



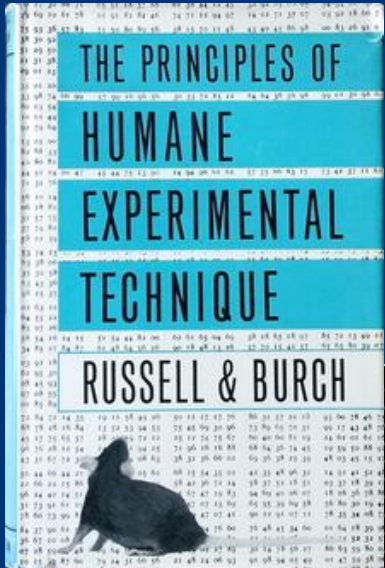
Have the 3Rs made a difference?

DR ELLIOT LILLEY

All right...all right...but apart from better sanitation, the medicine, education, wine, public order, irrigation, roads, a fresh water system and public health....
what have the Romans ever done for us?

What are the 3Rs?

RUSSELL AND BURCH 1959



- Replacement - use of humane alternatives
- Reduction - using the minimum number to achieve satisfactory results
- Refinement - reducing suffering (in experiments and other procedures) and improving welfare; applies to the lifetime experience of each animal

What are the 3Rs?

Why are they important?

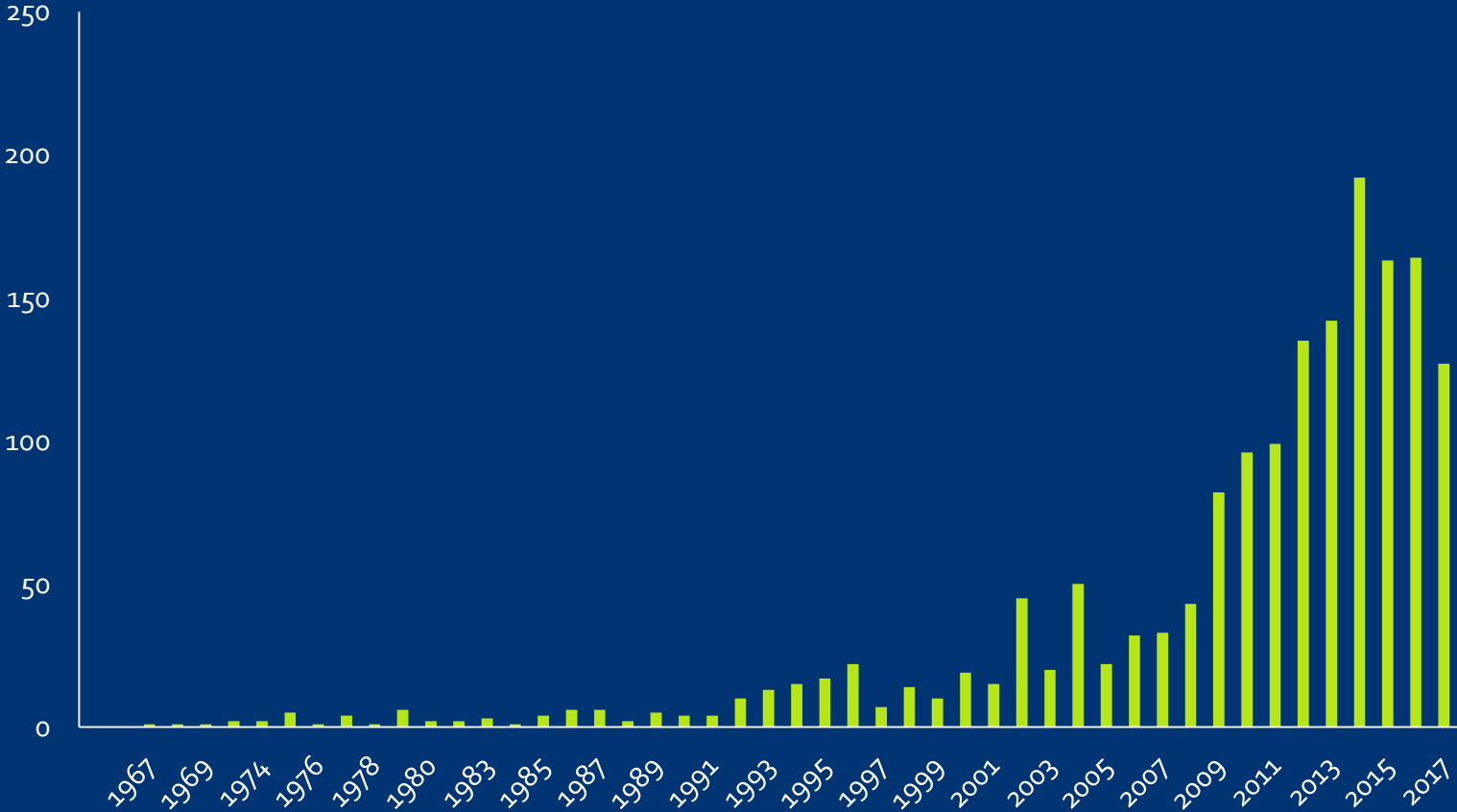
- Emphasis on **ultimate goal** of full replacement
- 3Rs as a framework to promote **humane** research
- UK/Europe convention is:

