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Abstract

Brazil has an exceptionally dynamic research sector in Latin America in health, biotechnology, and pharmacology, backed by defined government policies on science and technology and a health research agenda focusing on important neglected diseases: malaria, leishmaniasis, Chagas disease, turberculosis, leprosy, and dengue. The Brazilian health research policy promotes partnerships and networks among scientists in academic institutions in both wealthy industrialized and disease-endemic countries, and in these efforts the government's guidelines for animal use in biomedical research are considered fundamental to guarantee both animal welfare and the quality of research. Given international discussions of animal experimentation regulations and guidelines, in this article we describe current Brazilian legislation governing the use of animals in scientific investigations. We conclude that, despite advances in the implementation of the 3Rs (reduction, refinement, replacement), the new regulatory framework does not sufficiently incorporate ethical considerations, lacking explicit reference to the 3Rs as well as measures for their full application. The more humane use of animals in research will depend on the approach adopted by Brazil's National Council for the Control of Animal Experimentation to promote the 3Rs and to improve internal regulations as well as data collection and analysis in research institutions. In Brazil as elsewhere, one of the greatest challenges to policymakers is to harmonize the myriad and intertwined legal provisions without hindering biomedical research.

Key Words: biomedical research; Brazil; harmonization; laboratory animal; law; legislation; regulation

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Introduction

Global Regulation of Animal Care and Use

During the second half of the 20th century the use of animals in research, testing, and education became subject to a number of laws, regulations, policies, and standards that vary among countries (Garner 1998; Garthoff 2005; Kong and Qin 2010; Kulpa-Eddy et al. 2007; Kurosawa 2007; Monamy 2000; Pereira et al. 2004). According to the Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, the diversity of these regulatory procedures and authorization criteria generates economic, laboratory animal welfare, scientific, and public/societal problems; for example, the European Medical Research Councils (EMRC) and the Standing Committee for Medical Sciences at the European Science Foundation (ESF) argue that a total ban on great ape research in Europe "would also logically and ethically require that the EU bar its citizens from any medical advances achieved outside the EU based on great apes" (ESF-EMRC 2009, 1).

The need for international harmonization of guidelines has been broadly emphasized (Demers et al. 2006; Gauthier and Griffin 2005; Ohno 2002; van Zutphen and Valk 2001). Many discussions focus on the implications of differences in standards on animal care and procedures such as anesthesia, euthanasia, categories of invasiveness, and animal reuse (NRC 2004; Vanderberg and Stone 2002).

Brazilian Regulation: Overview

For the past 10 years Brazil has invested considerable resources in a health research and development agenda focusing on neglected diseases. The Ministries of Health and of Science and Technology are funding efforts to develop novel drugs and vaccines for tropical diseases—malaria, tuberculosis, dengue, leishmaniasis, Chagas disease, and leprosy—that disproportionately affect poor and marginalized populations. One of the strategies of the policy on health research involves partnerships and networks among scientists in academic institutions of both wealthy industrialized and disease-endemic countries (Morel et al. 2009). In this context, guidelines for animal use in biomedical research are fundamental to guarantee both animal welfare and research quality.

A Brazilian federal law on the scientific use of animals was approved in 2008 (Law 11794/2008). It establishes the

National Council for the Control of Animal Experimentation (CONCEA[1]; somewhat comparable to the Canadian Council on Animal Care, CCAC) and requires institutions to establish an ethics committee on the use of animals (CEUA[1]; comparable to the US institutional animal care and use committee, IACUC) for day-to-day enforcement of the law and regulations.

In 2009, CONCEA's operational standards were set out by Decree 6899/2009,[2] defining the Council as a governing and advisory body, under the Ministry of Science and Technology (MCT[1]), that has the authority to provide accreditation to registered institutions and to license activities that use animals in research. However, CONCEA has not yet defined the accreditation process; it is expected that the procedures will be comparable to those of AAALAC International. The decree also called for the creation of an electronic database where breeding and research facilities must register in order to apply for CONCEA accreditation (Sistema para Cadastro das Instituições de Uso Científico de Animais, CIUCA[1]).

