Activities undertaken under Article 47 of Directive 2010/63/EU on the protection of animals used for scientific purposes to contribute to the development, validation and promotion of alternative approaches, and dissemination of information thereon at national level

Member State: **United Kingdom** Time period: **2013-14**

Submitted by: **Animals in Science Regulation Unit**

ACTIVITY	ACTION TAKEN	OBJECTIVE	RESULTS - IMPACT	MONETARY VALUE (where appropriate)
1. Three Rs policy and investment	**List any changes in, or amendments to the Three Rs policy (including legislative changes) aimed at promoting and accelerating the development and uptake of alternative approaches. Describe the steps taken to encourage research in this field.**			
Policy changes	Full implementation of Directive 2010/63/EU: effective on 1st January 2013. Guidance on the operation of the Animals (Scientific Procedures) Act 1986 UK Coalition Government Commitment: Working to reduce the use of animals in scientific research.	Implementation of the objectives in Directive 2010/63/EU into the national legislation Gives guidance to stakeholders on implementing the 3Rs in their work National programme for Government committing to work to reduce the use of animals in scientific research by placing 3Rs approaches at the heart of a science-led programme.	Ensures the 3Rs are a primary consideration in all aspects of our legislation. Delivery Plan published at: https://www.gov.uk/government/publications/working-to-reduce-the-use-of-animals-in-research-delivery-plan Prioritises the 3Rs with target actions and milestones to be achieved	

Public research investment	The NC3Rs is the main funder of 3Rs research in the UK. It typically commits over £6 million each year on research awards over a three year period. In 2013/14 it spent £2.8 million on research, training and career development awards. An additional £1.3 million was spent on open innovation and commercialisation of 3Rs technologies via its CRACK IT scheme.	To develop new research models, tools and approaches with reduced reliance on animal use and improved animal welfare.	For details of NC3Rs-funded projects see: www.nc3rs.org.uk/our-science For examples of impacts arising from NC3Rs research see: www.nc3rs.org.uk/our-impacts	Currently ~ €10 million per year
	A special programme set up as NC3Rs-Innovate UK partnership	To stimulate innovation in developing 3Rs technologies.		€5 million in 2014-15
	The Dr Hadwen Trust, during 2013-14, committed £0.86 million to a programme of animal replacement research and education. This was achieved by funding 9 new research activities ranging from undergraduate training opportunities to 3 year post-doctoral research fellows. Additionally, the Dr Hadwen Trust continued its support of a further 19 large scale and novel animal replacement research projects.	To develop new research models and methods to replace the use of animals in medical research	For details of the new projects see: http://www.drhadwentrust.org/research-and-funding/current-portfolio and http://www.drhadwentrust.org/research-and-funding/summer-studentship-past-projects	£1.4 million in 2013-14 (~€1.8 million)

Private research investment	Both NC3Rs and FRAME receive support from private industry. The FRAME Alternatives Laboratory (FAL) forms mutually beneficial collaborations, which both benefit their industry partners, and promote the use of non-animal methods	This enables them mainly to carry out specific projects of interest to industry. It may also be used to support some of their core work.	Example projects include: examining the effects of cannabinoids upon immune cell function in vitro and conducting gene expression analysis into the role of inflammation and infection in IBD	

2. Validation and regulatory acceptance of alternative approaches	List measures taken to validate alternatives which are intended to reduce or eliminate the need for animal use or intended to reduce suffering by application of less painful (more refined) procedures. List measures taken to facilitate and promote regulatory acceptance of alternative approaches.			
EU-NETVAL laboratory membership(s)	Huntingdon Life Sciences (HLS) is a UK-based member of EU-NETVAL.	To become actively involved in the validation of new in vitro alternative assays.	HLS is now actively involved in the validation of new in vitro alternative assays.	
EU-NETVAL task participation	HLS successfully applied to be a participating laboratory for the validation of the AR-CALUX® assay.	Validation of an in vitro transactivation assay for the detection of compounds with (anti)androgenic potential using AR-CALUX® cells. Currently the in vivo Hershberger assay is used to test for androgenicity. In a tiered testing approach, the in vitro assay would be conducted first.	This non-animal alternative test for the detection of compounds with (anti)androgenic potential could be the subject of an OECD regulatory guideline for the detection of endocrine disruptors.	
Participation in other validation studies	Home Office (ASRU) working with MHRA and manufacturers regarding batch testing of biologicals e.g. botulinum toxin	Development of non-animal alternative to the mouse bioassay; refinement of mouse bioassay pending acceptance of alternative	Non-animal alternative test for botulinum toxin testing developed; will be validated during 2015.	~ €8 million spent so far on the alternative development.

