

# Animal experimentation: historical overview and perspectives

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## Abstract

Every year, millions of vertebrate animals are used worldwide in scientific research. Although many countries have already, for decades, legislation regulating experiments with animals, there was a legal gap in Brazil. In this context, a historical and comparative overview of Brazilian normative situation was drawn up. The reference used was the Law 11,794/08, the first legislation specifically regulating experiments with animal in the country. The Law established the adoption of research practices that value animal wellbeing by reducing suffering and the number of specimens used, aligning to the “3Rs” concept. The effects of the new regulation will only be observed in some years from now, when the entire regulatory system is implemented and generated statistical data are available for analysis. Still, it is clear that the Law 11.794/08 represents a major advance in the face of the incorporation of guiding principles aimed at animal wellbeing and the previously existing legal vacuum.

**Key words:** Animal experimentation. Legislation. Ethics. Animals.

## Resumo

### Experimentação animal: panorama histórico e perspectivas

No mundo, milhões de animais vertebrados são utilizados, por ano, em pesquisas científicas. Embora vários países possuam, há décadas, uma legislação para regulamentar a experimentação animal, no Brasil havia uma lacuna legal. Nesse contexto, traçou-se um panorama histórico e comparativo da situação normativa brasileira. A referência utilizada foi a Lei 11.794/08, primeira legislação a especificamente regulamentar a experimentação animal. A lei determinou a adoção de práticas de pesquisa que prezem pelo bem-estar animal, pela redução do sofrimento e do número de espécimes utilizados, alinhando-se ao conceito dos “3Rs”. Os efeitos da nova normatização só serão observados em alguns anos, quando todo o sistema regulatório for implantado e os dados estatísticos gerados estiverem disponíveis para análise. Ainda assim, percebe-se que a Lei 11.794/08 representa significativo avanço em face da incorporação de princípios norteadores que visam ao bem-estar animal e ao vácuo legislativo anteriormente existente.

**Palavras-chave:** Experimentação animal. Legislação. Ética. Animal.

## Resumen

### Experimentación animal: panorama histórico y perspectivas

En el mundo, millones de animales vertebrados son utilizados cada año en investigaciones científicas. Aunque varios países posean, desde hace décadas, una legislación para reglamentar la experimentación animal, en Brasil había vacío legal. En este contexto, se ha hecho un panorama histórico y un comparativo de la situación normativa brasileña. La referencia utilizada fue la Ley 11.794/08, primera legislación a regular específicamente la experimentación animal. La ley determinó la adopción de prácticas de investigación que objetiven el bienestar animal, mediante la reducción del sufrimiento y del número de especies utilizadas, adecuándose al concepto de las “3Rs”. Los efectos de la nueva legislación sólo se observarán dentro de algunos años, cuando todo el sistema normativo sea implementado y los datos estadísticos generados estén disponibles para análisis. Aún así se observa que la Ley 11.794/08 representa un avance significativo ante la incorporación de principios orientadores que objetivan el bienestar animal y el vacío legal anteriormente existente.

**Palabras-clave:** Experimentación animal. Legislación. Ética. Animales.

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They declare that there is not any conflict of interest.

## Relations between human beings and other animals

The age of Earth was estimated by the scientific community, as about 4.6 billion years old and the oldest discovered fossil remains dated from about 3.5 billion years<sup>1-3</sup>. The ancestors of modern humans, in turn, appeared around 6 to 2 million years ago and began producing tools only in the last 200 to 100 thousand years<sup>4,5</sup>. Because the ability to develop tools, humans have become the dominant species on the planet today, even if biologically devoid of natural morphological or physiological characteristics such as speed, night vision, poison, thorns, ability to fly, deadly claws, protective carapace, among others<sup>6</sup>.

Historically, humans went from fear and admiration for the wild world, from real inferiority towards the animals in primitive cultures - since they considered wildlife as powerful spirits, true gods - to a position of taming, artificializing and humanizing nature. Thus, wild animals lost their condition of powerful spirits, because it became difficult to admire, fear or deify the sheep in the barn or the pig in the sty<sup>6</sup>.

Grounded in religious view, Western civilization has maintained a control relationship with animals because, according to this view, humans were created in the image and likeness of God, who has explicitly determined that humans should take advantage of all animals and plants<sup>7</sup>. Later, there was the development of philosophical thought based on the anthropocentric concept, in which man is the measure of all things, the center of the universe, as noted in the philosophical schools of romanticism, humanism and rationalism<sup>8</sup>.