Replacement / Reduction / Refinement

- US convention is:

Refinement / Reduction / Replacement

Three Rs in the literature



Three Rs in UK law

ASPA

- **Animals (Scientific Procedures) Act 1986**
 - **Based on the principles that:**
 - **harm-benefit analysis and should inform decision making as to whether animal experiments should take place.**
 - **Efforts should be made to reduce suffering**
- **The Three Rs are one way that this can be achieved.**

Three Rs in UK law

'New' ASPA January 2013

- **Animals (Scientific Procedures) Act 1986**
 - Updated to take into account European Directive 2010/63
 - Original ASPA makes no specific reference to the Three Rs. (closest section below).

10.—(1) Subject to the provisions of this section, a licence or certificate under this Act may contain such conditions as the Secretary of State thinks fit.

(2) The conditions of a personal licence shall include—

(a) a condition to the effect that the holder shall take precautions to prevent or reduce to the minimum consistent with the purposes of the authorised procedures any pain, distress or discomfort to the animals to which those procedures may be applied ; and

Three Rs in UK law

'New' ASPA January 2013

- **Animals (Scientific Procedures) Act 1986**
- **New ASPA references Three Rs throughout the legislation. (9 separate, specific mentions)**

Principles of replacement, reduction and refinement

5. After section 2 insert—

“2A Principles of replacement, reduction and refinement

(1) The Secretary of State must exercise his or her functions under this Act with a view to ensuring compliance with the principles of replacement, reduction and refinement.