PARERE membership and activities within PARERE network	UK representative attended PARERE meeting.	See PARERE website.	Feedback from the UK regulatory network to ECVAM on the regulatory relevance of the GreenScreen (for genotoxicity) and hCLAT (for skin sensitisation) methods, as well as on ECVAM's draft strategies on 1) acute toxicity testing and 2) fish toxicity and bioaccumulation testing.	
Other	NC3Rs working groups and Centre-led activities involve national and international regulators, e.g. EMA, FDA. The NC3Rs also has a formal collaboration with the MHRA in areas of joint interest, e.g. the use of recovery animals in drug development, the use of non-human primate for biosimilars. Home Office (ASRU) inspectors, working with other relevant bodies such as MHRA, HSE, VMD, RSPCA, private companies etc. to promote alternatives.	To share data on the use of animals in safety pharmacology and regulatory toxicology studies which will generate an evidence-base to reduce animal use in regulatory practice. To develop alternative (3Rs based) approaches, particularly for the most severe procedures.	Input into regulatory change and revisions, e.g. ICH M3 (R2), ICH S6, acute toxicology. Publication of guidance on use of Experimental Autoimmune Encephalomyelitis model; guidance on refining models of seizures, arthritis, sepsis; development of non-animal test for botulinum toxin to replace mouse bioassay; review of batch testing of biologicals such as veterinary vaccines; etc.	

	Home Office (ASRU) inspectors have developed strategies for 3Rs knowledge access and transfer through regular conferences and virtual meetings as well as developing IT solutions. The FRAME Alternatives Laboratory (FAL): http://www.frame.org.uk/the-frame-alternatives-laboratory/	To share information about 3Rs between inspectors, and to engage with NC3Rs to maintain current knowledge of 3Rs advances. Its mission is to produce human based systems that are better and more relevant to humans than current animal models	Increased impact in disseminating 3Rs advances and advising about implementation by inspectors as part of project authorisation. For examples of some of the current projects see: http://www.frame.org.uk/fal-projects/	

3. Promotion of alternative approaches at national level	Describe specific measures taken to promote alternative approaches at national level.			
Communication/ awareness activities and events	In 2014 the NC3Rs organised 12 scientific symposia/workshops and funded a programme of public engagement. A review of 10 years of working with the pharmaceutical industry was launched in Parliament: www.nc3rs.org.uk/our-reviews FRAME holds an annual lecture where an invited speaker presents work related to the Three Rs and alternative approaches. In 2014, the Dr Hadwen Trust launched its annual Animal Replacement Science Conference.	The objective was to disseminate to the scientific community the latest findings and research methodologies for the replacement of animals in fundamental biomedical research.	The impact of the event was that nearly 100 international research scientists and affiliates were informed of the latest replacement approaches in areas such as gastroenterology, neuro-oncology, neuroscience and antibody production. A selection of speaker presentations and poster abstracts from the event can be viewed on the DHT conference website. www.animalreplacementscience.com	

Portals – web-sites, databases and publications	The NC3Rs launched a new, comprehensive website in 2014: www.nc3rs.org.uk FRAME updated its website in 2014 and is continuing to develop it: www.frame.org.uk			
	FRAME publishes the journal Alternatives to Laboratory Animals (ATLA) which is available in hardcopy or online via www.atla.org.uk	To promote and disseminate all aspects of the development, validation, introduction and use of alternatives to laboratory animals at a national and international level.	For example, in 2013 ATLA issues included publication of the Lush Prize Awards and the outcomes of an EU-funded project, the Marie Curie Initial Training Network Project, Environmental ChemOinformatics.	
	FRAME publishes Perspectives in Laboratory Animal Science (PiLAS). This is circulated as part of ATLA and through a dedicated website: www.pilas.org.uk	PiLAS offers an opportunity for discussion about issues raised by animal experimentation and the Three Rs through discursive articles and opinion pieces that invite replies.	For example in 2013 there were pieces raising awareness of the need to improve experimental design, and looking at ways in which animal alternatives are used in training and education.	
	In 2014, the Dr Hadwen Trust published a revised and updated serum-free media guide.	The objective was to collate a database of the commercially available serum-free media to assist scientists when culturing cells *in vitro*.	The output was a searchable catalogue of all the serum-free media available to scientists conducting research using cell culture. The catalogue is available to everyone at www.drhadwentrust.org/serum	

