# Planning and dissemination of research as a parameter of integrity in animal research

*Marta Luciane Fischer* [1], *Gabriela Santos Rodrigues* [2]

**Abstract**

Integrity in animal research, coupled with scientific and social responsibility, demands rigor in the construction and execution of the protocol, commitment to the promotion of animal welfare and the dissemination of suitable data. Protocols for submitting projects to the Ethics Committee on Animal Use, editorial policies and dissemination of the methodology as tools to promote research integrity were analysed based on the questioning of the vulnerability of researchers not trained to fulfill this demand. The results supported the insertion of planning and dissemination of research as a parameter of integrity and adherence to the principle of 3R (Replacement, Reduction and Refinement) as a guide to the decision of how much and how and why to use animals in research. We verified the efficiency of the administrative and legal instrument as a promoter of reflection on technical, ethical, social and legal conception and society. These should be subsidized by the educational role of Bioethics, carried out by committees to mitigate vulnerabilities of the researcher.
**Keywords:** Animal welfare. Animal experimentation. Animal care committees. Scientific integrity review.

**Resumo**

**Planejamento e divulgação da pesquisa com animais como parâmetro de integridade**

A integridade na pesquisa com animais, atrelada à responsabilidade científica e social, demanda rigor na elaboração e execução de protocolos, no comprometimento com o bem-estar do animal e divulgação de dados idôneos. A partir do questionamento da vulnerabilidade do pesquisador para cumprir essa demanda, analisaram-se protocolos de submissão de projetos para Comissões de Ética no Uso de Animais, políticas editoriais e divulgações de método como instrumentos para garantir a integridade da pesquisa. Os resultados subsidiaram o planejamento e a divulgação da pesquisa como parâmetro de integridade e adesão ao princípio de redução, substituição e refinamento. Atestou-se a eficiência do instrumento administrativo e legal como meio de refletir sobre a concepção técnica, ética, social e jurídica para se obter dados consistentes e confiáveis, além de fortalecer a confiança entre ciência e sociedade. Essa reflexão deve ser apoiada pelo papel educativo da bioética, desempenhado pelas comissões para mitigar as vulnerabilidades do pesquisador.
**Palavras-chave:** Bem-estar do animal. Comitês de cuidado animal. Experimentação animal. Revisão de integridade científica.

**Resumen**

**Planificación y divulgación de la Investigación con animales como parámetro de integridad**

La integridad en la investigación con animales, ligada a la responsabilidad científica y social, demanda rigor en la construcción y ejecución del protocolo, compromiso en la promoción del bienestar animal y difusión de datos adecuados. Partiendo del cuestionamiento de la vulnerabilidad del investigador no instrumentado para satisfacer esta demanda, se analizaron protocolos de proyectos presentados al Comité de Ética en el Uso de Animales, políticas editoriales y de difusión de la metodología como herramientas para la promoción de la integridad en la investigación. Los resultados apoyaron la inserción de la planificación y divulgación de la investigación como parámetro de integridad y adhesión al principio de las 3R como guías de la decisión de cuánto, cómo y por qué usar animales. Se comprobó la eficiencia del instrumento administrativo y legal como promotor de reflexión sobre la concepción técnica, ética, social y legal con el objetivo de obtener datos consistentes y adecuados, fortaleciendo la relación de confianza entre Ciencia y Sociedad. Estas deben ser apoyadas por el papel educativo de la Bioética, desempeñado por las comisiones para mitigar las vulnerabilidades del investigador.
**Palabras clave:** Bienestar del animal. Ética animal. Comités de atención animal. Experimentación animal. Revisión de integridad científica.

**Aprovação CEP-PUCPR 887908/14**

**1.** **Doutora** marta.fischer@outlook.com – Pontifícia Universidade Católica do Paraná (PUCPR), Curitiba/PR **2.** **Mestre** rodriguesga@hotmail.com – PUCRS, Porto Alegre/RS, Brasil.

**Correspondência**
Marta Luciane Fischer – Rua Imaculada Conceição, 1.155, Prado Velho CEP 80215-901. Curitiba/PR, Brasil.

Declaram não haver conflito de interesse.

