

Special Topic Overview

FELASA Guidelines and Recommendations

Javier Guillen

The Federation of European Laboratory Animal Science Associations (FELASA) has been releasing guidelines and recommendations on several laboratory animal science disciplines for more than 15 y. The Working Groups producing these documents comprise specialists in each of the addressed topics, are nominated by the FELASA constituent associations, and are elected by the FELASA Board of Management. The FELASA guidelines and recommendations are not regulatory but rather are proposals based on scientific knowledge and the state of the art of laboratory animal science activities. Because they are supported by laboratory animal science associations that represent the vast majority of European professionals, these guidelines and recommendations have influenced the development of various regulatory requirements in Europe, including those related to education and training, routine laboratory animal activities, and animal health monitoring. Some reports fill existing gaps in the European legal framework or complement it. The Working Groups occasionally collaborate with other European organizations, thus enhancing the professional input and effect of the documents produced. The recently established AALAS–FELASA Liaison Body may result in future international cooperation that benefits laboratory animal science and welfare in a global context.

Abbreviations: ECLAM, European College of Laboratory Animal Medicine; ESLAV, European Society of Laboratory Animal Veterinarians; FELASA, Federation of European Laboratory Animal Science Associations.

The Federation of European Laboratory Animal Science Associations (FELASA) was established in 1978 and currently comprises 18 national or regional laboratory animal science associations that represent laboratory animal professionals in more than 20 European countries. As a major representative of the laboratory animal science community in Europe, FELASA has held observer status at both the Council of Europe and the European Union during the revision process of Appendix A to the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (ETS 123)⁴ and the development of the European Directive 2010/63/EU²² on the protection of animals used for scientific purposes, respectively. Currently, FELASA also is involved with expert working groups established by the European Commission for transposition and implementation of the new Directive. The FELASA Board of Management is made up of representatives from the constituent associations. The Board appoints the Executive Committee (President, Secretary, Treasurer and Vice Presidents) to run the daily business of the organization.

One of the main activities of FELASA is related to the establishment of Working Groups to issue and publish recommendations, guidelines, and reports on different areas of laboratory animal science. The topics addressed by the Working Groups can be proposed by the Executive Committee or by any constituent association and must be approved along with the Terms of Reference for the Working Group by the Board of Management. The Terms of Reference describe the context, aims, budget, and deadlines for the work. Once the Terms of Reference are approved, constituent associations may nominate

experts on the selected topic to be members of the Working Group. After review of the nominated candidates, the Executive Committee makes an official proposal on the composition of the Working Group to the Board of Management, where it is voted on and the final composition approved. There are no specific requirements for membership. The selection process is based on professional background and expertise. One of the members serves as the Convener of the Working Group and is responsible for organizing the work to comply with the proposed objectives, budget, and deadlines. The efforts of all Working Groups are coordinated by the FELASA Vice President for Working Groups.

Working Groups are expected to produce a report to be published. In most, but not all, cases, the original manuscripts are submitted to the *Laboratory Animals Limited* journal, which is the official journal of FELASA and several constituent associations. When reports cannot be published, they are made available on the FELASA and *Laboratory Animals Limited* websites (<http://www.felasa.eu>; <http://www.lal.org.uk/>). Since 1994, FELASA has produced and published reports containing recommendations and guidelines that have been of paramount importance in the development of several areas of laboratory animal science in Europe. Especially noteworthy are the sets of recommendations on health monitoring and education and training. The health monitoring recommendations, especially those dedicated to rodents, are followed by most rodent breeders and many user establishments to control and report the health status of the animals that are bred, supplied, and used in Europe. The education and training categories proposed by FELASA are widely followed by course organizers and have served as the basis of regulatory requirements for personnel working with laboratory animals in several European countries.

Because FELASA does not represent any government body or agency, its guidelines and recommendations are not regula-

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European Office, Association for Assessment and Accreditation of Laboratory Animal Care
International (AAALAC), Pamplona, Spain and FELASA former President.
Email: jguillen@aaalac.org

tory in nature, despite their wide adoption by the laboratory animal community in Europe. However, in some cases, FELASA recommendations have offered important guidance in areas not well covered by the European legal framework or complement existing legal requirements. The objective of these documents is to advance and coordinate the development of all aspects of laboratory animal science and practice in Europe and worldwide.

FELASA Recommendations on Health Monitoring

FELASA has published recommendations on health monitoring for several species including rodents, rabbits, cats, dogs, pigs, calves, sheep, goats, and nonhuman primates. The first publication focused on health monitoring of rodent and rabbit breeding colonies⁹ and prompted interest in this kind of FELASA recommendations. These recommendations soon were followed by those for rodent and rabbit experimental units.¹⁸ The European context was appropriate for beginning efforts on health monitoring recommendations: researchers and laboratory animal professionals became increasingly aware of the importance to control the health status of the animals used; state of the art animal facilities and equipment were being developed to improve animal biosecurity; and the transfer of genetically altered mouse strains between institutions was increasing. The effect of such recommendations, especially those for rodents, was dramatic. Despite initial reservations, the recommendations were adopted by the main breeders in Europe to control the microbiologic quality of their animals and to report the results to customers. In addition, many users started health monitoring programs based on the recommendations.

In this initial set of recommendations, a minimal frequency of monitoring of sentinel animals of every 3 mo was recommended. In addition to the observation of pathologic lesions, a list of bacterial, fungal, viral, and parasitic agents was recommended for monitoring. At that time, *Helicobacter* spp. were not included in the list, although they already were beginning to be observed as a pathologic agent in mice. The concept of a common health monitoring report was proposed. This proposed report form included historical results, latest results, the name of the laboratory performing the tests, and the method used. At a time when the use of SPF animals was becoming more popular, both breeders and users started considering the list of pathogens as an exclusion list. This limited interpretation has been usual for FELASA recommendations on health monitoring. However, these recommendations were intended to be flexible, and this flexibility was emphasized in the revision of the recommendations for rodents published years later.¹⁵

The revision included updates on new scientific knowledge on infectious agents (for example, *Helicobacter* spp., mouse rotavirus, mouse adenovirus, mouse and rat parvoviruses, and so forth) and diagnostic techniques. The revision also included a recommendation that the health monitoring program be tailored in the diverse environment of the experimental units, where needs might be influenced by research objectives, prevalence of specific agents, or applicable regulations. The use of different housing systems was considered, and the definition of 'unit' as a self-contained microbiologic entity was considered material to understanding and implementing the recommendations appropriately. Information on the importance of personnel and the use of biologic materials were discussed as part of an effective health monitoring program, including the appropriate use of sentinel animals, frequency of monitoring and sample size, test methods and samples, agents to be monitored, and (most importantly) reporting of the results. For this last purpose, ex-

amples of health monitoring reports were included in Appendix 3 of the publication, which is the part of the recommendations best known by laboratory animal professionals. The proposed frequency of the tests, which varied depending on the agent tested, was a new component to the proposed reports.

