A resource book for lay members of ethical review and similar bodies worldwide

3rd edition

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FOREWORD

The RSPCA is a long-standing advocate of ethical review and similar bodies (ERBs) as a means of promoting:

- recognition and consideration of ethical matters related to the use of laboratory animals;
- involvement of a wider range of perspectives in decisions regarding the justification for animal use; and
- more active implementation of the Three Rs (Jennings 1994; see definitions, page 6).

This Resource Book is one of a series of RSPCA publications designed to facilitate the work of ethical review and similar bodies, and especially their lay members. The first edition was published in 2003, and a second updated and revised edition followed in 2009. Both were written from a UK perspective, but have been used by lay members and other participants in ERBs across a range of countries and continents. Given this widespread interest, we have updated the text to provide a more international view.

For UK readers, the book complements the RSPCA/LASA *Guiding principles on good practice for Ethical Review Processes* (2010), which discuss the functions of UK institutional ethical review bodies, now known as Animal Welfare and Ethical Review Bodies, in more detail. The RSPCA/LASA document is being updated at the time of writing in 2014.

The RSPCA also organises an annual UK Lay Members' Forum, which provides an opportunity for lay members to share their experiences of participating in ethical review bodies and hear presentations on a variety of relevant topics.

All of these resources, including reports of past Lay Members' Forums, are published on the RSPCA's website, where you can also join an e-mail list to receive information about forthcoming events and publications. Go to www.rspca.org.uk/laymembers.

Acknowledgements

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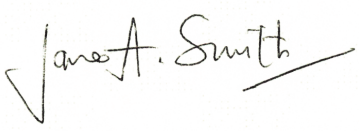

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Definition of terms

We have tried to explain 'technical' terms wherever they appear. However, there are a few names and key concepts that are mentioned throughout the book, which it is helpful to explain at the start. Terms in *bold italics* (the first time they appear) are defined lower down the list.

Ethical review body (ERB)

We have used the phrase 'ethical review body' (ERB) to describe any institutional, regional or national committee or similar process that brings together a range of people offering relevant expertise and perspectives, in order to:

- consider ethical, welfare and ***Three Rs*** questions arising in the use of ***animals*** in science;
- consider the ethical acceptability of proposed or on-going work, i.e. carry out ***project review*** and, in some cases, license or otherwise 'approve' proposed or on-going work;
- consider other aspects of laboratory animal use, such as animal breeding, husbandry and care, and staff training; and
- provide a forum for discussion on such matters and offer advice and support to relevant staff.

The aims, tasks and level of authority of ERBs around the world vary according to the regulatory framework, as do the terms used to describe them (for example, Animal Welfare and Ethical Review Bodies in the UK, Ethics Committees in Sweden, Institutional Animal Care and Use Committees in the USA), but the role of lay members will be similar in each case.

Animals

Most jurisdictions define an 'animal' as a non-human adult vertebrate (i.e. fish, amphibian, reptile, bird or mammal). Some also include larvae and/or embryos from specified stages of development; and some include particular invertebrates (e.g. cephalopods, such as octopus and squid).

Project review (or project evaluation)

This phrase refers to one aspect of an ERB's work, as described in the list above. It involves assessing the justification for a scientific ***project*** involving animals, for example within an application for a project licence in the UK, and as part of the project authorisation process required under EU Directive 2010/63 (European Parliament and Council of the European Union, 2010).

This will take the form of a harm/benefit assessment, in which the likely harms to animals, in terms of pain, suffering and distress, are 'weighed' against the potential benefits to humans, animals or the environment. Sometimes such reviews are carried out at the ***procedure*** or ***protocol*** level, but the aims are the same.

Procedure, project, protocol

A procedure is any use of an animal for experimental or other scientific or educational purposes, "*which may cause that animal pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice*" (Directive 2010/63/EU).

A project is "*a programme of work having a defined scientific objective and involving one or more procedures*" (Directive 2010/63/EU). In the European Union an authorised project may last for up to five years, after which time it must be reviewed and, if appropriate, re-authorised.

A protocol describes the procedure(s) that will be carried out on a given animal, from the time the animal enters the project until humanely killed or otherwise released from the project. A project will usually include a number of protocols.

The Three Rs (3Rs)

The Three Rs are principles of humane experimental technique that were first set out by Russell and Burch in 1959. They are now widely accepted within the international scientific community and in associated legislation and guidelines, as a means of avoiding or reducing animal use and suffering and helping to improve the quality of science.

Replacement: using methods or strategies that replace or avoid the use of animals in research and testing.

Reduction: reducing the number of animals used to achieve the scientific objectives, for example by improving experimental design and statistical analyses.

Refinement: refining scientific procedures and other factors affecting animals (for example, transport, housing, restraint) to reduce suffering and improve the animals' welfare at every stage of their lives.

CHAPTER 1

The lay member's role

Lay involvement in ethical review bodies (ERBs) overseeing laboratory animal use is common practice in a number of countries around the world, and in some cases is a regulatory requirement. This chapter explores the valuable contributions that lay members can make and discusses some practical matters associated with the role.

Defining a 'lay member'

Lay participants in ERBs come from a variety of backgrounds and fields of work. Examples include academics from the arts or social sciences, managers in areas unrelated to animal use, lawyers, ethicists, administrative staff, librarians, safety officers, and people from the local community, clergy or public services.

Some countries require that certain types of lay participant are represented in their ERBs and examples are listed below. These definitions make clear that lay members should have no vested interest in the matters under review, and may also be independent of the institution where the research is conducted; but beyond this, opinions differ on exactly who counts as 'lay'. However, rather than placing too much emphasis on the definition of 'lay member', it is more important to focus on the *roles* that lay members can play and the benefits that these bring.

Examples of 'required' lay participants

N.B. these are minimum requirements, and other kinds of lay people may also be involved.

Australia: "*a person who is both independent of the institution and who has never been involved in the use of animals in scientific or teaching activities, either in their employment or beyond undergraduate education*" (Australian Government National Health and Medical Research Council 2013).

Canada: "*an institutional member whose normal activities, past or present, do not depend on or involve animal use for research, teaching or testing*" and "*person(s) representing community interests and concerns who have not been involved in animal use for research, teaching or testing*" (Canadian Council on Animal Care 2006).

New Zealand: a person who "*should bring the perspective of a member of the public",* who is *"not employed by, or associated with*" the organisation concerned, "*nor associated with the scientific community or an animal welfare agency*" (New Zealand Ministry of Agriculture and Forestry 2000).

UK: "*....actively seek a wider membership taking into account the views of people who do not have responsibilities under [UK law on laboratory animal use] as well as one or more persons who are independent of the establishment*" (Home Office 2014).

USA (PHS Policy): a "*member whose primary concerns are in a non-scientific area (for example ethicist, lawyer or clergy)*" and "*at least one public member to represent the general community interests in proper care and use of animals*", who "*should not be a laboratory animal user"* and a *"member not affiliated in any way with the institution*" (National Research Council 2011).

Benefits of lay participation

There is widespread agreement that lay people can bring a range of benefits to ethical review in its widest sense (APC 2003; Smith *et al.* [FELASA] 2007). These include:

- **Providing a different perspective**
  Asking questions that people more deeply involved in the research might not identify or consider asking; viewing established practice and accepted norms with a 'fresh eye'; and stimulating new or different ways of thinking about the ethical, animal welfare or scientific issues.
- **Helping to ensure the integrity of the ethical review body**
  From an independent stand-point, either within or outside the institution: checking that the ERB's procedures are rigorous, that all participants play an active part, and that decisions and advice are acted upon.
- **Supplying a degree of public representation**
  Bringing a societal perspective to consideration of animal experiments, which are often funded by public money and carried out in the public's name. It is unrealistic to expect individual lay members to represent the full spectrum of public opinion, but lay participation is a contribution to openness and can help scientists see how members of the public might view their work.

The three types of benefit listed above all rest on lay members asking questions, which:

- can be from the animals' point of view, with the aim of making a positive difference for animal welfare
- may address scientific aspects, with the aim of understanding the benefits that are sought, how these can be achieved with the least possible impact on the animals, and why alternatives cannot be used, and
- can help to ensure that the justification for using animals is rigorously evaluated.

Lay involvement in other similar contexts

Lay participation is also valued, and is becoming the norm, in many areas of scientific and medical decision-making where lay voices bring a societal perspective to the issues under discussion. Examples include: research ethics committees for clinical (human medical) research; government scientific advisory bodies; and research funding and priority setting processes.

Empirical studies of the lay role in such contexts indicate that there is widespread agreement that lay perspectives are important and can bring substantive procedural benefits, by helping to ensure that the ERB's procedures are rigorous. However, it is also acknowledged that it is not easy for lay people to contribute in all the ways listed above. For instance, it can be difficult to ask pertinent and challenging questions when complex scientific issues are discussed (for example, Entwistle *et al*. 1998; Dyer 2004; and Stilgoe *et al.* 2006).

Nevertheless, it is important to remember that other members of the ERB are likely to be in a similar position when the discussions fall outside their own specialist areas. Indeed, some commentators argue that the term 'lay' is unhelpful, because it suggests that there are two classes of member (lay *vs*. expert), rather than a group of equal but diverse experts to which lay members bring wisdom gained in other fields (Stilgoe *et al*. 2006).

Becoming a lay member

In order to achieve the benefits of lay participation listed above, lay members need to feel confident and comfortable in the role. The following practical steps and personal qualities can assist in making a strong contribution and most of these will be helpful for all participants, not just lay members (see also RSPCA/LASA 2010).

Practical steps that help participants contribute to the ERB

- **Do not worry about lack of scientific expertise in the particular issues under consideration.** By definition, lay members are not experts – just like other members when discussions move outside their particular areas of expertise.
- **Ask any question you feel is important**, especially as this might also enable other members of the ERB to enter more fully into the discussions. This book includes ideas for questions to ask in a range of different contexts.
- **Get to know the other participants in the ERB and, at an institutional level, other relevant staff.** Talking with other lay members can be especially helpful and the support of a challenging ERB chairman is very valuable, particularly when that chair is also a layperson.
- **Obtain as much information as possible to help you in your work**, e.g. about the ERB itself (see Chapter 2), the work discussed, and where to go to for advice on issues such as the 3Rs (see Chapter 3). Good non-technical summaries of project applications (see page 28), visits to animal facilities (see Chapter 7) and discussions with relevant animal care and scientific staff are also very helpful.

Useful personal qualities for ERB participants

- Being open-minded, fair and impartial.
- Being prepared to listen and respond thoughtfully to differing views.
- Being prepared to 'think outside the box' and challenge the status quo.
- Having the confidence to ask questions and initiate discussion in a committee environment.
- Having realistic expectations of what can be achieved.
- Having the commitment and time to take an active role.

Consensus, compromise and disagreement

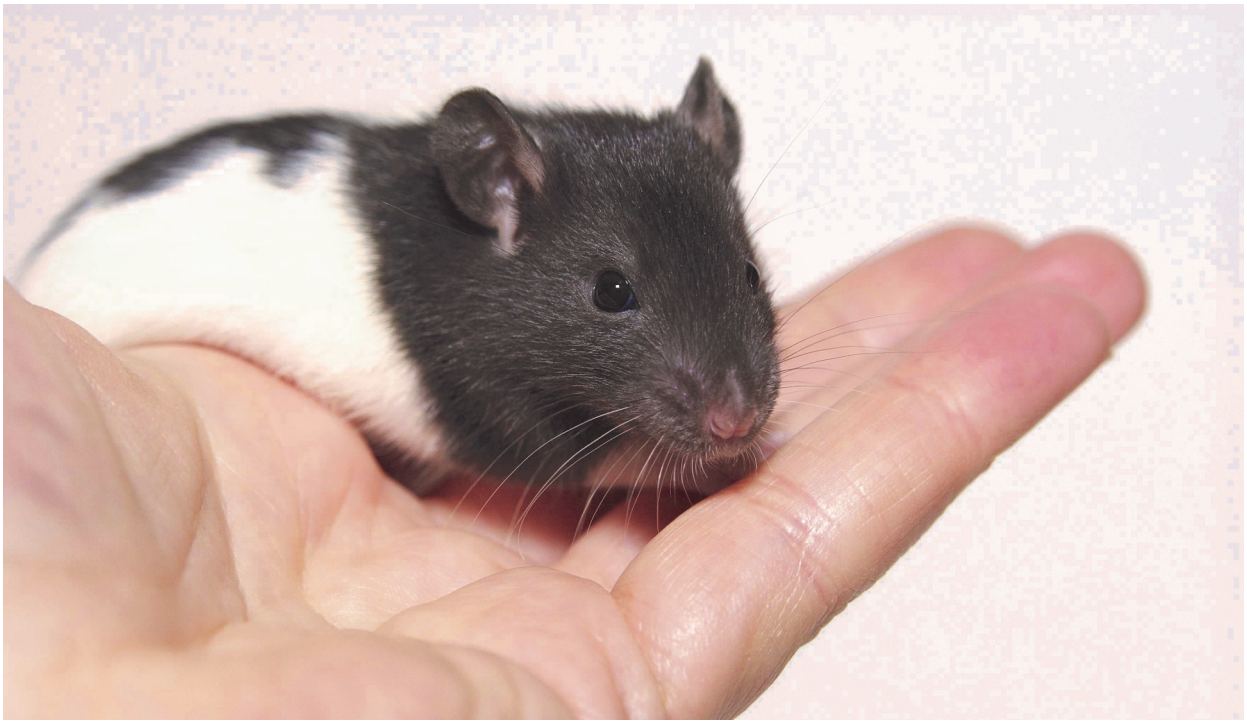
For the ERB to be effective, participants need to work together to try to achieve consensus. However, there may be times when some members disagree with the majority view and feel unable to compromise their position. Expressing and standing by a difference of opinion can be difficult, but is important, since always compromising in such circumstances diminishes the value of involving a diversity of perspectives. Likewise, it is important that differing views, and the reasons for these, are recorded and communicated to other relevant people.

The ERB should allow participants who have concerns to feel that these are taken seriously, and should not subject lay or other members to cross examination that can close down, rather than open up, discussion of differences of opinion.

When deciding whether or not to accept an invitation to become a lay member it is useful to consider the questions overleaf, drawing on information about the organisation and goals of the ERB concerned (see Chapter 2).

Becoming a lay member: questions for consideration

- What would you like to achieve by participating in the ERB? How far do your hopes for the role match the expectations of the ERB and, if relevant, the particular institution?
- Do you have strong views on animal experiments, and is participating in the ERB likely to involve compromising your personal principles?
- Will you be able to commit sufficient time and energy to enable you to play an active role e.g. attending formal ERB meetings, reading and commenting on what might be a large volume of written material in preparation for and between formal meetings, visiting animal facilities, and getting to know the work of the institution(s)?
- Would you be concerned about minutes of meetings and other documentation being made available to others within the institution or more widely?



