

Accreditation of animal care and use programmes: the use of performance standards in a global environment

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Summary

Revisions of several important documents establishing standards of animal care and use in the United States and Europe have been released recently, including the *Guide for the Care and Use of Laboratory Animals* (*Guide*), the European Directive on the Protection of Animals Used for Scientific Purposes (that includes the care and accommodation standards of the ETS 123 Appendix A) and the *Guide for the Care and Use of Agricultural Animals in Research and Testing* (*Ag Guide*). Although these documents differ in their origin and structure, they all share the same ethical principles based on Replacement, Refinement and Reduction. The Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC International) evaluates the performance of animal care and use programmes across the world with regard to ETS 123, the *Guide* and the *Ag Guide* (considered as the Three Primary Standards), applicable local regulations/guidelines, and other recognised reference publications. While always respecting the engineering standards of local regulations, AAALAC International applies the performance goals of the Three Primary Standards globally. Performance standards, which are outcome oriented and focused on goals or expected results rather than the process used to achieve the results, are essential in determining what can be considered appropriate animal care and use at each institution. Performance standards can be applied to all areas of the animal care and use programme. When different engineering standards required by law exist internationally, performance standards serve as a tool for harmonisation of animal care and use, especially in the current context of increasing globalisation.

Introduction

A combination of scientific reasons and ethical principles is defining the current framework for the care and use of laboratory animals. Science does not demand only animal quality in microbiological and genetic terms, but also high standards of animal care

and use. It is generally accepted that there is a correlation between the level of animal care and use and the quality of the experimental data, and that animals whose well-being is less compromised can offer more reliable scientific results¹, except for some particular experimental needs (e.g. deliberately infected animals who can offer valid data for specific research questions). Science and ethical interests converge because well performed experiments with healthy animals that are maintained in appropriate conditions avoid unnecessary repetitions. Therefore, the number of animals used is reduced while the level of welfare of the animals used is better, the cost and time of research decrease, and data are more reliable, leading to improved human and animal health.

There are several mechanisms for control of animal care and use at research institutions. Internal mechanisms are represented by institutional specialists, such as veterinarians, animal technologists, animal care personnel, researchers etc. as well as institutional oversight bodies such as the Ethical Review Processes (ERP) in the UK, Institutional Animal Care and Use Committees (IACUC) in the US or Ethics Committees in other countries. These internal mechanisms, in addition to ensuring compliance with the applicable legal requirements, may result in the implementation of institutional policies and procedures based on adopted guidelines, recommendations and best practice. The composition and functions of institutional oversight bodies may vary across countries. Some of these bodies only perform ethical evaluation of research proposals, while others are also responsible for inspecting facilities, reviewing the animal care and use programme, monitoring that studies are performed according to the approved protocol and reviewing/establishing policies and procedures. In general, the effectiveness of internal mechanisms of control differs significantly across countries and among institutions within the same country, as it depends on both institutional and individual commitment as well as the competence of the personnel involved.

The external control mechanisms are related to:

- Government bodies/inspectors. Government oversight systems also differ among countries, but typically, the government control includes local/regional personnel responsible for inspections of institutions, and central bodies/committees at a regional and/or central level that may participate in ethical evaluation, authorisation processes or have an advisory role. Inspectors may have very variable level of laboratory animal science background and focus. In some cases they are fully dedicated to laboratory animals (e.g., the UK and a few other European countries) but in the majority of cases, as happens in most of Europe and globally, they are not specialists in the field because laboratory animal activities represent only a small portion of their job responsibilities. Government commitment and resources are the variables that influence the effectiveness of this control process. Government bodies/inspectors must refer to applicable legislation. Therefore, except in the few cases where they are well versed in laboratory animal science and medicine, they tend to use the measurable engineering standards contained in the legal framework, sometimes obviating other performance standards.
- Quality systems, such as Good Laboratory Practices (GLP) and International Organisation for Standardisation (ISO). GLP standards are regulatory in nature and are typically implemented in institutions performing preclinical studies, as they are obligatory for some of these studies. ISO standards can be found in use at animal breeders and institutions producing and offering goods or services to external customers as a symbol of the consistency in the quality of the product or service. They can be also applied to other kinds of institutions on a voluntary basis. The implementation of these quality systems normally includes the animal-related activities as part of the general institutional quality implementation process. Review of the organisation's animal care and use is typically part of a much larger evaluation, and in many of the cases the personnel involved in the audits or inspections are not necessarily experts in the laboratory animal science field. Quality systems refer to their own specific organisation requirements and mainly ensure that institutional activities (including animal care and use) are performed according to established standard operating procedures. A FELASA Working Group published a report describing these systems and AAALAC International, and summarising their strengths, weaknesses, similarities and differences².
- International accreditation of animal care and use programmes. AAALAC International is the only global system specifically focused on laboratory animal

