The CCAC is the national organization responsible for setting and maintaining standards for the care and use of animals in science in Canada.
Overview

- A bit of history
- CCAC and the Three Rs
- Recommendations from CIHR/NSERC review panels
- Establishment of the Three Rs Program
- Promotion of the Three Rs
- Implementation of the Three Rs
THE PRINCIPLES OF
Humane Experimental Technique

W. M. S. RUSSELL
AND
R. L. BURCH

Special Edition
Three Rs History

Originated in a proposal made in 1954 by Charles Hume, founder of the Universities Federation for Animal Welfare (UFAW),

- scientific study of humane technique in laboratory animal experiments
- project managed by a committee
  - Sir Peter Medawar, (Chair)
  - William Lane-Petter, Secretary of the Research Defence Society of Great Britain, (member)
  - Christine Stevens, founder of the Animal Welfare Institute (AWI) in the U.S. (funder)
Three Rs

Fundamental basis for most systems overseeing the use of animals in research

- US Public Health Policy (1985)
- EU Directive 86/609
- UK Animals (Scientific Procedures Act) 1986
- International Guiding Principles for Biomedical Research Involving Animals (1985)
CCAC Ethics of Animal Investigation

- Animals should be used only if the researcher’s best efforts to find an alternative have failed...
- Those using animals should employ the most humane methods on the smallest number of appropriate animal required to obtain valid information

CCAC policy statement on: the ethics of animal investigation (1989)
CCAC and the Three Rs

- 1983 – funding provided by CCAC to support cell culture course
- 1989 – CCAC Alternatives Committee
- 1993 – last entry for the Alternatives Committee
  - guidelines on alternatives/annotated bibliography on alternatives for ACCs
- 1995 – Distributed management
  - scientific subcommittee – Guidelines Committee
    - one individual responsible for the topic of alternatives
The Work of the Assessment Program has Always Been Based on the Three Rs

Animal use protocols must include information with regard to the Three Rs…

- a description of why sentient animals must be used for the project, … of possible replacement alternatives… and justification if these are not to be employed

- justification of the species and numbers of animals to be used

- a description of all of the refinements to be employed

CCAC policy statement on: terms of reference for animal care committees (2006)
Implementation of the Three Rs through the Guidelines program

- Guidelines Program
  - Tennessen & Griffin (2006) Application of the Three Rs in Agricultural Research and Teaching
Recommendations from the Granting Agencies

- Continued attention needs to be given to exploring and promoting the fundamental principles of the 3Rs…we believe that the concept of Replacement of animals…should receive equal emphasis (NSERC/CIHR, 2001)

- …additional activities which could contribute to ensuring a credible national program are…ensuring a solid scientific basis for standards and practices by promoting research in support of replacing animal use, refining procedures…and reducing the number of animals… (CIHR/NSERC, 2005)
CCAC Board of Directors
Task Force on the Three Rs (2006-2007)

Chair’s report to the Board of Directors

“given the lack of personnel resources to support the Task Force, it may be appropriate to consider moving the Task Force to a subcommittee of the Guidelines Committee”
Response from the Board of Directors

Establishment of a Three Rs Program for CCAC

- Three Rs Committee
  - Inaugural face-to-face meeting
    October 4, 2008
Three Rs Committee

- François Auger, CIHR (Chair)
- Doug Morck, CFAVM
- Peter Greer, NCI
- Darren Grandel, CFHS

Ex officio
- Jim Thornhill, Chair, Council
- Clément Gauthier, Executive Director
- Gilly Griffin, Guidelines and Three Rs Programs Director

Committee Liaison
- Nicole Fenwick, Consultant (Committee liaison)
Three Rs Committee – Mandate

- focus for the implementation of replacement, reduction and refinement by the CCAC and its constituents, and for the recognition of significant contributions by individuals or organizations to advancing the Three Rs concept in Canada

- develop effective communications and partnerships with other relevant national and international agencies and organizations

- recommend... mechanisms to collaborate with the granting Agencies... to ensure that funded research is fully implementing the Three Rs
Three Rs Committee – Mandate

- …establishment of an appropriate relationship with regulatory agencies to encourage the adoption of validated alternative methods
- …recommend… policies to stimulate the development of replacement alternatives
- …assist in the evaluation and dissemination of relevant Three Rs information including… user-friendly format for the CCAC website
Three Rs Program

Two main focuses:

- Promotion of the Three Rs
- Implementation of the Three Rs
Promotion of the Three Rs

- Communication of CCAC’s ethic of animal experimentation
- Maintenance of an up-to-date Three Rs microsite on the CCAC website
- Consolidation of CCAC’s role as Canada’s National Centre for the Three Rs
The Three Rs as an Ethic of Animal Experimentation

- Basis for most oversight systems

- Challenges
  - Agricultural research
  - Wildlife research
  - Genetically-engineered animals
  - Tension between reduction and refinement
Maintenance of an Up-to-date Microsite

- Recommendations (task force)
  - Create an area on website to post resources for ACCs and investigators

- Hired Nicole Fenwick MSc on contract
CCAC Three Rs Microsite

Welcome to the Three Rs section of the Canadian Council on Animal Care (CCAC) website. This microsite aims to provide those involved with the use of animals in science with easily accessible, useful, and relevant information and resources on the Three Rs - Replacement, Reduction and Refinement alternatives.