CHAPTER 2

Finding out about the ERB

As a new or prospective lay member, it can take a while to gain a clear picture of the role and functions of the ethical review body and how it is organised. This chapter aims to assist in getting to know your particular ERB and the context in which it operates. It covers the following questions:

- **Level and scope:** Does the ERB operate at national, regional and/or institutional level?
- **Responsibility:** Is the ERB responsible for the legal authorisation of scientific projects involving animals? Is it solely concerned with project review or does it also form a wider system of oversight of animal use within institution(s)?
- **Aims and tasks:** What are the aims of the ERB? What practical tasks does it carry out to achieve its objectives?
- **Participants:** Who are the other members of the ERB and what are their roles and responsibilities?
- **Authority:** How does the ERB ensure that its decisions and recommendations are acted on?
- **For institutional ERBs:** Why and how animals are used within the institution?
- **Wider context:** What other national or local activities impact on, or relate to, the work of the ERB?
- **Communication and evaluation:** How does the ERB communicate with staff involved in laboratory

Level and scope of ethical review by the ERB

The 'level' at which ERBs operate varies between countries, according to their laws and regulations. In some countries, national or regional ERBs are responsible for all aspects of ethical review of laboratory animal use. For example, Denmark has a national committee which directs a government inspectorate, and in Germany regional committees advise government authorities. Other countries, such as Australia, Canada, New Zealand, and USA have institutional ERBs and some regulatory systems include both national and institutional ethical review, for example the UK system which is described in detail in Appendix 1. In some parts of the world, systems of ethical review are still under development, such as in China where the intention is to involve national, regional and local levels of review (Kong and Qin 2010).

Although there is no absolute rule, national and regional ERBs generally focus on review of applications to use animals in scientific projects (project review) and usually bear responsibility for legal authorisation of work and enforcement of legislation; whereas institutional ERBs are able to operate a system of oversight of day-to-day care and use of animals, as well as contributing to project review, focussing on ‘local’ institutional perspectives and practices. Note, too, that the names given to ERBs differ around the world: some emphasise their role in 'ethics', (e.g. Animal Ethics Committees (AECs) in Australia and New Zealand); others their role in animal care (e.g. Institutional Animal Care and Use Committees (IACUCs) in the USA) and Animal Care Committees (ACCs) in Canada); and some reflect both aspects (e.g. Animal Welfare and Ethical Review Bodies (AWERBs) in the UK).

The ERB’s aims and tasks

There is no standard approach to the organisation of an ERB whether at institutional, regional or national level. This will vary according to regulatory, scientific, political and cultural factors. However, there is widespread agreement on the principles of ethical review and hence what ERBs should aim to achieve (see international statements of principle such as ICLAS 2010 and CIOMS-ICLAS 2012).

These aims are described in national laws and/or codes of practice and were summarised in 2000 by the UK Home Office as:

"*To ensure that all use of animals is … carefully considered and justified; that proper account is taken of all possibilities for reduction, refinement and replacement (the 3Rs); and that high standards of accommodation and care are achieved*".

A similar statement was made by the Australian Government National Health and Medical Research Council (2013), in its *Code of practice for the care and use of animals for scientific purposes*:

"*There are difficult ethical judgements to be made regarding the use of animals for scientific purposes. The Code requires (AECs) Animal Ethics Committees to determine whether the case for animal use is justified and to ensure adherence to the principles of Replacement, Reduction and Refinement (3Rs)*."

The general aims above can be broken down into **a series of practical tasks**, covering both project review and oversight of the wider aspects of animal care and use, as shown in the box below.

Tasks for Ethical Review Bodies*

1. Providing a forum for discussion on all matters related to animal welfare, care and use [Chapter 6].
2. Promoting the development and uptake of the 3Rs (replacement, reduction and refinement of animal use) in all projects/protocols throughout their duration; advising staff how to apply them [all chapters, and especially Chapter 3].
3. Considering standards of animal care and accommodation to ensure high standards are developed and maintained [Chapters 6 and 7].
4. Evaluating applications (and any subsequent amendments) to carry out projects/protocols involving laboratory animals [Chapter 4].
5. Carrying out interim or retrospective reviews of projects/protocols in progress or completed [Chapter 5].
6. Supporting all staff dealing with animals, including those with statutory responsibilities, regarding animal welfare and ethical issues [all chapters].
7. Establishing and regularly reviewing procedures and protocols, including management systems, for monitoring, reporting and following up on acquisition, welfare and proper use of animals [all chapters].
8. Ensuring that relevant staff have appropriate education and training [Chapter 6].
9. Reviewing methods of humane killing; encouraging the sharing of tissues and organs; exploring options for reducing animal wastage, rehoming or releasing animals [Chapters 3, 4 and 6].
10. Helping to promote a 'culture of care' within the institution and the wider community [all chapters].

Your ERB may not carry out all of these tasks, especially if it is a national or regional rather than an institutional body, or it might have additional roles not listed here.

***See Appendix 1 for the list of tasks specifically for UK AWERBs.**

Responsibility for the ethical conduct of research and testing rests with the researchers and others who use and care for the animals, and so the ERB also has an important educational role to play in helping to create a "*culture of care and conscience*" within institutions (CIOMS-ICLAS 2012). This is easier to achieve when there is an institutional forum for consideration of ethical aspects of animal use, which can help to ensure that "*everyone plays their part in practising 'ethical science'*" (Jennings and Smith 2012). It is therefore worthwhile noting that even in countries that have no regulatory requirement for local ERBs, institutions often voluntarily set up their own review processes to help achieve this goal.

Participants in the ERB

Regulations lay down minimum requirements for membership of ERBs which usually must include animal care staff, one or more veterinarians, and scientists. Some jurisdictions also require representatives of the local community (e.g. the USA, Australia) and animal welfare organisations (e.g. Sweden, where half the members must be "*laymen, some representing animal welfare organisations*", CODEX 2013). However, to be effective, ERBs need to include a wide variety of participants who together provide a comprehensive range of knowledge, competencies and perspectives and, at an institutional level, a balance of different levels of seniority. A good ERB will therefore also include people with expertise in each of the 3Rs, experimental design, animal welfare, education and training, ethics and relevant scientific fields.

Participants also need to have the personal qualities required to contribute to discussions (see Chapter 1 page 9) so the composition of an ERB needs careful thought. In particular, there is a need for a strong, impartial chairperson to "*make sure that the focus is on outcomes, the process is efficient*" and in particular to "*create a supportive, inclusive environment that will encourage open and forthright discussion*" (RSPCA/LASA 2010).

Authority of the ERB

ERBs need to ensure that their decisions and recommendations are taken forward and implemented, that conditions of project authorisation and codes of practice are complied with, and that laboratory animals are always treated with appropriate care and respect.

Some countries have government inspectorates and penalties set out in law to help detect and deal with non-compliance (e.g. these are requirements of EU law). In others, institutions alone bear responsibility for monitoring compliance and dealing with cases of non-compliance (e.g. Australia, where in addition to their own day-to-day responsibilities, "*Institutions must also ensure that an independent external review is conducted at least every four years to assess ... compliance*" (Australian Government National Health and Medical Research Council 2013).

Whatever regulatory system is in place, it is vital that institutions themselves have rigorous processes for monitoring animal welfare, detecting non-compliance, encouraging and enabling staff to express any concerns, ensuring that the concerns are properly addressed, and generally fostering a 'culture of care' in which high ethical standards of animal care and use are the norm (see Chapter 6). An institutional ERB provides an ideal driver in this respect.

For institutional ERBs

Research institutions vary considerably in size, in the nature and diversity of their scientific studies and animal work, and in their organisation and management. If you are participating in an institutional ERB, it is important to gain an overview of the institution's research interests, including why and how animals are used, and a feel for the local culture, including the priority given to animal welfare and the 3Rs.

It can take time to acquire a strong sense of these aspects, particularly when coming from outside the institution. Discussion of the points overleaf with other participants in the ERB can help build up a picture of the animal work. It is also helpful to visit the animal facilities to see the animals, view procedures where possible and talk to staff (see Chapter 7)

Finding out about the institution's animal work: points to consider

- The **type of institution**, for example whether it is predominantly an academic, industry or contract research organisation. This will influence the type of work and the reasons it is done, e.g. the balance between fundamental and applied research and whether tests are carried out to satisfy regulatory requirements.
- The **diversity of research interests** across the institution as a whole and within individual departments, and the **lines of responsibility** involved in managing animal care and use.
- The **scale of animal research**, for example the numbers of projects involving animals and researchers working within them, and the frequency of submissions of new proposals to use animals to the ERB.
- The variety of **animal species used**, where they come from, how they are **housed and cared for**, and the **numbers** of each species kept at the institution.
- The broad range of **types of scientific procedures** carried out, and whether the institution has decided **any absolute limits** on the kinds of work that can be done. For example, some institutions will not use primates or dogs, or carry out safety testing of certain categories of non-medicinal products.
- The **management structure** and other organisational issues such as **staff induction and training**.
- Any **financial constraints**, restructuring issues or site limitations.

The wider context in which the ERB operates

A range of activities can affect whether and how laboratory animals are used, and hence have an impact on the work of ERBs. An ERB should complement, not duplicate, these other activities (some of which are listed overleaf), and it is helpful to have an understanding of this wider context order to appreciate where and how the ERB can 'add value'.

Communication and evaluation of the ERB

The outcomes and effects of ethical review are more important than exactly how it is done – and good outcomes rest on effective communication between all relevant staff. Details of the form and function of ERBs should therefore be part of the induction and training process for all relevant staff, with information on the ERB's ongoing work made freely available. ERB websites, newsletters and posters are just some of the ways that this is being done. Seeking feedback from staff on the approach and work of the ERB is also useful, since this not only aids communication but also helps the ERB evaluate its own efficiency and effectiveness from time to time.

Engaging scientists with the ERB is particularly important so that its role and value is clear and it is not just viewed as 'another hurdle' to negotiate in developing and implementing their projects.

Examples of activities that can impact on the use of animals and the work of the ERB

The work of groups that consider specific aspects of animal care and use, such as:

- institutional animal users' groups; animal house management/policy committees; animal care staff discussion forums; on-going project review carried out by project teams and involving animal care staff
- internal or external audits of standards of animal care and welfare.

These activities can all have positive impacts on both animal welfare and science and are likely to form part of an institutional ERB's activities.

Activities that drive research directions and thus the animal research that is done, such as:

- review of research proposals and on-going projects by funding bodies
- research priority-setting by government, funding bodies, academic institutions and industry
- audits of research quality, carried out by internal or external assessors.

The outcomes of these activities clearly have impacts on whether and how animals are used. However, their focus is on scientific quality and priorities, and/or commercial applications; and they vary as to whether, and in what detail, they consider animal use and associated welfare and ethical issues.

The work of a national Inspectorate or authorising body, which might include:

- visits to inspect animal facilities and check compliance with the relevant legislation
- meetings with animal users and/or animal care staff to discuss their work and provide advice
- in some countries, formal review and authorisation of project applications once they have been considered by the institutional ERB. For example, in the UK the Home Office inspectorate advises the Home Secretary [government minister] whether or not to grant project licences, after applications have been considered by a local Animal Welfare and Ethical Review Body.

Processes that review the results of animal research, including:

- editorial peer review prior to publication in journals or other media
- other reviews, for example, by scientific peers or senior management within the institution, externally at conferences and/or by the bodies that fund the work.

These processes can affect animal use in a number of ways, e.g. an editor may require replication of a study before publication, or certain experimental methods or approaches may be required to meet reviewers' expectations.

CHAPTER 3

The Three Rs

The Three Rs (3Rs) strategies of *replacement*, *reduction* and *refinement* of the use of laboratory animals are key guiding principles for everyone involved in animal research and testing, and they permeate all aspects of the work of ERBs. This chapter explains each 'R', with examples; and examines how ERBs can help to support and promote their application.

The 3Rs principles of humane experimental technique were first set out by Russell and Burch in 1959 and are now widely accepted in the international scientific community and translated into associated laws and guidelines. The 3Rs have to be *actively* addressed, and the work of the ERB can be pivotal in creating a 'culture of care' that provides a driver and fosters progress in this respect.

Applying the 3Rs thoughtfully and consistently is not only an ethical imperative to reduce or avoid animal suffering, but is also vital in ensuring the quality of science (see box below). As Russell and Burch (1959) point out: treating animals in the most humane way possible *"is actually a prerequisite for successful animal experiments*".

The Three Rs (3Rs)

Replacement: methods or strategies that *replace or avoid* the use of animals in research and testing.

Reduction: reducing the numbers of animals used to the *minimum necessary* to achieve the scientific objectives, for example by improving experimental design and statistical analyses.

Refinement: refining scientific procedures and other factors affecting animals (for example, transport, housing, restraint) to *reduce suffering and improve the animals' welfare* at every stage of their lives.

Good animal welfare is essential for good science

Good animal welfare is vital not only because of its positive effects on the animals, but because it is essential to good science. This emphasises the importance of *all* the functions of the ERB.

When animals are stressed, they may appear outwardly normal but their physiology may be affected in a number of ways (e.g. changes in heart rate and the levels of 'stress' hormones in the blood). This can influence the variability, reliability and reproducibility of scientific data.

Reducing animal suffering and improving welfare increases the reliability and reproducibility of data, which helps to reduce the likelihood that experiments will have to be repeated, and can reduce the variability of results, allowing smaller group sizes to be used.

What lay members should expect

Different ERBs may approach the 3Rs in different ways, but they key tasks are to:

- review how well the 3Rs are applied in project applications
- encourage and promote 3Rs initiatives and activities throughout the institution, encompassing all aspects of laboratory animal care and use
- collect and disseminate 3Rs information within institutions and more widely.

At an institutional level, this may be done by the ERB itself or there may be one or more nominated individuals and groups (active champions) where scientists, animal care and other staff with relevant expertise take responsibility for leading on the 3Rs, working together to advance their implementation and provide information and advice to others, keeping staff up to date with developments in good practice (see also RSPCA/LASA, 2010).

As a lay person, you are not expected to be expert in the practical possibilities for applying the 3Rs, as other members of the ERB should provide this expertise. However, you should feel free to ask questions to help understand why and how it is proposed to use animals. This should include consideration of any and all possibilities for avoiding the animal studies, and reducing the numbers of animals used and the harms caused. The following explanations of approaches to the 3Rs are intended to provide background information to help with this process.

Replacement

Ideally, all uses of laboratory animals should be replaced with non-animal alternative methods that would achieve the scientific objectives. However, animal research and testing is currently considered unavoidable in many areas of science. Nevertheless, with innovative and challenging thinking the replacement of specific procedures, tests or animal models on a case by case basis should be possible, especially as science and technology continue to develop and alternative approaches become better resourced and more widely accepted.