With the addition of new agents that are now identified in rodent colonies, such as norovirus, the list of agents included in these health monitoring reports currently is associated with the SPF concept in Europe and, as discussed earlier, is sometimes used as an exclusion list without taking into consideration many other factors. Poor reporting and too literal interpretation of the list of agents as an obligatory exclusion list may create problems related to the transfer of genetically altered strains among institutions, thus increasing expenses due to unnecessary rederivation processes and delaying the onset of research projects. FELASA recommendations on health monitoring should be interpreted in their entirety to implement an efficient program. These recommendations have represented a major advance in the harmonization of health monitoring and reporting in Europe and could serve as a model for global recommendations and harmonization: "given the increased significance of accurate health information when exchanging animals, research institutions and universities would benefit from universal standards, which would also help scientists and reviewers and readers of publications to better assess the validity of research results."¹³

The FELASA Board of Management is aware that new scientific knowledge is constantly produced and has therefore decided to periodically review and update the health monitoring recommendations. A Working Group is finalizing a new revision that could be published during 2012. To garner broader acceptance of the final document, this new version has considered input from an expert in the United States who has been contributing to the Working Group. This collaboration with an American expert is in accordance with the objectives of the recently created AALAS–FELASA Liaison Body, which is exploring areas of mutual benefit for laboratory animal science communities in both continents and ideally will produce joint recommendations in the future.

FELASA also has worked on health monitoring for nonhuman primates. FELASA has published reports on the sanitary aspects of handling nonhuman primate during transport²⁴ and on health monitoring recommendations for nonhuman primate colonies.²⁵ The first report focused on the potential risks of transmission of diseases between nonhuman primates and humans during transport and included a list of these transmissible diseases, but did not address the health monitoring of animal colonies. The health monitoring recommendations for nonhuman primates²⁵ addressed zoonotic concerns, animal health, and how animal health could influence research. The recommendations focused on the most commonly used species in Europe, including cynomolgus monkeys, rhesus monkeys, vervets, baboons, squirrel monkeys, and marmosets but did not include apes. Pathogenic and other undesirable microbiologic agents were listed, information related to nonhuman primate carrier species, disease symptoms, transmission, zoonotic potential, proposed testing frequency, proof of absence criteria, and eradication possibilities is included for all agents, and a sample health status report form based on the list of agents for each species is provided. A new Working Group is currently being established to revise these recommendations to reflect new scientific knowledge on pathogenic agents and diagnostic methods and to consider the harmonization of schemes in main breeders' geographic areas, especially taking into account upcoming requirements

in the European Union regarding the use of second-generation purpose-bred nonhuman primates.

Recommendations on the health monitoring of breeding colonies and experimental units of cats, dogs, and pigs¹⁹ and of experimental units of calves, sheep, and goats¹⁷ have been produced by FELASA. Although these documents are not as well known as those focusing on rodents, they follow the same pattern and represent a useful tool for harmonization of practices and standardization of reporting. Specific agents are listed by species, and the proposed health report form maintains the structure of including historical results, latest tests, and the laboratory and method used. The frequency of testing is less rigidly defined so that it may be adjusted to national disease control programs, but frequencies of 1 y for calves, sheep, and goats and 3 mo for cats, dogs, and pigs were recommended.

The Accreditation Board of Health Monitoring and Testing Laboratories. Since the publication of FELASA recommendations on health monitoring of rodent breeding and experimental colonies, breeders and users have implemented them with varying rigor. Regardless of the procedures used and the quality of local health monitoring programs, institutions have been using different terms to define their health monitoring programs with reference to the FELASA recommendations without external assessment of compliance with them. Terms such as ‘following,’ ‘based on,’ ‘in accordance with,’ and others have been used in past years. In one particular case, a health monitoring report used by a breeder was defined as ‘FELASA-approved,’ when in fact FELASA had never assessed or qualified, let alone approved, any particular health monitoring program or report.

The idea of promoting accreditation of diagnostic laboratories to ensure the quality of health monitoring reports had already been discussed and published by FELASA previously,⁶ but these guidelines referred to external accreditation systems, such as EN 45001 and ISO 25. Years later, the FELASA Board of Management decided to establish an Accreditation Board of Health Monitoring Programs and Testing Laboratories.^{14,16} The Accreditation Board currently evaluates health monitoring programs after voluntary application for accreditation. Official FELASA accreditation can be awarded to health monitoring schemes or laboratories if they conform to the quality standards described in the FELASA recommendations, as assessed by the Accreditation Board. Only health monitoring programs (related to defined microbiologic units) or diagnostic laboratories that have been accredited by FELASA are entitled to use the term ‘FELASA-accredited.’ More information on this Accreditation Board can be found at: <http://www.felasa.eu/accreditation-boards/accreditation-board-for-health-monitoring-programmes-and-testing-labor/>.

FELASA Recommendations on Education and Training

Education and training historically has been one of the main topics of FELASA activities and the area in which FELASA has had the most influence in Europe. Education and training requirements for personnel who care for or use laboratory animals and the actual implementation of education and training programs vary across Europe. FELASA recognized years ago the need for a universal and quality scheme of education and training that could serve as the common basis for these activities among all European laboratory animal professionals. This scheme would serve 2 main purposes: first, to promote quality education and training for all personnel based on both minimum requirements and competence, and second, to recognize

| Category | Description |
|----------|--|
| A | Persons caring for animals |
| B | Persons performing animal experiments |
| C | Persons responsible for directing animal experiments |
| D | Laboratory animal science specialists |

Figure 1. FELASA education and training categories.

professional competence among European countries and facilitate the mobility of professionals across Europe. Although different national requirements still exist, the FELASA scheme of categories A, B, C, and D (Figure 1) is widely recognized within the European laboratory animal science community; courses in many European countries follow the FELASA recommendations for all categories; and some countries follow the functional scheme in their legal requirements. This functional scheme is in agreement with the resolution of the Council of Europe of 1993 (http://www.coe.int/t/e/legal_affairs/legal_co-operation/biological_safety_and_use_of_animals/laboratory_animals/Res%20training.asp).