**Replacement alternatives** refers to methods which avoid or replace the use of animals in an area where animals would otherwise have been used. This includes both absolute replacements (i.e. replacing animals with inanimate systems, such as computer programs) and relative replacements (i.e. replacing more sentient animals, such as vertebrates, with animals that current scientific evidence indicates have a significantly lower potential for pain perception, such as some invertebrates).

**Reduction alternatives** refers to any strategy that will result in fewer animals being used to obtain sufficient data to answer the research question, or in maximizing the information obtained per animal and thus potentially limiting or avoiding the subsequent use of additional animals, without compromising animal welfare.

**Refinement alternatives** refers to the modification of husbandry or experimental procedures to minimize pain and distress, and to enhance the welfare of an animal used in science from the time it is born until its death.

The CCAC is recognized at home and internationally as the centre for the Three Rs in Canada. Integration of the Three Rs within Canada's national organization for the stewardship of animal use in science ensures translation of the broadest range of scientific knowledge into best practice for animal use.

Please be aware that information on this site is not intended to replace CCAC's guidance statements.
Sections on Each of the Three Rs

Refrinement Alternatives

Refinement alternatives refers to the modification of husbandry or experimental procedures to minimize pain and distress, and to enhance the welfare of an animal used in science from the time it is born until its death.

Key to the implementation of refinement alternatives is the consideration of the entire lifetime experience of the animal, not just the animal's experience during an experiment. There is also evidence that refinement not only benefits animals, but also improves the quality of research findings. For example, the experience of pain and other distress is likely to result in physiological changes that may increase the variability of experimental results and/or decrease their validity.

Last updated: 2009-02-26
Three Rs Search Guide

If you plan to use animals for scientific purposes, you must complete an animal use protocol and submit it to an animal care committee for approval prior to commencement of the study. The animal use protocol outlines how the Three Rs will be implemented in the proposed animal-based procedures. To find the most up-to-date information on the Three Rs, investigators typically conduct a structured information search. To assist investigators with this search, the CCAC has produced the Three Rs Search Guide.

The Three Rs Search Guide provides detailed instructions on how to conduct a Three Rs information search in the Step-by-Step Three Rs Search Strategy.

Specific information can be found more quickly by selecting one of the following Quick Info topics:

- CCAC guidelines & policies on animal use protocols
- Where to do a Three Rs literature search
- Questions to assess if your Three Rs search is complete
- Animal use protocol worksheet

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We would like to know whether this tool is useful for Canadian investigators and would be grateful if you could send us your feedback at ThreeRs@ccac.ca.
Special Topics

Genetically - Engineered Animals

A genetically-engineered animal is an animal which has had a random or targeted change in its nuclear or mitochondrial DNA (addition, deletion or substitution of some part on the animal’s genetic material) achieved through a deliberate human technological intervention.

Genetically-Engineered (GE) animal models may contribute positively to refinement and reduction in an experiment, for instance when the model more closely resembles the human disease of interest. However, the production of GE animals presents distinct challenges to the application of reduction and refinement. One key concern is the large number of surplus animals that must be generated to achieve a small number with the desired genome (challenging reduction). A second key concern is the unpredictability of phenotype expression. This can adversely affect individual animal welfare by causing pain, distress, and/or difficulties related to the husbandry and maintenance of breeding colonies (challenging refinement).

Animal Welfare and Genetic Engineering

Genetic engineering may adversely affect the welfare of individual animals used to produce the genetically-engineered strain (i.e. egg donors, surrogate mothers and stud males) because invasive techniques are required.

Genetic engineering may also adversely affect the welfare of the resultant genetically-engineered offspring because:

- disruption is caused to animals’ physiological processes;
Three Rs Program Activities

Three Rs Search Guide

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## Three Rs Program Activities