The goal of replacement is reinforced by legislation and/or international and institutional guidelines, which require researchers to make every effort to replace the use of animals. For example:

- European Directive 2010/63/EU (Recital point 10) explicitly requires replacement wherever possible, as "*an important step towards achieving the final goal of full replacement of animals for scientific and educational purposes as soon as it is scientifically possible to do so"* (European Parliament and Council of the European Union 2010)
- under UK law, project licence holders (responsible for the direction of scientific projects involving animals) must not use any procedures for which "*there is a scientifically satisfactory alternative method or testing strategy not entailing the use of a protected animal*[1]*"* (Home Office 2014).

There can be scientific advantages and cost and time savings in developing and using alternatives. For example, some studies of human cells and tissues enable more precise, detailed and direct insight into the mechanisms underlying human disease and other disorders; can generate data more quickly; and are usually cheaper than animal studies when the costs of housing and care and other related factors are taken into account.

Replacement methods can be either complete or incomplete. Complete replacement does not involve any use of living animals, nor any material derived from animals. Incomplete replacement may involve the use of animal material such as cells or tissues, or invertebrate animals not covered by legislation.

Examples of complete replacements

- **Computer (*in silico*) and mathematical simulations** that use existing biological information (e.g. results of biochemical, cellular, physiological and behavioural studies) in 'virtual' models, to predict effects in humans and other animals.
- **Mechanical and chemical devices**, which may also include human cells, to model human organs and systems. For example:
  - "**Organ-on-a-chip**" which simulates a human organ in miniature. The 'lung-on-a-chip' is a micro-device, about the size of a USB memory stick, containing human cells, which accurately replicates conditions inside normal and diseased human lungs, including the passage of air (Huh *et al.* 2012; Ingber 2013).
  - **"TIM models"** which are complex, computer-controlled mechanical and chemical simulations of the digestive system. TIM-1 mimics the stomach and small intestine, and TIM-2 the colon (TNO, Netherlands 2013; Dickinson *et al.* 2012).

[1] An animal of species and stage of development covered by the Animals (Scientific Procedures) Act 1986 (as amended 2012).

- **Human cells and tissues**, donated or grown in culture, and **human volunteers**. Human studies yield results that are directly relevant to the clinical situation, but are not without ethical concerns relating to health and safety, informed consent and confidentiality. Moreover, sourcing human tissue can be difficult. However, recent technological advances are increasing the possibilities for using human tissue and volunteer studies to replace the use of animals. For example:
  - Advances in tissue engineering are enabling researchers to grow 3D human tissues, which mimic the structure and function of 'real-life' tissues much better than single-layer (2D) cultures. Examples include the development of 3D normal and diseased human skin tissue for studying skin diseases and irritation. (Carlson *et al.* 2008); 3D 'micro-tumours' for cancer research (Vinci *et al.* 2012; NC3Rs 2013); and the first 3D human liver tissue model generated by 'bioprinting', i.e. 3D printing using cells instead of plastic (Organovo 2013a and 2013b), which could have a wide range of applications.
  - Advances in medical imaging methods and techniques such as micro-dosing that can be used safely in human volunteers. This involves administering tiny doses of potential new medicines to study how they are distributed and broken down by the human body.

Some human tissue and cell cultures are maintained using products derived from animals, such as fetal calf serum (FCS), so they are not entirely complete replacements.

Examples of incomplete replacements

- **Invertebrates** such as nematode (round) worms and fruit flies, used extensively in areas such as genetic studies and research on the nervous system.
- **Vertebrate animals at early stages of development**, such as rat embryos before two-thirds gestation, fish before they are capable of independent feeding, or chickens' eggs before two-thirds of the way through incubation (the latter used in influenza vaccine studies).
- **Cells, tissues and organs from humanely killed vertebrate animals**, e.g. from animals killed for other projects, whose cells and tissues may also be grown in culture. Some cell lines can be 'immortalised', so that they can grow indefinitely, and hence may be considered to be a complete replacement (provided there is no use of animal-derived products such as FCS to maintain the cultures, as noted above).

Approaches to replacement

Direct replacement

One approach to replacement focuses on finding a non-animal method that can directly replace a specific animal method. An example from the safety tests required for the regulation of chemicals is a 3D model of human skin, made of human tissues grown in culture. This is used to replace guinea pigs and rabbits in tests to see whether chemicals might cause skin irritation or corrosion in humans (OECD 2013, Tests 439 and 431).

This direct 'one-for-one' approach to replacement can be a slow process; it took around 10 years to complete validation and acceptance of the human 3D skin model. The direct approach also tends to assume that data from the animal studies are the 'gold standard' against which data from alternative approaches must be validated, even though the animal methods themselves may never have been subject to similar validation.

The scientific community is increasingly questioning the predictive value of some regulatory test requirements as well as some currently used animal models of human diseases. This is driving efforts to find new alternative methods (Holmes *et al.* 2011, CAMARADES 2011, Seok *et al.* 2013).

Avoidance of animal use

Another approach to replacement is simply to avoid the use of animals, by increasing the use of non-animal methods within the overall research strategy, or by re-framing the scientific 'questions'. In this approach, the focus is not on direct replacement of currently-used animal tests, but on finding ways to use cutting-edge technologies to study the molecular and cellular mechanisms underlying the biological processes being studied and/or to use a variety of *in vitro* human cell systems to replace the animal models (Westmoreland 2013).

Indeed, some commentators believe that we may be on the cusp of a 'paradigm shift', where, with imaginative, creative and bold thinking, new and emerging technological solutions could replace whole swathes of animal use, for example in toxicity (safety) testing (National Research Council 2007; Basketter *et al.* 2012; RSPCA undated; Kimber *et al*. 2012).

A targeted approach

Targeted efforts to develop replacements can also be very productive (e.g. by drawing together a variety of relevant expertise to critically evaluate current animal models and see how the research area might be progressed using non-animal methods). For example, a workshop organised by the UK National Centre for the Three Rs (NC3Rs) brought together scientists from a range of disciplines to identify non-animal approaches for predicting whether potential new medicines might cause nausea and vomiting (Andrews 2012; Holmes *et al.* 2009). Proposals included:

- compiling a database of available information and developing criteria (an algorithm) to predict which compounds are likely to cause nausea and/or vomiting (Percie du Sert *et al.* 2012)
- using social amoebae (simple organisms, commonly known as slime moulds) to identify emetic (vomit-causing), bitter or pungent- tasting molecules (Robery *et al.* 2011)
- carrying out *in vitro* (test-tube) studies of human gut tissue to identify the effects of molecules implicated in nausea.

When reviewing a project, one important question that the ERB can ask is: "How could the research questions be addressed if the use of animals was not possible?" There may not be a simple solution for the project under consideration, but the question might stimulate debate and present a good opportunity to focus thinking on the search for alternative approaches.

Reduction

The goal of reduction is to ensure that animal studies always use the minimum number of animals needed to achieve the scientific objectives; neither too many nor too few animals, as the latter might mean that the whole study has to be repeated. Although reduction might seem a straightforward task, it can be difficult to predict how many animals a study requires, and a variety of factors relating to experimental design and statistical analysis need to be taken into account. These include:

- **Clear definition of the aims** of a study (e.g. according to SMART criteria – specific, measurable, achievable, realistic and timely)
- Identification of **the most appropriate experimental design** to achieve the scientific objectives, and consideration of **how the results will be analysed**, ***before* carrying out the study**, taking advice from a statistician or other expert colleague as necessary
- Identification and **removal of unwanted variation between individual animals and their experiences**, by controlling factors such as:
  - weight, age, sex, strain, health status, and genetic status (where relevant) of the animals

N.B. Reducing variation helps the 'signal' (i.e. the experimental findings) come through loud and clear, because the 'noise' surrounding the signal (i.e. other, unwanted sources of variation and distraction) is reduced. This, in turn, means that fewer animals need to be used to achieve a statistically valid result. However, **controlling variation does not mean withholding provisions necessary for animal welfare, such as refuges and enrichment**. Indeed, lack of such requirements can cause the animals stress, which is likely to increase variation.

- housing and husbandry, transport and handling
- environmental conditions, e.g. light levels, temperature and humidity, 'day' length, noise levels, ultrasound
- level of suffering, ensuring this is minimised
- all aspects of the experimental procedures, except the specific factors that are being investigated, which are varied in a carefully controlled way.

- Consideration of **a pilot study** using small numbers of animals to resolve any technical or animal welfare issues, prior to any larger definitive study.
- **Discussion of the study with all staff involved**, so that they understand the purpose and design of the work, their roles in carrying out the scientific techniques, monitoring the animals, and record-keeping, for example.
- Provision of full details of the experimental design and analysis, use of animals and implementation of the 3Rs, when publishing findings so that advances in the 3Rs can be shared – **following publication guidelines such as ARRIVE or ILAR Guidance** (Kilkenny *et al.* 2010; ILAR and National Research Council 2011).

Refinement

The aims of refinement are to reduce animal suffering to the absolute minimum consistent with the scientific objectives, ideally avoiding suffering altogether, and to improve animal wellbeing.

To achieve this goal it is necessary to:

- identify all potential sources of suffering and the impact of each on the animals throughout their lives (i.e. to identify the 'harms' or 'adverse effects' caused to the animals)
- provide animal housing, husbandry and care that minimises stress and promotes wellbeing
- design experiments and procedures so that harms are avoided or minimised as far as possible
- ensure that any pain, suffering or distress is promptly recognised, assessed, and alleviated.

This requires that:

- the staff who use and care for the animals are appropriately trained and experienced in recognising 'normal' animals, and identifying those experiencing adverse effects
- procedures for observing, assessing and monitoring animals are developed and agreed in advance of studies (e.g. specific 'welfare indicators' and behaviours to look for; use of 'score sheets' or other recording systems; frequency of checking, see Hawkins *et al.* 2011)
- the steps to be taken to relieve or reduce any suffering, including humane endpoints[2], are clear and agreed by all involved before procedures are started
- all staff understand who has responsibility for implementing each of these actions.

[2] The earliest point at which there will be specific intervention to end an animal's suffering, e.g. by removing the animal from the study, humanely killing the animal and/or terminating the study.

Types of harm/adverse effects

Harms for animals can be physical (e.g. pain, nausea, fever, skin irritation, convulsions) or psychological (e.g. distress, behavioural disorders, fear, anxiety, boredom) and, just as in humans, these different types of harms can be linked. For example, chronic pain can cause depression, and boredom can exacerbate the perception of pain.

It is important for the adverse effects to be understood in terms of what they actually mean for the animals (see box) and their degree and duration must also be considered (see Chapter 4, page 30 for discussion of severity of adverse effects). This will depend on the species, strain, sex, stage of development, and temperament and experience of each individual animal.

Understanding adverse effects

In a study where, for example, dogs are singly housed, the adverse effect is not 'single housing'. That is just a description of what will happen to the animals.

The real harms are lack of comfort and stimulation from social contact, together with associated boredom and frustration. Recognising the nature of harms in this way gives everyone a better understanding of the impact of the research on the animals and can help in identifying ways of reducing and avoiding the adverse effects.

Sources of harm

Physical or psychological suffering can occur at any stage from birth to death of the animals and may be caused by:

- **animal sourcing**, for instance in many standard breeding protocols, juvenile laboratory animals are separated from their mother earlier than this would naturally occur, causing distress. This happens with rodents as well as larger animals such as dogs and primates
- **transport**, even if it is just between laboratory buildings
- **housing and husbandry**, and whether or not this allows the animals to perform a wide variety of normal behaviours such as social behaviour, foraging for food and exercise
- **handling animals**, which can cause stress in many species, or **methods of restraint** that confine the animals more closely, especially for prolonged periods
- **scientific procedures and their effects**, including the **cumulative effects** of repeated interventions
- **taking tissue**, e.g. from the ear in mice, for 'genotyping' to test whether the animal has a desired genetic alteration; or for **identification** purposes
- **what happens to the animals at the end of the procedures**, for example, how they are killed or whether they are re-used or rehomed.

Refinement strategies

The list below includes some points to help in thinking through strategies that can be used to refine laboratory animal use, for each of the potential sources of suffering noted above.

Some refinement strategies

Choice and source of animals

- Use the **species or strain** of animal that will be least affected by the procedures.
- Reduce adverse effects caused in animal **breeding procedures**.
- Avoid the use of **wild-caught** animals, and where this is not possible, refine the method of **capture** of the animals.
- Critically review harms and benefits of **transport** of animals. If transport is justified, ensure all aspects are refined including container design, provision of food and water, minimal journey time.

Animal housing, husbandry and handling

- Take all steps possible to reduce stress caused by **housing and husbandry** of the animals, and provide **environmental enrichment** to enable them to express their normal behaviours.
- Better **acclimatise** the animals to the experimental set-up and general laboratory environment.
- Refine methods of **handling** of the animals, so as to cause the animals less stress.
- Avoid **restraint** of the animals, or refine the method of restraint used during procedures.
- **Train** the animals to co-operate in the experiments using **positive re-enforcement techniques**, as a means of reducing stress and avoiding restraint.

Conduct of scientific procedures

- If appropriate, carry out **pilot studies** with a small number of animals and use the information obtained to help minimise adverse effects in larger-scale work.
- Take all possible steps to **alleviate adverse effects** e.g. use pain relief (analgesia) wherever appropriate; provide special nursing or other care, such as use of especially comfortable bedding, softened food, extra warmth.
- Improve **observation and monitoring** of the animals' condition, e.g. using **score sheets** to provide objective assessments.
- Ensure that personnel carrying out procedures are fully **trained and competent**, and aware of their duties under the legislation.
- Consider how **cumulative suffering** might be reduced e.g. by increasing recovery times between interventions and reducing the number of interventions in each animal’s lifetime.
- Reduce the **duration** of procedures, provided this can be done without increasing suffering.

End of procedures

- Use earlier, less severe **humane end-points** (i.e. set 'stop' points for the studies that are triggered at lower levels of suffering).
- Use a more humane technique for **killing** the animals once procedures are finished; or **re- home** the animals, provided that there is a well thought out process for doing so and it is in the animals’ best interests.

You could ask for further information about some of these points and how they are addressed within your institution, region or nation. For example, at an institutional level, staff could provide examples of systems for recording observations (e.g. score sheets) used for a particular procedure and explain how the indicators of suffering were identified and the humane endpoints defined. See also Chapter 4 pages 31-33 for discussion of the Three Rs in project review, including points to consider for each 'R'.

Conflict between reduction and refinement

On some occasions, there may be a conflict between reduction and refinement, when animal numbers could be reduced, but only by increasing the severity of harms caused to each animal. The ERB should consider this issue very carefully. In general, reducing the suffering of individual animals is considered more important than reducing overall numbers, so refinement should be given priority.