Plagiarism of ideas, data or texts, authorship conflicts, data falsification, among other issues, have been generating more and more discussions in the field of research integrity in the last thirty years [1-3]. This integrity is linked to the ethical conduct of researchers in their professional practice and considers the intention of the study, planning, conduct, analyses and dissemination of results [4]. In addition, it includes aspects such as correction of academic literature, intellectual property and moral rights [1], in the expectation that they are based on values such as responsibility, precaution and honesty [5].

The discussion is incipient in Brazil and focuses mainly on plagiarism and authorship conflicts [3]. The concept of integrity used in this study was conceived during the second World Conference on Research Integrity, held in Singapore in July 2010. The document resulting [6] from the event defined as principles of integrity: honesty in all aspects of research, accountability in the conduct of the research, professional courtesy and fairness in working with others and good stewardship of research on behalf of others.

The terminology "research misconduct" is linked to " research integrity", and refers to data falsification [6] and untrue results [7], in which case the dissemination of illicit results, taken as true, may be considered a fraud mode [8]. Honest results are desired by society, which supports and places confidence in researchers and scientific institutions [9]. In addition, this confidence is strengthened when the dialogue between science and society [1,4] becomes collective responsibility. Fraud affects not only research itself but also the lives of all citizens [2].

The success of a study is conditioned by its planning and dissemination, demanding a reproducible methodological outline [10]. Although this premise is based on Cartesian thinking and has permeated scientific conduct, it has not been unanimous. The Open Science Collaboration [11] tested the reproducibility of 100 psychology studies where only 36% were a replication success, while Begley and Ellis [12] reported a 11% rate of success in the reproducibility of oncology studies. According to a survey carried out by Baker [13] 70% of researchers failed to reproduce another scientist's experiments and more than 50% of researchers failed to reproduce their own experiments. This is attributed to methodological failures, pressure to publish and selectivity reporting [13].

The demand for publications, especially in high-impact journals, has resulted in the limitation of the space provided by the dissemination vehicle. The restriction to the size of the text makes it unfeasible to report biases, such as inadequate procedures and instrument technology, which consequently reflects in the interpretation and exploitation of results [2,12,13].

Animal-based research stands out in this scenario, since there are other ethical issues in addition to the the already mentioned, such as implied suffering, indifference to standards of animal welfare (AW) and inevitable waste of life caused by lack of integrity in research [14-18]. The animal welfare pioneer instrument dates back to 1965 and refers to the Brambell Committee [16]. Consolidated by Broom [16], animal welfare refers to the state of an individual in its attempts to adjust to the environment, and reaches a higher standard when there is more chance of naturally solve the challenges of survival.

The vulnerability of animals directed to research demanded legal and ethical guidelines based on the principle of 3R [20], which recommends reducing the number of animals; refine handling, manipulation and experimentation techniques; and replace the use of animals by alternative methods. Increasing animal welfare standards affects the direct costs of interventions and also their indirect costs which are related to care and production [20].

Fischer et al. [17] proposed environmental enrichment as a guideline for norms of ethical behaviour in order to increase animal welfare standards, which could generate benefits both for scientific development and for the quality of animal life and, above all, the social and ethical responsibility of the researcher.

Therefore, the omission of the researcher [17] could constitute misconduct once the benefits of animal welfare have been proven and if the responsibility is linked to the consequences of acts [2]. In view of this argument, this study asks if the researcher has the necessary conditions to attend to this demand without becoming even more vulnerable to technical, legal and ethical demands. The hypotheses tested were:

1. The protocols for submitting projects for evaluation by the Comissão de Ética no Uso de Animais (Ethical Commission on the Use of Animals - Ceua), legally determined, guarantee the integrity of the research;
2. The researcher compromises the integrity of his or her research by neglecting ethical guiding principles on animal use guidelines, both in the elaboration and dissemination of the research results, when valuing professional demands to the detriment of animal welfare;

3. Instruments and norms created to regulate the use of animals improve the evaluation system, but may deviate from the principles of bioethics if they are designed as bureaucratic procedures only.

Therefore, the objective was to evaluate the instruments available to elaborate and disseminate animal research projects as determinants of research integrity. The results were analysed from the bioethical perspective of identifying the vulnerabilities of the actors involved in the issue, according to which the commitment to animal welfare can be enhanced due to the plurality of moral agents and the complexity of the interrelationships established between them. It was also sought to stimulate the resumption of the educational, promoter of dialogues and formative roles of the Ceua in the resolution of conflicts and reduction of vulnerabilities.