Briefly, in the time line, animals lost the initial superior condition, sacred beings due to their domestication, and in a later stage, based on religious grounds, followed by the development of humanist thinking. From animal domestication, humans used them to satisfy needs such as food, clothing, transportation, entertainment, companionship, scientific research, among others<sup>9,10</sup>.

## Use of animals in scientific research

Animal experimentation in scientific research walked alongside the development of medicine, having, according to the Dictionary of Bioethics, the following definition: experimentation on animals is the use of living laboratory animals within the scope of pure or

applied research experiences, as well as for teaching purposes<sup>11</sup>. The use of animals in the field of medical knowledge refers to ancient Greece, where Aristotle and Hippocrates acquired their knowledge about the human body through the dissection of animals. These skills were expressed, respectively, in the *Historia Animalium* and *Corpus hippocraticum* productions<sup>10</sup>.

In 1540, Vesalius, in his work *De humani corporis fabrica*, outlined the mechanisms that govern the human body and William Harvey, in 1628, demonstrated the functioning of blood circulation, both using the animal model for their studies<sup>12</sup>. The 17<sup>th</sup> century philosopher Rene Descartes, when postulating that thought and sensitivity were part of the soul, strengthened and legitimized the use of animals in scientific research<sup>13</sup>. Since, in his opinion, animals did not have soul, they would not be able to feel pain.

Charles Darwin's discoveries, which culminated in the book 'The Origin of the Species', in 1859, established the premises of the link between different species through common ancestors during the evolutionary process. With these discoveries, Darwin's theory provided support for the extrapolation of results obtained in experiments with animal models to humans<sup>14</sup>. Claude Bernard, in 'An introduction to the study of experimental medicine', based the use of species in research on the grounds that it would be strange if we recognized the right to use animals for housework, food and to prohibit its use for instruction in one of the most useful sciences to mankind<sup>15</sup>.

Currently, the animal model is used in almost all branches of biological research and in various fields of biomedical research, on the condition it meets the following requirements: permits the study of biological phenomena or behavior of the animal, permits a spontaneous or induced pathological process to be investigated, and that the phenomenon in one or more respects, is similar to the phenomenon in humans<sup>9</sup>. Scientific research and product testing occur to improve knowledge about the physiopathological mechanisms of disease, undertake clinical trials with new drugs, study biomarkers and assess new techniques with prospects for applicability in humans<sup>16</sup>.

It is possible to systematize some relevant examples of advances in basic research obtained through animal experimentation as follows:

discovery of blood circulation, understanding of infectious diseases, discovery of antibiotics, mechanisms of nerve impulse, understanding of embryonic development, discovery of monoclonal antibodies and prostaglandins. Some examples of advances in the medical field are: insulin for diabetes, the modern anesthetics for surgery, pacemakers and replacement heart valves, heart transplantation, improved sutures and other surgical techniques, and life support system for premature babies<sup>17</sup>.

In Brazil, from the 1990s onwards, we have the example of studies involving the use of animals in research in observing the development of Chagas' disease, in the quest for understanding the epidemiological determinants of the disease, although the human being is the ideal model for experimental studies, for ethical reasons, only observational studies can be performed, while in animals can be observed the penetration, multiplication and development of the parasite in the quest to eradicate the disease.

Although experimental models do not accurately reproduce the infection of the human disease, animal models have been used successfully: the acute and chronic phases of Chagas' disease, with its parasitological, immunological and histopathological characteristics, in varying degrees of severity, as well as congenital infection, were reproduced in mice; the identification of heart, digestive tract and nervous system lesions in histopathological study, which are alike in humans, was observed in rats; in rabbits were histopathologically identified heart and digestive tract lesions which are similar in humans; dogs are a model of great interest because they are the single animal model that develops the various clinic-pathological forms of the disease. Also monkeys have been used in the search for a model that reproduces immunopathogenic aspects satisfactorily; the genus *Callitrix Kpenicillata* was the first non-human primate species used by Carlos Chagas in 1909<sup>18</sup>. One hundred years after the discovery of the disease, the convergence between basic and clinical research raises new perspectives for the treatment of chronic Chagas' disease<sup>19</sup>.

