

# The International Symposium on Regulatory Testing and Animal Welfare: Recommendations on Best Scientific Practices for Animal Care Committees and Animal Use Oversight

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## Introduction

This Breakout Group addressed the current best practices and future possibilities involved in animal use oversight undertaken for regulatory purposes. Participants in the group (listed at the end of this report) had previously reviewed a number of key background references (also listed at the end of this report) that had been selected by the group's leaders prior to the meeting.

Participants were asked to consider the following questions as part of their general discussion:

1. Regulatory Testing Requirements
  - a. How is the need to develop new test requirements identified?
  - b. How transparent and inclusive are the processes?
2. Stakeholders and Oversight
  - a. How can a productive dialogue between stakeholders be facilitated?
  - b. What positive outputs can be produced?
3. ACCs/IACUCs/Local Ethical Review Processes
  - a. From where is their authority derived—legislation, guidance, public relations, etc.?
  - b. Regarding their terms of reference (advisory/decision making/executive):
    - i. Do they consider proposed studies/on going studies/retrospective reviews?
    - ii. Should they look at large programs of work, or individual studies?
    - iii. Should they consider the ethics, science, welfare, and accommodation and care?
  - c. Regarding competencies of animal care committee members:
    - i. What interests should be represented?
    - ii. What competencies should the members have to demonstrate best practice?
4. National Legislation
  - a. Compare and contrast North American and European models: What are the best features of each?
  - b. Are national regulatory assessments

- i. Based on animal test data sensitive to the animal welfare issues?
    - ii. Prepared to give advice before testing programs are undertaken and feedback after submissions have been received?
5. The 3Rs
  - a. Is “best welfare best science”?
  - b. Is the imperative to minimize “suffering” or minimize numbers?
  - c. How can refinement be measured?
6. Report on Group Discussion

In the context of current best practice, certain regional differences of view that are based on the framework of particular systems exist. Nevertheless, in considering the future and disregarding the limitations imposed by current frameworks, we unanimously agree on certain characteristics of best future practice. We also agree that best practice in one context might not be best practice in another and unanimously endorse the proposition that “best welfare is best science.” The investigator, the animal care and use committee (ACC<sup>1</sup>), and the veterinarian share responsibility for the practical application of this principle.

## Regulatory Testing Requirements

We appreciate that regulatory test requirements are developed in response to scientific need and political imperative. Indeed, it is necessary to develop new test requirements by inclusive and transparent processes that ensure they are based on sound science and humane animal use. However, we are concerned that some animal studies that satisfy regulatory requirements still reflect “what the regulators expect” rather than best contemporary science or animal welfare. We believe that until recently, animal welfare was not a priority or concern to regulatory authorities. However, we believe that the following organizations now offer necessary vision and leadership in this field: US Department of Agriculture, Health Canada, Office of Laboratory Animal Welfare (OLAW), International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), and Organisation for Economic Co-operation and Development (OECD).

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<sup>1</sup>Abbreviation used in this presentation: ACC, animal care and use committee.

In our view, progress necessitates a constructive, inclusive dialogue between stakeholders. Examples of prospective benefits include the recent UK guidance on humane regulatory testing and concordats on data sharing (OECD 1981; 1987a,b; 2001a,b) and the 3Rs (Russell and Burch 1959).

Clearly, support for such initiatives ideally comes at the national level from both governments and stakeholders. In addition, the established forum should be apolitical and without influence from constituencies and the media. Regulatory authorities are responsible for ensuring that those involved with ACCs understand regulatory requirements and their interpretation. They also should consider developing and providing basic training material and regular accessible updates.

## Current Best Practice

Examples of current best practice make use of constructive dialogue, as is taking place in the United Kingdom among those who develop and implement regulatory requirements, those who conduct the animal testing, and those who regulate animal testing.

## Future Progress

We believe the following provisions will ensure future progress:

- Regulatory test requirements should be built on good science and good animal welfare;
- Induction training for members of ACCs should include a grounding in regulatory requirements and their interpretation; and
- Regulatory authorities should supply ACCs with accessible and easily digestible updates on trends and developments.

## Mandate and Remit of Animal Care and Use Committees

ACCs have a role in overseeing animal care and use in all establishments that use vertebrate animals for regulatory testing, regardless of the size or nature of the establishment. However, we are concerned that some committees may exist simply to meet legal or other obligations, rather than as an effort to “add value” to the animal studies performed. If this concern is indeed justified, we believe it indicates a poor institutional culture.

ACCs must help visibly to foster the “culture of care” that should be in evidence at all establishments where animals are used for experimental or other scientific purposes. Means must be found to allow people involved in such processes to network with individuals at other institutions,

including committees and processes established under other jurisdictions. The committees should have the authority and confidence to challenge ethical concerns as well as issues relating to scientific validity and animal welfare (including the training and technical proficiency of the scientists and animal care staff involved).

ACC members are responsible for ensuring that all animal studies conducted by their respective organizations are consistent with the organizations’ standards and values. In addition, administrators should consult with committee members regarding any studies that are being considered for out-sourcing. We believe there is no defense for the out-sourcing of studies that are not compliant with national policy or practice, or that are not considered to have sufficient scientific or ethical merit to be conducted in-house (“scientific tourism”).

The success of ACCs and the committee process is generally the product of two important factors: the quality of the people involved (particularly the choice of chairperson) and the senior management’s strong and visible support for the committee’s process and outputs. We consider these factors to be more important determinants of success than whether the committees are established voluntarily or mandated by legislation.

