to 50% reduction in the number of fish needed for this test. A calculation of the number of chemicals requiring FSDT testing in Europe alone shows that use of sticklebacks in this test will result in about 90,000 fewer fish being sacrificed. iii) Project report demonstrating better fish welfare in experimental systems, but also more widely in farmed fish in aquaculture.	i) Underwater cameras have been established in 30 tanks. This is giving a clear picture of animal behaviour, clinical signs and welfare without the need to disturb the fish unnecessarily for checks. Fish that are displaying signs of morbidity can be removed before they die, substantially reducing their suffering. ii) The refinement of the test is complete and it is now available for use. The new model species (sticklebacks) is now in the regulatory guideline (TG234). iii) This is in the middle of the experimental phase. Preliminary results indicate that small changes in the aquaria make large differences to fish behaviour. The aim is to link this with markers in the water that can be measured non-invasively.
1.6 "Actual Severity" reporting in Annual Statistics on Use of Animals in Science **(HO)**	Implement retrospective reporting of the "Actual Severity" of all scientific procedures on protected animals in line with the Directive (2010/63/EU). This will enable us to better understand: - levels of overall animal suffering in terms of numbers of animals experiencing each category of severity – sub-threshold, mild, moderate or severe; - which procedures are most severe and in which species; and - whether 3Rs implementation is having an impact on reducing overall severity.	i) Completion and review of pilot trial for retrospective (actual) severity reporting. ii) Development of Guidance on recording Actual Severity. iii) Commence project to map phenotyping of GA mouse strains to actual severity categories commenced (with external stakeholders e.g. MRC Harwell). iv) Completion of analysis of pilot data for limited publication. v) Publication of first complete year of retrospective actual severity data. vi) Provision of complete year data to the EU Commission.	i) Completed and published in the ASRU Annual report.[3] ii) Guidance on Actual Severity published on the Home Office website[4] iii) Phenotyping project workshop with MRC Harwell held with Home Office Inspectors. ASRU intend to publish material in 2015 as a tool for establishments to ensure effective breeding practices, specifically for GA animals. iv) Pilot data published in 2013 Animals in Science Regulation Unit (ASRU) annual report. First full year data to be published in July 2015.
1.7 Capture of information on scientific outputs relevant to 3Rs and the implementation of 3Rs advances **(MRC and BBSRC)**	Research Councils to improve the capture of information on scientific outputs relevant to 3Rs and the implementation of 3Rs advances in funded projects. Data on 3Rs implementation and relevant outputs captured via the introduction of new questions in the Research Councils' computerised data-gathering systems. Encouragement of other charitable funders to do likewise.	i) Successful collection of captured data. ii) Publication of analysis of data collected. iii) Other major charitable funders of animal research able to collect comparable data.	A new set of questions about the 3Rs has been introduced into Researchfish, the online system for collecting information on research outputs, outcomes and impact, and researchers funded by Medical Research Council (MRC), Biotechnology and Biological Sciences Research Council (BBSRC) and some medical charities submitted data for the first time in November 2014. The first analysis of data on implementation of the 3Rs and outputs relevant to the 3Rs will be available in 2015.

3 https://www.gov.uk/government/publications/animals-in-science-regulation-unit-annual-report-2013

4 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/276014/NotesActualSeverityReporting.pdf