### The adoption of the 3Rs benchmarks

This century, between 75 and 100 million vertebrate animals are used in research yearly<sup>20</sup>, according to a study conducted in the databases of the Regional Library of Medicine, including Medline (USA National Library of Medicine), Lilacs

(Literature Latin American and Caribbean Health Sciences), Scielo (Scientific Electronic Library Online) and the Cochrane Library (The Cochrane Database of Systematic Reviews), over a period of four years, it was shown that rats, mice, rabbits and dogs represent over 90% of the specimens used in scientific research, according to a total of 278,779 published and analyzed articles<sup>9</sup>.

The big conceptual reference regarding animal experimentation adopted by the scientific community was proposed by WMS Wussel and WL Burch in the book 'The principles of humane experimental technique'<sup>21</sup>, whose first edition dates from 1959. This work established the adoption of the concepts of replacement, reduction and refinement, known as the "3Rs" concept. Replacement postulates that one must seek to replace the use of vertebrate animals with other materials that do not feel pain, e.g., plants, microorganisms or computer simulations. In turn, reduction indicates that one should try to minimize the number of animals used for performing a given research. Refinement guides the use of methods for lapidating the research, aiming to decrease the discomfort and pain caused to the animal research subjects<sup>22-24</sup>.

Although the '3Rs' proposal is adopted internationally, it is not exempt from criticism because the idea of lapidating the research (refinement) still retains the use of animals and the fact of replacing vertebrates by other animals (replacement) assumes that the existing system of animal use is valid<sup>25</sup>. The orientation to decrease (reduction) the use of animals can cause a risk of losing statistical analysis capacity of the results due to the use of fewer animals. In parallel, we should not use an unnecessary and excessive number of animals, claiming lives without any additional scientific benefit<sup>26</sup>.

### Historical overview of international law

In the legal field, the oldest law about the use of animals in research appeared in England in 1822, and forbade cruelty only against large animals – it was the British Anticruelty Act. Over the years, England passed new laws for procedures in scientific research involving animals. Other countries followed in the drafting of laws on the protection of animals used for experiments<sup>26</sup>. In the UK, the first specific legislation regarding animal experimentation was the British Cruelty to Animals Act in 1976, - updated in 1986, called 1986 Animals (Scientific Procedures) Act. From the

legal update emanated an operational guide - Guidance on the Operation of the 1986 Animals (Scientific Procedures) Act - and also a code of technical procedures - Code Practice for the Housing and Care Animals Used in Scientific Procedures<sup>27-28</sup>.

In the United States, the first law that provided for the use of animals in research was the Laboratory Animal Welfare Act, of 1966 - today after modifications, it remains as Animal Welfare Act<sup>29</sup>. This law has been amended in 1970, 1976, and 1985 and changed in 1990, 2002, 2007, and 2008. Its spectrum of activity was enlarged on each amendment suffered, with the important feature of making compulsory the institutional ethics committees on the use of animals (Institutional Animal Care and Use Committee - IACUC)<sup>30,31</sup>.

In general, the countries' laws related to protection of vertebrate animals, except Sweden, which included invertebrates, and Canada and the UK, which also include in their sphere of protection the cephalopods (the class of invertebrates to which octopuses, cuttlefish and squid belong)<sup>32</sup>.

The most important international document for animal protection is the Universal Declaration of Animal Rights, by the United Nations Educational, Scientific and Cultural Organization (UNESCO) adopted in January 1978. This statement strives to ensure animal freedom, the right to not suffer abuse and the prohibition of experiments involving physical pain, as well to guide for the use of procedures in which animals are replaced by other test methods<sup>33</sup>.

The Universal Declaration of Animal Rights is the international document in which there is an exception to the anthropocentric view. It glimpses the protection of animals, also including animals used in research, through the prism of equality between all living beings, recognizing, among others, the guarantee to life, liberty and protection from abuse. Meanwhile, the recent Universal Declaration on Bioethics and Human Rights, from October 2005, expresses a more anthropocentric position<sup>34</sup>.

The World Veterinary Association (WVA), aiming at the wellbeing of animals used in research, adopted the position that during the experiment the animals should not feel hunger, thirst, pain or discomfort (the environment must be suitable and comfortable), nor suffer injury, illness, fear or distress, and should feel free to develop their normal behavior<sup>35</sup>. With this positioning, the WVA corroborated an understanding on the need of using animals in research, provided their wellbeing is ensured.