Advancing the Three Rs in practice

In order to achieve active implementation of the 3Rs at all stages in animal research and testing at an institutional level, there needs to be:

- **senior management and strategic leadership** which actively supports the 3Rs, e.g. by providing resources and encouraging staff to work to develop, and publish, their 3Rs ideas
- a **proactive approach**, keeping the 3Rs on the ERB's agenda
- **teamwork**, in which scientists and support staff with relevant expertise (e.g. animal care staff, veterinary surgeons, statisticians) work together to advance the 3Rs
- nominated individuals and groups (**active champions)** who take responsibility for leading on the 3Rs, working to advance their implementation and providing information and advice to others
- **easy access to information**, to keep staff up to date with developments in 3Rs, good practice guidance and standard operating procedures for common techniques, and sources of advice and support for new procedures, e.g. via intranet sites and workshops
- **empowered animal care and veterinary staff** who feel 'listened to' and supported
- **openness, trust and strong, effective communication** between all relevant staff, providing opportunities for anyone to express concerns and make suggestions for improvement
- opportunities to **recognise and reward achievement** in advancing the 3Rs within institutions and more widely e.g. through 3Rs prizes or publications.

These points all demonstrate, and are part of, an overall 'culture of care' (see Chapter 6 for further information). They are matters to consider when thinking about how the 3Rs are being advanced in your ERB's institution, region or nation (see also Chapter 2); and when carrying out project review (Chapters 4 and 5), or addressing wider ERB functions (Chapter 6), and visiting animal facilities (Chapter 7).

Sources of further information

Information on all Three Rs

RSPCA Research Animals (UK) has a wide range of 3Rs resources, including documents specifically prepared for lay members: www.rspca.org.uk/researchanimals

The UK's National Centre for the 3Rs (NC3Rs) has an extensive *Information portal*: www.nc3rs.org.uk/our-resources

NORECOPA (Norway) and the US Animal Welfare Information Center have produced a database of 3Rs guidelines, databases and journals: www.3RGuide.info

The EURL ECVAM Search Guide (2013) includes lists of 3Rs databases, journals and other sources of information: http://tinyurl.com/ECVAM-guide

The European Commission Working Document on the Availability of Information on the Three Rs can be downloaded at: www.ec.europa.eu/environment/chemicals/lab_animals/pdf/Endorsed_consensus_doc.pdf

Other useful sources include:

UK Fund for Replacement of Animal Experiments (FRAME): www.frame.org.uk/

Australian and New Zealand Council for the Care of Animals In Research and Teaching (ANZCCART): www.adelaide.edu.au/ANZCCART/links/

Canadian Council on Animal Care, 3Rs Microsite: http://3rs.ccac.ca/en/

US Department of Agriculture: http://awic.nal.usda.gov/alternatives/3rs

US John Hopkins University Altweb: http://altweb.jhsph.edu/

Resources specific to replacement

The RSPCA has produced a slide set on replacement, which discusses approaches to replacement in more detail, and includes a wide range of examples: www.rspca.org.uk/allaboutanimals/laboratory/replacinganimals – click on "*The 'R' of Replacement"*

The US John Hopkins University Altweb and UK FRAME webs-sites focus on replacement: http://altweb.jhsph.edu/ and www.frame.org.uk/

Resources specific to reduction

Useful sources include books by Bate and Clark (2014) and Festing *et al.* (2002); also the report of an ECVAM (European Centre for the Validation of Alternative Methods) workshop on reduction (Festing *et al.* 1998)

FRAME runs regular *Training Schools in Experimental Design and Statistics*, to help researchers reduce their use of animals (go to www.frame.org.uk/ and search for 'training schools'); and

Michael Festing has set up a free on-line training course at: www.3rs-reduction.co.uk/

The NC3Rs has a webpage on experimental design and statistical analysis: www.nc3rs.org.uk/our-resources

'Planning for reduction' by Das *et al.* (2009) includes a useful experimental planning flowchart: www.3rs-reduction.co.uk/assets/applets/planning_for_reduction.pdf

Resources specific to refinement

RSPCA Research Animals has a wide range of resources on reducing laboratory animal suffering. Go to www.science.rspca.org.uk/sciencegroup/researchanimals/implementingthe3rs and follow the links

RSPCA Research Animals has also produced a series of *Good Practice Guidelines for Laboratory Housing and Care*, covering a wide range of species commonly used in laboratories: www.rspca.org.uk/sciencegroup/researchanimals/ethicalreview/functiontasks/housingandcare

The NC3Rs Information Portal covers many aspects of refinement: www.nc3rs.org.uk/our-resources

The *Enrichment Record* is an online portal for discussing environmental enrichment: http://enrichmentrecord.com/

The journal *Laboratory Animals* has published some useful 'overview' papers on the 3Rs, including Flecknell (1994) and Lloyd *et al.* (2008) on refinement. Available via: www.la.rsmjournals.com. Use the search facility (and reference details at the end of this Resource Book) to find both papers as free, full-text PDFs.

CHAPTER 4

Reviewing project applications

Review of applications to carry out studies on animals is a major part of the work of most ERBs. This chapter examines the ERB's role in project review and describes the principles involved in carrying out a harm-benefit analysis, together with some practical factors for consideration.

The ERB's role in project review

All ERBs, whether national, regional or institutional, will usually carry out some form of project review[1]. This is a crucial part of the ethical framework of legislation regulating animal use and involves evaluating:

- the likely harms to animals and potential benefits of a project and how these balance i.e. a harm-benefit analysis, and
- how the 3Rs will be implemented, throughout the duration of the project, from initial idea through to completion.

Project review is carried out prospectively (at the project application stage) and there may also be interim review (while a project is on-going) and retrospective review (after the project is completed).

Processes for review of project applications vary[2]. In some ERBs a single committee reviews all applications and amendments. In others (usually ERBs in large institutions), smaller 'project review groups' may carry out this work and report to a central, overarching committee. The central committee may then choose to review applications of particular concern, such as those involving novel techniques or procedures that cause severe suffering.

Some ERBs (mainly institutional) review individual studies carried out within a project as they arise, particularly if the project itself is very broadly framed. There may also be 'fast track' procedures for review of certain categories of work, such as minor amendments to existing project authorisations. Some ERBs always meet face to face, whereas others conduct much of their business via e-mail. The latter can be expedient, but the former enables better dialogue. Applicants for project authorisation may attend ERB meetings to present their proposed work, and this is particularly helpful in facilitating discussion of applications and resolving any concerns swiftly.

Whatever form it takes, it is important for the ERB to be clear about the outcomes it expects from the review process, and about how these outcomes are achieved and evaluated in practice.

Institutional factors that impact on project review

It is difficult to appreciate potential benefits and likely harms without knowledge of institutional factors that impact on animal care and use and quality of science. This includes the facilities and the expertise available to carry out the work, and especially how the use of animals will be managed (e.g. the institutional processes for monitoring animals and implementing humane end-points). Understanding such factors is important, as both harms and benefits can be influenced as much by *how* a procedure is carried out, as by the nature of the procedure itself.

Developing a comprehensive knowledge of these issues will be much easier for participants in ERBs at an institutional level rather than in national or regional ERBs. Moreover, institutional review can bring a range of other benefits to project review, such as those listed overleaf.

[1] Or procedure, or protocol (see definitions, page 5) or study review.
[2] See Appendix 1 for how the UK AWERB review relates to the formal authorisation process by the Home Office.

Benefits of project review by institutional ERBs

- Reviews are based on first-hand knowledge of local factors likely to impact on harms and benefits.
- Project applications are reviewed in light of the institution's own goals and ethical values, involving a wide range of local perspectives and expertise from within the institution, including animal care staff, veterinarians, researchers and lay people.
- Facilitates communication and provides a forum for discussion between scientists, animal care staff and others within the institution e.g. regarding conduct of studies, refinements to techniques or special husbandry needs.
- Provides a forum for consideration of any wider ethical questions or concerns arising in project reviews.
- Ensures that advice given and lessons learned in project review (e.g. examples of 3Rs initiatives) are disseminated more widely within the institution.
- More generally, helps to foster and maintain the culture of care within the institution.

What lay members should expect

The process of review should enable everyone to understand the potential benefits of each project and the harms likely to be caused to the animals throughout their lifetime. It should be clear why the researchers believe that the goals of the project justify using animals, why they believe that the project will be a success, what efforts they have made to avoid or replace procedures involving animals, how the numbers of animals have been minimised, and how animal suffering will be reduced and welfare improved.

There should be plenty of opportunity to ask questions and discuss issues with other ERB members so as to develop your own views, provide feedback to the researchers, and, depending on the regulatory context, work towards a collective ERB view on whether the work should be authorised as it is, or whether it should be amended or rejected.

At the end of the process you need to feel comfortable that:

- **the review has covered all relevant factors and has addressed any concerns**
- **the ERB's advice and decisions have been informed by participants from a range of perspectives and expertise, and that**
- **the ERB's advice and decisions will be acted upon.**

Key steps in project review

Participants in the ERB will develop their own particular approaches to reviewing project applications, but everyone will need to take the following steps:

1. Gather information in order to understand what the project entails
2. Ask questions about anything that is not clear and discuss issues with other ERB participants and relevant staff
3. Provide advice to applicants and draw conclusions, both personally and with other ERB members

1 Gathering information

Application for authorisation of a project (a project licence application in the UK)

You should expect to see the formal application forms required when applying for authorisation to carry out a project involving animals, together with any associated documentation such as local good practice guidelines for specific techniques or score sheets for assessing animals. These papers should be circulated well in advance of a meeting. They should include the details needed to understand and assess whether there is justification for the work, and the care taken to minimise its impacts on the animals. However, applications are usually complex documents, written in scientific and technical language which can be difficult for a lay member, or anyone outside the specific scientific field, to access. To help with this, ERBs may also require applicants to provide additional material, such as a non-technical summary, a presentation on the project, and/or a summary of previous work. There may also be guidance for ERB participants highlighting particular issues that need considering in individual applications.

Non-technical (lay) summaries

A well written summary that explains the salient features of the project in non-technical terms, highlighting the main issues of harm and benefit, can be very useful for all ERB participants, not just lay members. In some countries, including the EU, regulations require non-technical summaries to be provided as part of the project authorisation process and specify the information they should contain (European Commission, 2013b). These may be published as a contribution to greater openness. In the UK for example, the summaries appear on the Home Office website.

If good quality lay summaries (see box overleaf) are not prepared as part of project review it would be worth asking for these to be provided. If summaries are provided, your views on their clarity and helpfulness can be useful as feedback to researchers.

Other sources of information

Discussion with researchers can provide a clearer understanding of a project, so it is helpful for applicants to attend ERB meetings at which their work is reviewed. Other members of the ERB can also answer queries and clarify points of concern. For example, the animal care staff and veterinary surgeons should be able to explain the effects on the animals and possible ways of reducing harms, as well as matters to do with animal care and husbandry.

Information about projects need not be confined to paperwork and discussions in committee. It can be difficult to envisage from a written description what effects the protocols will actually have on the animals, and so it is valuable to observe animals undergoing or affected by procedures, especially if the ERB feels that there is a particular cause for concern.

Sometimes, experimental or other constraints may mean that this is not possible (e.g. additional people present during procedures may cause additional stress to the animals that cannot be justified). However, more generally, visits to animal facilities can help to ensure that project review is rooted in a wider understanding of animal care and use in the institution (see Chapter 7).

Becky Murray/RSPCA Photolibrary

Key points to cover in lay summaries

Using non-technical language and avoiding jargon, the summary should:

- summarise the **objectives and potential benefits** of the project, focusing on **why the particular project is important**, not merely the general field of research
- outline the **sequence of the work**, indicating how all the different approaches and techniques (including non-animal studies) contribute towards answering the scientific questions
- state the reasons **why animals of the particular species, strain and stage of development** are needed
- explain **why alternative methods cannot be used**
- state the **number of animals** likely to be used and how this was determined
- indicate how the **experimental design** was developed, and whether statistical advice has been taken
- provide a candid synopsis of the **main adverse effects** likely to be caused to the animals, covering their experience from birth to death, including any adverse effects due to the methods of housing, husbandry and supply of animals, as well as the effects of the scientific procedures themselves:
  - state the likely **level of suffering** (mild, moderate, severe) and its **duration**
  - explain **what will happen to the animals at the end of the procedures** (e.g. humane killing, re-use[3], or rehoming)
- outline efforts made to **minimise the adverse effects**, for example, improvements in technique or husbandry, humane end-points, how animals will be monitored and any special arrangements for caring for them
- briefly explain how it is judged that the **benefits outweigh the harms** and why the research is justified
- state the **source of funding** and **any scientific collaborations.**

2 Questions and discussions

Many factors can influence the harm-benefit analysis, and it is important to bear this in mind when approaching project review. 'Reminder lists' of points to consider can be very useful in helping to ensure that reviews are as pertinent and comprehensive as possible and some suggestions are presented in the boxes in this chapter.

Assessing benefits

Identifying questions about the benefits of projects – and interpreting the answers – can be difficult because the science involved is often very detailed and the wider context into which the specific project fits may be hard to see. Furthermore, scientific outcomes are by their nature uncertain and perceived benefits may only be realised a long way in the future. In addition, and particularly in the case of testing for regulatory purposes, the benefit may be commercial, i.e. to enable a company to market a product.

A common complicating factor is that the scientific work may already have been peer reviewed and supported by reputable funding bodies which may make people reluctant to question its benefit. However, the focus of funding body review is on quality of science, and, although the use of animals may be considered, animal welfare and associated ethical issues are not the main priority. The ERB by contrast considers the potential benefits *in relation to the particular harms likely to be caused to the animals* and with *knowledge and understanding of local factors that need to be taken into account*. It therefore delivers a different and valuable perspective on questions of benefit.

[3] In most regulatory systems, re-use of animals is only allowed under certain carefully controlled circumstances and must be authorised in advance.

Even where the benefits of the work are agreed, the likelihood that these will be achieved needs to be considered. There are a range of factors that can influence the success of the project, and it is particularly important that such issues are addressed at an institutional level so that appropriate safeguards and practical responses can be put in place locally. As a result, the ERB might advise on requirements for staff training or particular facilities, equipment or expertise that the researchers and their institution need to address; or, if the project involves a novel method or is otherwise of special concern (e.g. involving severe procedures), the ERB could request a pilot study and regular feedback, especially in the early stages of the work.

The boxes below list some points to consider when thinking about both the potential benefits of a project and the likelihood that the benefits will be achieved (Smith and Boyd 1991; APC 2003; Smith *et al.* [FELASA] 2007).

Benefits: key questions for all ERB members

- Have the project application and ERB discussions made clear the objectives of the project and the benefits, and how they will be achieved in practice?
- Are you, and the ERB as a whole, satisfied that everything possible has and will be done to maximise the likelihood that the project will have significant benefits and that these will be taken forward in a positive way?

Benefits: points to consider

Are the following aspects clearly explained and addressed?

Potential benefits

- Features that makes the work original, relevant, timely and realistic.
- If the project is part of ongoing work, the progress made previously.
- If the project involves repetition of previous studies, why repetition is needed.
- The project's links to, and implications for, other areas of research.
- How the results will be taken forward and used.
- Arrangements for publishing or otherwise disseminating the findings.