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
1.8 Updated requirements for applications which include animal research **(MRC and BBSRC)**	Research Councils to issue updated requirements and guidance for applications which include research involving the use of animals. Ensure that every research programme and project proposal receives effective scrutiny before it is funded and that opportunities to implement scientific advances to replace, reduce or refine animal use are not missed.	i) Drafting and issuing of new guidance. ii) Evaluation of impact of new guidance.	Medical Research Council (MRC) and Biotechnology and Biological Sciences Research Council (BBSRC) have issued revised guidance for applicants about information that must be provided in proposals involving the use of animals. A workshop was held jointly with NC3Rs for Board and Panel members in September 2014 to promote the importance of improved scrutiny of experimental design in the peer review process.
1.9 Highlight on 'Animal Welfare: Measures and assessment' **(BBSRC and NC3Rs)**	Dissemination event: BBSRC joint highlight with NC3Rs on 'Animal Welfare: Measures and assessment'. 16 projects funded totalling nearly £5.8m.	BBSRC working with NC3Rs to ensure that outputs are captured and disseminated to ensure better monitoring and assessment of welfare in the future. Dissemination events during the course of the programme.	Plans for dissemination event in spring 2015.
1.10 Veterinary vaccine testing **(VMD and Defra)**	Review of batch testing of biologicals such as veterinary vaccines. Identification of areas for possible replacement in the batch testing of vaccines, especially areas of such testing involving animals where the replacement of the test would have the biggest impact in reducing number of animals used.	A report setting out the number of animals used during in-process and final product testing of batches of vaccines released by the VMD.	A report was published in April 2014 eliciting considerable interest among veterinary medicines regulators throughout Europe. A short presentation was given to the Immunological Working Party of the Committee for Medicinal Products for Veterinary Use (CVMP) and a poster about the report presented at the 50th Anniversary Conference of the European Directorate for the Quality of Medicines (EDQM). In 2014, further presentations were given to the European Medicines Agency Ad Hoc Joint Expert Group on the 3Rs and at a Veterinary Vaccines conference in Brussels.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
1.11 Human Vaccine testing **(PHE)**	Development of 3Rs techniques for use in human vaccine development. i) Working with academic and clinical partners to develop a BCG model that allows assessment of efficacy of novel TB vaccines which refine the use of animal models. ii) Actively developing cell-based assays for the characterisation of the manufacturing process and the batch release of the product, evaluating the potential to replace toxicity release tests.	i) This model has the potential to refine the current test to allow further development to take place at human clinical trials stage. ii) If developed, the Toxin Neutralisation Assay test will replace the current potency test resulting in a reduction in the numbers of animals used and the severity of the testing.	i) The use of advanced lung imaging, in non-human primates, has led to the establishment of more refined efficacy studies for TB vaccines and therapeutics by reducing the challenge dose that needs to be given. This has resulted in less disease severity and shortening the time taken to demonstrate efficacy, in addition to a reduction in the number of animals used. Furthermore, funding has been provided for the development of a welfare assessment system that will quantify refinement strategies. This will be published in due course. Software will be launched to allow the research community to apply the welfare assessment in a user-friendly manner. ii) The *in vitro* component of the assay (Toxin neutralisation assay) has been developed and validated. The development of the *in vivo* component is near completion and the validation will be completed this year. This will then lead to a reduction in both the number and severity of animal procedures required for the batch release assays.
1.12 Development of non-animal technologies **(TSB and NC3Rs)**	Technology Strategy Board (TSB) development of non-animal technologies. Competition to fund early stage feasibility studies investigating novel non-animal technologies to improve product development across a range of industries. Up to £4 million funding available.	Industry and sector informed of competition in autumn 2013 and awards made in 2014. Output from the funded studies will be novel non-animal technologies that produce approaches that are 'fit for purpose'.	Business-led feasibility studies were funded under the first non-animal technologies call (Innovate UK's emerging technologies and industries programme). The total budget was £4 million with funding from Innovate UK, the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), Engineering and Physical Sciences Research Council (EPSRC), Biotechnology and Biological Sciences Research Council (BBSRC) and Defence Science and Technology Laboratory (Dstl). A road map for the non-animal technologies programme is being prepared for publication by Innovate UK with input from NC3Rs and other expert groups. Consortia workshops were held in three locations in the UK throughout February 2015.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
1.13 Ensure government departments and agencies consider the 3Rs when commissioning or funding research involving animals **(GCS and CSAs)**	Government Chief Scientist and Departmental Chief Scientific Advisers (CSAs) to ensure that government departments and agencies consider the 3Rs when commissioning or funding research involving animals. Commitment from departments and their agencies on the 3Rs including policy statements overseen by the CSAs.	i) All government departments including DH, MoD, Defra, HO, BIS and agencies have statements on their websites.	Statement uploaded on Gov.UK, linked to all relevant Departments that regulate or fund research involving animals, including Home Office, DH, BIS, Defra and MoD.[5]
1.14 "Minimisation of animal testing" leaflet **(Defra and HSE)**	As UK Competent Authority for REACH, Defra and HSE already produce a leaflet entitled "Minimisation of animal testing". This is a popular publication and provides a brief summary of the opportunities that are available to REACH registrants to minimise the amount of animal testing needed to comply with REACH registration. This initiative will ensure new information about advances in *in vitro* testing, particularly of irritants, is communicated to UK-based duty holders.	i) Update the publication "Minimisation of animal testing" which is popular and effective in promoting the 3Rs in this area. ii) Encourage the European Chemicals Agency (ECHA) to similarly update its guidance in this area for those with registration duties in 2018.	The revised leaflet has been published by the REACH UK Competent Authority.[6]

5 https://www.gov.uk/research-and-testing-using-animals

6 http://www.hse.gov.uk/reach/resources/18animaltesting.pdf 4

Strategic Priority 2: Influencing the uptake and adoption of 3Rs approaches globally