It so happens that, due also to the disclosure of the atrocities committed by scientists in experiments involving human subjects during World War II, the use of animals in preclinical research still remains, in order to protect humanity itself. In this context, the Nuremberg Code was drafted, which contains recommendations for guiding the ethical aspects of research with humans<sup>36</sup>. This code has become a landmark in the history of mankind, because it was the first international document that established international recommendation on the ethical aspects involved in human research. And its text is clear in defining that experiments involving human subjects must be grounded in results obtained in animal experiments<sup>37</sup>.

With the growing number of studies, the World Medical Association (WMA) has developed and promulgated the Declaration of Helsinki in 1964, which highlights the importance of respecting human beings in their totality and the duty to defend populations in vulnerable situations<sup>36</sup>. Under such ethics, the WMA orientation, revised in October 2008, ratified the use of animals in biomedical research as indispensable for medical progress. However, the rules of good treatment and wellbeing of the specimens used in the study should be respected<sup>38</sup>.

Grounded on and supported by the Nuremberg Code and the Declaration of Helsinki, the majority of the thirty countries that have laws regulating the use of human subjects in research recognize the test phase in animals as necessary<sup>10</sup>.

### Brazilian legislative vacuum regarding animal experimentation

In Brazil, the first rule to regulate and protect animals was Decree 16,590/24, subsequently repealed by Decree 11/91. Decree 16,590/24 prohibited cattle races, poultry fights, as well as any leisure resulting from mistreatment of animals in houses of public entertainment<sup>39</sup>. Then, Decree Law 24,645/34 mandated in its Article 12 that all animals in the country were to be ruled by the State and Article 22 foresaw sanctions to those who practiced mistreatment of animals. The same legal text, in its Article 32, listed the actions considered mistreatment of animals<sup>40</sup>. Thus, due to the absence of specific legislation, the aforesaid ordinance was used as a standard by analogy to the practice of animal experimentation, as it regulated the prohibition of ill-treatment of animals<sup>41</sup>. Decree-Law 3,688/41 (Criminal Misdemeanor Law), in its Article 64, typified as a

misdeemeanor all animal cruelty, regardless whether for educational or scientific purposes<sup>42</sup>.

The sanctions imposed by Decree-Law 24.645/34 to practitioners of animal mistreatment are distinguished from those set forth in Decree-Law 3,688/41, for being more severe in relation to imprisonment and fine.

Due to the absence of specific legislation, Bill 1507 was introduced in August 1973 by Congressman Peixoto Filho<sup>43</sup>, changed into Law 6,638, of May 1979, which set the standards for the practice of educational and scientific vivisection of animals<sup>44</sup>. Law 6,638/79 authorized, across the national territory, animals vivisection practice (Article 12), except in primary and secondary schools (Article 32, section V).

According to Article 32 of that Act, seeking the wellbeing of animals, vivisection was not allowed without the use of anesthesia (section I) and without the animals having remained in an acclimatization period of fifteen days in a vivarium (section IV). For the vivisection practice, it is necessary to register the study at the competent agency (Article 32, section II), as well as the presence and supervision of an expert technician (Article 32, section III). Another important legal requirement was the need to apply special care to animals subjected to research protocols (Article 42)<sup>44</sup>.

Law 6,638/79, regarding its infractions, refers to Article 64, caput, of Decree Law 3,688/41, for first time offenders (Article 52, section I). For recidivist offenders, the penalty was disqualification and cancellation vivarium or research center registration (Article 52, section I). In spite of its Article 62 explicitly mandating the legislation to be regulated within 90 days, the norm never received proper regulation. Thus, there was no legal definition of the agency responsible for authorizing and issuing registry of vivariums and centers for experiments and demonstrations with live animals (section I); the general conditions required for registration and operation of animal facilities (section II); and the agency and authorities for inspection of animal facilities and centers mentioned in subsection I (section III)<sup>44</sup>.

Another rule regarding the mistreatment of animals is Law 9,605, of February 1998, known as the Environmental Crimes Law or Nature Law, which made punishment even more severe for the practice of mistreatment, with imprisonment from three months to one year and a fine (Article 32)<sup>45</sup>. The administrative sanctions were governed by Decree 3,179/99, which, in its Article 17, refers to the practice of animal mistreatment, even if for educational or scientific purposes<sup>46</sup>. The Constitution itself, in his Chapter on the

environment, prohibits the practice of animal cruelty<sup>47</sup>.