care and use. This voluntary scheme is performed by recognised laboratory animal science professionals and applies to all areas of the programme of animal care and use. AAALAC International applies the performance standards of the documents considered as the primary standards in addition to applicable regulations.

AAALAC International

The Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC International) is a voluntary accrediting organisation that enhances the quality of research, teaching, and testing by promoting humane and responsible animal care and use. AAALAC provides advice and independent assessments to participating institutions and accredits those that meet or exceed applicable standards.

AAALAC was established in 1965 as the American Association for Accreditation of Laboratory Animal Care. In 1996, after a number of international institutions had shown interest in the accreditation process, AAALAC adopted the current name and became truly international. The first non-US institution was accredited in 1981; the first European institution (in the UK) in 1986, and the first institution in Asia in 1995. Currently, there are over 820 accredited institutions in 35 countries.

AAALAC is managed by a Board of Trustees in which more than 60 scientific organisations are represented, including some European professional societies such as the European Federation of Pharmaceutical Industries and Associations (EFPIA), the European Society of Laboratory Animal Veterinarians (ESLAV), the Federation of European Laboratory Animal Science Associations (FELASA), and the Institute of Animal Technology (IAT). The headquarters office is located in the US and there are regional offices in Europe and South East Asia, where the AAALAC staff carry out the daily activities of the organisation. The group of individuals in charge of the assessments is denominated the Council on Accreditation, comprised of 56 highly respected, independent professionals distributed in three North American sections, one European section and one Pacific-Rim section. Council members are professionals who have experience at universities, pharmaceutical companies, CROs and NGOs and volunteer their time and expertise for AAALAC International. They lead the site visits and the assessment of animal care and use programmes, with assistance from other colleagues with similar or complementary expertise referred to as ad hoc Consultants or Specialists. Vacancies on Council are filled by experienced ad hoc Consultants/Specialists.

Any public or private institution, organisation, or agency maintaining, using, importing, or producing animals for

purposes of scientific research, teaching, or testing may be accredited. AAALAC accredits only active animal care and use programmes. An active animal care and use programme includes: animals; facilities; equipment; professional, technical, and administrative support; policies and programmes for institutional responsibilities, animal husbandry and veterinary care. Applicant institutions have to complete a questionnaire referred to as a Programme Description (PD) to describe the operations of all areas of the animal care and use programme. The PD is initially reviewed by the site visit team before the on-site assessment takes place. Once the assessment has been conducted, the site visitors prepare a report that is evaluated by the other members of the Council section, a peer review process culminating in deliberations at regularly scheduled Council meetings. The Council's decision regarding the accreditation status is communicated to the institution in the form of a letter. The letter may contain two categories of findings, mandatory items, which are serious deficiencies that must be corrected to obtain Full Accreditation; and/or suggestions for improvement, which in opinion of the Council would enhance the quality of the programme.

Accredited institutions have to undergo the process of completing a new PD and undergoing another on-site assessment (by a different site visit team) every three years. This process engages the institution in a continuing improvement process.

AAALAC relies on Three Primary Standards for evaluating laboratory animal care and use programmes: the eighth edition of the *Guide for the Care and Use of Laboratory Animals (Guide, NRC 2011)*; the *Guide for the Care and Use of Agricultural Animals in Research and Teaching (Ag Guide, FASS 2010)*; and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Council of Europe (ETS 123); along with other widely accepted guidelines. AAALAC International also refers to other specialty publications for supplemental information about procedures or techniques related to the care and use of laboratory animals. These specialty publications are designated as Reference Resources. Reference Resources are intended to serve as references and guidelines for laboratory animal care and use programmes. Reference Resources are formally reviewed and adopted by the Council and assist site visitors as they evaluate animal programmes.