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
2.1 NC3Rs international science-led programmes **2.1.1 Human tissues and pharmaceutical development programmes** **(NC3Rs and MHRA)**	**NC3Rs/MHRA joint working group on human tissue for safety pharmacology** – Joint working group to generate an evidence base to support the use of human tissue to reduce animals in safety pharmacology studies. The group consists of 25 pharmaceutical companies, contract research organisations, academics and regulators from the UK, Europe and USA. This forms the basis of a wider programme of work on the use of human tissue for basic and applied research, including in the areas of asthma and pain.	An evidence base is developed to support the use of human tissue to reduce the use of animals in safety pharmacology studies.	Data have been collected on human tissue-based assays for safety pharmacology studies and have shown that the use of human tissue is limited; mainly focused on cardiovascular assays and wider use is inhibited by concerns about the regulatory acceptability of the data generated. Access to tissue is a problem. The data are being prepared for publication. An online hub to support human tissue use for safety pharmacology studies will be launched in 2015 to promote better access to tissue and standard operating procedures for assays.
	NC3Rs/MHRA joint working group on recovery animals in pharmaceutical development – Joint working group to consider potential opportunities for minimising the use of recovery animals (rats, dogs or non-human primates) in pharmaceutical development. The group consists of 32 pharmaceutical companies, contract research organisations and regulators from the UK, Europe and USA, including the FDA.	Potential opportunities are identified to minimise the use of recovery animals in pharmaceutical studies.	Analysis has been conducted on data for 259 studies and 137 compounds to explore whether the use of recovery animals can be reduced. Recovery animals are used to determine whether any adverse effects observed are reversible. The data analysis has shown that it is possible to reduce the use of recovery animals by 66% in studies to support first-in-human clinical trials, avoiding the use of thousands of animals worldwide. It has shown that where recovery animals are needed it is not necessary to include them for all dose groups or all studies. The data analysis was published in the journal Regulatory Toxicology and Pharmacology in 2014.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
2.1.2 Chemical safety programme **(NC3Rs, HSE and PHE)**	**NC3Rs working group on the fixed concentration procedure (chemical safety)** – This working group supports the international adoption of the fixed concentration procedure (FCP) for acute inhalation toxicity testing. The NC3Rs is working with inhalation toxicity experts from contract research organisations, academia, and other government bodies, to make the FCP more objective to encourage wider adoption of the approach across Organisation for Economic Co-operation and Development (OECD) Member States.	Objective scoring system to encourage wider adoption of FCP across OECD member states.	Focus has been given on building a case for evident toxicity instead of death of the animals as the end-point for inhalation toxicity studies. Evident toxicity is key to the FCP but there are concerns from some countries about how to recognise it. Evident toxicity is defined as the clinical sign(s) that predict severe toxicity or death at the next highest dose used. Analysis on inhalation toxicity data was conducted on 188 substances at two or more concentrations. There is evidence to support the use of evident toxicity and preparations are now in place for publication and for discussion at the OECD. This is international participation from regulators and CROs from North America, Europe and Korea.
2.2 Review of OECD Test Guidelines **2.2.1 Systematic review of OECD Test Guidelines to address 3Rs.** **(Defra and PHE)**	Systematic review of Organisation for Economic Co-operation and Development (OECD) Test Guidelines (TGs) to address 3Rs. In liaison with industry partners as well as regulatory authorities, we will review TGs where a potential to replace, reduce or refine animal studies is identified. Current work is on skin and eye sensitisation and irritation (see also Action 1.14). Proposed additional work is on the acute dermal toxicity. All are areas where the a review of the protocols would not only address 3Rs but provide an advance in science.	i) Adoption of TG under review TG430 and TG431 – Skin irritation and corrosion. ii) Submit proposal to OECD for review of the use of both genders in the acute dermal toxicity assay (TG402). iii) Commence review of data for the use of both genders in the acute dermal toxicity assay (TG402).	A proposal to update TG402 has been accepted by the OECD. Data have been gathered to support the reduction in the use of animals for acute dermal toxicity test. A report will be submitted to OECD in April 2015. Working with Swiss OECD partners to amend TG203 (Fish Acute Toxicity Test) to reduce numbers of fish and promote early termination for moribund individuals, thus avoiding unnecessary suffering. Proposal to be considered further at OECD National Co-ordinators meeting in April 2015.
2.2.2 Reproductive toxicology (EOGRTS) **(Defra and HSE)**	The Extended One Generation Reproductive Toxicity Study (EOGRTS) offers a much more flexible study design than the traditional two-generation approach (OECD TG416). The EOGRTS has been shown to generate sufficient information for regulatory purposes without the mandatory production of a second generation. The EOGRTS uses about half the number of animals – reducing from 2,600 to 1,400 rats per test. It was adopted by the OECD into its test guidelines in 2009.	i) In association with competent authorities from other key EU Member States, to promote the adoption of the EOGRTS in the EU. ii) To complete the process by achieving adoption of the EOGRTS in the REACH Test Methods Regulation.	Agreement has been reached at the REACH Article 133 Committee on revisions to the REACH information annexes to accommodate the Extended One Generation Reproductive Toxicity Study (EOGRTS) (OECD TG443). Formal adoption is dependent on the political processes.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
