Science and Society – Why the 3Rs Matter

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Plenary Address: CCAC National Workshop – Enhancing Ethics and Welfare, Hyatt Regency Hotel, Montreal, Canada.

Saturday 30th May 2015
Summary

- Why we use animals in research?
- Why promote the 3Rs?
- What is a Harm-Benefit analysis?
- Transparency & openness – why it matters
- New ethical dilemmas – be prepared
- Conclusions & Questions
What Animals Are We Using?

UK Statistics 2013
(numbers of procedures – total 4.12m)

- Rats, mice & other small mammals & rabbits: 82.2%
- Fish, amphibians, reptiles & birds: 15.9%
- Sheep, cows, pigs & other large mammals: 1.53%
- Dogs, cats (no strays), ferrets & small carnivores: 0.14%
- Primates: marmoset & macaque monkeys (no apes): 0.08%
Trends in Numbers of Procedures 1995-2013

Procedures on Living Animals, 1995-2013

- Mouse
- Rat
- All other rodents
- Cats, dogs, ferrets and other carnivores
- Ungulate
- Primate
- Other mammal
- Bird
- Reptile/Amphibian
- Fish

Millions of procedures
What Are These Animals Being Used For?

Permissible purposes in UK 2013
(based on numbers of procedures)

- Breeding genetically altered animals: 51%
- Basic biological and medical research: 28%
- Developing and testing new medical & veterinary treatments for diseases: 17%
- Safety testing of non-medical products used in the home, farm and industry: 2%
- Developing new methods of diagnosis: 1%
Mice By Genetic Status

Procedures using mice by genetic status, 1995-2013

- Normal animals
- Genetically modified animals
- Animals with a harmful genetic mutation

Millions of procedures

Home Office
Fish By Genetic Status

**Procedures using fish by genetic status, 1995-2013**

*Millions of procedures*

- Normal animals
- Genetically modified animals
- Animals with a harmful genetic mutation

Home Office
Focus on Alternatives: The 3Rs

- “Principles of Humane Experimental Technique”
- Published by UFAW in 1959
- Introduced the concept of the 3Rs
  - Replacement
  - Reduction &
  - Refinement

William Russell & Rex Burch
Promote and Implement the 3Rs

- **Replacement:**
  - Using totally non-animal methods e.g. *in silico*, human data (absolute)
  - Using cells, tissues, organs of animals *in vitro* (relative)

- **Reduction:**
  - Using fewer animals, often through good experimental design
  - Obtain same information from fewer animals or more information from the same number of animals

- **Refinement:**
  - Using methods which minimise pain or distress
  - Using species with less capacity to feel pain
  - Includes improvements in housing and care e.g. environmental enrichment

- **Why do the 3Rs matter?**
In 2010, a UK Government commitment to:

“Work to reduce the use of animals in scientific research”

Published a Delivery Plan: February 2014

- Advancing the use of the 3Rs by putting them at the heart of science-led programmes;
- Influencing the uptake and adoption of 3Rs approaches globally;
- Promoting an understanding and awareness about the use of animals where no alternatives exist.

UK Government Commitment: A One-Year Delivery Report

Published: March 2015

- Describes progress made on actions taken during the first year after publication of the Delivery Plan;
- Follows a similar structure and priorities as the 2014 Delivery Plan;
- Shows significant progress that can be made on all three priorities with engagement and commitment

Science Led Implementation of the 3Rs: Example - Safety Testing

- Focus on mechanisms of toxicity using *in vitro* and *in silico* predictive models
  - e.g. Tox. 21 program – for improved toxicity assessment
  - “Lung-on-a-chip”: [http://wyss.harvard.edu/](http://wyss.harvard.edu/)

- Regulatory Safety Assessment is a global enterprise
  - Encourage validated alternatives globally

- Review of batch testing of biologicals
  - e.g. vaccines, toxins, etc.

- Use of human tissues for safety pharmacology
- Refinement of inhalation toxicology methods
- Review of OECD test guidelines for new medicines and vaccines
- Promote 3Rs in food safety regulation
Examples of Implementing the 3Rs: What Can You Do Locally?

- Refinement of most severe models
  - e.g. arthritis; sepsis, seizures, stroke, dementia; etc.
- Improved reporting of severity & 3Rs advances
- Early career training for research scientists
- Create awards for 3Rs initiatives

- The drive for alternatives comes from scientists - to improve their science
  - “Better, faster, cheaper science”
  - Veterinarians and ACCs can actively encourage

- Total numbers may remain level or may rise
  - More may be fish, invertebrates and other lower species
Harm-Benefit Analysis (HBA)

- Important ethical evaluation of projects
- Needs to be done on a case by case basis
- Significant role for ACCs
  - including vets and care staff as well as scientists and lay members
- Implement 3Rs to minimise harms
- Must continue throughout life of project
Harms: What to Consider?

- Numbers of animals, species, genotype, phenotype and life-stage;
- Type of manipulation, handling and training;
- Nature of pain, suffering, distress or lasting harm caused;
- Intensity, duration and frequency of techniques;
- Cumulative suffering or habituation within a procedure; and
- Prevention from expressing natural behavior including housing, husbandry and care.