Due to the absence of specific federal legislation to regulate the matter until October 2008, agencies and entities were forced to issue their own rules and regulations regarding procedures and ethical aspects concerning the use of animals in research. In practice, the Brazilian Institute of Environment and Renewable Natural Resources (IBAMA) hosted and performed the mentioned duties, through ordinances and regulatory instructions. Ibama's Ordinance 16/94 determined that institutions using the Brazilian wildlife for research purposes must register with the state superintendents of IBAMA (Articles 12 and 22). However, the ordinance did not refer to any specific procedure regarding animal testing, only the capture and accommodation of specimens<sup>48</sup>. Ordinance 93/98 regulated the importation, exportation and exploitation of live animals, with scientific purposes (Articles 22- 24, 27, 28)<sup>49</sup>.

The Federal Council of Veterinary Medicine (CFMV), in its turn, issued Resolution 714/02, which lays down the rules governing euthanasia procedure in animals (Article 12). The hypotheses are envisaged when animal wellbeing is threatened, when the animal imposes a threat to public health or for being a research subject (Article 22)<sup>50</sup>.

### Current legislation in Brazil

In Brazil, Law 11,794 was enacted only in 2008<sup>51</sup>, which established procedures for the scientific use of animals, meeting the expectations of the scientific community by regulation<sup>52,53</sup>, closing the existing legal gap. Thus, there was the repeal of Law 6,638/79 and the regulation of Article 225, Item 12, section VII of the Federal Constitution. The new legal text also disciplined that the use of animals in educational activities will be restricted to higher education and biomedical technical professional education (Article 12, Item 12, sections I and II), as well as excluding non-experimental agricultural practices from the list of animal experimentation techniques (Article 32, section II)<sup>54</sup>.

Article 22 of the law specifies that existing dispositions apply to animals of species classified as *phylum Chordata, subphylum Vertebrate*. Decree 6,899/09, which regulates this law, explained that its dispositions do not apply to humans (Article 12, and Article 22, section I)<sup>54</sup>. Law 11,794/08 determines, in its Article 42, the creation of the National Council for Control of Animal Experimentation (Concea), as well as the mandatory establishment of ethics committees in

the use of animals (CEUA) at the institutions wishing to conduct research involving animals<sup>51</sup>. The CEUA, guided by the Conceia resolutions, will be responsible for evaluating and monitoring the use of animals (Decree 6,899/09, Article 44). The Conceia, chaired by the Minister of Science and Technology (Article 72), has the function of monitoring/evaluating the introduction of alternative techniques that replace the use of animals in teaching and research, without, however, explaining the way in which these alternative techniques will be introduced.

CEUAs are indispensable for the accreditation of institutions that aim to use animals in research (Articles 82 and 12). The law provides for administrative penalties, without prejudice to the criminal liability (Article 21), which can range from warnings, fines, temporary suspension, funding suspension, and permanent banning for legal entities (Article 17); and between warning, fine, temporary suspension and permanent banning for research involving animals (Article 18)<sup>54</sup>.

Article 14 discusses the requirements and procedures to be adopted when using animals in research, essentially aiming at reducing the number of animals used and minimizing suffering, among them: the practice of euthanasia to stop intense suffering caused by the experiment (Item 12); reduction specimens and using alternative means, when possible (Items 32 to 42), use of sedation or analgesics to minimize pain resulting from the research process (Item 52); specific CEUA authorization with the objective of studying pain and anguish (Item 62); prohibiting or blocking the use of neuromuscular relaxants to replace the use of sedation or analgesia (Item 72); and in the case of education programs if traumatic procedures are employed, several processes can be carried out in the same animal (Item 92). It should be noted that §22 provides, in exceptional cases, for the adoption of animals used in research, avoiding their death<sup>54</sup>.

The law consists of six chapters and presents the following structure: Preliminary and general provisions; the National Animal Control and Experimentation - Conceia; the Ethics Committees on Animal Use (CEUA); the terms for raising and using animals for education and scientific research; Penalties; Transitional and final provisions<sup>54</sup>.

Decree 6,899/09 lists Conceia's nature, purpose, responsibilities, composition, administrative structure, meetings and deliberations, resources management and processes. The decree stipulates that the Conceia will be necessarily composed by Brazilian citizens, with a PhD degree or equivalent notorious academic and scientific knowledge and activities

**Experimentação animal: panorama histórico e perspectivas** (agricultural and biological sciences, human and animal health, biotechnology, biochemistry or ethics areas). In turn, the CEUA shall consist of Brazilian citizens of recognized technical competence and remarkable knowledge, undergraduate, graduate or post-graduate, and with outstanding professional activity in these areas (Articles 92 and 43)<sup>54</sup>.