Biomedical researchers considered Law 11794/2008 an invaluable advance (Marques et al. 2009), but it left challenging issues (Machado et al. 2009) to be resolved by CONCEA, among them coordination of the new legislation with the existing legal framework concerning research animals. Depending on the research animal used and the process of acquiring it, scientific investigations are subject to various laws overseen by a number of agencies. We analyze the new legislation based on major issues in the legal and regulatory debate about the use of animals in research (Balls 2009; Griffin et al. 2007; Højgaard and Makarow 2009; Perry 2007) and we consider whether it sufficiently reinforces the 3Rs.[3]

We begin by describing the ministries, agencies, and commissions in charge of the legal framework involving animals that CONCEA will have to consider when defining guidelines. We explain the Brazilian legal system and administrative divisions and the responsibilities of CONCEA and CEUAs, the terms of the new legislation, and the standards established by Law 11794/2008 and Decree 6899/2009.[4] Last, we identify unresolved issues in the new legislation that need urgent guidance from CONCEA to resolve unclear provisions, inconsistencies, and ambiguities that will generate operational problems for oversight agencies, research institutions and investigators. We translate selected articles of the new legislation on the scientific use of animals to illustrate the weakness of the legal framework regarding the consistency of the terms and expressions used, within and between the texts of the law and the decree.

Organizations Involved in Animal Research Oversight

Ministries, Agencies, and Commissions

Brazil is a civil law country with a legal system based on codes and legislations enacted primarily by the federal legislative power as well as states and municipalities. The Brazilian Constitution, ratified on October 5, 1988, organizes the country into a federative republic with three levels of government: federal, state, and municipal (there are 26 states and one federal district). It defines the legislative, judicial, and executive power of each federal branch as well as the boundaries between federal, state, and municipal law. State and municipal governments enact and enforce their own laws; when there are conflicts between federal, state, and municipal legislations, federal regulations prevail.

At the federal level, the executive branch is headed by the President of the Republic and supported by presidentially appointed ministers of state who create regulations, monitor and evaluate federal programs, and implement policies for the sectors in their purview.[5] The National Congress, composed of the Chamber of Deputies and the Senate, exercises legislative power and has responsibility for rule making; the ministries and various branches implement the rules and define with more accuracy the procedures that must be followed. The purview of each ministry is defined by Law 10683/2003.

The Ministry of Environment (MMA) is responsible for formulating and executing the national environmental policy. It is also in charge of both legislation concerning the protection of flora and fauna (e.g., the Brazilian Law on Environmental Crimes, Law 9605/1998) and risk classification of exotic animals. Researchers who wish to conduct scientific research using wild animals require MMA authorization and must indicate the corresponding license number in their scientific publication.

National policy and legislation on biosafety fall under the MCT. The use of genetically modified animals or other organisms (GMOs) requires authorization from the MCT-based National Technical Commission for Biosafety (CTNBio). The Law on Biosafety (Law 11794/2008) mandates that only institutions with a local biosafety commission and CTNBio accreditation are allowed to manipulate GMOs. Investigators must submit their protocol to the local biosafety commission, which forwards to the CTNBio all requests and documents involving projects and activities with GMOs and their derivatives.

The Ministry of Agriculture, Livestock, and Food Supply (MAPA; similar to the US Department of Agriculture, USDA)

[1]Abbreviations that appear 3x throughout this article: APO, animal protection organization; CEUA, ethics committee on the use of animals; CFMV, Brazilian Veterinary Regulatory Board; CIUCA, Sistema para Cadastro das Instituições de Uso Científico de Animais (electronic database for the registration of institutions and procedures that use nonhuman vertebrates in teaching, testing, and research); CONCEA, National Council for the Control of Animal Experimentation; MCT, Ministry of Science and Technology

[2]A Law (or Act) is a regulation passed by a legislative body. A decree is an order or regulation that specifies the practical implementation of a law; it is proposed by the executive branch (e.g., a minister) and approved by the president.

[3]The 3Rs—reduction, refinement, and replacement—are widely accepted as the guiding principles for research using animals (Russell and Burch 1959). They call for reducing the use of animals to a minimun, refining the way experiments are done to make sure animals suffer as little as possible, and replacing animals with nonanimal techniques whenever possible.

[4]Both are available online (www6.senado.gov.br/sicon/ExecutaPesquisaLegislacao.action), accessed on June 6, 2010.