The first FELASA recommendations on education and training addressed categories A and C.²⁷ This document stated that the recommendations were based on functions rather than nomenclature, which may differ from country to country. The original recommendations for category A²⁷ (persons taking care of animals) included subdivision into 4 levels—level 1 was assigned to the more basic training and functions of laboratory animal care whereas level 4 focused on higher management or specialization. Levels 2 and 3 could be acquired with years of experience after level 1 was obtained. Personnel reaching level 4 could later qualify to apply to category D, which applied to specialists in laboratory animal science. Activities, responsibilities, and teaching syllabus for each level were described in detail.

A new Working Group critically assessed the 1995 recommendations and delivered a revised and simplified educational concept for category A²⁶ that completely replaced previous recommendations. The new recommendations are more flexible to facilitate adoption of this scheme by national educational systems in a step-by-step manner. The revised recommendations offer the possibility to enter the system through a short introductory course (theoretical and practical) to reach category A0. The learning topics of category A0 include hygiene and supplies, husbandry, safety, and ethics and legislation.

This introduction is followed by experience, education, and regular assessments of competency to reach category A1, which represents a comprehensively educated laboratory animal technician with theoretical background knowledge and practical skills. The desired learning outcomes demonstrated by a category A1 person include knowledge and practice of: basic biology of frequently used laboratory animal species; housing and care; animal handling; care and husbandry; nutrition; breeding; animal facility routines; disease prevention and control; euthanasia; environment; safety; legislation/ethics; animal welfare; and additional topics such as computer skills.

After a similar process (Figure 2), category A2 is achieved after gaining deeper knowledge and expertise in the areas listed for category A1, as well as in communication and information technology, animal health, and disease prevention and control. Category A2 personnel also have basic supervisory and basic managerial skills.

| | Level | | |
|--------------|-------------------------------|---------------------------------|---------------------------------|
| | A0 | A1 | A2 |
| Prerequisite | School education | A0 level | A1 level |
| Duration | 30 h | 1 y minimum | 1 y minimum |
| Education | 20 h theory; 10 h practice | 200 h theory; 200 h practice | 200 h theory; 200 h practice |

Figure 2. FELASA education and training timelines for category A levels.

The initial proposal of the Working Group in charge of the revision of category A did not include the A0 level, which would have generated problems in countries with less developed education and training systems. Several FELASA constituent associations raised this concern, and after much debate, the Board of Management subsequently established an introductory education and training level (later called A0) to allow for easier recruitment of personnel. This debate and the final decision, which was the establishment of the A0 level, are excellent examples of how laboratory animal practices can be harmonized internationally when, first, all parties have the same aim and, second, when they opt for a positive approach to address the differences.

With regard to category C personnel (those responsible for directing animal experiments), the 1995 recommendations²⁷ included a scheme still in use in many education and training programs across Europe. These recommendations have 2 basic pillars. First, persons responsible for directing animal experiments should hold a full university degree in a biomedical discipline such as (animal) biology, medicine, or veterinary medicine. Second, these persons should complete a basic course of not less than 80 h that addresses at least the 8 main topics listed and described in the syllabus of the 1995 recommendations:²⁷ biology and husbandry of laboratory animals; microbiology and disease; health hazards and safe practices in the animal house; design and conduct of animal experiments; anesthesia, analgesia, and experimental procedures; alternatives to animal use; ethical aspects and legislation; and analysis of scientific literature. The courses should be concluded by an examination or other form of assessment of the competence obtained. The concept of competence is particularly important in the FELASA recommendations, and it has also been recognized in Directive 2010/63/EU.²² Thousands of researchers have attended courses that adhere to these recommendations in many European countries and generally have appreciated both the theoretical and practical components of the courses.³ In addition, some national competent authorities may currently acknowledge the curriculum of researchers who have attended courses in other countries.

The following FELASA recommendations on education and training focused on category D (specialists in laboratory animal science) and were published in 1999.¹⁰ FELASA realized that the applicable Directive at that time (Directive 86/609/EEC)⁵ made reference to a 'competent person' who would be responsible for the health and welfare of the animals but that no clear definition of the necessary competency was given. Pursuant to the concept of competence already used in the previous recommendations on education and training, the Working Group defined the competence of a specialist in laboratory animal science after acquiring appropriate qualifications and experience. The defined areas of competence include management, animal health and welfare, assistance to researchers, law compliance, educational programs, and participation in research. Category

D persons are anticipated to hold a degree in biomedical or veterinary sciences so that the specific educational program would be at a postgraduate level, with a minimal duration of 2 y. The recommendations provide a detailed curriculum for the coursework desired, at the end of which competency is assessed by some kind of examination. Furthermore, these recommendations include mention of the concept of accreditation of courses, to harmonize specialist education in Europe. The work of this Working Group led to the establishment of the Accreditation Board of Laboratory Animal Education and Training, which is described in following paragraphs. In addition, an initiative of the European Society of Laboratory Animal Veterinarians (ESLAV) led shortly afterward to the creation of the European College of Laboratory Animal Medicine (ECLAM), which offers further specialization in laboratory animal science. The common interpretation within the European laboratory animal science community is that FELASA category D is considered a basic requirement for a laboratory animal specialist and that the ECLAM diploma represents additional voluntary specialized training.

The FELASA recommendations for category B (persons carrying out animal experiments) were published in 2000¹² with the same aim of enhancing consistency of the definition of competence and facilitating universal recognition of acquired skill and knowledge sets through harmonized and mutually acceptable criteria. These recommendations describe the duties in which category B personnel are trained and provide a detailed curriculum based on 7 areas: legislation, ethics and the '3Rs,' the basic biology and husbandry of relevant laboratory animal species; assurance of the physiologic needs and welfare of animals without compromising scientific integrity of the investigation or procedure; animal handling techniques; conduct of basic techniques and euthanasia; recognition of lack of wellbeing and other complicating factors; anesthesia, analgesia, and basic principles of surgery; and occupational health and safety. Although these category B recommendations stress the concept of acquired competence compared with a specific duration of training, they also assume that a typical a course of 40 h, half of which were practical in nature, is sufficient to establish a basic level of competence. This particular recommendation has resulted in many category B courses in Europe being 40 h long. This duration may seem short as compared with that of the recent revision of category A recommendations,²⁶ which propose much longer periods of training to achieve category A levels. Regardless, the category B recommendations clearly state that "no award recognizing competence should be granted without a thorough evaluation of the candidate"¹² and that practical skills, perhaps even more than theoretical knowledge, must be assessed. To be universally accepted within Europe, the diploma should explicitly describe both the theoretical and practical elements of competence achieved.