The Conceia was officially installed on December 8, 2009, comprised by 28 representatives (officials and substitutes). Its bylaws (RI) were established on April 5, 2010, by Ordinance 263/10, and the requirements in the new law will be implemented according to the established transitional provisions. The licensing and accreditation of institutions will be required after system implementation by competent agencies<sup>55</sup>.

The Conceia RI, in its Article 15, sets forth the Constitution of four permanent chambers for prior analysis of themes, and claims to be submitted to the plenary of the Council (Permanent Board for Scientific Research, Permanent Board for Education, Permanent Board for Animal Raising and Permanent Board for Alternative Methods). The RI gives the Conceia's executive secretariat the task to prepare and publish an annual report of its activities (Article 19, section XV) and in its Article 20 discourses on the conduct of the proceedings, establishing procedures and deadlines that must be observed and respected during the procedural action, and on Conceia's advertising<sup>55</sup>.

Until 2008 there was no official data available, both in numbers and taxonomic groups of animals used in research in Brazil or procedures employed and institutions involved<sup>56</sup>, a reason that explains the importance of the provisions of RI, in Article 44 related to the necessity of knowledge of Brazilian statistical data by the scientific community and society at large.

In July 2010, Conceia issued its first normative resolution, which provides for CEUA installation and operation<sup>57</sup>. In late October 2010, the system provided for Registry of Institutions for the Scientific Use of Animals (Ciuca) and enacted Ordinance 870/10<sup>58</sup>, by the Ministry of Science and Technology (MCT), which determined their respective assignments. In December 2011, it issued Normative Resolution 3<sup>59</sup>, establishing the Institutional Accreditation for Activities with Animals in Research and Teaching (Ciaep) and establishing criteria and procedures for application, issuance, revision, extension, suspension and cancellation of accreditation of institutions that raise, possess, or use animals in teaching or research. It should be noted that the MCT official website, in the Conceia area, discloses information on its members; schedule, agendas and minutes of

meetings, resolutions, legal advice and opinions<sup>60</sup>. The law stipulates, in its Article 22, the lapse of 90 days after its regulations for institutions to create the CEUA, and five years from its publication in order to adapt to the Concea provisions concerning the regulation of breeding centers, animal facilities and laboratories<sup>61</sup>.

### Research funding through CEUA/ Concea system

The research ethics committees (REC) assist researchers in the adequacy of the proposed projects, as well as observing the protocols and conditions to which the animals are exposed, acting independently, competently, transparently and plural. It is its responsibility to offer opinion on need and conditions of research, as well as to carry out the monitoring of the entire development<sup>36</sup>.

The repealed Law 6,638/79 did not provide for the establishment of committees or commissions related to animal testing and housed in the body of its text only the concept of reducing the suffering inflicted on animals (when established that vivisection is prohibited without the use of anesthesia and determining the practice of special care for animals), although the "3Rs" concept was proposed in 1959<sup>44</sup>. Historically, Sweden was the first country to create ethics on animal research committees in 1979, and the United States established its first committee in 1984<sup>62,63</sup>.

Even if Brazil did not have specific committees system to examine the use of animals in research, it was already guided, timidly, by the "3Rs" principles, with research protocols reviewed by the system established by National Health Council (CNS) Resolution 196/96. CEPs, by this resolution, are coordinated by the National Research Ethics Committee (CONEP): the CEP/Concep system. By June 2009, there were 598 registered CEPs, which included all branches of research involving humans, and not specifically those involving the use of animals<sup>64</sup>.

From the enactment of Law 11,794/08, experiments involving animals became co-opted by Ciuca and analyzed by CEUA, coordinated by Concea: CEUA/Concea system. Thus, there is a rupture with the CEP/Concep system and transfer of research involving animals to the CEUA/Concea system. Thus, a more specialized and refined system is generated, when the analysis of compliance with the "3Rs" concepts and animal wellbeing, positioning itself, in theory, as the most prepared in terms of scientific knowledge to offer

advice - both in relation to methodological issues and regarding ethical questions.