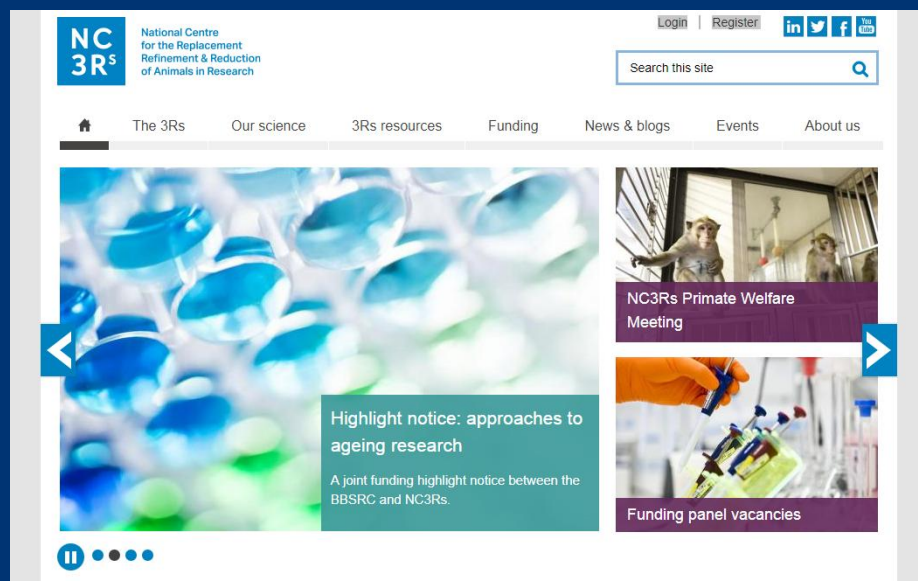
(2) For the purposes of this Act—

- (a) the principle of replacement is the principle that, wherever possible, a scientifically satisfactory method or testing strategy not entailing the use of protected animals must be used instead of a regulated procedure;
- (b) the principle of reduction is the principle that whenever a programme of work involving the use of protected animals is carried out the number of protected animals used must be reduced to a minimum without compromising the objectives of the programme;
- (c) the principle of refinement is the principle that the breeding, accommodation and care of protected animals and the methods used in regulated procedures applied to such animals must be refined so as to eliminate or reduce to the minimum any possible pain, suffering, distress or lasting harm to those animals.”

Three Rs in UK scientific practice

Much improved.....

- **NC3Rs formed in 2004**
 - Following 2002 HoL select committee report on animals in scientific procedures



- **Raised the profile of the 3Rs in the UK**
 - Others had been working on the issue for several years before this!

Three Rs in UK scientific practice

But....

- **Overall** Government funding for 3Rs has not **significantly** increased
- **MRC/BBSRC** funding of 3Rs research pre 2008 now given to **NC3Rs** (based on data from PQs)

Current state of play

THE POSITIVES

- As a framework the 3Rs is delivering
 - Scientific meetings
 - Working groups
 - Common language
 - Improved animal welfare
- Debate is re-shaping
 - Importance of welfare for good science is recognised
 - How research is conducted is a hot topic

Benefits to science

Higher welfare standards \propto better science

"The OIE emphasises the need for humane treatment of animals and that good quality science depends upon good animal welfare.. Good husbandry practices enhance the health and welfare of the animals used and contributes to the scientific validity of animal research."

World Organisation for Animal Health (OIE)

"Good animal welfare and full implementation of the 3Rs are essential for good science and for retaining the support of the public in the use of animals in research."

Medical Research Council

Current state of play

NOT UNIVERSALLY ACCEPTED....

“Please no. the 3Rs is not the accepted global religion of biomedical research. Some people, me included, think it is nonsense. It certainly has NOTHING to do with science and if it is to be policed then this should be at the level of regulators (HO etc) not journals. The best way to comply with 3Rs is to get out of the lab and do something else.”

Current state of play

NOT UNIVERSALLY UNDERSTOOD....

“I ‘do’ reduction: I throw compounds at my model until I see something interesting and then increase the ‘n’ until I can put a star on the graph – I use the fewest number of animals possible”

Current state of play

WHICH R IS MOST IMPORTANT?

- Some animal protection groups only want **full replacement**
- Reduction and Refinement **suggest approval** for animal use?
- Refinement is **poor** relation?
- **Conflict** between reduction and refinement

Current state of play

REFINEMENT AS A GATEWAY TO REPLACEMENT?

- **Mechanism** based approaches lend themselves to:
 - reduced **suffering**
 - development of non-animal **alternatives**.

ATLA 45, 159–160, 2017

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Comment

Animal 'Models': How a Mechanistic Approach can Reduce Suffering and Improve Translatability

Elliot Lilley

Poorly predictive animal models of disease cause avoidable suffering and hamper the discovery of new treatments for patients. A focus on mechanistic modelling has the potential to reduce animal suffering as well as improving translation from the bench to the bedside.

Current state of play

AVOIDANCE OF ACCOUNTABILITY?

- The 3Rs are **valuable**, like ARRIVE, if they are **embedded** in research **culture**.
- Do dedicated **3Rs funders** encourage this?
- 3Rs as an **ethical** framework
 - Focus on **how** not **why** or **if**
 - **BHA** ≠ ethical evaluation
 - Too much **box ticking**?