[5]Regulatory bodies (similar to the US public utilities commissions; OECD 2008) have been set up to inspect the provision of public services offered by private companies, establishing rules and ensuring quality of service.

is responsible for the regulation, classification, and inspection of live animals, including research animals, and it determines the classification of biological agents that affect animals. It is in charge of federal laws and regulations to protect and improve animal health and to control and eradicate animal diseases. (But the authority to control stray animals that put wild animals at risk is shared by the Ministries of Health, Environment, and Agriculture, through their state and municipal secretariats.) MAPA has exclusive authority to inspect activities involving animals. In addition, it determines the airports and borders through which animals may enter the country; enforces regulations on the import and export of live animals,[6] semen, and embryos; and defends Brazilian borders against foreign and exotic animal diseases.

Three regulatory agencies establish provisions regarding transportation, including for research animals: the National Agency for Land Transportation (ANTT), National Agency for Waterway Transportation (ANTAQ), and National Civil Aviation Agency (ANAC).

There are several other provisions to consider when using animals in research, including those concerning the veterinary profession. According to the Brazilian Veterinary Regulatory Board (CFMV[1]; somewhat comparable to the American Veterinary Medical Association, AVMA), only a licensed veterinarian may diagnose and treat the injuries and ailments of animals and perform anesthesia, analgesia, and euthanasia. National and state veterinary regulatory boards are responsible for inspecting the practice of veterinary doctors and, through regional regulatory boards, for guiding, supervising, and disciplining veterinary activities (Law 5517/1968, Articles 7 and 8).

The Ministry of Health (similar to the US Department of Health and Human Services, HHS) is responsible for public health. The National Health Surveillance Agency (ANVISA), a regulatory body associated with the Ministry of Health, protects public health by ensuring sanitary control in the production and marketing of products and services that require sanitary inspection, and by inspecting the sites, processes, supplies, and technologies related to these products and services. The agency exercises control over ports, airports, and borders and acts as a liaison between the Brazilian Ministry of Foreign Affairs and foreign institutions in matters concerning international aspects of sanitary surveillance. ANVISA establishes provisions for the approval of new medicines, pesticides, or toxic substances as well as guidelines for epidemiological surveillance, including zoonosis control. The Ministries of Health and of Labor set rules concerning human health and protection in working environments.

As this overview shows, animal research in Brazil is subject to various laws and regulations overseen by a number of agencies. One of CONCEA's challenges is to integrate these into a single comprehensive regulatory framework for all animal experimentation and to ensure coordination of their oversight.

[6]Brazil does not, however, have specific regulations concerning the importation of research animals.

National Council for the Control of Animal Experimentation (CONCEA)

CONCEA is composed of 14 members: five ministerial representatives (one each from the ministries of Science and Technology, Education, Environment, Health, and Agriculture), one representative each from a range of national scientific/technical organizations (the National Council for Scientific and Technological Development, Rectors Council of Brazilian Universities, Brazilian Academy of Sciences, Brazilian Society for the Progress of Science, Federation of Societies for Experimental Biology, Brazilian College of Animal Experimentation, and National Federation of Pharmaceutical Industries), and two representatives of legally established animal protection organizations (APOs[1]). Article 9 of Decree 6899/2009 is explicit in its requirements for the APO members: they must be "Brazilian citizens, with a doctoral degree or equivalent in one of the following areas: agricultural sciences, biological sciences, human health, animal health, biotechnology, biochemistry, or ethics. Moreover, their scientific knowledge and performance must be recognized, with outstanding professional activities in these areas." It is worth noting that the CFMV and the Brazilian Society of Bioethics do not have a seat on CONCEA.

In addition, CONCEA has four permanent committees: for scientific research, education, animal breeding, and alternative methods.

Law 11794/2008 establishes the following responsibilities for CONCEA (Article 5):

(I) formulate and oversee adherence to guidelines related to the humane and ethical use of animals for research purposes;
(II) grant accreditation to institutions that breed or use animals for educational or scientific purposes;
(III) monitor and assess the introduction of alternative techniques that replace the use of animals in education and research;
(IV) develop and review standards for the care and use of animals for educational or scientific purposes, according to the international conventions to which Brazil is a signatory;
(V) establish and periodically review technical standards for the installation and functioning of animal housing facilities, breeding centers, and animal experiment laboratories, including facility working conditions;
(VI) develop and periodically review standards for the accreditation of institutions that use animals for teaching and research;
(VII) based on reports provided by an institution's CEUA, maintain up-to-date records of teaching and research procedures using animals, completed or in progress, and the researchers involved;
(VIII) review and decide on actions taken by researchers against CEUA decisions;
(IX) define standard operating procedures and submit these to the MCT for approval; and
(X) advise the executive branch in matters associated with the procedures regulated by this law.