2.3 Influence regulatory frameworks which require animal testing **2.3.1. Adverse Outcome Pathways for chemicals** **(PHE and Defra)**	**Adverse Outcome Pathways** – International Development of New Approaches to Chemicals Testing. Historically, identifying adverse effects of chemicals has relied on using large numbers of animals to test their toxicity, one by one. If we could identify the chain of linked events from an initial chemical impact at the molecular level to responses at higher biological levels, we might be able to use *in vitro* techniques such as genomics to predict impacts up to the level of an organism or even populations. This would offer ways of reducing the need for tests using intact animals, as well as speeding up the assessment of chemicals. The concept of Adverse Outcome Pathways (AOPs) offers a mechanistic way to describe such a sequential chain of causally linked events. In 2012, the OECD launched a new programme to develop AOPs, in which the UK is collaborating. Appropriate AOPs to be validated and incorporated into OECD Test Methods toolkit as quickly as possible, via outputs of UK-funded research made available to the OECD programme.	Three relevant projects are underway: i) UK–Japan collaborative project – Critical review of key knowledge gaps to support AOPs for OECD test guidelines for aquatic organisms. Delivery of critical review of key knowledge gaps to support AOPs for OECD test guidelines for aquatic organisms delivered by UK and Japan. ii) Defra-funded project (Cranfield University) – In Silico Predictions of *In vivo* Toxicity: Are interspecies extrapolations off tangent? Final report published on accuracy of inter-species extrapolations of in silico predictions of *in vivo* toxicity. iii) Defra-funded project (Cefas, Universities of Birmingham and Liverpool) – The use of systems toxicology to reconstruct molecular AOPs – can chemical mixture toxicity be predicted to aid environmental risk assessment and regulation? Final report published on the use of systems toxicology to reconstruct molecular AOPs.	Public Health England (PHE) in collaboration with international partners is taking forward a large piece of work to improve *in vitro* methods in toxicity testing for genotoxic and non-genotoxic carcinogens. This is a long-term project which will lead to reduction in animal testing and improvements in testing strategies.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
2.3.2 Approaches for pharmaceuticals **(MHRA and VMD)**	**Harmonisation of approaches within regulatory frameworks:** - Harmonise approaches with respect to the 3Rs, and promote their uptake in pharmaceutical development. - Contribute to ongoing exploration of alternatives to using animals in testing of hazardous materials. Support the harmonisation of global regulatory standards. Unless all regulators accept an alternative to an animal test, the animal test would still be carried out by industry to ensure widespread marketing – essentially performing to the 'lowest common dominator' (and highest animal use) despite better and more economic tests being available. Continue to work with other regulatory agencies to interpret ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) and VICH (Veterinary ICH) flexibly, especially in light of emerging markets which are known to be less flexible. Continue to insist on adherence of OECD Good Laboratory Practice (GLP) requirements to avoid duplication of studies, especially important for emerging markets which are not party to the Mutual Acceptance of Data procedures. Provide a challenge to industry for already authorised projects and highlight where they are performing unnecessary animal testing and set out our expectations for change.	i) MHRA engaged at European and wider international levels with pharmaceutical regulators to promote the uptake of the 3Rs and harmonise approaches at all stages of pharmaceutical development. ii) MHRA encouraging the use of multiple end-points in one study to work to reduce the use of animals – an example would be including genotoxicity testing in animals in other toxicity studies. iii) VMD and MHRA influencing the development and revision of European Pharmacopoeia monographs such that, wherever feasible, testing in animals is replaced or removed or refined. (This creates a wider outreach than simply the EU as more countries are signed up to the pharmacopeia.) iv) VMD participating in the CXMP 3Rs group which is intended to identify and progress areas for regulatory change which can enable reduced testing in animals. v) VMD and MHRA actively challenging industry for already authorised projects and highlighting where they may be performing unnecessary animal testing. Setting out our expectations for change. vi) Defra project to review accuracy of inter-species extrapolations of in silico predictions of *in vivo* toxicity.	i) MHRA staff have been engaged at EU Safety Working Party and International ICH level promoting the 3Rs in new/revised guidelines. MHRA staff also discussed the 3Rs with delegates from China's FDA. ii) MHRA staff have been involved with the revision of EU and International guidelines promoting multiple end-points in one study. MHRA staff have also promoted this view in scientific advice meetings with pharmaceutical companies and academic groups. iii) Requirement for a safety test to be carried out in the target species for each batch of veterinary vaccines produced has been deleted from the European Pharmacopoeia – this requirement has now been deleted from all marketing authorisations saving approximately 5,000–6,000 animals per year. Veterinary International Conference on harmonisation (VICH) is working on guidelines for waiving batch safety tests for veterinary vaccines. This will not affect the EU because the requirement for these tests has already been removed from the European Pharmacopoeia, and consequently from all vaccines authorised in the EU, but should eventually reduce the number of animals used for this purpose worldwide. Humane end-points have been introduced into the 'rabies vaccines (inactivated) for veterinary use' monograph along with an alternative batch potency test based on serological responses instead of virulent challenge. Uptake of this alternative method has been slow because of the need for product-specific validation.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