The Future of FELASA Recommendations on Education and Training. Article 23 of Directive 2010/63/EU²² identifies those

persons requiring education and training and lists a set of elements in Annex V for which minimum requirements should be established by Member States. FELASA has realized that implementation of the Directive offers a unique opportunity to establish a harmonized framework across Europe that assures the competence of all persons involved in laboratory animal experiments. Achieving this goal is a major challenge, because at the level of the European Union, only nonbinding guidelines may be adopted, and the Member States will have to devise and publish minimal requirements with regard to education and training and those for obtaining, maintaining, and demonstrating requisite competence. Because the 4 different functions listed in the article 23 of the Directive (carrying out procedures on animals; designing procedures and projects; taking care on animals; killing animals) do not correspond exactly with the FELASA education and training scheme, Member States might develop individual schemes to meet those specific roles unless FELASA offers a revised system that can be generally accepted and that facilitates harmonization and mutual recognition. After having evaluated this situation, and because FELASA categories contain all the elements to meet the requirements of the Directive, FELASA established a Working Group in cooperation with the European Federation of Animal Technology (EFAT) to develop a new education and training scheme that will allow for more flexibility, proportionality, and availability. An important feature of this scheme is its modular nature, which facilitates tailoring to the specific needs of persons, institutions, the species used, and the research being conducted. The draft scheme is already serving as the basis for the ongoing discussions of the Expert Working Group established by the European Commission to develop an education and training framework within the European Union which would assure the competence of staff caring for or using animals in procedures and facilitate the free movement of personnel within the European Union.

The Accreditation Board of Laboratory Animal Education and Training. Once recommendations for all categories were published, FELASA set up a Working Group to establish the structure and recommendations for accreditation of education and training programs. The published recommendations on education and training did not address the qualifications of the educators and the actual quality of the education. Furthermore, as occurred with health monitoring programs, course organizers had begun to claim that courses were conducted ‘following’ or ‘in accordance’ with FELASA recommendations, when in fact compliance was not being assessed externally. The use of terms such as ‘following,’ ‘in accordance,’ and other similar terms does not necessarily mean that the courses are accredited. The FELASA recommendations for the accreditation of laboratory animal science education and training¹¹ describe the scope and requirements for accreditation of education and training programs. The accreditation process includes instruction on how the accreditation should be maintained and describes the structure of the Accreditation Board in charge of the process. The Accreditation Board on Laboratory Animal Education and Training was approved by the FELASA Board and Management and started accrediting any programs or courses that voluntarily requested accreditation. Only programs or courses that undergo this process, which involves a site visit, and obtain accreditation are entitled to use the term ‘accredited by FELASA.’ More than 20 courses in 10 European countries and representing all of the FELASA categories have been accredited by FELASA. All future FELASA recommendations on education and training will coordinate with this accreditation system, which is

playing an important role in the harmonization of education and training programs across Europe. Moreover, as stated in the published document, “FELASA is committed to working globally to secure mutual acceptance of this accreditation system with assured programs offered by comparable bodies, so as to assist with the development of an internationally recognizable training program.”¹¹

The current recommendations for FELASA categories A and B and the training programs for achieving ALAT, LAT, and LATG certification were compared and discussed during the 2011 AALAS Meeting at the session organized by the AALAS-FELASA Liaison Body. More information on the Accreditation Board can be found at <http://www.felasa.eu/accreditation-boards/accreditation-board-for-education-and-training1/>.

Continuing Professional Development. The FELASA recommendations for all education and training categories are updated regularly; the legislation also requires institutions to ensure that personnel are competent and trained continually. FELASA is aware that laboratory animal science professionals are expected to seek continuing professional development to learn and implement new scientific knowledge and regulatory requirements.

A FELASA Working Group on continuing professional development was established to produce guidelines for continuing education for persons involved in animal experiments. The Working Group produced a report available through the FELASA website (http://www.felasa.eu/media/uploads/Guidelines%20for%20Continuing%20Education%20of%20Animal%20Technologists_%20final.pdf). The Working Group used the results of a questionnaire distributed to constituent associations, which evidenced that half of them did not have any type of continuing professional development program in their respective countries. One of the aims of this report is to harmonize the principles of continuing professional development across Europe so that they can be adapted to each territory. The first principle in the document recommends that all people working with animals (FELASA categories A, B, C, and D) should have and maintain state-of-the-art knowledge and skills. Second, continuing professional development should be available and organized in a flexible way. The third principle recommends that continuing professional development should commence when a person starts working with animals and continue through the working career. The fourth principle bases the continuing professional development scheme on the awarding of credits over a certain period. For example, the number of credits can be averaged over a period of as long as 5 y, and all participants need to achieve a minimal number of credits (likely with 1 credit being equal to 1 h) during that period, depending on their category: category A, 5 credits annually; category B, 10 credits annually; category C, 15 credits annually; category D, 20 credits annually. The fifth and sixth principles refer to the review and evaluation of continuing professional development activities and the operational scheme. For this purpose, 3 levels are proposed: accreditation (the strictest), endorsement, and recognition. Accreditation can be awarded only by FELASA; endorsement by other recognized third parties, such as constituent associations or competent authorities; and recognition by local management. The seventh principle encourages communication among countries. If these principles were implemented similarly in all countries, obtaining mutual recognition of the adapted national continuing professional development schemes would be facilitated. Examples of how activities such as lectures and meetings could be endorsed or recognized are included as an appendix.