Factors influencing the likelihood of success

- How the selected scientific approach and animal model(s) will help in achieving the objectives.
- Steps taken to ensure validity of experimental design, e.g. use of optimum numbers of animals, neither too many nor too few; and appropriate use of control and experimental groups and statistical analyses.
- Resources available to support the project, such as:
  - whether appropriate facilities, for example, for animal housing and husbandry, laboratory space and equipment, are available to meet the requirements of the project, and whether any special arrangements are needed
  - the project team's experience of the methods and whether there are any needs for training; if so, how the necessary competencies will be ensured
  - whether other resources for the project, such as staff time and funding, are sufficient to meet its aims.
- Where the proposed work sits in relation to other research in the field.
- Any opportunities for consultation/collaboration with others working in the field, to learn from their experiences, optimise the experimental approach and avoid unnecessary duplication.

Assessing harms to animals

The aim of the ERB should be to ensure that everything possible is done to identify, minimise and preferably avoid all potential harms at all stages of a project.

There are many sources of harms and types of suffering, both physical and psychological, which need to be identified, recognised and addressed (see Chapter 3 page 21). Adverse effects are sometimes obvious, particularly if significant suffering is involved, or if the species of animal used displays signs of suffering that are easy for humans to observe and interpret. However, indicators of suffering can be relatively subtle in many commonly used species, such as mice, rats and rabbits. Factors such as staff training and expertise in monitoring the animals, recognising and reducing adverse effects, and implementing humane end-points are therefore very important, alongside the lines of responsibility for these actions. The ERB needs to ensure that all of these issues are addressed.

Describing harms for project review

In official application forms or other material brought to the ERB, project applicants should be clear about what the animals are likely to experience and the steps taken to minimise any suffering. They should:

- identify all possible sources of adverse effects from start to finish of each procedure, and show awareness of other sources of harms (e.g. from sourcing, transport, handling, housing and husbandry, and method of killing animals) and the impact these are likely to have on the actual experience of the animals
- explain how the 3Rs have been applied, in order to avoid or minimise animal use and suffering from all potential sources, covering strategies for recognising, assessing and reducing suffering
- describe the nature, degree and duration of all potential adverse effects, *in terms of what they actually mean for the animals* – see Chapter 3 page 21 for further discussion
- indicate the proportion of animals likely to experience mild, moderate or severe effects, or non-recovery procedures, and define a severity limit for each procedure (see box below).

Classifying the severity of harms to animals and severity limits

Severity classification

Most countries with well-developed laboratory animal regulations have a system for classifying the severity of harms to animals (e.g. Smith *et al.* [FELASA] 2007; Fenwick *et al.* 2011). Under EU and UK law, the adverse effects caused by scientific procedures must be prospectively classified as ‘mild’, ‘moderate’ or ‘severe’ – or ‘non-recovery’ for procedures carried out under general anaesthesia from which the animal is not allowed to recover. Annex VIII of the EU Directive 63/2010 lists examples procedures that generally fall within the different categories and a European Commission Expert Working group has produced guidance and a series of illustrative examples which are very helpful (European Commission 2012, 2013a).

Severity limits

Severity classifications describe the upper limit on the suffering that an animal used in a particular protocol is allowed to experience, i.e. they set a ‘severity limit’. This prospective severity classification is based on the highest severity anticipated for any animal on the study, but the aim should be for the *actual* severity to be less than this. Severity limits should help to manage and minimise adverse effects. For example, if a procedure is allocated a mild rather than a moderate limit, it must be ensured that the adverse effects do not progress further than the permitted mild limit (APC 2003, page 45; Boyd Group/RSPCA 2004, page 3).

Retrospective reporting of actual severity

Some regulatory systems, notably EU Directive 2010, also require *retrospective reporting of the actual* severity of adverse effects experienced by animals used in scientific procedures, for publication in annual statistical reports – using the same categories (mild, moderate, severe, or non-recovery). This is intended to enhance openness on the use of laboratory animals and how much suffering is involved. Another important benefit is that review of actual (retrospective) severity data by ERBs (at national, regional, and especially institutional levels) can help to highlight priority areas for refinement of animal procedures. (See also Chapter 5 on retrospective review.)

Asking questions about harms

As a lay person, you are not expected to be expert in the potential harms caused to animals, nor how to avoid or alleviate these. Other members of the ERB should provide this expertise, but you should feel free to ask questions that enable you to understand the impacts on animals, so that you can consider the balance of benefit *versus* harm in the project as a whole, and in individual procedures where relevant.

Harms to animals: key questions for all ERB members

- Is it clear what will happen to the animals throughout their lifetimes?
- Are all the potential adverse effects (both physical and psychological) identified and described in terms of what they will actually mean for the animals?
- Do you get a clear sense of the severity of adverse effects likely to be caused to animals in individual procedures within the project?
- Are you satisfied that everything possible will be done to minimise and avoid harms to animals in the project?
- Are you confident that all of the 3Rs have been adequately addressed?

Reducing harms

The boxes below and overleaf include points to help consider whether the 3Rs have been applied and the potential harms to animals have been reduced as far as possible (see also Chapter 3 for definitions and additional examples of the 3Rs).

Implementing the Three Rs in practice: points to consider

1. Replacement

Are the following aspects clearly explained and addressed?

- **The need to use animals** to achieve the objectives and why non-animal approaches are considered unsuitable.
- **Efforts made to search for alternatives** to the use of animals and consider **ways of avoiding** animal use.
- **Use of non-animal methods** in any part of the project; and how animal and non-animal methods relate to and build on one another.

2. Reduction

Are the following aspects clearly explained and addressed?

- **Number of animals** likely to be used in the project as a whole and in individual studies/protocols within it.
- **How the numbers have been optimised**, for example by:
  - taking statistical advice to optimise experimental design and statistical analyses
  - using the results of other similar studies to inform the approach
  - carrying out pilot studies to help improve the design of larger definitive studies
  - N.B. in some cases the number of animals used will be stipulated in a regulatory protocol
- If reducing animal numbers has increased the level of harm caused to individuals, whether and how this has been justified.
- When animals are humanely killed during or after studies, whether their tissues will be shared with other researchers, to avoid any additional use of animals to supply tissue for *in vitro* studies.

The box below and continued overleaf includes examples of steps that a good research team would take to implement refinement. There should be evidence in the project application and/or discussions that such aspects have been considered, although not all will be relevant to every project.

3. Refinement

Are the following aspects clearly explained and addressed?

Choice and source of animals

- Reasons for **choice of species and strain** of animals: e.g. why the animals are considered most relevant for the science, but least affected by the procedures.
- Any adverse effects due to **source and transport** of animals to the laboratory and/or quarantine requirements, and how these will be reduced and alleviated.
- If the animals are **genetically altered**, whether the alteration is likely to cause adverse effects and, if so, how these will be reduced and alleviated.

Animal housing and care

- How animal housing and care has been refined, so as to minimise adverse effects and provide a stimulating environment that enables the animals to express their normal behaviours (see also chapter 7).
- Any special housing and care requirements required by the procedures (e.g. confinement of animals in 'metabolism cages' that allow collection of the animals' faecal and urine output), their likely adverse effects, and how these will be reduced and/or alleviated.
- If social animals are to be housed singly at any time: why this is considered unavoidable for scientific or welfare reasons; and how adverse effects will be reduced.
- N.B. if single housing is unavoidable, action should be taken to mitigate the effects e.g. by additional enrichment or, if appropriate for the species and individuals concerned, the animals should be housed within sight, sound and smell of their conspecifics.

3. Refinement (continued)

Pain, distress, anxiety or other harms likely to be caused by the procedures

- **Clear description of the likely adverse effects** of the procedures, in terms of what they will actually mean for the animals, including their anticipated severity levels and proportion of animals likely to be affected.
- **How the procedures have been refined** to reduce their adverse effects on the animals.
- The **steps that will be taken to alleviate the remaining adverse effects** as far as possible.
- **How animals will be acclimatised** to the laboratory environment and to the experimental set-up, where relevant.
- **If animals will be restrained** during any of the procedures, steps taken to refine the method as far as possible; whether the animals will be **trained to co-operate** as a means of reducing stress and whether the training method used is positive rather than negative re-enforcement.

Monitoring and implementation of humane end-points

- **Plans for monitoring the animals' condition**, including:
  - how frequently the animals will be checked, including provision for out of hours cover
  - the particular signs ('welfare indicators') that will be looked for
  - how the observations will be recorded and their severity assessed, e.g. using score sheets
  - which particular observations will be considered to give cause for concern, and what action will be taken to alleviate and reduce animal suffering.
- **Clear definition of humane end-points for all procedures**, including:
  - how it will be ensured that agreed end-points are not exceeded, and
  - plans for reviewing the end-points for appropriateness and further refinement.

What happens to the animals at the end of the procedures

- If animals will be **humanely killed**:
  - whether a standard method is used, e.g. as set out in Annex IV of the EU Directive
  - if not, what scientific justification there is for using a different method; and whether the method has been refined as far as possible.
- If any animals are to be **re-used**, in what circumstances this will be considered acceptable and how adverse effects will be minimised[4].
- If animals are to be **re-homed**, how the institution will ensure that this is in the best interests of the individual animals.

Facilities, expertise and competence to carry out the procedures

- The project team's **experience and competence** with the particular species and techniques, and identification of any **needs for training, supervision and/or advice**
- Whether the **facilities** required to support the project (e.g. animal housing, laboratory space, equipment, funding) are readily available and sufficient

[4] In most regulatory systems, re-use of animals is only allowed under certain carefully controlled circumstances and must be authorised in advance.

3 Drawing conclusions

Having examined likely harms and benefits and discussed ways of maximising the benefits and minimising the harms, members of an ERB will need to decide whether or not they are comfortable with the balance of benefit over harm in the project application. They then need to provide advice to the applicants and, if required by regulations, authorise the work. These judgements can be difficult. As a consequence, whilst ERBs have been shown to be very good at addressing the 3Rs in project applications, they may avoid explicit consideration of the ethical 'weighing' of harms and benefits (Ideland, 2009; Hansen, 2013).

One of the problems is that there is debate about what exactly the 'weighing' of harms and benefits should mean in practice. A particular difficulty is that the factors to be weighed are not directly comparable. *Animal suffering* must be weighed against *benefit to humans* or, in some cases, other animals. It is therefore debatable whether it is possible, or indeed desirable, ever to say that the predicted benefits 'exceed' the harms to animals.

However, this 'weighing' is not in any sense a quantitative procedure; rather, it is a matter of *moral judgement* which, by its nature, depends on the particular circumstances involved. In this sense, it does not seem a unique or even unusual process of judgement:

"*In everyday life... personal, professional and political judgements on moral issues normally require the weighing of factors and considerations which cannot be quantified with mathematical precision. A judge, for example, weighing a plea for mitigation of sentence in the 'scales of justice' carries out a procedure of this kind*" Smith and Boyd (1991, p.140).

In any discussion of the use of animals in research there is likely to be a range of views expressed. Some people argue that no amount of benefit can permit the infliction of any form of suffering on animals, and thus that the benefits of using animals in research and testing are never sufficient to sanction the harms. Other people feel that it would be wrong to forgo potential benefits of animal use and accept that at least some uses of animals in research and testing should be allowed, provided that the benefits are judged sufficiently worthwhile and no alternatives are available that could reduce or avoid harm to animals. Most members of ERBs are likely to be in the latter group. For them, the justification, or lack of justification, for using animals varies with context, and so they must make their judgements case by case.

In practice, it can be relatively easy to reach consensus on what definitely should not be done. When the benefits are considered to be very low or unlikely to be achieved (e.g. because the experimental design is poor or other non-animal approaches could be taken), animal use should not be sanctioned, even when the predicted harms are mild. Similarly, at the other end of the spectrum, there are harms that are so high that no benefit can be considered to justify their use. However, both personal and consensus judgements about the balance of benefit over harm are more challenging within the grey area between these extremes.

In such situations, "*confidence in the soundness of judgements largely depends on the approach of those who make them: upon whether they have taken all the known morally relevant factors... and interests*" (Smith and Boyd, 1991 p.141) and can be trusted to come to balanced, informed decisions that take into account all reasonable perspectives on the issues. Involving a diversity of people in the decision-making process is an important step in achieving and enhancing such trust, especially where this includes lay members who are widely regarded as having no vested interest in the outcomes of the review.

In the end, you will need to draw conclusions and/or come to decisions, both personally and collectively with other participants in the review, but if these result from the kind of comprehensive thinking described above, they will not rest on 'gut feelings' alone. Rather, the judgements and associated advice will be supported by arguments that are well-informed and sensitive to the different ethical nuances and perspectives brought forward.

There may be times when some participants disagree with the majority view. Expressing and standing by an informed perspective that differs from the majority can be difficult, but is important, as always compromising in such circumstances diminishes the value of involving a diversity of perspectives. Indeed, it may also be that other participants feel the same, but do not feel able to voice their disagreement. In such circumstances, it is important to ensure that differing views, and the reasons for them, are recognised by the ERB as a whole and are recorded and communicated to all relevant people.

Challenging the assumptions underlying harm-benefit discussions

The language used in answers to questions about harms and benefits may sometimes need further probing, to find out exactly what is being said or claimed. The box below lists some examples of more general questions that might arise in harm-benefit discussions, which the ERB might want to consider from time to time.

Some general questions underlying harm-benefit discussions

- If a particular use of animals is said to be 'necessary', what exactly does that mean? How has necessity been determined?
- Is it considered 'better' to use some species (say fish or mice) than others (say primates or dogs) in research? If so, what are the grounds for giving different species different status?
- What level of harm would be permissible for a particular purpose?
- What do people actually mean by 'best possible' animal welfare or 'best practice'?
- What exactly is meant when it is said that a particular technique is 'better' or 'worse' than another for the animals concerned?
- Is all scientific knowledge 'worthwhile'? Who actually benefits and how?
- Can an economic or career benefit ever form part of a justification for using laboratory animals?

Lay members can be particularly alert to these broader questions, and encourage the ERB to consider them. Appendix 3 explores further thoughts on 'doing ethics' in practice and the benefits this can bring.

CHAPTER 5

Retrospective review of projects

As well as examining new project applications, ERBs may undertake reviews of completed projects and/or on-going projects at particular time-points, and the term 'retrospective review' is often used to cover both options. This chapter examines the aims and benefits of retrospective review and suggests how lay participants can help to achieve them.

Aims and benefits of retrospective review of projects

Retrospective review of projects is generally regarded as good practice and is beginning to appear in legislation and be recommended in guidance documents. For example, Directive 2010/63/EU and the UK Animals (Scientific Procedures) Act 1986 both require retrospective review of all projects involving primates and those involving procedures classified as severe (although the term retrospective assessment is used instead). According to the EU Directive a decision as to "*whether and when the project should be assessed retrospectively*" must be made as part of initial project evaluation prior to authorisation. In addition, an EU consensus document regards retrospective assessment of projects involving animals as "*an extremely powerful tool to facilitate critical review of the use of animals in scientific procedures, to identify future 3Rs improvements, and… to inform future studies*" (European Commission, 2013c).