			iv) The group has reviewed all Committee for Medicinal Products for Veterinary use (CVMP) and Committee for Medicinal Products for Human use (CHMP) guidelines with a view to reducing recommended animal numbers and removing unnecessary animal tests. Following this review, one guideline on veterinary vaccines is to be withdrawn and a revised version of a guideline removing the option for *in vivo* tests, at the request of JEG 3Rs, is being presented to CVMP for endorsement. Veterinary vaccines authorised via the European centralised procedure are being reviewed with a view to identifying animal testing procedures that might be able to be modified or replaced according to 3Rs principles. This is ongoing. v) The Veterinary Medicines Directorate (VMD) has published a report on animal usage during quality control testing of veterinary vaccines during 2007 to 2012 and have given presentations on this at the JEG 3Rs meeting and the Veterinary Vaccines conference. This has enabled the identification of vaccines that require the use of particularly large numbers of animals to be identified, facilitate monitoring trends and evaluate the impact of other initiatives, such as changes to European Pharmacopoeia monographs. As a result of the above mentioned study, clostridial vaccines have been identified as using particularly large numbers of animals. The VMD has written to all of the manufacturers of veterinary clostridial vaccines asking about plans for refining the methods to reduce the numbers of animals used or to replace them by *in vitro* methods.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
2.3.3. Promote 3Rs in food safety regulation **(FSA and Cefas for Mouse bioassay replacement)** **(FSA for other opportunities)**	**Uptake of 3Rs and research/risk assessment to promote alternatives.** - Promote uptake of 3Rs in food safety regulation and support testing requirements in the UK and EU. - Promote and support research and risk assessment to underpin adoption of alternatives to animal-based testing for food safety where this can be done while maintaining an adequate level of consumer protection. Key opportunities exist: - replace mouse bioassay in testing for shellfish bio toxins (i and ii). - continue to encourage the European Commission and other Member States to consider the 3Rs principles when determining the need for animal studies in the risk assessment of Genetically Modified Organisims (GMOs) (iii). - engagement worldwide with food risk assessment and regulatory bodies to develop and harmonise approaches and to reflect these and the 3Rs in new or updated food regulations and testing requirements. Unless all regulators accept an alternative to an animal test, the animal test may still be carried out by industry to ensure widespread access to markets despite better and more economic tests being available (iv). - consider the most appropriate means of generating data on approved food chemicals, including human studies where these are ethical and appropriate (v). - clear guidance on the requirements for authorisation of novel foods and processes (vi).	i) Successful replacement of mouse bioassay in controls on shellfish toxins in UK. ii) Seek commitment from Commission to ensure other EU Member States replace mouse bioassay. iii) Key opportunities to influence include when the EU FP7 “GRACE” project comes to fruition, and when the Commission’s two-year feeding study with GM maize is completed. iv) FSA and its independent scientific advisory committees are engaged at EU and wider international levels, including strong engagement with the EFSA, the Commission, JECFA and Codex Alimentarius. v) Producing the most appropriate means to generate data on approved food chemicals, including human studies where these are ethical and appropriate. vi) FSA provide clear guidance to industry on the requirements for applications for authorisation of novel foods and processes on where animal testing is and is not necessary for approval.	i) and ii) The monitoring of shellfish toxins for official control purposes in the UK uses analytical chemistry methods. There was no reported use of mouse bioassays in the latest period for which Home Office statistics on animal use are available. EU Member States have also moved the majority or all of their testing to the analytical chemistry methods and it is anticipated that this will replace the mouse bioassay in the few remaining laboratories shortly. iii) The GRACE project is due to finish in November 2015. Once the final report and recommendations are published the Commission has made a commitment to review the necessity for mandatory 90-day feeding studies as part of the risk assessment for GMOs. FSA will of course remind the Commission of this commitment when the time comes.[7] It is of note that a newer EU-funded research project called G-TwYST, which stands for, ‘GM Two Year Safety Testing’, is looking at longer-term safety testing for GMOs. This project lasts for four years and does not end until April 2018. No information is yet available, but it is possible the Commission may seek to delay a decision on animal testing until this project is completed.[8] iv) Food Safety Agency (FSA) supported by its independent scientific advisory committees continues to have strong engagement with European Food Safety Authority (EFSA), the Commission, Joint Expert Committee on Food Additives (JECFA) and Codex Alimentarius. FSA continues to champion proportionate and appropriate testing which maintains adequate consumer protection.