Other FELASA Guidelines and Reports

Report on Ethical Evaluation of Animal Experiments. Before the publication of Directive 2010/63/EU,²² the European legal framework contained no specific requirement for prior ethical review of proposed animal studies, although such a requirement existed at national or regional level in some countries. At the time that a Technical Expert Working Group was advising the European Commission on how to address the needed ethical review in the new Directive, FELASA established a Working Group to provide unified guidance on the best manner in which to conduct the ethical review process across different institutions and countries in Europe. The Working Group produced a full report (http://www.felasa.eu/media/uploads/Principles-practice-ethical-review_full%20report%20.pdf) that was summarized for publication.²¹

The report on ethical evaluation of animal experiments describes and explores a set of principles for the conduct of ethical review of laboratory animal use. It also presents the results of a questionnaire that was distributed to the countries represented in FELASA and that queried what approaches to ethical review were taken in these countries. The questionnaire showed that the ethical review processes existing at that time in Europe were performed either at the national, regional, institutional, or even individual level or by combinations thereof. The accumulated experiences obtained from the different approaches being performed across Europe are the foundation of these recommendations. The report proposes and describes 30 recommendations to implement an appropriate ethical review process. These recommendations include the definition, scope level and quality of the ethical review, the organization, the initial and ongoing review, the participants and the relation with the legal requirements.

The initial recommendation states that “ethical review should aim to ensure that, at all stages in scientific work involving animals, from initial planning, to completion of the studies and review of the outcomes, there is adequate, clearly explained ‘ethical justification’ for using animals, which is subjected to ongoing, critical evaluation.”²¹ This evaluation should consider a harm–benefit analysis and the implementation of the 3Rs. Other recommendations propose that the ethical review should be mandatory for all animal use, be an ongoing process, and have sufficient authority to intervene (that is, stop animal experiments) when authorizations are exceeded or unexpected events that affect animal welfare occur.

With regard to the organization of the process, a combination of local elements and an overarching external (either regional or national) process is recommended. Local elements would ensure that the review can be responsive to local factors, and the overarching process would act as an independent monitor of the performance of the local processes and as a body to which local processes can refer difficult cases. With regard to the participants in the ethical review process, the involvement of reviewers with a wide range of expertise is recommended, including specialized veterinarians and animal care staff, scientists, and lay persons. In addition, the concept of a ‘culture of care’ as another outcome of the ethical review process is highlighted. In this regard, the recommendation suggests that the ethical review process should not be limited to the review of research proposals, but that it should also serve as a tool to influence the ethos of the whole institution with regard to the care and use of the animals.

Several FELASA recommendations parallel articles in the new Directive. For example, recommendation 8 proposes that the initial ethical review be performed at the project level and sug-

gests that review occur at least every 5 y. Several articles of the Directive (36 to 45) mandate the evaluation and authorization of projects and state that authorization will last 5 y. Recommendation 13 requires a harm–benefit analysis, as does article 38 of the Directive. Also, recommendation no. 18 discusses the usefulness of including nontechnical summaries, which are required in article 43 of the Directive.

As in earlier versions of FELASA recommendations, one of the recommendations (no. 30) focuses on international harmonization and considers it “vitaly important that efforts be made to develop common ethical goals and outputs as well as common processes of ethical review both within and between countries.”²¹ The report may serve as guidance to institutions both within and beyond Europe regarding the implementation of ethical review processes that exceed applicable legal requirements.

Guidelines for the Veterinary Care of Laboratory Animals. FELASA has a close relation with other European organizations such as ECLAM and ESLAV. When FELASA was considering a Working Group on veterinary care, it seemed natural to seek the collaboration of these veterinary organizations to produce a joint report, which subsequently was published as *The Guidelines for the Veterinary Care of Laboratory Animals*.²³ Veterinarians are an essential component of successful animal care and use programs. Although other competent persons have responsibilities regarding animal care and use, veterinarians are undoubtedly the most appropriate to bear the ultimate responsibility for the veterinary care of laboratory animals. The European legal framework acknowledges and requires the role of the veterinarians in laboratory animal care, but in many cases this role is advisory in nature, and few details or requirements regarding inclusion of a program of veterinary care are provided in the regulations. In addition, the authority granted through regulations to laboratory animal veterinarians differs across Europe, sometimes negatively affecting the involvement and activities of veterinarians in the animal care and use program. Lack of regulatory support should not curtail the level of authority and involvement of veterinarians in the institutional animal care and use program. This joint report is aimed not only at veterinarians but also at employers and regulators.

The report on veterinary care acknowledges that medical care takes up a relatively small proportion of the laboratory animal veterinarian’s time and that adequate veterinary care encompasses several activities: those related directly to animal welfare (transportation, health monitoring and management, husbandry, environmental enrichment, surgery, anesthesia, analgesia, and euthanasia); scientific activities; regulatory and administrative compliance (including ethical review process); and education and training of personnel. The following topics are discussed in the report: educational requirements and competencies; animal health and welfare aspects; veterinary care of animals undergoing procedures; regulatory and ethical aspects; and managerial aspects and occupational health and safety.

With regard to the proposed education requirements for laboratory animal veterinarians, the FELASA category D competence, and additional specialization through ECLAM and continuing professional development programs, is recommended. The animal and welfare part reviews the activities in which the veterinarian should be involved when managing animal colonies: introduction of animals; disease prevention; health monitoring, attention to diseased or injured animals or to those having harmful genetic modifications; and medical records. The veterinary care of animals undergoing procedures applies to habituation of animals, training of personnel

performing experiments, refinement of procedures, anesthesia and analgesia. The importance of the involvement of the veterinarians in the surgical program and perioperative care is also stressed. Advice, training, and oversight regarding euthanasia procedures and the control of drugs also are considered to be functions of the veterinarian.

The report reviews the different levels of authority and responsibilities given by the European regulations to laboratory animal veterinarians and considers it necessary that veterinarians have access to all research protocols and participate in regular visits to the animal facilities to inspect animals and their accommodations and to assess animal health and welfare. Keeping inspection and medical records should be another responsibility of the veterinarians. Finally, veterinarians should acquire skills and be involved in managerial activities that affect the overall program, such as facility planning, design and management, occupational health and safety, training of personnel, and emergency plans.

At a meeting during the 2007 FELASA and ICLAS Symposium, international representatives described and discussed similarities and differences between these FELASA guidelines and other documents on veterinary care from around the world.²⁸

Report on the Evaluation of Quality Systems for Animal Units.