Engineering and performance standards

Engineering standards for the care and use of laboratory animals are those that are strictly defined, often based on numeric or other specific parameters, and can normally be measured. The most typical

example of an engineering standard is cage size, but many others may also be found especially in regulations and guidelines, such as the environmental range levels (temperature, humidity, ventilation rates), composition of committees, etc. They occur more often in regulations than in guidance documents, and normally are presented in the form of minimum requirements. They are used by government bodies to establish a minimum acceptable level and serve as the basis to inspect animal research facilities, since they represent specific and measurable standards that are easy to apply. Although they are useful in the sense that they define the basic framework, they also have the problem of allowing little or no flexibility at all when applied, not taking in account all the potential situations that can be found in the research environment.

Performance standards are outcome oriented, focused on goals or expected results rather than the process used to achieve the results. The assessment of the implementation of performance standards may be more complicated, as the outcome is to be defined in detail and the criteria to assess it provided. Professional input and judgement are necessary to evaluate the application of the standard in diverse research environments. On the other hand, performance standards allow flexibility to fit different situations. This is what makes them so important for the assessment of animal care and use programmes³. The engineering standards of current regulations across the world differ with regard to several areas of animal care and use programmes, and for some other areas they are written in general terms and give broad recommendations. Performance standards facilitate global harmonisation and evaluation of desired outcomes^{4,5}. Using the example of cage size, a performance based approach would focus more on the health, activity and behaviour of the animals housed rather than on a defined cage size. A cage size that may be appropriate for some animals in a particular situation might not be appropriate for other animals of a different strain, age, health status or experimental condition.

Current standards framework

During 2010 and 2011, three important documents were published: the European Directive 2010/63/EU on the protection of animals used for scientific purposes⁶, the eighth edition of the *Guide for the Care and Use of Laboratory Animals (Guide, NRC 2011)*⁷ and the third edition of the *Guide for the Care and Use of Agricultural Animals in Research and Teaching (Ag Guide, FASS 2010)*⁸.

Annex III of the Directive 2010/63/EU contains part (the engineering part rather than the performance one) of the accommodation and care standards of the

European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, (ETS 123, Council of Europe 1986)⁹, that are defined in its Appendix A¹⁰. The Directive is intended to level the playing field across Europe while enforcing the principles of the 3Rs, and establishes requirements for a number of issues including the purpose and severity of procedures; origin of animals; the use of nonhuman primates; authorisation of establishments; personnel; project (ethical) evaluation and authorisation; institutional responsibilities (e.g.: animal welfare body); animal care and accommodation; euthanasia; and others. However, it includes little information on important areas such as husbandry, veterinary care or facilities. The Directive is mostly written in engineering terms, and uses the term “shall” as an imperative for the requirements in the articles. A majority of the extensive performance standards contained in ETS 123 Appendix A are not in the Directive, which has transposed from Appendix A mainly the cage sizes as mandatory engineering standards. The Directive applies to the 27 countries of the European Union, and is in the process of transposition into the legislation of the Member States. The transposition must be finished by November 2012, and it will be enforced beginning 1 January 2013.

Also in Europe, ETS 123 can apply to any of the 47 countries of the Council of Europe (including all in the European Union) that sign and ratify the Convention, though only 19 countries have undergone the process so far. Appendix A (Guidelines on accommodation and care of animals) in ETS 123 contains extensive performance standards on the accommodation and care of many species of laboratory animals, focusing specially on housing and enrichment. Other areas of animal care and use programmes are more succinctly covered. ETS 123 uses the term “should” when defining all recommendations.

The *Guide for the Care and Use of Laboratory Animals (Guide)*, is the most widely followed document in the United States, but also has broad international acceptance and has even served as the basis for the legislation in other countries, especially in Asia. The *Guide* is written in a performance based approach, and gives extensive recommendations on all areas of the animal care and use programme, including programme management (key institutional personnel); personnel management; occupational health and safety; programme oversight (ethical review); environment, housing and management (including husbandry, housing, enrichment); veterinary care; physical plant. The *Guide* mostly uses the term “should” (intended as strong recommendation), but also other terms such as “may” (intended as a suggestion) and “must” (intended as imperative) are used. The recommendations are intended to be used as a foundation for the development of a comprehensive animal care and use

programme, recognising that the concept and application of performance standards is essential to this process. The *Guide* has served historically as AAALAC’s main reference to evaluate animal care and use programmes.