## Material and method

### *Analysis of submission forms to the Ceua*

Forms of evaluation of research projects submitted to the Ceua from public and private universities were collected. The documents, made available on the Internet by the commissions, were obtained by conditioning the search for the terms "college" and "university" to each state of the federation. Institutions whose Ceua had been established and received protocols of submission of projects before the publication of legal guidance were adopted as inclusion criterion [21].

The analysed data were based on the protocol recommended by the Diretriz Brasileira para o Cuidado e a Utilização de Animais - DBCA (Brazilian Guidelines for the Care and Use of Animals) [21]. Data from 57 protocols ( 27 from federal , 19 from private and 11 from state universities), were classified according to the presence or absence of items related to integrity and the general or specific content of the request, considering: 1) justification and relevance; 2) alternative methods; 3) animal model; 4) creation and management environment; 5) statistics; 6) drug use and postoperative; 7) risk analysis; 8) mitigating measures; 9) finalisation; 10) inspection; and 11) term of responsibility.

In order to evaluate the content of the research protocols five years before, during and after the legal implementation of Ceua, protocols of a private university commission from Southern Brazil were analysed. Coded method records were accessed, and 10 documents were drawn from each year, from 2004 to 2015. The content was categorised according to: 1) origin of the research; 2) animal; 3) category of invasiveness (A = invertebrates / observation, B = small or no discomfort, C = minor stress or short duration pain and D = significant stress and pain), 4) conditions of maintenance and manipulation of animals; 5) aspects of welfare animal, risks and mitigating measures.

### *Integrity in the dissemination of animal surveys*

In the Sucupira Portal, 30 scientific journals were selected, 15 of which were national publications (NP) and 15 from international publications (IP). They were distributed in qualification strata A, B and C in the 2012 Qualis classification, in the area of interdisciplinary evaluation [22], whose scope included topics of biology, biomedicine, biochemistry, toxicology and surgery. The editorial policies indicated in instructions to researchers were analysed, being confirmed the presence/ absence of: 1) animals: approval of Ceua, compliance with official documents, mention of animal welfare conducts and application of the 3R principle; 2) human: request for informed consent, compliance with the Declaration of Helsinki [23] and Resolution of Conselho Nacional de Sa*úde (*National Health Council - CNS) 466/2012 [24] (for Brazilian publications); 3) integrity: plagiarism, falsification and fabrication of data; and 4) statement by the author: conflict of interest.

To access the information published by the authors about their research, the method of 100 scientific papers was analysed: 50 published in national publications and 50 in International publications. The magazines were accessed in their electronic pages, following the order of the most recent editions to the oldest ones. We excluded from the sample publications that did not present experimental studies with animals, being recovered one article per newspaper.

The analysis of the texts considered the following items: 1) documents and guidelines related to the methodological design; 2) ethical parameters; 3) description of the macro and microenvironment considering type of environment, housing, nutrition, hydration, manipulation, population and promotion of environmental enrichment.

### *Statistical and legal procedures*

The homogeneity of the categorisation variables (protocols, projects and data conveyed) was verified by the goodness of fit (G-test) test, and the comparison between the categories by means of the chi-square test, considering the level of significance of 95% in both tests. This study also met the ethical guidelines, being conducted in accordance with the *Declaration of Helsinki* [23] and Resolution CNS 466/2012 [24], respecting