Although some institutions seek to comply with minimum legal requirements only, the introduction of the report of the FELASA Working Group on the evaluation of quality assurance systems states “an increasing number of them are seeking to progress beyond them and to benchmark the provision by reference to an external standard.”⁷ The successful development of quality systems in laboratory animal units improves the standards of animal care and use, facilitates implementation of the 3Rs, and improves the quality of the scientific results. The Working Group on evaluation of quality systems for animal units reviewed and compared 3 systems that are used internationally and are applicable to institutional laboratory animal care and use programs: Good Laboratory Practice guidelines, ISO 9000:2000, and AAALAC International.⁷ The report of this group summarizes the characteristics of each system, describes the strengths and weaknesses of each, and compares them with regard to the following points: principal focus, applicability, animal welfare and law, external consideration, internal quality assurance, working processes, inspection, direct costs, ongoing costs, flexibility, bureaucracy, resources, standards and applicability, and subjectivity.

The main difference in these systems is related to the focus of the quality assurance process: “AAALAC principally addresses the quality of the broad environment within which animal care and use takes place; Good Laboratory Practice addresses the reliability and reproducibility of experimental data which is generated by the use of animals; and ISO 9000:2000 focuses on customers, the persons to whom the animals and their products or services are provided.”⁷ The Good Laboratory Practice process was considered the most bureaucratic. AAALAC accreditation includes both animal care and use in research and deals directly with animal welfare, in contrast to ISO 9000:2000 and Good Laboratory Practice, which focus principally on customer satisfaction and specific studies, respectively. Another difference identified was related to the voluntary or obligatory nature of the processes: Good Laboratory Practice is obligatory for certain studies, whereas AAALAC and ISO 9000:2000 are voluntary. The report on these quality evaluation systems recommended that the implementation decision should consider that “ISO is primarily a business-independent

management tool to master and optimize the business, aiming at implementing ‘customer satisfaction’; AAALAC is primarily a peer-reviewed system which evaluates the organization and practices in a laboratory animal facility for adequate use of animals, safeguards for animal well-being (‘state-of-the-art’ housing, techniques, etc.) as well as health and safety risks to staff, and emphasizes the concept that quality animal care and use yields quality scientific data; and Good Laboratory Practice is a legally defined system for institutes and companies which have to be ‘GLP-compliant’.”⁷

The report concludes that “applying one or more of these three quality standards in an animal unit will, in principle, be of benefit as they improve scientific working methods and animal welfare.”⁷ In fact, the systems described can perfectly coexist because of different needs and interests at a single institution. This may happen, for example, at institutions performing preclinical regulated studies (Good Laboratory Practice), manufacturing goods or producing animals (ISO 9000:2000), and voluntarily willing to promote humane treatment of animals by improving all areas of the animal care and use program (AAALAC). At the time the report was produced, FELASA discussed the possibility of creating a European system of accreditation, but this idea was rejected due to the existence of a specialized international organization such as AAALAC International. FELASA has been a member of the AAALAC International Board of Trustees since 1998.

Report on the Production and Nomenclature of Transgenic Rodents.

The increase in the use of transgenic rodents during the last 30 y has had a dramatic effect on both science and laboratory animal practices. Transgenic strains shared between institutions often lack appropriate information on the characteristics of the strains, and, as stated in the FELASA guidelines for the production and nomenclature of transgenic rodents,²⁰ “many publications, especially on transgenic rodents, still use vague and inappropriate strain designation.” The outcome is that in some instances scientists may not know the specific strain actually used in certain experiments. The use of standardized, effective nomenclature system is essential if investigators are to understand, accurately interpret, and communicate findings resulting from transgenic animals. The aims of this FELASA report were to “raise awareness about specific features of production and of current nomenclature systems used for transgenic rodents” and to “highlight the limitations of current nomenclature systems to encourage the development of a more robust classification scheme.”²⁰

To achieve these aims, this report first overviews the characteristics of the different type of mutations: spontaneous mutations; chemically and physically induced mutations; transgenic animals; and conditional mutagenesis. The second part reviews the importance of the genetic background of transgenic rodents, recommends the use of inbred or F1 hybrid backgrounds, explains when and how a change of background is recommended, and highlights the importance of regularly monitoring the background to detect any genetic contamination. Third, for the reasons presented earlier, the report focuses on the nomenclature of transgenic rodents. The existing sources for nomenclature guidelines are shown, giving particular importance to the Jackson Laboratory Mouse Genome Database (www.informatics.jax.org) and the Rat Genome Database (<http://www.rgd.mcg.edu/>). The report then describes the standardized nomenclature rules that should be used and propose the use of a strain data sheet to be associated to the use, transfer, and stock of transgenic strains. This strain data sheet should be sent to user laboratories and central repositories and includes

12 questions related to the name, mutation, protocols (genetic, breeding, husbandry), and health status of the animals.

In the conclusions, the report on transgenics and nomenclature recognizes that "the nomenclature of very complex genetic modifications, such as occur in double or multiple mutants, was still challenging and sometimes not compatible with line management databases."²⁰ Similarly, "the nomenclature of transgenic rodents developed by reproductive cloning, i.e., transfer of the nucleus of in vitro mutated somatic cells into enucleated oocytes, remained to be defined."¹⁷ Nevertheless, in all such cases "the information necessary to describe such complex genotypes should be documented in a way that is available and understandable by scientific colleagues."²⁰

Report on Standardization of Enrichment. Since environmental enrichment for laboratory animals was introduced in the 1980s, considerable progress has been made concerning the knowledge about and the introduction of environmental enrichment as part of laboratory animal care and husbandry. When the Terms of Reference for this Working Group were defined, FELASA knew the text of the draft of the revised Appendix A of the ETS 123,⁴ which contained numerous recommendations on enrichment for all species. However, implementation of environmental enrichment is variable and adopts many different forms. In addition, the effectiveness, implementation procedures, cost, and research implications of environmental enrichment remains a topic of much discussion.⁸

A FELASA Working Group was established with "the goal to provide guidance on how to standardize enrichment in laboratory animal enclosures such that essential species-specific needs and individual needs of gender and life stage are fulfilled to guarantee animal welfare while at the same time minimizing interference with experimental results."² The Working Group focused on the concept of harmonization compared with standardization, so that their efforts would not be limited by future innovation in environmental enrichment, and on formulation of "principles intended as guidance, as a navigation tool for the future development in this particular area of animal welfare."²

The first chapter of this report comments on the principles of environmental enrichment and their harmonization, to facilitate understanding of the key question, of how enrichment can benefit animal welfare and what needs to be kept in mind when aiming at the harmonization of enrichment. The report acknowledges that "it is not necessarily true that an environmental enrichment strategy should be aimed at letting the animal express as much as possible of its natural behavioral repertoire"² but that it should instead focus on the possibility for the animal to respond in a species-typical manner to a series of stimuli provided in captivity. The report also states that "a basic principle to be taken into account is that the behavior of the species used in laboratory settings evolved in complex environments, characterized by a certain degree of predictability, and on which they can exert a certain degree of control. Therefore, complexity, predictability, and control are three concepts to bear in mind when applying an environmental enrichment strategy."² By knowing the natural history of the species, animal welfare can be increased by introducing enrichment that gives the animal the possibility to select a behavior of its repertoire, especially if the animal has some control on the frequency and use of the introduced enrichment. The reports recommends that when trying to harmonize enrichment features, social enrichment should have priority, always considering that animals are given some degree of control over it (for example, possibility to hide or escape from dominant individuals). Ideally,

a harmonized combination of social and physical enrichment should be provided.