The key objectives of retrospective review are to: evaluate the actual harms and benefits of projects; to identify, build on and encourage implementation of the 3Rs; and to facilitate project management (Jennings *et al*. 2007). The box opposite lists some of the specific benefits that can result from the process (see also RSPCA/LASA 2010).

Your ERB's approach

Some regulatory systems specify the timing of retrospective review. For example, in Canada each protocol [project] must be reviewed annually by the institutional ERB (i.e. the Animal Care Committee); whereas other systems allow more flexibility in deciding the most appropriate time for review, depending on the nature and pattern of the work involved. Even within an institutional ERB there may be a different approach for different projects. For example, projects involving novel or severe procedures may be reviewed more frequently than those using small numbers of animals in mild procedures.

Some regulatory systems also set out the factors that must be addressed in retrospective review. For example, in the European Union, the following at least must be evaluated (EU Directive 2010/63/EU):

(a) *whether the objectives of the project were achieved;*

(b) *the harm inflicted on the animals, including the numbers and species of animals used, and the severity of the procedures; and*

(c) *any elements that may contribute to the further implementation of the requirement for replacement, reduction and refinement*

As well as variation in timing and the factors that are addressed, there are also differences in the way that individual ERBs carry out retrospective reviews, how the outcomes are recorded, and to whom these are communicated. In particular, the amount of written documentation that ERBs require from researchers can vary widely. Some ask for written feedback on specially designed review forms of varying complexity, while others rely more on oral presentations from one or more members of a research team. RSPCA/LASA (2010) state that: "*The most productive retrospective reviews focus on face to face discussion and outputs and how to take things forward, not the filling in of forms! In most cases they are best achieved by inviting [researchers] to present the key issues to the ERB in person*."

Whatever approach is used, the focus should be on delivering useful outputs from retrospective reviews, making it a positive and constructive experience that benefits research teams, the institution and, of course, animals.

Benefits of retrospective review

Examining harms and benefits and informing future work, by:

- providing feedback to the ERB on progress with the project, its achievements, the impact of any amendments, and any problems or difficulties
- comparing the actual harms and benefits of the work with those predicted at the application stage, in order to inform future judgements.

Enhancing implementation of the 3Rs, by:

- identifying any 3Rs advances made during the project, and helping to ensure that they are implemented in the institution wherever possible and publicised more widely
- bringing together a range of expertise to provide advice and assistance to research teams, to help in:
  - addressing any technical or scientific difficulties not yet resolved
  - raising awareness of any steps that can be taken to implement the 3Rs more fully.

Optimising project management, by:

- identifying and addressing any concerns about project or animal facility management, including resources, staffing, training requirements, communication and dissemination of information
- planning ahead, e.g. for authorisation of future work and/or amendments to on-going work.

Assisting with collection and reporting of data on the actual severity of adverse effects, and:

- using these data to help identify priority areas for further application of the 3Rs (see Chapter 4, page 30 for discussion of severity classification and reporting).

What lay members should expect

Everyone involved needs to have a clear idea of what the retrospective review process is intended to achieve, the issues that are to be considered, the questions that need to be addressed and any actions that should be taken forward (see Jennings *et al.* 2007 for further discussion).

The process should be designed to enable lay and other ERB participants to gain a clear sense of the scientific outcomes of the project and its effects on the animals to date, and you should feel able to ask any question you think is important, and which might help in achieving the benefits listed above.

The box overleaf lists some points for consideration during retrospective review – but note that not every topic will be relevant for every project.

At the end of the process, you should feel confident that:

- **any emerging ethical issues have been recognised and will be addressed**
- **all possibilities for further implementation of the 3Rs will be taken forward**
- **the process has helped to optimise project management, and address any difficulties or concerns**
- **developments in the 3Rs and/or any other lessons learned will be shared with others in the institution and/or more widely, so that they can inform future work**
- **the benefits of the retrospective review match the efforts put into it.**

Points to consider during retrospective review

Assessing actual versus predicted harms and benefits and informing future work

- Have the researchers explained progress with the project so far, and is it as anticipated?
- Are the *actual* adverse effects on the animals, and the numbers used, in line with predictions? Has the ERB explored the reasons for any differences and proposed actions if adverse effects are greater than expected?
- Do the research team and the ERB feel that the particular animal models and study designs are still the most appropriate for achieving the aims of the project?
- Has the ERB discussed with the research team whether there are any recent developments in science or technology that could influence the future direction or conduct of the work, especially any developments that might help to avoid or replace the use of animals in some or all of the project, or cause less suffering?
- Have any wider ethical issues arisen during the project (e.g. concerns about use of particular species or in work carried out in association with research teams abroad), and what steps does the institution plan to take to respond to these issues in future?

Enhancing implementation of the 3Rs

- Has the review process revealed any additional possibilities for implementing the 3Rs in the project (e.g. refinement of housing and husbandry or experimental procedures, or experimental design)? If so, have appropriate actions been agreed within the research team?
- Is everyone satisfied that welfare monitoring systems and processes are working well and that humane end-points are as refined as possible?
- Has the supply and use of animals been balanced so that none are wasted?
- Have any special housing and care needs arisen? If so, how have these been addressed?
- Are there examples of good practice or implementation of the 3Rs that it would be beneficial to communicate to other research teams either internally or externally?

Optimising project management

- Are the researchers, animal care staff and others satisfied that facilities for procedures and animal housing and care are still appropriate for the work? Are there any difficulties that need addressing?
- Does there seem to be good communication between the animal care staff, veterinarians and the researchers working on the project particularly regarding any concerns between animal care and scientific staff? Has the ERB helped to address these?
- Has the review process identified any additional needs for staff training or supervision?
- Has the ERB helped to identify and plan for any future amendments to the project authorisation?
- Have there been any particular developments or lessons learnt that should be communicated to others in the institution?

CHAPTER 6

Beyond project review: wider functions for ERBs

ERBs, and particularly institutional ERBs, have a much wider range of functions than just prospective and retrospective project review. The wider, oversight functions listed in Chapter 2 and below, are important and can all have a significant impact on standards of care and use of animals, implementation of the 3Rs, delivery of good quality science, and compliance with legislation. This chapter discusses these functions and explores how ERBs, and specifically lay members, can help to address them in practice.

Tasks for ERBs

A study of ethical review across Europe emphasises that ERBs "*should not be 'merely committees for review of particular projects' but should aim to permeate and influence the ethos of every institution in which animals are used – creating an appropriate 'culture of care', and providing advice and resources to ensure proper consideration of ethical aspects and application of the 3Rs in all scientific work involving animals*" (Smith *et al.* [FELASA] 2007).

In other words, ethical review should consider not only the harms and benefits of proposals to use animals, but also how more humane and beneficial science will be developed and maintained on a day-to-day basis. This is influenced by institutional factors such as: access to information about the 3Rs; standards of animal care and accommodation; management of animal use; and training, expertise and competence of staff. External factors that will also have an effect include developments in science, better understanding of animals and changes in public opinion and attitudes.

The box below lists tasks for ERBs in this context (see Appendix 1 for specific details of the UK system).

Tasks for ERBs

1. Providing a forum for discussion on all matters related to animal welfare, care and use.
2. Promoting the development and uptake of the 3Rs (replacement, reduction and refinement of animal use) in all projects/protocols throughout their duration; advising staff how to apply them.
3. Considering standards of animal care and accommodation to ensure high standards are developed and maintained.
4. Evaluating applications (and any subsequent amendments) to carry out projects/protocols involving laboratory animals.
5. Carrying out interim or retrospective reviews of projects/protocols in progress or completed.
6. Supporting all staff dealing with animals, including those with statutory responsibilities, regarding animal welfare and ethical issues.
7. Establishing and regularly reviewing procedures and protocols, including management systems, for monitoring, reporting and following up on acquisition, welfare and proper use of animals.
8. Ensuring that relevant staff have appropriate education and training.
9. Reviewing methods of humane killing; encouraging the sharing of tissues and organs; exploring options for reducing animal wastage, rehoming or releasing animals.
10. Helping to promote a 'culture of care' within the institution and the wider community.

Institutional ERBs: the wider functions in practice

The ten tasks in the box are all functions that any responsible establishment using animals in scientific procedures should be addressing, regardless of whether an ERB exists. However, an ERB can bring considerable benefits by *providing a focal point* for efforts to address such matters. Its role is to mobilise institutional expertise and resources, and to drive and coordinate the various local systems and processes needed to ensure good animal welfare, rigorous implementation of the 3Rs, and sound, humane science (Home Office 2000; RSPCA/LASA, 2010; European Commission, 2014). Clearly, it is easier to do this at an institutional, rather than a regional or national, ERB level, but the examples below show how the different tasks can fit together whatever type of ERB is in place.

Example 1

An ERB's evaluation of an application for project authorisation (task 4) raises questions about the best way to carry out a procedure that is also used in a number of other projects within an institution, region or nation. These questions are discussed by the ERB (task 1). As a result, the ERB decides to draw up general guidance on how the procedure should be performed (task 7) and ensures that training is provided for relevant animal users (task 8). This helps to refine the procedure so that it causes less harm to the animals, which, in turn, leads to a reduction in the number of animals needed to achieve the scientific goals (task 2). The ERB encourages publication of the refinement which leads to its wider dissemination and implementation (task 2).

Example 2

An ERB's retrospective review of data on the actual severity of adverse effects on animals shows an increase in the number of animals that experience severe suffering over the course of a project (task 5). Following discussion, the ERB decides to review the use of severe procedures within the institution, region or nation, with a view to reducing their use in future (tasks 2 and 7). As a result, it implements a series of actions intended to eliminate severe suffering wherever possible.

These include:

- training to generate greater awareness of sources and nature of suffering (task 8)
- better use of ‘welfare assessment’ or ‘scoring’ systems for monitoring animals and implementing early humane end-points, emphasising the pivotal role of people with statutory responsibilities for animal welfare in decisions to stop procedures before severe suffering occurs (tasks 3, 6 and 7)
- written guidance and staff training on specific, probing questions that *must* be addressed when considering whether or not a severe procedure might be authorised and/or carried out within the institution (e.g. tasks 2, 4, 6, 7, 8)
- an institutional (or regional or national) reporting system detailing the context and reasons for any severe suffering, to assist the ERB in critically evaluating the use of severe procedures, and so to identify possibilities for avoiding or refining them in the future (e.g. tasks 2, 5 and 7), and
- regular review of strategies for refinement of severe procedures to evaluate progress in reducing the number of animals that experience severe effects (tasks 2 and 5).

As already noted, the way in which an institutional ERB addresses its wider functions will vary according to the nature of the individual establishment and the work that it does. Often, an ERB will set up working groups to identify and address particular topics (such as specific aspects of housing and care or refinement of procedures), which will then report back to a ‘central’ ERB committee for further discussion and to support implementation of any recommendations. Other ideas for activities an ERB could initiate or co-ordinate are listed opposite.

Ideas for institutional activities to address the wider functions

Identifying topics and activities

- Encourage and enable any member of staff to raise a question or concern for consideration e.g. via an ERB post-box or email facility.
- Encourage ERB participants to visit the animal facilities regularly and, where possible, see animals undergoing procedures so that everyone has a feel for how the animals are cared for and used, and can feedback their responses and ideas (see also Chapter 7).
- Invite staff to give presentations about animal care and use in their areas of work, highlighting any 3Rs advances and questions that the ERB might help address.
- Ensure that lessons learned and ideas from prospective and retrospective project evaluation are picked up by the ERB for further consideration and action.
- Organise or co-ordinate regular reviews of facilities and methods of animal care and use, humane killing and strategies for reducing animal 'wastage' at the institution, perhaps involving external experts.
- Encourage and support staff to attend relevant external workshops and ask them to provide updates to the ERB.
- Invite staff who are not formally involved to sit in on ERB discussions from time to time, and to feedback their impressions and suggestions.

Driving and co-ordinating progress

- Nominate specific people - 'champions' - to stimulate progress on each function, by acting as a point of contact and catalyst for further action and/or set up sub-groups to work on each function – with regular updates to the ERB.
- Encourage staff to apply for grants to help them develop approaches that better implement the 3Rs and improve husbandry and care.
- Ensure staff are allowed time and other resources to test out their ideas (e.g. for refinements).
- Develop in-house guidelines to implement new innovations and agreed current 'best practice' for particular procedures and uses of animals across the institution.
- Organise annual prizes for the best advances e.g. in each of the 3Rs and husbandry and care.
- Provide support for staff who have specific responsibilities for care and welfare of animals (e.g. veterinary surgeons, animal care managers) and a framework to help them engage in dialogue with other stakeholders; also ensure that they have adequate resources, including time, to fulfil their roles properly.
- Play a role in strategic planning e.g. in considering the need for new facilities and developing these, and co-ordinating joint bids for expensive equipment.
- Review the ERB's own procedures and outputs, to help to ensure that the benefits of its work match the efforts put into it.

Keeping staff up to date

- Act as a focal point to provide/coordinate advice for researchers and animal care staff on relevant issues, including the institution's information officers in the ERB membership.
- Develop an intranet site, library collections and/or regular mailings of information on the 3Rs, ethical issues, good practice, training opportunities, legislation and guidelines, and other relevant aspects, for all staff.
- Organise seminars or similar events, open to all staff, to explore the above topics.
- Ensure that successful 3Rs approaches developed within the institution are communicated to relevant staff and implemented wherever possible, and encourage publication and promotion internally and externally.

The ERB and education and training’

Education and training in all aspects of laboratory animal care and use including ethics, animal welfare and the 3Rs, is increasingly recognised as a key factor in delivering good science. All establishments need to ensure that they have a robust framework for training in place, with a focus on attaining and maintaining competence and subsequent continuing professional development (see European Commission 2014). The ERB may not itself be involved in such training, but it does have a role in ensuring that training is taken seriously and that it is adequately resourced.

The ERB and the ‘culture of care’

The concept of an institutional ‘culture of care’ within research establishments has been around since the 1990s but has only recently started to be formally discussed and defined. In essence, the concept is that every scientific institution which uses animals should have a culture that demonstrates caring and respectful attitudes and behaviour towards animals and encourages acceptance of responsibility and accountability in all aspects of animal care and use. This is in everyone’s interests, as it will promote improved animal (and staff) welfare, and enhance scientific outcomes.

Defining, developing and fostering such a culture of care within an institution is a key role for the ERB. The activities described in the box on the previous page will all help to deliver a good culture, but first it is important to think through what the institution itself means by a ‘culture of care’ and how it will interpret and demonstrate that it has one. Ideas for what this can mean in practice are given below.