But also:

- Any transport or change of environment;
- Expected mortality rate;
- Experience of death;
- Whole life experience of the animal;
- Any proposed re-use.
Prospective & Actual Severity

- Estimated ‘prospective severity’ of a proposed procedure
  - Used to inform the Harm-Benefit Analysis
- Monitor ‘actual severity’ at the end of a procedure
- Why is this important?
  - We learn the ‘total cost’ of animal research
  - We monitor reduction in that ‘total cost’ through applying the 3Rs
  - We can focus on the most severe procedures

- Retrospective assessment – a structured review of the entire project
  - to identify further 3Rs opportunities
  - Important veterinary and animal welfare insight
UK Pilot Study: Actual Severity Reported

- Data on 35,409 procedures supplied from 75 project licence holders at 21 establishments over a two month period in 2012.
- The pilot study covered 2.8% of all active project licences and involved 12% of all licensed establishments.
Assessing the Benefits

What?
- Scientific outputs

Who?
- Patients
- Other researchers

How?
- Improved therapy, survival

When?
- In life-time of project
- Much later
Consider Likelihood of Benefit

- **Proven track record**
  - Recent publications – how many, quality of journal?
  - Background of applicant. What has been achieved before?

- **Funding**
  - Is there funding available for this work?

- **Other resources needed**
  - Practical, technical and specialist support needed.
  - e.g. Veterinary support for surgery, anaesthesia, post-operative care, special expertise, etc.
The 3Rs Across Government: Working with China

• Project with three work-streams:

1. Eliminate unnecessary testing of cosmetics in animals
   - Removes barriers to trade

2. Support OECD GLP membership for Mutual Acceptance of Data
   - Speeds up registration of new medicines

3. Develop compatible standards of welfare and ethical use
   - Supports scientific collaborations between UK and China
Openness & Transparency: Why Bother?

- Public confidence is diminished by ‘closed doors’ image
- Lack of public trust feeds extremism – but extremism drives ‘closed doors’
- Vicious circle of mistrust
- Increasing use of Freedom of Information laws:
  - overwhelming both the scientific community & regulators
- Beware a ‘Jungle Vision’
Openness & Transparency: What Do We Know?

- Positive relationship exists between transparency and trust in government
  - Applies to objective and perceived transparency
  - Not cause and effect
- Includes:
  - accessibility to processes in decision making as well as
  - outcome and information itself
- Must be comprehensible and timely
- Probably also applies to institutions (e.g. universities)

Mahoney & Webley, 2004
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Mahoney & Webley, 2004
What Does the Research Tell Us?

Perceived trustworthiness of Government

- If the audience has low knowledge:
  - ↑Transparency → ↑ Trust

- If the audience has high knowledge:
  - ↑Transparency → no change in Trust

- Majority of “the public” have low knowledge about animal research

- Potential 3Rs benefits for scientists through greater transparency

Grimmelikhuijsen & Meijer, 2014
Acceptance of Animal Experimentation Has, Generally, Increased
“Why would you want to be open? Is it so people will LIKE you?”

Public dialogue participant, Cardiff
What people think happens to research animals is much worse than the reality.
1. We will be clear about when, how and why we use animals in research

2. We will enhance our communications with the media and the public about our research using animals

3. We will be proactive in providing opportunities for the public to find out about research using animals

4. We will report on progress annually and share our experiences
Our research environment

Supporting researchers
Working collaboratively

Integrity and ethics
Good practice and quality
Research ethics
Clinical research
Animal research

Animal research

We are committed to providing open and transparent information about our research involving animals and our standards of animal care and welfare.

We have signed the Concordat on Openness on Animal Research in the UK.

Replacement, reduction and refinement
Consideration of the 3Rs is the basis of everything we do related to animal research.

Find out more about the 3Rs

Related links
The Home Office - Science Research and Statistics
National Centre for the Replacement, Refinement and Reduction of Animals in Research
Understanding Animal Research
Fund for the Replacement of Animals in Medical Experiments (FRAME)
The Institute of Animal Technology
Publishing Animal Numbers

Frequently asked questions

How many procedures do you carry out on animals each year?

In 2013, we carried out 63,578 procedures. This includes the natural breeding of genetically altered animals, where the birth of each animal counts as one procedure.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Number of procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>48,587</td>
</tr>
<tr>
<td>Rat</td>
<td>3,345</td>
</tr>
<tr>
<td>Guinea pig</td>
<td>24</td>
</tr>
<tr>
<td>Rabbit</td>
<td>3</td>
</tr>
<tr>
<td>Fish</td>
<td>11,297</td>
</tr>
<tr>
<td>Tree shrew</td>
<td>2</td>
</tr>
<tr>
<td>Pigeon</td>
<td>155</td>
</tr>
<tr>
<td>Frog</td>
<td>165</td>
</tr>
</tbody>
</table>

Do you test cosmetics or household products on animals?

No, never. This has been illegal in the European Union since 2009.
Next Steps

- Strategy meetings
- Steering group meeting
- Annual event
- AALAS
- Openness awards
Ethical Dilemmas: Use of Animals Containing Human Material (ACHM)

- Increasing use of ACHM to cross the boundary between animals and humans
  - e.g. personalised cancer models; ‘humanised’ immune systems in mice.
- Raises ethical issues, e.g. what if we could:
  - Culture functional human gametes and human brain tissue in animals?
  - Develop animals with human characteristics e.g. skin, speech?
- We can now induce human cells to become pluripotent
  - Opportunity to replace some animal use
  - Likely also to increase relevance of animal models
- Need ethical access to diverse sources of human tissue banks for research
  - Will require public confidence for informed consent
Achieving a Balance

Ensuring Animal Welfare
Achieving a Balance

Delivering Quality Science

Ensuring Animal Welfare
Achieving a Balance

Questions?

Delivering Public Confidence

Delivering Quality Science

Ensuring Animal Welfare