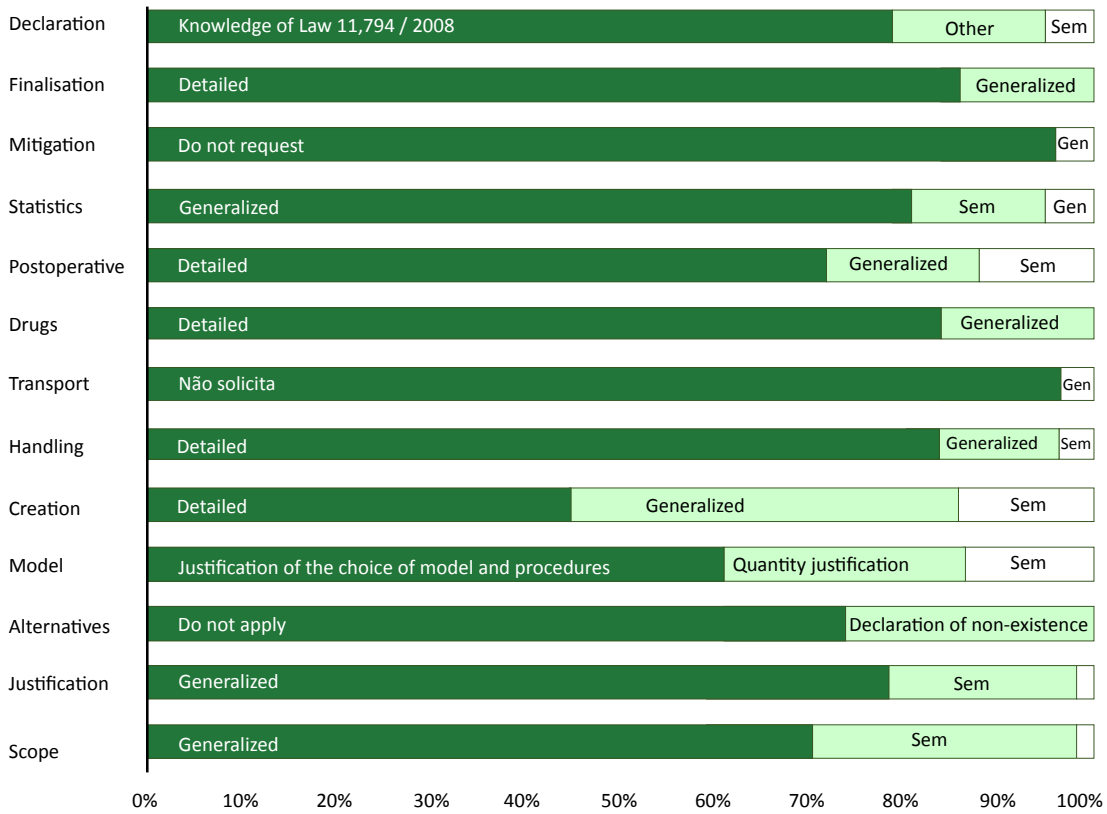
the integrity and anonymity of institutions and authors, as well as the preservation of data.

## Results

### *Analysis of submission forms to Ceua*

The comparison between public and private institutions regarding the application of DBCA standards before their implementation [21] did not show significant differences. In addition, there was a predominance of vague or generalised requests about the relevance and justification of the project, and there were few requests for risk analysis and mitigation attitudes, enforcement, alternative methods and transportation. However, the focus was on statistical design and characterisation of the animal model, on drugs, postoperative and euthanasia / destination (Figure 1). The term of responsibility was outdated in 8.5% of institutions and absent in 17.5%.

**Figure 1.** Relative frequency by category in protocols of submission of projects to Ceua of Brazilian private, state and federal educational institutions.