The next chapters of the report explain the principles of the evaluation of environmental enrichment, and comment on validity and variability. Several ways to assess the effect of environmental enrichment are described, including the comparison of behavior between enriched and home cages, the use of behavioral tests, and the measure of physiologic parameters. Evaluation of potential interference of environmental enrichment with experimental research is considered also, and the use of enrichment items in regulatory studies that have been certified previously is recommended.

The report on enrichment practices discusses the abnormal behaviors induced by unenriched environments and the effects of enrichment on variability of results and experimental bias. It recommends that "enrichment should be designed with the species' needs in mind taking into account strain, age (pups or senescent animal), and health of the animals including sensorimotor capability and the history of the animal" and that "different enrichments have different stimulatory effects on different nervous pathways."² In the development of a practical enrichment program, the needs of the species must be understood first. Then existing literature on enrichment recommended for the species must be evaluated. The enrichment's potential effect on experimental variables must be weighed, so that an enrichment program that considers both social and environmental factors can be selected.

The decision tree for assessment of new enrichment ideas would start with the question whether the proposed enrichment is an extension of a proven enrichment concept. If the answer is no, expert advice from welfare experts should be considered. If the answer is yes, whether an ad hoc study is necessary to validate it for efficacy, safety, and lack of experimental effect should be addressed.

The next chapter of the report describes types of enrichment: social (contact and noncontact) and physical (complexity, sensory, nutritional), and gives examples of species specific environmental enrichment. Social enrichment is recommended as default for gregarious species, and examples of additional physical enrichment (mainly based on nesting, bedding, and gnawing materials) for rodents, rabbits, nonhuman primates, dogs, pigs, and minipigs are provided.

Another chapter reviews practical points to consider when implementing environmental enrichment programs: interaction with experiments (also discussed previously); potential increase in workload for staff; attention to occupational and safety aspects; financial aspects; Good Laboratory Practices implications (certification, standardization, and validation of enrichment are particularly important for these types of studies); training of staff and communication to researchers (who typically are concerned with changes in study protocols); unwanted side effects on animal welfare (for example, aggressive behavior, accidents, toxic compounds); observability of animals (made more difficult, depending on the use of some materials); changes of enrichment program after animal transfer (information on enrichment programs should be communicated); and reporting of enrichment program in the Methods section of scientific publications (recommended).

The report on standardization of enrichment for laboratory animals ends with a set of 7 conclusions and recommendations. The first conclusion acknowledges the complexity of this issue. The second refers to the principles discussed previously (that is, animal physiologic and behavioral needs; complexity control and predictability; knowledge of natural history of species).

The third states that scientific evaluation of the effect on animal welfare is needed. The fourth places the benefits of working with more 'normal' animals (rather than with animals that show abnormal behaviors) over the potential increase in variability of results. The fifth recommends a systematic approach for the design of enrichment programs. The sixth states that the use of performance standards when applying the enrichment principles is the only way to address the complexity of the issue. The seventh recommends improved study, review, and communication of applied environmental enrichment programs.

The new Directive 2010/63/EU²² (published after this FELASA report was produced) mandates the implementation of enrichment programs appropriate to the species. The concepts of this Working Group report may help not only European institutions in their compliance with the Directive, but also any institution worldwide that may be considering the development of enrichment programs.

Report on Pain and Distress in Laboratory Rodents and Lagomorphs. The minimization of the pain, distress, and suffering of laboratory animals is a legal and ethical imperative.^{5,22} To that end, laboratory animal professionals must know how to define, identify and categorize pain, distress, and suffering. The first section of this report, which was published in 1994,¹ defines pain, distress, and suffering. Following sections are focused on the mechanism of pain, measurement of analgesia, and sensitivity of tissues and organs to pain. The effects, sources, and signs of pain and distress are each addressed in separate sections. The legal obligations in Europe with regard to pain and distress in laboratory animals that were in effect at publication time are described in another section. The last section focuses on the grading of the severity of pain and distress.

One of the main conclusions stated by the Working Group is the need for a relatively simple means of accurately grading the levels of pain and distress, a means that can be applied to the wide range of circumstances and procedures used in animal laboratories throughout Europe by animal care specialists, technicians, and scientists. Although this report is one of the first produced by FELASA (it was approved by the Board of Management in 1992), the conclusions are still valid. Directive 2010/63/EU²² has established a simple classification of severity of procedures that includes 4 categories: nonrecovery, mild, moderate, and severe. This legal classification and its implications with regard to other legal requirements in the Directive (that is, retrospective assessment of severity and statistical reporting) is prompting the European laboratory animal community to become proactive in offering guidance on harmonization of criteria. FELASA is taking a leading role in this process (described further in the following section).

Reports in Progress

At any time, FELASA has several Working Groups at different stages of report preparation. At present, 9 Working Groups are active, discussions are ongoing with regard to the potential establishment of 2 additional Working Groups, and the process of establishing 2 joint Working Groups with AALAS (on health monitoring for rodent transfer and on harm-benefit analysis) is well advanced. The number of active Working Groups is relatively high due to the activity initiated through the publication of Directive 2010/63/EU.²²

Reports on Animal Identification and Genotyping Methods. Two different Working Groups are focused on systems for identifying individual animals and on guidelines for refining the methods for genotyping genetically modified rodents. Because animal identification and the collection of samples

for genotyping can in some instances be achieved through a single technique, the progress and contents of the reports of these two Working Groups have been interrelated. Both reports have been finished and are awaiting consensus and approval by the FELASA Board of Management. Methods of identification, collection of samples for genotyping, and genotyping techniques are reviewed and described and recommendations on their use are offered.