Features of a culture of care

- **A corporate expectation of high standards in legal, ethical, animal welfare and scientific aspects of the use of animals that extend above and beyond the legal minimum, and which are endorsed and implemented at all levels throughout the establishment.**
- Strong commitment, support and leadership from senior management.
- Demonstrable respect for animals and for differing ethical perspectives on animal use.
- Effective and well supported ethical review of scientific work; willingness to challenge the status quo.
- A proactive attitude and approach to improving standards of animal care and use and related organisational and management practices, rather than merely reacting to problems as they arise.
- Acceptance of individual responsibility and accountability for animal use, with collective responsibility where appropriate.
- Good establishment-wide processes to facilitate communication regarding animal care and use issues, providing opportunities for any concerns to be raised and dealt with effectively.
- A clear operational structure with clarity of roles, in which animal care staff and veterinarians, information officers and trainers and assessors are listened to and supported.
- A robust framework for training and assessment of competence, together with recognition of the importance of continuing professional development for all staff, and with adequate opportunities and resources provided.
- Co-ordination across animal suppliers, contracted organisations, and research partners abroad to ensure that their standards are consistent with the good practice in animal housing, care and use that is implemented in-house.
- Commitment to openness and honesty about animal use both internally and in the public domain.

Lay members' input to the wider functions

Perhaps the most important way in which lay members can contribute is to ensure that all of the wider functions are firmly on the ERB's agenda, both literally and metaphorically.

With that in mind, the box below lists some ideas for steps you can take to help.

Progressing the ERB's wider functions

- Remind the ERB of the need to devote sufficient time to functions that help to promote good animal welfare and humane science.
- Ask that each function is included as a regular item on the meeting agenda.
- Help to ensure that wider questions identified during project review and visits to animal facilities are picked up and dealt with.
- Request feedback on what the ERB is doing to address its full range of functions, including the benefits that have been achieved for animals and science, and whether the ERB is making the most of the various strategies at its disposal.
- Ask to review the culture of care 'checklist' given in this document to see how well the institution does.

CHAPTER 7

Visiting animal facilities

The day-to-day housing and care of animals has a major impact on their welfare and can also influence the quality and consistency of scientific data. All ERBs should therefore consider standards of animal housing and care, and members should be able to visit animal facilities, talk with relevant staff and discuss any issues that concern them. This chapter presents some points to think about when preparing for and reflecting on such visits and when discussing animal housing and care more generally.

Standards of animal housing and care

It is widely recognised that good housing and care for animals is important for scientific as well as animal welfare and ethical reasons, and many countries have regulations that set out the minimum standards with which institutions must comply. For example, in the USA, standards of housing and care are described in the *Guide for the Care and Use of Laboratory Animals* (National Research Council 2011). In Europe, binding general and species-specific requirements for the care and accommodation of animals are set out in Annex III of Directive 2010/63/EU (European Parliament and Council of the European Union 2010). Individual member states may then develop these into their own national Codes of Practice.

However, understanding of the behaviour and needs of animals is constantly evolving, as is understanding of how animal welfare can affect science. This means that the provisions set out in such codes and guidelines are the minimum required at the time they were published. They do not, as sometimes stated, represent the 'highest possible standards', and institutions should always strive to improve upon them.

There is a wealth of published material available on laboratory animal housing and care, but this is not always easy for non-specialists to interpret. The RSPCA's Research Animals Department has produced a series of guidance notes, in an easy-to-use format, which summarise the scientific literature and set out good practice for the housing and care of a range of species commonly used in the laboratory (see sources of further information at the end of this chapter).

You may find it helpful to read the RSPCA *Guidance notes* for each species you will see, before visiting an animal facility.

What lay members should expect

The ERB's role

Institutional ERBs address animal housing and care in a variety of ways. There may be sub-groups of the main ERB dedicated to housing and care issues, or individual groups of animal care staff or project teams may get together independently to consider specific housing and care issues. Examples of topics they may address are: the development of better environmental enrichment for strains of genetically altered mice; challenging perceived needs to keep animals in barren environments for some types of study; reviewing rodent cage cleaning protocols; or developing positive reinforcement training of animals to reduce the stress associated with handling and restraint. These sub-groups will then report their ideas and conclusions to the main ERB for discussion and appropriate action.

Preparing for animal facility visits

If you are a participant in an institutional ERB you should be invited to visit the animal facilities on a regular basis, to see animal housing and care and ideally procedures taking place. If this is not the case, you can ask to visit.

Visiting animal facilities will help in gaining an appreciation of standards of animal care and welfare and the effects of procedures. This, in turn, will help to inform prospective and retrospective project review and the ERB's wider functions. It may also be helpful to visit to see things that arise from ERB discussions (e.g. to help to understand a husbandry matter or to see a new procedure).

Visits also provide an opportunity to talk informally with animal care staff and so can help in getting a feel for the overall culture of the institution. When viewing procedures, it is particularly helpful if a member of the animal care staff, or a veterinarian, and/or a relevant scientist is available to explain the procedure and answer any questions, and good ERBs will ensure this happens.

If you are a part of a national or regional ERB it is also important to gain an understanding of how animals are cared for and used, and so you should also be offered the chance to visit institutional animal facilities.

Practical matters

The RSPCA's housing and care guidelines mentioned above are designed to help consider how well the animals' needs are catered for. Some additional, general points to think about are listed overleaf. Other points to bear in mind are:

- It can be helpful to visit with one or two other members of the ERB (if the facility can accommodate this), to compare perspectives on what you see.
- Usually you will be given protective clothing to wear during the visit, such as a lab coat or overalls, latex gloves, overshoes and a face-mask. This is to avoid infection entering the animal house and to protect staff and visitors from allergy.
- For the same reasons you may need to shower before entering a particular area, and if you have visited another animal facility recently, you may be asked to delay your visit for a set time afterwards, to avoid any possibility of cross-contamination.
- Be aware that your presence can be stressful for some animals, so take advice from experienced staff about how to behave and interact with the animals. Your interaction starts when you approach and open the door to the room, not just when in front of the animals' cage or enclosure, as sudden noises can be startling.
- Also consider how to approach animals of different species, and how they interpret human body language. For example, it may be acceptable to stare at a cage of mice from across a room, and many dogs respond to eye contact by coming over to interact with humans, but most primates consider a direct stare to be aggressive and threatening.

Reporting back after a visit

The ERB should be interested in your views as a lay member, so reporting back is important. After each visit, you should have the opportunity to feedback your impressions to the ERB, ask any additional questions and/or raise any concerns for discussion by the ERB. It is important to be honest about what you think and to make sure any concerns are followed up.

Some points to consider when visiting animal facilities

General organisational issues

- Whether there appears to be good interaction and understanding between animal care staff, veterinarians and scientists.
- Whether the animal care staff feel that their perspectives are valued, and have clear and effective channels for expressing any concerns.
- How housing and care standards are assessed, and against what benchmarks.
- Whether innovative animal welfare ideas are encouraged and, if so, how.
- Whether there are any aspects that the animal care staff would like to see changed or improved.
- Whether you feel comfortable with the environment and care provided for the animals and with the overall culture.

Carrying out procedures and monitoring animals

- How compliance with project authorisations is monitored when procedures are performed.
- Who carries out the procedures. In some institutions almost all the procedures are carried out by the animal care staff; in others, researchers carry out more of the work. There are pros and cons for both approaches, which you might want to discuss.
- Whether staff receive the specific training that they feel they need (for example, for particular techniques or care of individual species).
- How the competence of people carrying out procedures is monitored and assessed, and what processes there are for supervising inexperienced staff.
- How refinement of procedures is addressed.
- How animals are monitored for adverse effects during and after procedures, and how humane end-points are developed and implemented.
- Whether you feel that any questions about animal suffering are adequately answered (e.g. in relation to particular procedures or if you see an animal displaying abnormal behaviour).

Animal supply and breeding

- Where animals are obtained from and how any stress caused to animals transported to, or within, the institution is minimised.
- If animals are bred in-house, what is done to try to ensure that supply matches demand so as to avoid any over-production of one or both sexes resulting in wastage of animals.
- When animals are killed, the steps taken to ensure that the most humane method is used, and that as many tissues and organs as possible are used, so as to avoid killing additional animals for that purpose.
- If animals are housed in the laboratory in the long term, or reused, what policies and criteria are in place for setting upper limits on the duration of their life in the facility and/or the number of procedures they undergo.
- Whether any animals are re-homed, or released from the institution (for example to a farm or sanctuary), and, if so, whether there is a system in place to ensure that this is well managed and in the best interests of the animals concerned (LASA 2004, Prescott 2006).

Some sources of further information

The RSPCA Research Animals Department's *Good Practice Guidelines for Laboratory Housing and Care*, cover a wide range of species commonly used in laboratories, and are available, together with longer reports on refining housing and care, at: www.science.rspca.org.uk/researchanimals/functionstasks/housingandcare

The Canadian Council for Animal Care has a 3Rs microsite which covers housing and care issues: http://3rs.ccac.ca/en/

The *Enrichment Record* is an online portal that shares ideas and promotes discussion of strategies for advancing the welfare of the animals in housed in laboratories: http://enrichmentrecord.com

The UK NC3Rs Information Portal has a section on housing and husbandry, with links to further information and resources specifically for rodents, rabbits, cats, ferrets and non-human primates: www.nc3rs.org.uk/our-resources

The US National Research Council's *Guide for the Care and Use of Laboratory Animals* (8th edition, 2011) sets out standards for animal housing and husbandry. These standards are also used by AAALAC (The Association for Assessment and Accreditation of Laboratory Animal Care International) to help evaluate and accredit laboratory animal care systems around the world
http://grants.nih.gov/grants/olaw/Guide-for-the-care-and-use-of-laboratory-animals.pdf

The UFAW Handbook is a large, authoritative source on housing and husbandry of laboratory animals: Hubrecht RC, Kirkwood J (2010). *UFAW [Universities Federation for Animal Welfare] handbook on the care and management of laboratory and other research animals*. 8th edition. Wiley-Blackwell.

NOTES

NOTES

APPENDIX 1

UK law on animal experiments

In the UK, the use of laboratory animals is regulated by the Animals (Scientific Procedures) Act 1986 (ASPA). The Act was amended in 2012 to incorporate the requirements of European Directive 2010/63/EU on the protection of animals used for scientific purposes. The amended Act came into force on January 1st 2013. In 2014, detailed Guidance on the Operation of the Act was published. The Guidance document provides a comprehensive, easy to read description of how the requirements of the Act should be interpreted in practice.

This Appendix summarises the main provisions of the UK law and the Guidance on its operation. All quotations are from Home Office (2014) and/or ASPA itself.

Scope of UK regulation

The Animals (Scientific Procedures) Act 1986 (ASPA, as amended) regulates the use of vertebrate animals (mammals, birds, reptiles, amphibians and fish) and cephalopods (a group of invertebrates that includes octopus, squid and cuttlefish), in procedures carried out for scientific purposes, which may have the effect of causing the animals pain, suffering, distress or lasting harm.

Developmental stages of animals covered

Embryos and fetuses of mammals, birds and reptiles are covered by ASPA during the last third of their gestation or incubation period. Fish and amphibians are covered from the time they become capable of feeding independently, and cephalopods from when they hatch. This means that chicken embryos, fetal rats and mice, fish larvae and frog tadpoles may all be covered depending on their stages of development. For example mouse and chicken embryos are covered from 14 days of development.

Level of pain, suffering or distress that is regulated

Under UK and European law, regulation of scientific procedures on animals starts at "*a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice*". In the UK, the Home Office provides guidance on the thresholds at which different kinds of procedure, such as causing psychological stress, studying nutritional deficiencies and attaching external monitoring devices, become regulated. Procedures include acts of commission (e.g. surgery) and of omission (e.g. food or fluid restriction).

Licences required

Before scientific procedures can be carried out on animals, three kinds of licence must be obtained, covering the place, the project and the people involved:

- Places which breed, supply or use animals for scientific research and testing must have an **establishment licence**.[1]
- The scientific programme of work in which the animals are used must be authorised in a **project licence**. Project licence authorisation lasts for up to 5 years, after which the project must be re-evaluated and the licence renewed if it is to continue.
- Anyone who carries out scientific procedures on animals must hold a **personal licence**. This 'qualifies' him or her "*to carry out regulated procedures of specified descriptions to animals of specified descriptions*" within the context of a project licence and at a specified licensed establishment.

[1] Procedures (for example field studies) may also be carried out at places other than licensed establishments (POLES), when specifically authorised in a project licence.

Legal responsibilities

The responsibilities of the establishment licence holder and personal and project licensees are set out in detail in the ASPA and in the 'standard conditions' attached to each licence (see Appendix A, B and C in the Guidance document www.gov.uk/government/publications/operation-of-aspa). Some key points regarding each role are set out below.

The **establishment licence holder** bears overall responsibility for compliance with ASPA. This includes ensuring that animals have appropriate care and accommodation, preventing unauthorised procedures, applying the 3Rs, and establishing and maintaining an Animal Welfare and Ethical Review Body (AWERB). The establishment licence holder must appoint a number of **named people** to help fulfil his or her responsibilities – see box. These people should "*play a central role and be actively involved on a daily basis in the AWERB*".

Named people with responsibilities under ASPA

- The **Named Compliance Officer (NCO)** is responsible for ensuring that the requirements of ASPA and conditions of the establishment licence are complied with – usually the establishment licence holder will be the NCO.
- The **Named Animal Care and Welfare Officer (NACWO)** is responsible for overseeing the welfare and care of the animals.
- The **Named Information Officer (NIO)** is responsible for ensuring that those dealing with animals have access to any information they need about the species they are using.
- The **Named Training and Competence Officer (NTCO)** is responsible for ensuring that those dealing with animals are adequately educated, trained and supervised until they are competent, and that undertake appropriate further training to maintain their expertise.
- The **Named Veterinary Surgeon (NVS)** with expertise in laboratory animal medicine is responsible for advising on the health, welfare and treatment of the animals.

There may be more than one of each NACWO, NIO, NTCO and NVS at an establishment; in some cases the individual roles are shared.

Project licence holders are "*responsible for the overall implementation of the programme of work specified*" in their licences and for ensuring "*compliance with the conditions of the licence"*. They are responsible for applying all 3Rs and ensuring that "*the appropriate level of supervision is provided for all personal licensees carrying out regulated procedures under the authority of the licence*".

Personal licence holders are entrusted with "*primary responsibility for the welfare of the animals*" on which they have performed regulated procedures. They must act "*in a manner consistent with the principles of the 3Rs*" and make sure that "*any animal that is in severe pain or severe distress which cannot be alleviated is painlessly killed using an appropriate method"*. Personal licensees must have had "*appropriate education and training*" and there is additional emphasis on the need for them to be competent in the techniques they carry out, and for them to be supervised until they demonstrate such competency.

Most establishments also appoint a **Home Office Liaison Contact** (HOLC) who provides a link with the Home Office, advises on personal and project licence applications and may organise the AWERB.

Administration of the law

The law is administered by the Home Office through a team of **Home Office Inspectors**, who:

- review applications for, and any amendments to, personal, project and establishment licences, and advise the Secretary of State (a Minister for the Home Office) whether or not to grant them
- encourage good practice, advising on implementation of the **Three Rs**
- visit licensed establishments to monitor their standards and practice, and compliance with ASPA, and
- report all non-compliance to the Secretary of State and recommend any action to be taken.