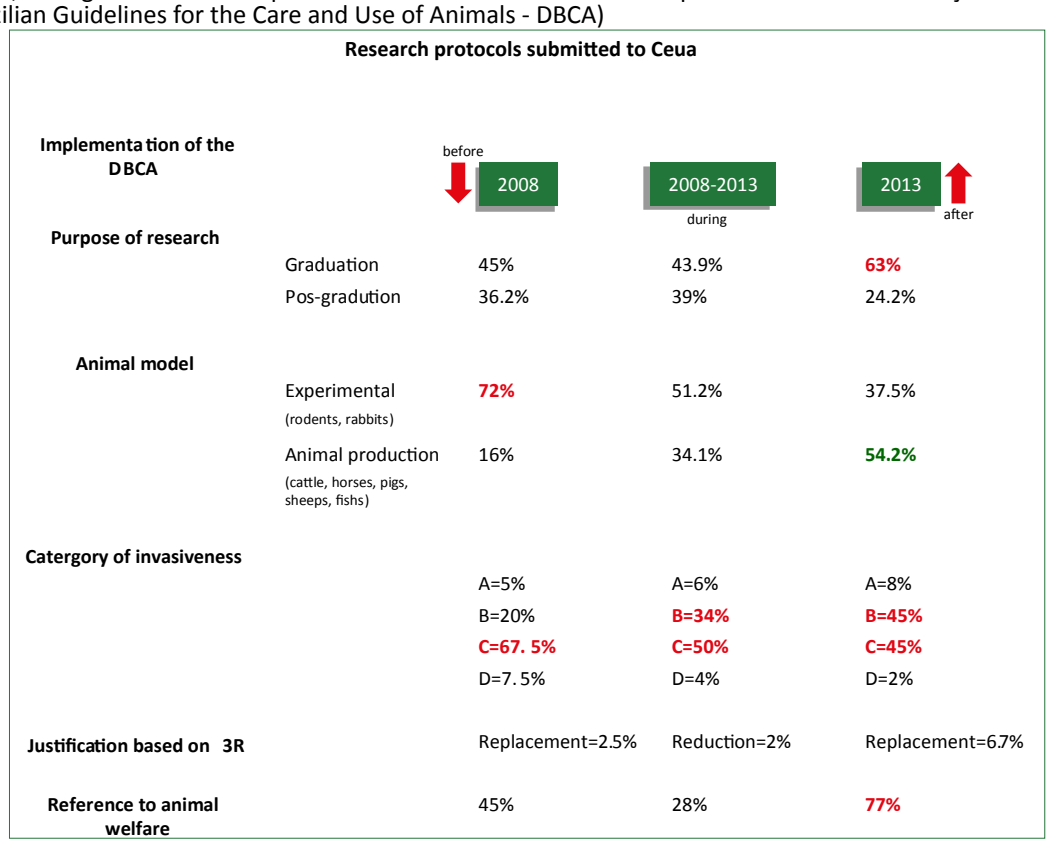

### *Analysis of research protocols before, during and after the implementation of DBCA*

The research protocols evaluated in the characterisation of Ceua from a private educational institution (Figure 2) covered mainly undergraduate studies, being registered researches with rodents (rats and mice) (46.3%), dogs (13.2%), rabbits (4.3%), poultry (1.7%), fish (4.1%), invertebrates (3.4%), birds and animals typically South American such as paca (0.8%) and jaboti (0.8%). The researches have predominantly inflicted intermediate category of invasiveness on animals (C = 52.8% and B = 31.2%), the highest category of invasiveness occurring to a lesser extent (D = 14.4%) as well as the lowest category (A = 1.6%).

The application of the 3R principle in the justification was identified in only 3.2% of the protocols, with one mention to reduction and three to replacement. The application of animal welfare in the methodological description totalled 36% of the protocols and 22.4% of the experiments descriptions. Comparison of the phases before, during and after the implementation of the DBCA indicated a decrease in the use of rats and a decrease of more invasive interventions, in addition to an increase in reference to animal welfare (Figure 2).


Rev. bioét. (Impr.). 2018; 26 (4): 543-55
http://dx.doi.org/10.1590/1983-80422018264273

**Figure 2.** Outline of the characterisation of the research protocols submitted to the Ceua of a private institution before, during and after the implementation of the Diretriz Brasileira para o Cuidado e a Utilização de Animais ( Brazilian Guidelines for the Care and Use of Animals - DBCA)




### *Integrity in the dissemination of animal research*

The editorial policies found on national publications (NPs) differed from those on international publications (IPs) in aspects such as human research papers and issues related to animal welfare. Regarding the integrity of the research, nine IPs mentioned falsification, fabrication, plagiarism, authorship and honesty as to the validity of the results, while only two NPs did so. Although most of the journals requested Ceua's approval, none of them claimed to refuse an article that did not meet ethical or animal welfare standards. Also, many journals did not request compliance with specific documents or indicated concern about pain, discomfort, or animal welfare (Table 1).

Although all Qualis qualification strata were consulted, journals that submitted articles with animal testing were more frequent in stratum B1 (23% ($\chi^2_{(7)}$ = 19.8, p <0.00)) compared to A1 ( 16%), A2 (13%), B2 (16%), B3 (12%), B4 (8%), B5 (4%) and C (8%). There were differences between NP and IP with strata A1 / A2 most sampled from international publications and C from national publications ($\chi^2_{(8)}$ = 285.9, p <0.000).