7 http://www.grace-fp7.eu/content/project (note weblink)

8 http://www.g-twyst.eu/

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
			v) Historically FSA have used human studies to investigate issues with approved food chemicals whenever appropriate e.g. with caffeine and pregnancy and to investigate alleged side effects of aspartame and that this approach will continue to be embedded in their future science strategy vi) Regarding novel foods, we plan to consult the ACNFP at the next Committee meeting on 29 April regarding guidance to applicants for minimising the use of animals in the risk assessment of novel foods. The guidance will draw attention to the statutory requirements for animal testing in the regulations and highlight areas identified where alternatives are acceptable.
2.4 Cosmetics alternatives **(BIS and industry with support from HO and FCO – see also 2.5 below)**	Work plan being developed to influence other non-EU countries in using alternatives to animal testing in bringing cosmetics to market (see also 2.5 below) Consider options of how the EU system (reliance on ingredient safety) could be adapted for third countries such as China to facilitate trade.	i) Paper developed. ii) Outline of geographies and types of test where we think there is redundant animal testing to target focus. iii) Options for revising (possibly based on the EU model) including opportunities for reform identified (e.g. in China).	Home Office Officials hosted a visit by a senior delegation of officials from the China Food & Drug Administration (CFDA) to discuss ways in which human safety can be assured through rigorous risk assessments which do not include unnecessary animal data. Demonstrated was best practice in cosmetic safety testing and showcase of UK expertise in the 3Rs with a particular focus on non-animal testing methods. The programme included visits to the National Centre for the 3Rs (NC3Rs); Unilever; Walgreens Boots Alliance; and meetings with the EU Commission and Cosmetics Europe as well as UK government teams. Having established a consortium with the companies (Unilever, Walgreens Boots Alliance, L'Oreal, and Proctor & Gamble) and UK, EU and Chinese trade associations (CTPA, Cosmetics Europe and CAFFCI) and in partnership with the EU Commission (DG Enterprise) a workshop was planned for March 2015 in Beijing to explain the principles of safety risk assessments with industry-led examples. As the UK/EU is a world leader in this field and is strongly positioned to support China in developing the skills to carry out and evaluate safety risk assessments among both its SMEs and its regulators through the development of a Risk Assessment Training Programme designed for China. The workshop is the first stage in the process that will continue from April 2015 onwards.

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
2.5 Developing Action Plan priorities into an effective international communication and influencing strategy **(FCO, HO and BIS-SIN)**	Using BIS-SIN Global Partnership Fund, to support a UK collaboration with China (e.g. Chinese Association for Laboratory Animal Science – CALAS) for a two-day seminar, funded jointly by UK Government and the relevant pharmaceutical and cosmetics industries, for invited experts (government, academia and industry) from China and overseas (UK/EU/US) to be held in Beijing.	i) Organise seminar in Beijing to support development of standards for animal care, welfare and ethical use in research. ii) Work towards endorsement of CALAS standards by Chinese authorities. iii) Initiate a dialogue on harmonising pharmaceutical safety testing guidelines and develop a forward plan. iv) Explore a strategy to cease animal testing of cosmetics in China wherever it is not scientifically necessary.	A strong working relationship with the Chinese Association for Laboratory Animal Sciences (CALAS) has been established. In March 2014 UK government officials, with CALAS, held a scene-setting seminar in Beijing that mapped out opportunities for UK–China co-operation in the development of standards for the welfare of research animals and their ethical use in China. Support has been given to CALAS in developing animal welfare and ethical research standards and it was demonstrated, through visits to the UK, how these can be made comparable. A familiarisation exercise with our regulatory scheme demonstrated our approach to developing standards in the UK. As part of this the delegation visited both industry and academic establishments to see standards being implemented in practice. In partnership with CALAS a second UK–China Seminar has been organised to be held in March 2015 which will support the further development of current voluntary standards for research animal care, welfare and ethical use to become mandatory national standards in China.
	International lobbying, influencing and evidence-gathering communications managed by FCO Science and Innovation Network, in partnership with BIS and Home Office leads, through the FCO global structure.	International Action Plan priorities delivered: Delivery Plan partners with an international component to their activity able to access FCO network efficiently/effectively with timely input of international feedback and evidence as required.	The Home Office, in collaboration with industry and the European Commission, is creating Science Innovation Network (SIN) toolkit. Once developed this will become the tool which the Science and Innovation Network in FCO posts will use to promote both animal welfare and its beneficial impacts to human well-being. The plan is to target Embassies, including Brazil, India and Taiwan, who can take on the work of engaging on the 3Rs regarding cosmetics testing to a local level. Brazil is the world's third largest cosmetics market. Discussions have been initiated to support proposed legislation which will ban animal testing of finished cosmetic products and promote acceptance of overseas (e.g.UK) generated non-animal test data.