The Animals in Science Committee

An independent non-departmental statutory public body, the **Animals in Science Committee (ASC)**, advises the inspectorate, Home Secretary and Animal Welfare and Ethical Review Bodies on issues relating to ASPA and the use of animals in scientific procedures. Members have a variety of expertise and perspectives, are independent, do not represent any organisations and include lay participants. In its work, the Committee "*must have regard to both the legitimate requirements of science and industry and to the protection of animals against avoidable suffering and unnecessary use in scientific procedures*".

The ASC is also responsible for sharing good practice within the European Union on the operation of Animal Welfare Bodies, including the UK AWERB. Your AWERB should include a point of contact for communicating with the ASC. www.gov.uk/government/organisations/animals-in-science-committee

Ethical framework of the ASPA

The ASPA sets out **an ethical framework for evaluating project licence applications**, as a basis for deciding whether or not a project licence can be authorised. The framework includes:

- an evaluation of whether the project is justified from a scientific or educational point of view or is required by law, and that the objectives justify using animals
- an assessment of whether the project will be carried out in the most humane way and in particular that:
  - the work does not involve any procedures for which there is a scientifically satisfactory alternative that does not involve the use of animals covered by the ASPA
  - **the project will comply with the Three Rs**, by employing procedures that:
    - use the minimum number of animals
    - involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm
    - cause the least pain, suffering, distress or lasting harm, and
    - are most likely to produce satisfactory scientific results
- **a harm-benefit analysis of the project** to assess whether "*the harm likely to be caused to animals in terms of the suffering pain and distress is justified by the expected outcome taking into account ethical considerations, and may ultimately benefit human beings, animals or the environment* ".

Local ethical review: Animal Welfare and Ethical Review Bodies

UK law requires that every licensed establishment must have an Animal Welfare and Ethical Review Body (AWERB). The AWERB's required tasks and members are listed in the boxes overleaf. In practice, AWERBs will function in much the same way as the local Ethical Review Processes (ERPs) that they replaced in 2013 and which have been a feature of UK regulation of laboratory animal use since 1999.

Membership of the AWERB

The minimum requirement is at least one of the establishment's:

- Named Animal Care and Welfare Officers (NACWOs)
- Named Veterinary Surgeons (NVSs)

plus

- a scientific member (if the establishment is a user establishment).

In addition:

- The Named Information Officer(s) (NIOs) and Named Training and Competence Officer(s) (NTCOs) must also be "*actively engaged with the AWERB given the breadth of its tasks*".
- In order to help ensure the integrity of the process, the establishment licence holder is expected "*to arrange for their AWERBs to actively seek a wider membership, taking into account, in a transparent manner, the views of people who do not have responsibilities under ASPA, as well as one or more persons who are independent of the establishment*".
- Home Office inspectors may also attend meetings from time to time as part of their responsibilities for monitoring compliance with the legislation.

Minimum tasks for AWERBs

The AWERB must carry out the tasks set out in the EU Directive. These are to:

a) advise staff dealing with animals in the licensed establishment on matters related to the welfare of the animals, in relation to their acquisition, accommodation, care and use

b) advise on the application of the 3Rs, and keep it informed of relevant technical and scientific developments

c) establish and review management and operational processes for monitoring, reporting and follow-up in relation to the welfare of animals housed or used in the licensed establishment

d) follow the development and outcome (retrospective review) of projects carried out in the establishment, taking into account the effect on the animals used; and to identify and advise on elements that could further contribute to the 3Rs

e) advise on rehoming schemes, including the appropriate socialisation of the animals to be re-homed.

In the UK, additional advisory and reviewing tasks are also allocated as follows:

- advise the establishment licence holder whether to support project proposals, primarily considering such proposals from a local perspective and bringing local knowledge and local expertise to bear
- assist with the retrospective assessment of relevant projects carried out at the establishment
- respond to enquiries, and consider advice received, from the Animals in Science Committee.

More generally, AWERBs should:

- promote awareness of animal welfare and the 3Rs
- provide a forum for discussion and development of ethical advice to the establishment licence holder on all matters related to animal welfare, care and use at their establishment
- support named persons, and other staff dealing with animals, on animal welfare, ethical issues and provision of appropriate training
- help to promote a 'culture of care' within the establishment and, as appropriate, in the wider community.

The establishment licence holder must ensure that a record is kept of any advice given by the AWERB and any decisions taken as a result. These records must be kept for at least three years and must be made available to an inspector, or the Secretary of State, on request.

Codes of practice and guidance notes

The Home Office issues policy statements and additional guidance and advice on specific issues which are available on the Home Office's website: www.gov.uk/research-and-testing-using-animals. The site contains a lot of explanatory material relating to personal and project licences and how to apply for these and, even as a lay person, it is well worth exploring.

Amongst other things there are a range of guidance documents, for example on assessing the severity of scientific procedures on animals; Codes of Practice, e.g. on animal housing and care; and ASPA e-newsletters; with links to non-technical summaries of project licences granted under ASPA, and to annual statistics on the use of animals in scientific procedures.

A series of guidance documents produced by the EU are also relevant and very helpful. These can be found at: http://ec.europa.eu/environment/chemicals/lab_animals/interpretation_en.htm. This page is part of a wider range of information about regulation of laboratory animal use in the EU, which covers, amongst other things, legislation and its implementation; the 3Rs; project evaluation and harm/benefit; retrospective assessment; severity assessment; Animal Welfare Bodies; and statistics of laboratory animal use in the EU. See also: http://ec.europa.eu/environment/chemicals/lab_animals/related_topics_en.htm.

What is – or are – ethics?

ERBs consider, and provide advice and support, on 'ethical' matters. To provide some background to the use of 'ethics' terminology, this Appendix explores what is meant by 'doing ethics' in practice and the benefits this can bring.

Different uses of the term 'ethics'

'Ethics' concerns ideas of right and wrong, what is good and bad, and how people ought and ought not to behave, both generally and in particular cases. The term ethics is used in at least four different but related ways, to describe:

- particular patterns or ways of life – as in, say, Buddhist ethics or Christian ethics
- sets of rules or guidelines for good, right or correct behaviour – as in professional codes of ethics or general ethical guidance, such as the Ten Commandments, or the Declaration of Helsinki, for medical research (World Medical Association, 1964, last amended 2008)
- general, theoretical inquiry into what it means to live a good life and do the right things
- exploration of how these ideas translate into practice when people are faced with dilemmas or decisions about what should (and should not) be done in specific situations.

In the last two senses, the term is being used as a verb – to 'do' ethics.

Ethics cf. morality

Morality (from the Latin *mores,* meaning customs, manners) also encompasses questions of right and wrong, what ought and ought not to be done. Nowadays, the terms 'ethical' and 'moral' are frequently used interchangeably, both in everyday conversation and in philosophical literature. Nevertheless, ethics is often the preferred term in a *professional* context. Codes of principles for professional conduct are usually described as codes of *ethics*, not codes of morals:

"*Anyone can be described as immoral", but only doctors, lawyers, scientists and "others who fail to live up to publicly professed obligations tend to be called 'unethical'*." (Boyd, 1997a)

This particular perspective might appear to encourage a narrow view of ethics, but the subject is not limited to professional practice – it includes all aspects of (everyday) morality. Moreover, professional codes of practice do not provide an escape from the need to make moral judgements, because they cannot cover all circumstances and are open to interpretation in different contexts.

Ethics cf. law

Behaving ethically (or being moral) "*involves more than keeping on the right side of the law*" (Boyd, 1997b). Laws lay down certain rules, or boundaries, which must not be breached; yet within these boundaries there can be considerable room for judgement about what is right and what is wrong.

The Animals (Scientific Procedures) Act 1986 (as amended) is not an easy-to-follow code of 'dos and don'ts' in animal use. Rather, it sets out a framework within which *ethical judgements* must be made about what is and is not acceptable. Guidance is provided (Home Office 2014), but it is recognised that this is not static and will evolve alongside advances in both scientific and moral understanding.

Identifying ethical questions

Ethical issues are most often encountered when there are difficult choices to be made about which courses of action *ought* to be taken in particular situations. We enter the realm of ethics when we make a move from considering what *can* be done (i.e. what is *possible*) in a given situation, to considering what *ought* to or *should* be done in that situation. For example, whether or not a particular research project that *can* provide knowledge to benefit humans or other animals, but which will involve causing pain, distress or suffering to animals, *ought* to go ahead.

The most dramatic dilemmas tend to make the headlines and it is sometimes forgotten that more day-to-day decisions and judgements can have ethical components. For example, in animal research, even a decision about how frequently to clean a mouse cage could have an ethical as well as a practical dimension, because it might involve balancing competing animal and human interests in order to decide what ought to be done. The decision could involve weighing scientific evidence about what would promote the best possible mouse welfare, against constraints of technician time and financial costs (if the evidence suggests that more frequent cleaning would be beneficial), or against human health hazards due to odour and allergen build-up (if the evidence points to less frequent cleaning).

'Doing ethics' in practice

The kind of practical decision making mentioned above is the visible "*tip of the [ethics] iceberg*" (Seedhouse, 2009). Practical decisions in particular cases are influenced by more fundamental questions that we run into as we think more deeply about the reasoning behind our ethical choices. For example, often unspoken questions that underlie and influence decisions on whether, and how, animals should be used in experiments, might include the following:

- do animals have 'rights' not to be harmed (either at all or in certain ways) by humans?
- what value we should place on an animal's life – how far, and in what ways, is killing an animal ethically similar to killing a human?
- is it more or less acceptable to use some species than others in experiments and, if so, why?
- what in practice should 'good animal welfare' mean?

At a deeper level still, there are ever-present questions, common to all moral choices, about how we should live our lives, what it means to be a good person and how, in the most general terms, we should decide how we ought to behave.

One useful working definition of 'doing ethics' is that this involves the "*critical evaluation of assumptions and arguments*" used to arrive at decisions and judgements about ethical matters (Raphael, 1994). Ethical questions often crop up in everyday lives, both private and professional, and we frequently make judgements or decisions on them. 'Doing ethics' involves careful consideration of the *reasoning* on which such judgements and decisions are based, so as to:

- make sure that the judgements are sound and consistent
- attempt to resolve disagreements, and
- promote better ethical decision making in future.

Inevitably, 'doing ethics' involves balancing competing arguments, trying to find out where exactly the disagreements and any points of agreement lie. Ethical judgements need to take into account a range of different perspectives, and this might involve engaging in discussion with people who hold different views.

Sometimes, consensus judgements can be reached; in other cases disagreements will remain, but better understanding of the reasons for the disagreements can help to strengthen the decisions that are eventually made. See, for example, Hope *et al.* (2008) for further discussion of ethical reasoning.

Some benefits

Ethical questions, by their very nature, are difficult questions on which people's opinions and judgements tend to differ. 'Doing ethics' can help to remove both muddle and intolerance from difficult debates by discouraging a rush to judgement and taking the time to think more clearly, deeply and precisely about the reasons for views and decisions.

In particular, doing ethics can help to:

- avoid being swayed by ill-founded, but at first sight persuasive, arguments, that is, to recognise bad rhetoric [1]
- develop a deeper understanding of the range of perspectives on the issue, and use this understanding to inform judgements
- make sure that decisions and judgements take into account all relevant features of the issue at stake
- engage in debate with people who hold different views and, by pin-pointing exactly where the agreements and disagreements lie, learn from each other, identify any common ground and move towards consensus
- feel more confident in the decisions that are made, knowing that, at the very least, all involved have done their best to identify the most acceptable standpoint or solution to a problem.

Ethics, however, cannot positively prove that one judgement is 'the correct solution' compared with all other possibilities, and choices must still be made. Indeed it can be argued that studying ethics *"makes it more necessary, not less, to stand on your own feet, to be self-critical, and to be obliged to choose for yourself. It makes you more rational, more responsible, more of a human being*" (Raphael, 1994, page 10).

Approaching ethical judgements in practice

As discussed above, the quality of ethical judgements depends largely on the depth and breadth of thought that those involved put into them. Higgs (1997) has set out a list of possible aims of ethical discussion that are important elements in the process of arriving at decisions, or ways forward, on ethical issues (see box below).

Aims of ethical discussion (Higgs 1997)

- Identification of issues at stake, whom they affect, and in what way.
- Further exploration of morally relevant facts, together with a reasonable attempt to assess the perspectives and purposes of all involved.
- Clarification of the concepts and arguments being used, including asking whether any person or group is distorting the discussion by manipulation, misuse of language, or distortion of concepts and arguments.
- Interaction and dialogue between the various parties to ventilate feelings, share points of view, and make sure everyone feels heard.
- Analysis or synthesis of different points of view and arguments in order to create a response or way forward.

This list emphasises that good ethical judgement requires:

- as comprehensive and accurate an understanding of the issues at stake as possible; and
- consideration of all the relevant factors and interests involved.

The latter includes an understanding of the *context* in which the judgement is made. This, in turn, includes any legal framework or relevant professional codes, historical precedent, range of current perspectives (both amongst people directly involved in the issue under consideration and perhaps across society more widely), and possible general frameworks for thinking on the issue.

Approached in this way, judgements will not result from 'gut feelings' alone. However, emotions do still play a part. Such feelings can, at least, help in identifying areas of ethical concern, suggesting a need to pause and allow time to consider the issues in depth (Hope *et al.* 2008, p. 7; Gillett, 1997).

[1] Rhetoric attempts to persuade others to adopt a particular point of view – in this case about what is right and what is wrong. Bad rhetoric is based on poor argument – it might merely play on the emotions, or it might exploit incomplete, disputable or incorrect facts, or it might use logically inconsistent arguments, for example.

Role of ethics 'experts'

Good ethical judgement is not limited to people with special training, but can be claimed by anyone with sufficient wisdom, intelligence and experience, who is prepared to make the effort to understand the issues and seriously consider the different perspectives involved.

Nevertheless, people trained in ethics have expertise that is particularly helpful in challenging others to think in new ways and in ensuring that the *process* of ethical reasoning is comprehensive, logical and consistent. Moreover, initial and/or continuing training in ethical reasoning can be helpful for everyone involved in considering ethical questions, such as those related to the use of animals in science. This is part of the long-term process of developing the experience needed to understand and evaluate the arguments, appreciate their context, and balance conflicting demands.

Suggestions for further reading

Ethics in general:

Blackburn, S. (2003). *Ethics: a very short introduction*. Oxford University Press: Oxford.

Compendium of essays:

Garrett JR (ed). (2012). *The ethics of animal research: exploring the controversy*. Basic Bioethics: The MIT Press.

Working group reports:

Nuffield Council on Bioethics (2005). *The ethics of research involving animals*. Nuffield Council on Bioethics. http://nuffieldbioethics.org/project/animal-research/

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Two anti-vivisection perspectives, which helped spark the 'animal liberation' movement:

Rights-based: Regan T (1985). The case for animal rights. In: Singer P (ed) *In defence of animals* pp. 13-26. www.animal-rights-library.com/texts-m/regan03.htm

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