Ethics Committee on the Use of Animals

The CEUA is the institutional body formally responsible for the care and use of animals in research, testing, and teaching. With CONCEA authorization, a research institution may have more than one CEUA. All teaching and research institutions that use vertebrate animals are required to appoint a CEUA. However, the law does not clearly indicate whether businesses involved in the breeding or sale of animals for teaching or research purposes must appoint such a committee.

CEUA members are veterinarians and biologists, professors and researchers, and one representative of a legally established APO. There is likely to be considerable variability in the number and profile of CEUA members at research institutions around the country (Machado et al. 2009) but the committee must include an APO member. Furthermore, Decree 6899/2009 (Article 43) stipulates that this member must be "a Brazilian citizen of recognized technical competence and remarkable knowledge, with a higher-education diploma (graduate or postgraduate), and a distinguished scholar in the areas related to the scope of Law 11794/2008." Such narrow criteria are questionable because in Western democracies the role of civil society organizations and community members in an animal ethics committee is to bring a different perspective to those engaged in scientific activities.

According to Law 11794/2008 (Article 10), the CEUA is responsible for

(XI) enforcing regulations concerning research animals, especially those of CONCEA;
(XII) examining teaching or research procedures performed in the institution to determine whether they are in accordance with the applicable legislation;
(XIII) maintaining up-to-date records of teaching and research procedures, both completed and in progress, and submitting a copy to CONCEA;
(XIV) maintaining records of researchers involved in teaching or research procedures, and submitting a copy to CONCEA;
(XV) providing certificates required by grant agencies, scientific journals, and others; and
(XVI) reporting immediately to CONCEA and relevant sanitary authorities any accidents involving animals that occur in accredited teaching or research facilities, with information that allows corrective actions.

In addition, the CEUA has the authority to halt any teaching or research procedure that does not comply with the legislation. The failure of a CEUA to stop procedures that do not comply results in sanctions to the institution, and failure to report accidents to CONCEA can result in administrative penalties for the institution, applied by CONCEA.

Law 11794/2008 does not define the CEUA's responsibility for reviewing and approving institutional assurances, advising research facilities about compliance, evaluating allegations of noncompliance with the legislation, or conducting site visits. However, the decree (Article 44) added two responsibilities for CEUAs that address these areas: (VII) establish prevention and inspection programs to guarantee the functioning and adequacy of the facilities, according to the standards defined by CONCEA, and (VIII) maintain records of both the reviews of each ongoing activity or project that involves animals and the researchers involved.

To promote harmonization among CEUAs, Decree 6899/2009 should have provided a more extensive list of definitions and components pertaining to research project review and inspection processes under CEUA authority. CONCEA strategies in this area remain unknown.

Law 11794/2008 and Decree 6899/2009

According to the Brazilian Constitution the federal government, states, and municipal districts are responsible for "protecting the fauna and the flora, and prohibiting practices that endanger their ecological function, cause the extinction of species, or submit animals to cruelty" (Federal Constitution [FC]/1988, Chapter VI, Environment, Article 225, §1.VII). Accordingly, Law 11974/2008 stipulates the conditions for breeding and using animals in teaching and scientific research.

Terms of the Law and Decree

Law 11794/2008 regulates the FC clause that establishes procedures for the scientific use of animals.[7] It describes conditions for the breeding and use of animals in teaching and scientific research (Article 1), covering all live vertebrate animals (phylum Chordata, subphylum Vertebrata) without attributing special status to any species or specifying conditions for early development (e.g., embryonic forms) or wild animals.

According to Law 11794/2008, scientific research activities involve, inter alia, basic and applied science, technological development, and production and quality control of drugs, medicaments, food, immunobiological agents, instruments, or other testing on animals.[8] The law replaced the term "vivisection" (used in Law 6638/1979) with the term "experiments," defined as "procedures performed on live animals in order to elucidate physiological and pathological phenomena, using specific and previously established techniques" (Article 3, III). Experiments are not defined in terms of causing the animal pain, suffering, distress, or lasting harm (although the law states that procedures should avoid causing suffering to research animals, as discussed below under Standards for the Use of Research Animals). The following procedures and practices are not covered: (1) prophylaxis and veterinary treatment of an animal if necessary; (2) the ringing, tagging, or marking of an animal, or the application of other methods to enable identification if they cause only momentary pain or distress and no lasting harm; and (3) nonexperimental practices related to farm animals.