Strategic Priority 3: Promoting an understanding and awareness about the use of animals where no alternatives exist

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
3.1 Improving public understanding of animal research **(BIS)**	Improving public understanding of the context of animal research and the licensing framework. - Review the responses to animal research questions contained within the Public Attitudes Survey 2014 managed by Science and Society and IPSOS Mori. - Office of Life Sciences (OLS) leading Poll on animal research.	Previous polls (BIS) show an enhanced public understanding of the regulatory framework within which animals are used in the UK. i) 2014 poll launched. ii) Evidence of enhanced public understanding through new poll results.	In March 2014 Business Innovation and Skills (BIS) ran two parallel public opinion surveys on the use of animals in scientific research. One survey was exactly the same as the previous iteration (Oct 2012 – the tenth wave of research in this series) and a new survey with some additional questions and updated language. The survey indicated that around two-thirds of the public continue to accept the use of animals for medical research where there is no validated alternative. The research as a whole provides an evidence base for future policy and engagement and to provide evidence for the sector to underpin their public engagement.[9]
3.2 Increased transparency about actual severity **(HO)**	Disaggregation of data to report procedures according to their actual severity. More clearly separate the number of procedures associated with the breeding of non-harmful GM animals (involving no suffering) from painful procedures in animals. Better inform the public about what animal research comprises (largely mild or sub-threshold) as well as to identify the most severe procedures and develop ways to reduce that severity.	i) Completion and review of pilot trial for retrospective (actual) severity reporting. ii) Development of guidance on recording actual severity. iii) Publication of first complete year of retrospective actual severity data. iv) Provision of complete year data to the EU Commission.	i) An actual severity pilot study was carried out over a two-month period in August and September 2013. The results were published in the 2013 ASRU annual report.[10] ii) The results of the pilot informed the development of guidance on actual severity, published on the Home Office website.[11] iii) The first complete year of data will be published as part of the Annual Statistics on the use of Animals in Scientific Procedures in 2015. iv) The first complete year of data will be submitted to the European Commission when available.

9 https://www.gov.uk/government/publications/public-attitudes-to-science-2014

10 https://www.gov.uk/government/publications/animals-in-science-regulation-unit-annual-report-2013 (page 12)

11 https://www.gov.uk/government/publications/animals-in-science-regulation-unit-annual-report-2013