Another Guide, the *Guide for the Care and Use of Agricultural Animals in Research and Teaching (Ag Guide)* was also revised recently. The *Ag Guide*, published by the Federation of Animal Science Societies, recognises needs and requirements of agricultural animals in research and testing and offers general performance based guidance for different species, using the terms “should” (intended as a strong recommendation) and “must” (intended as imperative). In addition to the species-specific sections, it offers guidance on institutional policies; health care; housing, husbandry and biosecurity; environmental enrichment; and animal handling and transport. An important new feature of this recent edition is that it is intended to address the care and use of agricultural animals, not only in agricultural research, but in research in general.

Three primary standards for international accreditation

After a thorough review by the AAALAC Council on Accreditation of the new European Directive, and the new editions of the *Guide* and *Ag Guide*, AAALAC International adopted the *Guide*, ETS 123 and the *Ag Guide* as Three Primary Standards for accreditation, and started using them officially to evaluate animal care and use programmes in the Autumn of 2011. In the European context, there were several reasons to choose ETS 123 instead of the Directive: first, the Directive is a regulatory document and institutions are already expected to comply with applicable legislation; second, ETS is structured as a guideline emphasising a performance based approach; third, ETS 123 is potentially applicable in a broader geographical area. The adoption of these documents by the AAALAC’s Board of Trustees as primary standards signifies the importance of these performance based guidelines in the accreditation process.

Although the Three Primary Standards differ in several aspects, they share the essential principles of animal care and use based on the implementation of the 3Rs. There are some differences related to the structure of the documents and the areas covered and also related to more specific recommendations, such as the minimum cage size. However, the use of performance standards and the combination of more than one Primary Standard facilitate a harmonised approach during the evaluation of programmes globally. While institutions can choose which primary standard is considered as the main standard, a combination of primary standards may be used to address the entire

animal care and use programme. For example, European institutions following ETS 123 and applicable regulations (i.e. Directive 2010/63/EU and/or national legislation) also may need to apply the recommendations of the *Guide* to ensure the areas of the programme not covered entirely by other guidelines and regulations are addressed by using at least one of the primary standards. This situation is very common in Europe, as the ETS 123 and applicable legislation may not address well areas such as the veterinary care programme, husbandry and facilities.

In summary, AAALAC applies the performance approach of the Three Primary Standards on top of the engineering standards normally required by the applicable legislation.

Performing standards in a global environment

Performance standards are paramount when trying to harmonise animal care and use practices in a global environment, where different regulations exist. People tend to think that what others do is different, and... oftentimes worse. But if we pay close attention to the documents described above, we can see that they share not only the principles, but many performance standards, which means that we are all seeking the same outcomes. The following are examples:

- Housing and environmental enrichment. In the European context, ETS 123 Appendix A states that “All animals should be allowed adequate space to express a wide behavioural repertoire. Animals should be socially housed wherever possible and provided with an adequately complex environment within the animal enclosure to enable them to carry out a range of normal behaviours. In addition to social activities, enrichment can be achieved by allowing and promoting physical exercise, foraging, manipulative and cognitive activities, as appropriate to the species.” That is a clear example of performance based recommendations, as it defines how housing should be implemented to obtain a desired outcome, which is that animals can express normal behaviour, etc. For those skeptical about another country’s framework, the *Guide* states that “All animals should be housed under conditions that provide sufficient space as well as supplementary structures and resources required to meet physical, physiologic, and behavioral needs. The primary aim of environmental enrichment is to enhance animal well-being by providing animals with sensory and motor stimulation through structures and resources that facilitate the expression of species-typical behaviors and promote psychological well-being through physical exercise, manipulative activities, and cognitive challenges according to species-specific characteristics”. The similarities are evident.
- Social Housing. ETS 123 Appendix A states that “Animals, except those which are naturally solitary, should be socially housed in stable groups of compatible individuals. Single housing should only occur if there is justification on veterinary or welfare grounds. In such cases, the duration should be limited to the minimum period necessary and, where possible, visual, auditory, olfactory and tactile contact should be maintained.” For the same topic, the *Guide* states that “Social animals should be housed in stable pairs or groups of compatible individuals unless they must be housed alone for experimental reasons or because of social incompatibility. Single housing of social species should be the exception and justified based on experimental requirements or veterinary-related concerns about animal well-being. In these cases, it should be limited to the minimum period necessary, and where possible, visual, auditory, olfactory, and tactile contact with compatible conspecifics should be provided.” These examples show how regardless of different engineering standards related to minimum cage size recommendations or requirements, common performance standards focus on the same desired outcomes.
- Ventilation: The ETS Appendix A states that “Adequate ventilation should be provided in the holding room and the animal enclosures to satisfy the requirements of the animals housed. The purpose of the ventilation system is to provide sufficient fresh air of an appropriate quality and to keep down the levels and spread of odours, noxious gases, dust and infectious agents of any kind. It also provides for the removal of excess heat and humidity.” With regard to ventilation, the *Guide* states that while the traditional range of 10-15 fresh air changed per hour “... is effective in many animal housing settings, it does not take into account the range of possible heat loads; the species, size, and number of animals involved; the type of primary enclosure and bedding utilized; the frequency of cage-changing; the room dimensions; or the efficiency of air distribution within the macroenvironment and between it and the microenvironment.” The recommendation of both documents is clearly the same, defining what is expected and avoiding the use of engineering standards.

The ethical oversight and review process is another area where different engineering standards are usually applied. Although all modern regulations and guidelines require or promote a system to review and ensure the application of the 3Rs in research proposals and institutional activities, this may take different forms. Systems can be based on oversight bodies or committees at institutional level (i.e.: Institutional Animal Care and Use Committees as per the *Guide*), government level, or a combination of both. Regardless

of the system in place, the important point is that the outcome, in the form of an appropriate ethical review (the common goal) is achieved^{5,11}. AAALAC International is aware that the same outcome can be achieved by using different approaches and does not require a uniform system of ethical review to achieve accreditation. This is particularly important in the European context where many different systems are in place at national level and still will be after the implementation of the new Directive because of different approaches in the transposition into national legislation. The competent authorities of the Member States are allowed to delegate some functions including the project (ethical) evaluation to other bodies (i.e.: local or external), an option that will be taken by some but not all, resulting again in a heterogeneous situation in Europe. The performance approach taken by AAALAC with regard to the assessment of ethical oversight is exemplified in the European version of the Programme Description template when referring to the description of the programme oversight: "Programmatic oversight of all aspects of the animal care and use programme must be described. Irrespective of whether the programmatic oversight is carried out by just one body or is delegated to several bodies (e.g., protocol review to an Ethics Committee, an Institutional Animal Care and Use Committee, the Competent Authority; oversight of animal care and welfare to an Animal Welfare Body; occupational health and safety to the Occupational Health Unit, etc.), it must be described how the comprehensive programmatic oversight, and the responsibility and authority of the body/bodies, are ensured."

Conclusion

The basic framework for animal care and use programmes is defined by the engineering standards in the existing regulations on the protection of laboratory animals. But the use of performance standards can transform and adapt the basic framework to address diverse animal and research needs, allowing harmonisation even in the context of different regulatory environments.

Irrespective of legal requirements and related engineering standards, AAALAC International applies the performance approach of the Three Primary Standards to assess and accredit animal care and use programmes globally. A detailed review of these Primary Standards reveals a common set of principles and expectations for key areas of the programme that can be applied in different geopolitical areas. International accreditation is one of the more powerful tools to achieve global harmonisation of animal care and use practices by ensuring the same desired outcomes.

Technicians/Technologists play a pivotal role in contributing to and harmonising of high quality

laboratory animal care and use, and to recognize those contributions and to promote their role, AAALAC International hosts annually the Technician Fellowship Award (<http://www.aaalac.org/about/fellowship.cfm>).

High quality animal care and use is a responsibility of all personnel involved, and should have no country boundaries. The use of performance standards overlaid on the different engineering standards required by law is clearly the way forward.

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