Law 11794/2008 applies to all facilities—public or private, academic or industry-based, whether or not they receive federal

[7]This law abrogated and supplanted Law 6638/1979.
[8]Animal agricultural practices are not covered.

funds. Only higher education institutions and biomedical technical schools are permitted to use animals in educational activities, but Law 11794/2008 and Decree 6899/2009 do not address animal experiments performed by students under the age of 18 (such experiments were previously subject to Law 6638/1979).

All research facilities covered by Law 11794/2008 must register with CONCEA, and only Council-accredited facilities may perform the activities covered under the Law.

Articles of Law 11794/2008 Concerning Animal Welfare

Articles 14, 15, and 16 of Chapter IV set the guidelines for animal welfare. Article 14 requires the provision of animal care before, during, and after an experimental or other scientific procedure. When appropriate or if the animal experiences severe chronic pain, the animal must be euthanized after or even during the procedure, using a method that is appropriate for the species and in keeping with the MCT guidelines (Article 14, §1). Animals that are not euthanized may be made available for adoption by individuals or APOs, in accordance with CEUA recommendations on biosafety criteria (Article 14, §2).

The law recommends the recording and dissemination of teaching practices to avoid unnecessary repetition of teaching procedures using animals (Article 14, §3). The number of animals used in a research project and the duration of each experiment must be the minimum necessary to produce conclusive results, and procedures should avoid causing suffering to research animals (Article 14, §4). Experiments that may cause pain or distress in the animal must be performed under sedation, analgesia, or anesthesia (Article 14, §5). Research projects that entail procedures related to pain and distress require CEUA special review and approval (Article 14, §6). The law forbids the use of neuromuscular blocking agents or muscle-relaxing agents as substitutes for sedation, analgesia, or anesthesia (Article 14, §7).

The reuse of research animals after achievement of the main objective of a project is not allowed (Article 14, §8). During a teaching activity, and whenever traumatic procedures are involved, other procedures on the same animal are permissible as long as they are all executed during the same course of anesthesia. The research animal must then be euthanized before recovering consciousness (Article 14, §9).

The breeding and use of scientific animals in an enclosed environment require adherence to the conditions and safety standards recommended by international organizations to which Brazil subscribes (Article 14, §10), such as the World Health Organization (WHO), World Organization for Animal Health (OIE), and the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).

According to Article 15, CONCEA may, after taking into account the relationship between the level of animal pain and the expected practical results, restrict or prohibit experiments in which animals experience severe or prolonged pain or distress.

Significant Omissions in the New Legal Framework

While the new law and its implementing decree are clearly steps forward in Brazil's regulation of the care and use of animals in research and teaching, we are concerned about areas that remain either ill defined or altogether absent from the legislative language.

Although the key role of a CEUA in research governance is well recognized in the literature (Gauthier 2007; Rollin 2007; Schuppli et al. 2004), Brazil's new regulatory framework does not define the content of research proposals that should be subject to CEUA scrutiny. Neither the law nor the decree requires (1) identification of the species and the approximate number of animals to be used; (2) a rationale for involving animals and for the species and number of animals to be used; (3) a complete description of the proposed use of the animals; (4) a description of procedures to minimize discomfort and pain to animals; or (5) a description of any euthanasia method to be used.

According to Article 16, all research projects must be supervised by a professional who has an undergraduate or graduate degree in an area of biomedicine and is employed in a CONCEA-accredited educational or research institution. However, neither the law nor the decree mentions that a qualified veterinarian must provide medical care. Furthermore, the legislation does not state that the personnel who conduct animal experimentation procedures must be appropriately qualified and trained in those procedures. In fact, Article 16 is the only clause related to staff education and training.

The new regulatory framework, except for Article 16, does not require a harm-benefit analysis (i.e., welfare cost to the animals involved versus benefits to humans, other animals, or the environment). Scientific merit is not specifically mentioned. Neither the law nor the decree contains clauses regarding the justification for carrying out animal experiments. In fact, no components of the new regulatory framework require that procedures involving animals be designed with consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.