Best practice and public accountability require an element of external oversight. Lay and external members should play an active role. The standards of care and accommodation provided by establishments should comply with recognized and reputable published guidelines. When mandatory oversight does not exist, administrators should encourage the membership of a reputable third party accreditation service.

Experience has shown that different frameworks provide effective oversight in different jurisdictions and within organizations with different cultures. Indeed, providing the process works in practice. Diversity, which can of itself promote continuous improvement, should not be discouraged.

## Current Best Practice

Committees that exemplify current best practice may be characterized as follows. They

- Establish an appropriate culture of care, make the appropriate institutional expertise and resources available to the investigators, and stamp the organization’s values and standards on the animal studies to be performed—including studies that are being out-sourced;
- Consider ethical, scientific, and animal welfare issues;
- Add value to animal studies that are undertaken—in some visible way;
- Have active and visible support from their organization’s senior management; and
- Involve lay and external members and other forms of independent oversight, including compliance with recognized and reputable third party standards.

## Future Progress

We believe that future progress requires the following:

- Encouraging diversity, providing the committees function effectively; and
- Finding the means for committees to network in an effort to identify, encourage, and share best practices.

## Composition of ACCs

The membership of ACCs should include appropriate technical competencies in addition to lay or external membership. As a minimum, the competencies should include knowledge of regulatory requirements and their interpretation, relevant aspects of the biological sciences and laboratory animal science, experimental design, and animal care and welfare. Committees should receive administrative support (including information specialists to provide relevant reference material), advice on statistical analysis, and advice on health and safety issues.

Experienced animal care staff and laboratory animal veterinarians who are properly trained and receive appropriate continued professional development are ideally suited for providing these latter inputs. They can also be key sources of information for lay and external members.

It is necessary to identify and resolve potential conflicts of interest (e.g., a committee member who is also the veterinarian or study director). Committee members should receive easily understood updates on issues relating to their functions, including updates on regulatory affairs and animal welfare. Induction training and continued professional development are important for committee members.

## Current Best Practice

Current best practice thus includes

- Committee members who have competencies and access to the support services, listed above; and
- Involvement of lay and external members, the laboratory animal veterinarian, and experienced animal care staff.

## Future Progress

There is a need for better induction training and continued professional development for those involved in such committees. Among the prospective professional development resources are appropriate literature, in-house presentations, attendance at meetings and symposia, and networking with committees from other establishments.

## Processes and Outputs of ACCs

The committees and their processes should make available to members the necessary advice and resources to ensure that best science is performed and that best welfare prevails. Whether the committee outputs are advice or decisions, there should be some reasonable appeals procedure.

Efficiency and effectiveness require that the right people offer the right advice at the right time. Advice and support should be available from the concept stage through to the completion of the study. Ideally, the support provided by the committee should be considered a *process* that underpins all stages of the animal studies, rather than only an “event” that must take place before animal studies begin.

Committees should consider not only the test protocol, but also the test strategy. Investigators should supply the committee with their proposals as well as a summary of the other options that were considered and rejected. In addition, committees should receive updates on programs of work they have advised and other information relating to the operation of the animal facility, including the impact of “more refined” husbandry and care practices.

It is important for committees to demonstrate value added to the science performed or to the welfare of the animals used—in terms of better animal welfare, better science, and reduced development times. In practice, this demonstration might best be achieved through case studies rather than some more abstract measurement.

It is imperative to minimize the pain and distress caused while maximizing scientific output. The number of animals used should never be reduced by the adoption of strategies that impose a disproportionately large additional welfare cost on the animals. Nevertheless, when it is possible to enhance the quality of the science, it is appropriate for committees to recommend increasing the number of animals or advise performing pilot studies.

ACCs should consider the development and maintenance of generic low-maintenance, minimum-severity protocols for common procedures, which would limit volumes and humane endpoints. Investigators should provide appropriate supportive, symptomatic, and specific treatments unless good cause is shown for them to be withheld.

## Current Best Practice

We believe that current best practice includes the following:

- Processes that provide support to investigators from the concept stage through to the review of results;
- Committees that consider all of the investigators’ options (not simply those selected, but also other options the investigator considered and rejected) and review the testing strategy as well as study protocols;
- Processes that allow the right of appeal if proposals are rejected; and
- Preparation of institutional (or endorsement of third

party) minimum-severity protocols for common procedures (including appropriate humane endpoints), which limit volumes for dosing and sampling.

## Future Progress

ACCs should better demonstrate and communicate value added to animal studies performed at their establishments. Committees should critically evaluate the impact of any “refinement” initiatives introduced for the accommodation, care, and use of animals.

## Recommendations

We recommend that

- All establishments that use vertebrate animals for regulatory testing have respective ACCs;
- Governments facilitate national apolitical forums in which there can be constructive dialogue involving all legitimate stakeholders on the issues of animal testing;
- Regulatory authorities provide material on regulatory test requirements and their interpretation to inform and facilitate the deliberations of ACCs; and
- A means be found to identify and publicize (within establishments, between establishments, and with a wider audience) the significant contributions ACCs make to the quality of science and the welfare of animals used for regulatory testing.

## Background References

- OECD [Organisation for Economic Co-operation and Development]. 1981. Guideline 403: Acute inhalation toxicity. Paris: OECD.
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## Participants

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As indicated, Breakout Group participants are principally from North America, with representation from Europe and the Pacific Rim. Their professional involvement includes both product development and overseeing and undertaking animal studies.