Current state of play

THINGS ARE GETTING BETTER

- Since the publication of 'The Principles' we have seen:
 - Huge expansion of **animal welfare science**
 - **Worldwide acceptance** of the 3Rs as a framework
 - Formation of dedicated **3Rs centres**
 - More robust **legislation**
 - Improved **collaboration** between welfarists and scientists

Refine. Reduce. Replace.

ADVANCING SCIENCE, INNOVATION
AND WELFARE THROUGH SHARING



ABOUT US



EVENTS



JOIN



COLLABORATE

Current state of play

RESOURCES AND PUBLICATIONS



The screenshot shows the Norecopa website homepage. At the top left is the Norecopa logo, a stylized star in a circle. To its right is the text "norecopa". In the top right corner, there are links for "NORSK" and "ENGLISH". Below the logo and name is a horizontal navigation menu with the following items: "About Norecopa", "Alternatives", "Databases & Guidelines", "Education & training", "Legislation", "Meetings", "More resources", "News", "PREPARE", and "Species". The main content area features a search bar with the placeholder text "Add search term" and a magnifying glass icon. Below the search bar, there is a welcome message: "Welcome to Norecopa, Norway's 3R centre!". Underneath this, there are several links: "Search engine help file", "Short cut: Guidelines for animal research", "More about Norecopa's databases: 3R Guide - NORINA - TextBase - Classic AVs", and "Reviews of the website".

NORSK [ENGLISH](#)

[About Norecopa](#) [Alternatives](#) [Databases & Guidelines](#) [Education & training](#) [Legislation](#) [Meetings](#) [More resources](#) [News](#) [PREPARE](#) [Species](#)

Search all Norecopa's databases and webpages simultaneously:

Add search term

[Welcome to Norecopa, Norway's 3R centre!](#)

[Search engine help file](#)

Short cut: [Guidelines for animal research](#)

More about Norecopa's databases: [3R Guide](#) - [NORINA](#) - [TextBase](#) - [Classic AVs](#)

[Reviews of the website](#)

The future

BLUE SKIES THINKING.....

- How **realistic** is full replacement?
- Should we set a **deadline**?
- How **much** should we **spend** on alternatives?
- What other ways can we **influence change**?

The future

FULL REPLACEMENT

- Therapeutics
 - Efficacy, plasma level, mechanism
- Target identification
 - Pathway, human disease relevance
 - Veterinary research-ethical conflict
- Fundamental research
 - Understanding disease mechanisms
 - Poorly understood pathology



The future

DEADLINES....

- Good for:
 - Directing resources
 - Highlighting issue
- Bad for:
 - Lack of realism
 - circularity of science

Ban on Animal Testing

The Cosmetics Directive provides the regulatory framework for the phasing out of animal testing for cosmetics purposes.

Specifically, it establishes:

- Testing ban – prohibition to test finished cosmetic products and cosmetic ingredients on animals;
- Marketing ban – prohibition to market finished cosmetic products and ingredients in the EU which were tested on animals.

VegNews

News Food Planet Travel Buzz

News

Dutch Government Bans Animal Testing

Mor

Popu
Chain
Vega

The future

HOW MUCH INVESTMENT?

- 2012/13 **£300million** of BIS funding by the four main research councils (MRC, BBSRC, EPSRC, NERC) to fund projects which **involved animal use**
- 2012/13 **£8.73million** on alternatives (£7.16million to NC3Rs)
- Less than **3%**
- Less than **0.2%** of total government funding of science and technology (**£4.6bn**)

The future

HOW MUCH INVESTMENT?

- What is a **reasonable** target?
 - 10% of animal use budget?
 - 2% of total research funding?
- **Fixed** proportion or **rising** over time?
 - 10% initially raising to 50% within 20 years?
- Must be directed to **high quality** science with clearly defined **KPIs**

The future

INFLUENCING CHANGE

- Education/CPD
- Buy-in from funders
- Support from Journals
- Emphasis on demonstrably better science
- Need to make humane research mainstream

All right...all right...but apart from better animal welfare, animal replacement science, pain faces, score sheets, ethical review, improved experimental design, initiatives to improve reporting, better facilities and improved training and competency....

what have the Three Rs ever done for us?

Thank you