The legislation does not define or adopt a severity classification or a category of invasiveness (CI). As Griffin and colleagues (2007) pointed out, assignment of the appropriate CI serves at a local and national level. At the local level, it is useful in signaling to investigators, CEUAs, and animal care staff which protocols require particular attention to ensure the minimization of animal pain and distress. At the national level, CI is useful to identify emerging trends and develop policy tools.

Except for teaching practices using animals (Article 14, §3), the legislation does not establish any provision to minimize research activities that unnecessarily duplicate previous experiments. Neither the law nor the decree presents a rationale for animal number justification except the minimum number to obtain conclusive results. In addition, the provision combines reduction and refinement principles in a single statement,

indicating a lack of clarity in the presentation of and support for the 3Rs.

Neither the law nor the decree requires consideration of alternatives to any research procedure using animals, especially those likely to cause pain and distress, ignoring the Law on Crimes against the Environment (Law 9605/1998).[9] Decree 6899/2009 substituted the phrase "alternative techniques" ("alternative methods" in Law 11794/2008) and defined it as "validated and internationally accepted procedures that guarantee results and reproducibility to attain, whenever possible, the same goal as procedures replaced by methods that (a) do not use animals, (b) use lower-order species, (c) use fewer animals, (d) use ex vivo organ systems, or (e) reduce or eliminate discomfort" (Article 2, II). Brazil does not have a Center for the Validation of Alternative Methods, and government funding to support collaborative studies on alternative methods has been almost nonexistent (Presgrave 2008).

It is worth noting that "humanely killed" is one of the few definitions presented by Law 11794/2008: "death of an animal by methods that involve, depending on the species, a minimum of physical and mental suffering" (Article 3, IV). However, neither the law nor the decree uses the term "humaneley killed," using instead the words "euthanasia" (without definition) and "sacrifice."

Law 11794/2008 forbids animal reuse "after the main objective of the research project has been achieved" (Article 14, §8) but does not define reuse or provide specific recommendations about the continuous use of the same animal in a research project. It does not take into account the Brazilian Official Pharmacopeia (ANVISA/Minister of Health) whose guidelines on biological methods for quality control (e.g., testing for pyrogens) allow animal reuse. Both the law and the decree ignore the difficulties surrounding reuse issues (Kovalcsik et al. 2006). This lack of precision may cause diverse interpretations by CEUA members reviewing research protocols.

There are, however, many possible scientific/research procedures using animals that fall under the legislation in which the reuse of animals would be acceptable. For example, animals suitable for reuse may include those used as controls in a nutrition experiment or for the testing of a telemetric device. Such reuse may be a promising method of reduction.

Neither the law nor the decree establishes minimum animal welfare requirements for breeding and supply facilities in terms of institutional policies (e.g., monitoring, veterinary care, and personnel qualifications, training, and safety), housing and management (e.g., space allowance, cage size, behavioral management, food, water, bedding, sanitation), and physical plant (e.g., animal environment, heating and cooling, water and air supply), in light of European and US regulations.

In addition, neither the law nor the decree addresses the sale or transportation of research animals, or mentions whether practices in these areas should comply with other applicable federal laws, guidelines, and policies.

[9]Law 9605/1998 (Article 32, §1) establishes that a person who performs a painful or cruel act on a live animal when there are alternative resources, even if for educational or scientific purposes, is subject to 3 months to 1 year imprisonment plus a fine.

Law 11794/2008 and Decree 6899/2009 do not address the use of stray dogs in research, but some state laws prohibit the use of pound animals in research and education. For example, the state codes on animal protection of Rio de Janeiro (State Law 3900/2002), Santa Catarina (State Law 12566/2003), and Parana (State Law 14037/2003), in their chapter on Laboratory Animals, stipulate that only animals bred in research centers may be used in experiments. The São Paulo State Code on Animal Protection prohibits the use of live animals from zoonosis control centers or municipal pounds and similar sources, public or private (State Law 11977/2005, Article 31). CONCEA will have to establish rules for granting credentials to animal pounds in states or municipalities that do not exercise jurisdiction over the research use of unclaimed animals. The Ministries of Environment, Health, and Agriculture together have the authority to control, through their state and municipal secretariats, stray dogs that may put wild animals at risk.