Education & training activities	The NC3Rs held its second Summer School for PhD students. The NC3Rs-funded Procedures With Care website (www.procedureswithcare.org.uk) was translated into Chinese. FRAME runs regular Training Schools in Experimental Design and Statistical Analysis of Biomedical Experiments http://www.frame.org.uk/training-schools/	Provides researchers from across Europe and beyond with an understanding of basic experimental design concepts that they do not seem to be gaining from other sources. To give them the ability to use more efficient designs for their experiments, and to stimulate engagement with the Three Rs and useful discussion between animal users in industry and academia on both refinement and reduction.	The key outcome is increased awareness and understanding among scientists about the need to reduce animal numbers in experiments and to refine procedures undertaken on them.	
Organisations in the field of Three Rs	National Centre for Replacement, Refinement and Reduction of Animals in Research (NC3Rs)	To lead the discovery and application of new technologies and approaches to replace, reduce and refine the use of animals for scientific purposes.	See NC3Rs Annual Report 2013: www.nc3rs.org.uk/about-us/corporate-publications and Vision 2015-2015: www.nc3rs.org.uk/our-vision	See above

	Fund for the Replacement of Animals in Medical Research (FRAME)	FRAME is an independent charity dedicated to the development of better scientific methods for the benefit of humans, animals and the environment. Its ultimate aim is the elimination of the need to use laboratory animals in any kind of medical or scientific procedure.	See http://www.frame.org.uk/	
	Dr Hadwen Trust (DHT)	A non-animal medical research charity entirely focused on the replacement of animals in medical research.	See www.drhadwentrust.org Latest annual report: www.drhadwentrust.org/downloads/Reports/dr-hadwen-trust-annual-report-2013-14.pdf	
	The Royal Society for the Prevention of Cruelty to Animals (RSPCA)	The world's oldest animal welfare organisation. For animals in research and testing, RSPCA works to develop and promote practical measures leading to better implementation of the 3Rs and more effective ethical review	See http://science.rspca.org.uk/sciencegroup/researchanimals	

4. Provide examples of the above described measures that have been successful in deriving specific benefits in each of the Three Rs.		
Measure	**Relevance to Replacement, Reduction or Refinement**	**Benefit**
Publication of the Coalition Commitment Delivery Plan (CCDP) in February 2014	The development of methods that replace the use of animals in specific biomedical research	The Delivery Plan was published at: https://www.gov.uk/government/publications/working-to-reduce-the-use-of-animals-in-research-delivery-plan The Plan prioritises the 3Rs with target actions and milestones to be achieved. A One-Year-On Progress Report will be published in early 2015 which will demonstrate the achievements against all the objectives and a number of new initiatives. This is an example of using leadership from the top of Government to raise the profile of the 3Rs right across the bioscience sector. In summer 2013, the UK Government Minister responsible for the regulation of animals used in science (Lord Taylor) visited the USA specifically to promote and encourage implementation of the 3Rs in US academia, industry and government. The benefit is seen in improved relationships with our US colleagues and in their participation in other UK led initiatives such as in China (see below). In addition, an Inter-Ministerial Group on International Animal Welfare has led on the international aspects of the Delivery Plan. As a result, the UK has held very productive discussions with, and hosted visits from, a number of countries including China and Brazil on topics such as using alternatives in the risk assessment both of pharmaceuticals and of cosmetics. We have also partnered with the Chinese Association for Laboratory Animal Sciences (CALAS) to run seminars in Beijing which focus on developing welfare standards for the ethical use of animals, including promoting the concept of putting the 3Rs at the heart of their science.

Publication of a serum free media list	Publication of a serum free media list	Scientists can investigate whether their *in vitro* cell culture work can be conducted without the use of FCS/FBS. The catalogue provides an overview of all the available serum-free and xeno-free media available for 74 different cell types. The catalogue is available from www.drhadwentrust.org/serum
Dr Hadwen Trust Research Projects	Allows researchers to reduce their reliance on FCS/FBS (Foetal Calf Serum/Foetal Bovine Serum) in their cell culture work by replacing it with serum-free or xeno-free media.	The Dr Hadwen Trust funds biomedical research projects that aim to replace the use of animals in biomedical research. The aim of all the projects is to demonstrate a scientifically satisfactory alternative method that has the potential to replace animal-models yet also improve human relevancy in the field of research. The benefit is that these projects aim to fulfil the mandate set out in Articles 4 and 13 of Directive 2010/63, where a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure on an animal. For more information about the Dr Hadwen Trust funded projects see: www.drhadwentrust.org/research-and-funding/current-portfolio