Title/lead organisation(s)	Actions published in the Delivery Plan	Measures of success and key milestones published in the Delivery Plan	Progress
3.3 Concordat on Openness and Transparency **(Academia, industry, health charities, funders, etc.)**	Concordat on Openness and Transparency to be more open about the ways in which animals are used in scientific, medical and veterinary research in the UK. - Concordat on Openness about animal research agreed between major funders, research organisations and industry. - IPSOS MORI report on Sciencewise supported public dialogue sessions will determine public expectations of openness, transparency and communication to inform the development of the Concordat on the use of animals in research.	i) Publication of declaration on openness. ii) Publication of Concordat. iii) Annual monitoring shows progress in implementation. iv) Polls show increased public understanding of the role of animal research.	The Concordat was published in May 2014 and signed by 86 companies, universities, medical research charities and other organisations across the UK life sciences sector. It puts the UK life sciences sector at the head of global efforts to increase openness and transparency in animal research. Every signatory organisation has given a clear commitment both to facilitate greater scrutiny of their animal research and to be visibly accountable by reporting annually on their progress towards implementing the Concordat. Institutions involved in animal science continue to sign up to the Concordat. A 'one year on' stock take is intended shortly to ensure signatories have made clear steps towards implementation.
3.4 Review of section 24 of ASPA **(HO)**	The Government to review section 24 of the Animals (Scientific Procedures) Act 1986 (ASPA). Section 24 provides for the protection of information, given in confidence, in connection with regulatory activities under ASPA. A breach of section 24 can result in criminal sanctions. The inflexible confidentiality requirements of section 24 are now out of step with government policy on openness and transparency and with the approach taken in other legislation, such as the Freedom of Information Act (FOIA). The intention is to design a more flexible framework that will protect proprietary rights, intellectual property and personal safety, provide greater transparency to assist public understanding, and not harm the competitiveness of the UK in the life sciences.	i) Public consultation on options for revision of section 24 commenced. ii) Response to public consultation reviewed and preferred option prepared. iii) Processes for legislative changes (as needed) pursued leading to revision of section 24.	The public consultation on options for the review of section 24 was published and four broad options were offered. These ranged from the complete repeal of the section through to no change. Almost 5,000 responses were received, the majority through the online survey system. Almost without exception, respondents expressed a desire for increased openness and transparency in this field whilst recognising the need to protect the identities of people and places as well as information that is academically or commercially sensitive. Further discussions with stakeholders have refined the proposals and we will revisit these in the next Parliament.

Glossary

3Rs	The principles of replacement, reduction and refinement – an ethical framework for conducting scientific experiments using animals humanely
AHVLA	Animal Health & Veterinary Laboratories Agency, an executive agency of Defra
ASPA	Animals (Scientific Procedures) Act 1986 (as amended in 2012)
ASRU	Animals in Science Regulation Unit, a unit of the Home Office responsible for regulating the use of animals in research under ASPA
AWERB	Animal Welfare and Ethical Review Body, a requirement of each research establishment licensed under ASPA
BBSRC	Biotechnology & Biological Sciences Research Council, an executive NDPB of BIS investing in bioscience research and training in the UK
BIS	Department for Business, Innovation and Skills
Cefas	Centre for Environment, Fisheries & Aquaculture Science, an executive agency of Defra
CFDA	The Food and Drug Administration responsible for registration, including pharmaceuticals, medical devices and cosmetics, in China
Defra	Department for Environment, Food and Rural Affairs
DH	Department of Health
ECHA	European Chemicals Agency responsible for the REACH Regulation
EOGRTS	Extended One-Generation Reproductive Toxicity Study
FCO	Foreign & Commonwealth Office
Fera	Food & Environment Research Agency, an executive agency of Defra
FRAME	Fund for the Replacement of Animals in Medical Experiments
FSA	Food Standards Agency, a non-ministerial department responsible for food safety and food hygiene across the UK
GA	Genetically altered (applied to animals)
GO-Science	The Government Office for Science which works within BIS and supports the Government Chief Scientific Adviser
HSE	Health & Safety Executive, an executive NDPB of the Department for Work & Pensions and the UK competent authority for REACH
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
in vitro	research using methods in components of an organism (e.g. tissue culture, cells, subcellular extracts or purified molecules)
in vivo	research using methods within a whole, living organism, usually an animal
MHRA	Medicines and Healthcare Products Regulatory Agency, an executive agency of DH responsible for registration of human medicines, vaccines and other healthcare products in the UK
MRC	Medical Research Council, an executive NDPB of BIS which aims to improve human health by supporting research in medical sciences
NC3Rs	The National Centre for the Replacement, Refinement & Reduction of Animals in Research
NDPB	Non-departmental public body
OECD	Organisation for Economic Co-operation and Development
PHE	Public Health England, an executive agency of DH which aims to protect and improve human health in the UK
REACH	Registration, Evaluation, Authorisation & restriction of Chemicals, an EU regulation which addresses the potential impact of chemicals on human health and the environment
RSPCA	Royal Society for the Prevention of Cruelty to Animals – a UK charity which aims to reduce the suffering of animals used in research
TSB	Technology Strategy Board, an executive NDPB sponsored and funded by BIS
UFAW	Universities Federation for Animal Welfare – an internationally recognised, independent, scientific and educational animal welfare charity which first promoted the concept of the 3Rs
US FDA	US Food and Drug Administration, an operating division of the US Department of Health & Human Services responsible for ensuring that human and animal pharmaceuticals, medical devices and cosmetics in the USA are safe and effective
VICH	The International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products
VMD	Veterinary Medicines Directorate, an executive agency of Defra responsible for registration of veterinary medicines, vaccines and other animal health products in the UK

ISBN: 978-1-78246-731-1