Inspections, Penalties, and Sanctions

The only Article of Law 11794/2008 that Brazilian President Luiz Inácio Lula da Silva vetoed concerned the inspection of facilities and activities involved in the breeding and use of research animals. The veto was based on an inconsistency between Articles 11 and 21 the former assigned to the executive branch the authority to inspect the facilities and activities, and the latter mandated shared responsibility among the ministries in accordance with their areas of expertise. As mentioned, it is the responsibility of the Ministry of Agriculture to inspect activities involving animals, except those related to workers' health and the management of exotic and wild species.

CONCEA imposes administrative penalties on research or teaching institutions that do not comply with regulated procedures. The nature of the penalty depends on the severity of the infringement; possible penalties include a temporary or permanent ban or suspension of funding from official agencies. CONCEA administrative penalties must not conflict with penal and administrative sanctions established by Law on Environmental Crimes (Law 9605/1998). Law 11794/2008 clarifies the relationship between scientific practices and financial sourcing by establishing that CONCEA may "recommend to research funding agencies the denial of funding" for projects either performed without CEUA approval or suspended by the CEUA. Penalties for individuals include the temporary or permanent suspension of the right to perform regulated procedures.

As Marques and colleagues (2009) point out, to implement funding restrictions at the state level would require the addition of a CONCEA representative of the National Council of State Foundations for the Support of Research.

Challenges for CONCEA

CONCEA must make specific references to federal legislation that concerns animal welfare and encourage state regulators and

research funding agencies to reference CONCEA standards in their legislation and programs.

One of the functions of CONCEA is to provide technical support to accredited institutions, including the training of personnel to use animals in research and teaching. The Council and the Brazilian Veterinary Regulatory Board must therefore work together to harmonize the future CONCEA accreditation and training program with the CFMV regulatory framework. As mentioned above, the CFMV does not have a seat on the Council. In this context it is worth noting that CFMV applied for membership on the Council soon after CONCEA was established; however, legally, to fulfill the CFMV request it would be necessary to change the article of the law defining CONCEA's composition.

CONCEA will have to be accountable to the general public and responsible for the dissemination of information on the scientific use of animals to Brazilians (CONCEA Internal Regiment, Article 44). The Council has not yet indicated whether annual statistics on animal research will be available to the public. Looking at international trends, it is a good time to consider strategies to reduce the number of animals used in scientific procedures. In addition, freely sharing information and publishing not only positive but also problematic or inconclusive research results are ways to avoid the needless repetition of experiments (Economist 2009).

Concluding Thoughts

Brazil has the most dynamic research sector in Latin America in the fields of health, biotechnology, and pharmacology, backed by defined government policies on science and technology and clear health research priorities (Moloney 2009). To ensure the continued effectiveness of this sector, one of CONCEA's greatest challenges is to harmonize the country's myriad and intertwined legal provisions without hindering biomedical research. We believe the first step in this direction should be the publication of a document explaining the technical terms presented in the legal framework, clarifying the strategies in progress to harmonize the legal framework concerning research animals, and, above all, clearly describing CONCEA policies on the 3Rs.

The current legislation does not clearly refer to or require implementation of the 3Rs. As pointed out by Thales de Astrogildo e Tréz (2010, 241), "refinement of experimental procedures is by far the most cited in the text of the new law, which draws little attention to the other two Rs." Advances have been made but a more humane approach to the use of animals in research will depend on CONCEA's strategies to promote the 3Rs and to improve regulations and data collection and analysis at research institutions.

It is the responsibility of animal researchers to ensure adherence to the law through CEUA project review and approval, biosafety licensing by the local biosafety committee, the coordination of animal production, and the establishment and implementation of effective standard operating procedures.

We believe it is important that institutional management coordinate the supply and demand for animals in order to avoid overproduction (Takahashi-Omoea and Omoe 2007). Customarily, Brazilian research institutions, public and private, breed the species and quantities of animals required by their researchers, but the breeding facility and the ethical committee either maintain very weak ties or act independently. Under the new legislation this will have to change. It is possible that breeding facilities will restrict the provision of animals based on CEUA approval of each animal research protocol.

Finally, timely and effective communication is needed to share and implement best practices (Gauthier 2002). Such communication must involve regulators and scientists as well as animal welfare organizations, the public, and decision makers as users of science. Internationally, it has been suggested that researchers should be more open to a two-way dialogue to improve and sustain public trust.

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