The Brazilian legislation established the CEUA to assist researchers in the appropriateness of projects. The CEUA in a wider sense, are also CEP. Thus, the criticism regarding the role and constitution of the CEP can also extend to the CEUA. Some of them refer to the fact that the committees or commissions act as entities that seek to legitimize the use of animal experimentation, since the protocols are conducted in the best possible way, i.e. with a view to reducing the use of specimens, pain and suffering inflicted. Another critical argument is based on the sense that the committees or commissions were unable to step into the merit of the research project itself and, therefore, its performance would be reduced.

Regarding the Constitution and the final decision there is wide divergence because the committees or commissions are plural agencies, comprising members from the scientific community and civil society, but the prevalence of the arguments, and consequent responsibility of one or another group generates intense dissent including in the very group whose arguments prevailed. There is still the risk of a bias towards institutional or scientific interests, resulting in a preponderance of institutional members and scientists and an intimidating atmosphere for members of the civil community<sup>25,65,66</sup>.

### Intersections of Federal Law and ethical discourses

There is evident influence of the "3Rs" contribution to Law 11,794/08, recognized in the substitution and reduction of used specimens and in the greater refinement in the research as well as in the maintenance of animal wellbeing.

There is an interface of the legislation with the speech of the philosopher Peter Singer solely at the point of recognition of not causing pain or suffering to animals, keeping in line with international documents, a stance which is anthropocentric and speciesist. Singer built the thesis of equal consideration of interests to animals, based on the fact that they admittedly have the capacity to feel pain and if a being suffers, there can be no moral justification for refusing to take that suffering into consideration<sup>67</sup>. Singer uses the term speciesist to, in analogy to the term racist, designate those who give precedence to the interests of their own species to the detriment of others<sup>68</sup>.

There is no point of convergence with Tom Regan's proposal, who brings the discussion to the legal field, advocating the thesis that animals have rights, are moral agents and, therefore, any practice that cause them pain or harm should be abolished<sup>69</sup>. An argument that although in the past has been marginalized and rejected as absurd and now increasingly accepted, has been widely debated and even legally incorporated by some countries<sup>70-71</sup>.

The legislation aligns itself to thinkers like H. Tristram Engelhardt Jr. and Ronald Dworkin, who are positioned towards the continued use of animals, but asserting mandatory benevolent practices and recognition of the value (intrinsic and instrumental)<sup>72-73</sup> of specimens participating in the research.

### Some final thoughts

The ethical debate about animal testing includes theoretical positions ranging from reducing the suffering inflicted to the total and unqualified prohibition of the use of animals in research. However, international documents express the need for experiments involving humans to be based upon results obtained in animal experimentation.

There is the prospect, given the provisions of the current regulations, that, after the whole new Brazilian system is deployed, there will be the production of periodic detailed reports on the use of animals in Brazil, considering that so far there is no official specific data. The next and new Brazilian ethical debates will arise after the production and analysis of statistical information on the subject (total number of animals used per year, species used for experimental purposes, type

of invasive technique used, amount of pain and suffering inflicted, among other information).

Law 11.794/08, which regulates animal experiments in Brazil, determined the adoption of research practices that respect animal wellbeing by reducing the suffering and number of specimens used. Thus, one can observe the incorporation of the contribution of the "3R" by the legal text, especially when looking at articles 14 and 15, which provide for the replacement and reduction of specimens, and refinement of research.

This was the first federal law to specifically regulate the use of animals used in research. However, the effects of standard will only be seen in a few years, because the regulatory system in this phase of implementation and legislation established the deadline of 90 days for the creation of CEUA by institutions breeding or using animals for teaching or research, and five years for the compatibility of physical spaces, according to the disciplined by Conceia - and remains awaiting the installation of the communication system for statistical data that will be produced and subsequently analyzed and used to improve the CEUA/Conceia system itself.

The Brazilian state, even though for some it seems to walk at a slow pace, has evolved its legislation to increase protections for animals, which is realized by the increasing in the penalties for those who commit abuse against them. It went from the legislative vacuum situation previously existing to a proper legislation to regulate experiments with animals, which is aligned with international documents. The creation of a dedicated system (CEUA/Conceia) signals for greater autonomy, expertise and speed in changing the rules of the matter when required, allowing to envision a system in constant evolution and analysis.

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### Authors' participation

The work was carried out during the preparation of the dissertation by Arthur Henry Bridges Regis, guided and supervised, in its entirety, by Gabriele Cornelli.

**Received: 5.11.2010 Reviewed: 7.2.2012 Approved: 22.2.2012**