Reports on Classification of Severity and Retrospective Assessment of Severity. Directive 2010/63/EU²² classifies the severity of procedures into 4 categories: nonrecovery, mild, moderate, and severe. Because one of the aims of the Directive is the harmonization of practices within the European Union, the interpretation of the severity classification must be applied uniformly in all Member States. During the final process of the Directive, the European Commission established a Working Group to produce assignment criteria for this classification scheme. FELASA and other European organizations were represented in the Working Group, and Annex VIII of the Directive is based on that work. However the opinion of FELASA is that the examples given in Annex VIII are limited, have little descriptive power to aid assignment, and relate to the procedure itself rather than to assessment of the outcome (for example, adverse effects) of the procedure. The Directive also contains a requirement for retrospective assessment of all projects categorized as severe, and that Member States shall collect and make publicly available, on an annual basis, statistical information on the use of animals in procedures, including information on the actual severity (rather than the assigned category) of the procedures. Only 2 European countries currently collect such information, and the remaining countries have no experience in this type of information collection. In cooperation with ESLAV and ECLAM, FELASA established 2 Working Groups that are working in concert with each other. The Working Group on severity classification is expanding the examples of Annex VIII to provide guidance and harmonization on the assignment of severity categories. The Working Group on retrospective assessment is evaluating the feasibility of a pilot scheme tested in the United Kingdom and is proposing a scheme of retrospective assessment of severity that can be incorporated by all Member States. Both Working Groups are striving to produce guidance reports that will be useful in the incorporation of the Directive into the legislation of Member States, a process that must be finalized by November 2012.

Report on Education of Students of Life and Medical Sciences. The use of animals in education and training of students is ethically controversial. A Working Group was established to: identify theoretical and practical methods of training in laboratory animal science and the 3Rs that are offered currently in life science and medicine faculties in Europe; assess the systems in place at these faculties; recommend minimal and maximal requirements for students that likely will work with directly animals as well as those for students that, to satisfy the criteria for earning a Bachelor or Master of Science degree, need only a basic understanding of animal methods and techniques without personal practical experience; and suggest an optimal time point to teach the 3Rs concepts so that a '3Rs ethos' is instilled in students before they become involved in performing in vivo animal studies. An additional goal of this final objective is to foster acceptance of the proposed type of education. The report is finished and should be published soon.

Revision of Education and Training Recommendations toward Directive 2010/63/EU. The scope of this work was explained

earlier in this article, in the section *The Future of the FELASA Recommendations on Education and Training*. FELASA is well situated to develop a strategy to deliver a harmonized system that could be adopted across Europe in accordance with the new Directive. The European Commission has established a Working Group on this subject, and the FELASA-EFAT draft document is serving as the basis for the discussion.

Glossary of Clinical Signs. Except in toxicology research, the use of glossaries of clinical signs is not customary. Animal wellbeing must be overseen daily, and any clinical abnormalities must be reported. Furthermore, in case of a breeding program or study, specific signs must be observed in a systematic way. In addition, some signs indicate a severe condition and are critical for the application of the principles of humane endpoints. In the opinion of FELASA, the introduction of a 'glossary of clinical signs' would greatly improve the reporting and follow-up of clinical pathology, the phenotyping of mutant animals, and the precise definition and application of humane endpoint criteria. This report is finalized and expected to be published soon and includes a review of existing documentation, a proposed glossary of clinical signs with definitions, explanations and background, and some examples of practical means for the registration of clinical signs.

Revision of the Recommendations on Health Monitoring of Rodents. As mentioned previously, FELASA is continuously updating this type of recommendations for rodents. The revision continues to attempt to balance responses to new developments, as scientific knowledge evolves, with individual and local needs. The revised recommendations for the health monitoring of rodents will be the basis for accreditation of health monitoring schemes and likely will suit this purpose. The Working Group receives input from a specialist from the United States, whose participation may facilitate the worldwide harmonization of these practices.

Report on Zebrafish Care and Use. This recent Working Group is a joint effort with the European Cooperation in Science and Technology (COST) Action EuFishBioMed. The zebrafish (*Danio rerio*) has become a very popular and useful animal model in recent years. Many research institutions are adapting facilities and educating personnel to work with this species, which differ in many ways from traditional species. Information in the literature that can help professionals at research institutions to cope with this new challenge currently is not easy to find. In addition, zebrafish are subject to a number of diseases, which may affect experimental results, be zoonotic, or both. The increasing traffic of zebrafish between institutions has increased the spread of disease in the same way as with genetically modified mice, and the need for management of disease spread through effective sanitation and quarantine and rederivation strategies is pressing. The Working Group has been charged to review available information, issue guidelines on basic housing and husbandry of zebrafish, and recommend health monitoring programs that address their natural diseases and zoonotic risks. FELASA expects that the resulting recommendations will become a most useful document for personnel caring for and using zebrafish as an animal model.

Conclusion

This review demonstrates the quality and importance of the work FELASA is doing for laboratory animal science in Europe. The FELASA Working Groups represent the main force of FELASA, and their reports, provided in the form of recommendations or guidelines, are followed widely across Europe. The documents are produced by recognized specialists

from the countries with representation in the FELASA Board of Management. The combination of contributors with different areas of expertise within each Working Group ensures the high quality and utility of the reports. Although FELASA reports are not regulatory, because FELASA does not represent any particular governmental body, they have influenced legislative developments in European countries. In this particular time of change in the legislative European framework, the European Commission is relying on the FELASA expertise to harmonize the transposition and implementation of the new Directive. In addition FELASA has increasingly developed collaborations with other European organizations such as ECLAM, ESLAV, EFAT and COST over the last several years, and this cooperation is now being extended to non-European organizations such as AALAS. These collaborations will increase the international acceptance of future reports. FELASA recommendations and guidelines, produced within the complex and diverse European environment, emphasize that good laboratory animal science has no frontiers. They are an example of what might be achieved at a global level should diverse international organizations join efforts for the benefit of the animals used in research and, as a consequence, of the quality of research. The recently created AALAS-FELASA Liaison Body is one such initiative that hopefully will result in future recommendations and guidelines that are accepted globally. Furthermore all FELASA reports result from the enthusiasm and dedication of many laboratory animal professionals, who have always worked on a voluntary basis.

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