### Alternative Test Methods: Validation and Regulatory Status

<table>
<thead>
<tr>
<th>Conventional Test Method</th>
<th>Alternative Test Method</th>
<th>Validation Status</th>
<th>Regulatory Status</th>
<th>Effect on Animal Use</th>
<th>Last Update</th>
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<tbody>
<tr>
<td>Acute Aquatic Toxicity</td>
<td>Upper Threshold Concentration (UTC) Step-Down Approach (a tiered testing strategy to be implemented with OECD TG 203)</td>
<td>EU: Endorsed as a valid testing strategy by ECVMAM.</td>
<td>EU: Accepted for the assessment of acute aquatic toxicity for hazard classification (2006).</td>
<td>Reduction (Reduces numbers of fish used by 65%)</td>
<td>October 2008</td>
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<tr>
<td>Fish Embryo Toxicity (FET) Test</td>
<td>OECD: Draft new Test Guideline</td>
<td>Replacement (Relate)</td>
<td>Replacement (Relate)</td>
<td>October 2008</td>
<td></td>
</tr>
<tr>
<td>Acute Mammalian Oral Toxicity</td>
<td>Fixed-Dose Procedure</td>
<td>EU: Endorsed as equivalent to scientifically validated by ECVMAM.</td>
<td>US: none</td>
<td>Reduction (Reduces the numbers of animals used per test from 25 to 5-9)</td>
<td>October 2008</td>
</tr>
<tr>
<td>Acute oral LD₅₀ (formerly OECD TG 401, now deleted as a test method)</td>
<td>OECD: TG 420 (2002)</td>
<td>Reduction (Reduces the numbers of animals used per test from 25 to 5-9)</td>
<td>Refinement (does not rely on death as an endpoint)</td>
<td>October 2008</td>
<td></td>
</tr>
</tbody>
</table>

### Coming Soon to the Three Rs Microsite: Table of Alternative Methods
Canada’s National Centre for the Three Rs

Three Rs Centres

- develop effective communications and partnerships with other relevant national and international agencies and organizations
Three Rs Centres

- Centre for the Documentation and Evaluation of Alternative Methods to Animal Experiments (ZEBET)
- European Centre for the Validation of Alternative Methods (ECVAM)
- European Consensus-Platform for Alternatives (ECOPA)
- European Resource Centre for Alternatives in Higher Education (EURCA)
- Finnish National Consensus Platform for Alternatives (FINCOPA)
- Fund for the Replacement of Animals in Medical Experiments (FRAME)
- National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)
- Netherlands Centre for Alternatives to Animal Use (NCA)
- Swedish Animal Welfare Association (SAWA)
- Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART)
- International Centre for Alternatives in Research and Education (I-CARE)
- Japanese Center for the Validation of Alternative Methods (JaCVAM)
- Canadian Council on Animal Care (CCAC)
- Center for Alternatives to Animal Testing (CAAT)
- Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)
- Institute for Laboratory Animal Research (ILAR)
Partnerships with Other Three Rs Centres

CCAC member of the Altweb project team

FRAME’s 40th anniversary

Assistance with CCAC’s fellowship program
August 21 – 25, 2011
Montréal, Canada
Hosted by the Canadian Council on Animal Care
www.ccac.ca
8th World Congress on Alternatives & Animal Use in the Life Sciences
Implementation of the Three Rs

- Research
- Teaching
- Testing
- Production (animals and biologicals)
Research and Teaching

Research
- Interaction with granting agencies

Teaching
- Improvement of Three Rs microsite
- Evaluation of pedagogical merit
ICLAS/CCAC International Symposium on Regulatory Testing and Animal Welfare June 2001, Québec City

- International Symposium
- Regulators, academics, people from industry and people from the field of animal welfare
- Recommendations emerged for how to improve animal welfare in regulatory testing
The successful implementation of change in scientific practice relating to the use of animals for regulatory testing depends on:

- Quality of science supporting the change
- Understanding, recognition and implementation of the change by all stakeholders in a timely manner
- Communication of best practices should involve regulators, scientists, animal welfare organizations, the public and decision makers as users of science
Canadian Stakeholders in Shellfish Toxin Testing

Public

Demands safe shellfish

Government of Canada

Ensures safety through regulatory testing

CCAC

More supportive of animal use in science when pain and distress are minimized

Animal use guidelines based on the Three Rs

Promote the use of alternative testing methods

Guy and Griffin, 2008
Shellfish Toxin Testing

- Regulators involved in shellfish toxin testing receive formal training on the alternative methods.
- Canada reduce its investment in the development of new alternative methods, and direct resources towards improving the pre-column HPLC method to suit the Canadian regulatory environment and furthering its international acceptance.
- More funding be dedicated to develop a complete set of standards for the HPLC method.
- Until a complete set of CRMs has been developed, the pre-column HPLC method be used as a screening method to reduce the number of samples that need to be confirmed using the MBA.

Guy & Griffin (in press) Regulatory Toxicology and Pharmacology
Conclusion

CCAC based on the Three Rs

Implementation of the Three Rs occurs in all CCAC Programs

New CCAC Three Rs Program

- Promotion of the Three Rs
  - Three Rs ethic
  - Three Rs Microsite
  - CCAC as Canada’s Three Rs Centre

- Implementation of the Three Rs
THANK YOU !!!

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