National and international journals in the areas of medicine (48%), biology (23%), psychology (6%), pharmacy (4%), nutrition and physiotherapy (3% each) were consulted in equal proportion. Only national nursing journals (1%) and dentistry journals (3%) were sampled. Periodicals from the veterinary area (8%) were predominantly Brazilian. The international journals that composed the sample were published in 15 countries (Saudi Arabia, Australia, Canada, China, Denmark, Egypt, Spain, United States, India, Iran, Italy, Japan, New Zealand, the Netherlands and Sweden).

As for the methodological design, 61.2% of the national texts consulted did not refer to any official guidelines, 18.3% cited the Colégio Brasileiro de Experimentação Animal (Brazilian College of Animal Experimentation) and 20.5% [referred to international documents. In the IPs, 44% did not indicate any documents. The ones that did indicate documentation cited guidelines and guides of which 25% were from the European Community. No ethical reference was found in 20% of the NP and 4% of the IP; 66% of the NPs and 22% of the IPs only referred to approval by the Ceua and 14% of the NPs and 74% of the IPs showed an intention to commit to directives or to the Ceua decision, while only 10% of the IPs already indicated measures to reduce and refine the experiments. We verified incipient data regarding the description of the experimental conditions in both NPs and IPs (Table 2).

**Table 1.** Relative frequency of the alternatives of each category analysed in the instructions to authors of national (NP) and international (IP) publications.

| Categories | Variables | PN | PI |
|---|---|---|---|
| Integrity | Request authorship of work | 13.3% | 6.7% |
| | Mentions plagiarism, fabrication, forgery | 13.3% | 60%* |
| | Does not mention integrity | 73.3%* | 33.3% |
| References for research with humans | Helsinki | 6.7% | 40% |
| | Cioms | 13.3% | - |
| | Others | 6.7% | 13.3% |
| | Does not mention | 73.3%* | 46.7% |
| References for research with animals | Yes | 40% | 53.7% |
| | No | 60% | 46.3% |
| General documents | Yes | 26.7% | 6.7% |
| | No | 73.3%* | 93.3%* |
| Conduct of the periodical | Refuses if it doesn't comply with ethics and animal welfare | 6.7% | 13.3% |
| | Refuses if it doesn't comply with ethics in general | 13.3% | 13.3% |
| | Doesn't mention | 80%* | 73.3%* |
| Condition for research on animals | Ask for Ceua's approval | 86.7%* | 53.3% |
| | Calls for authors to adhere to ethical standards | - | 13.3% |
| | Doesn't mention | 13.3% | 33.3% |
| Condition for research on humans | Consent form | 13.3% | 20% |
| | Request approval by Comitê de Ética em Pesquisa – CEP (Research Ethics Committee) | 40% | 20% |
| | Consent form plus CEP | 13.3% | 60%* |
| | Doesn't mention | 33.3% | - |
| Author declation | Copyright | 66.6%* | 86.6%* |
| | Letter of responsability | 6.6% | 6.6% |
| | Doesn't mention | 26.6% | 6.6% |
| Animal welfare | Mention | 20% | 60% |
| | Doesn't mention | 80%* | 40% |

*The homogeneity of the sample in each category was tested by Gtest. Values which are significantly larger are accompanied by an asterisk (*).*

**Table 2.** Relative frequency of selected criteria seen in NP and IP

| | Categoria | Total | PN | PI |
|---|---|---|---|---|
| **Macro e microenvironment** | Incomplete description | 90* | 82* | 96* |
| | No description | 10 | 18 | 4 |
| **Environment** | Temperature | 51 | 44 | 58 |
| | Air humidity | 20 | 10 | 10 |
| | Light/Dark cycle | 74* | 54 | 94* |
| **Enclosure** | Kind/material | 21 | 30 | 12 |
| | Size | 5 | 10 | 0 |
| | Substrate | 2 | 4 | 0 |
| | Population | 11 | 14 | 8 |
| **Handling** | Water and Feed availatility | 70* | 66* | 72* |
| | Kind of feed | 10 | 6 | 20 |
| | Kind of water | 13 | 10 | 0 |
| | Adaption period | 11 | 18 | 4 |
| | Environmental enrichment | 0.5 | 0 | 2 |

** Significantly higher values according to Gtest*

## Discussion

The data from this study subsidise the planning and delivery of animal research as a parameter of integrity and adherence to the principles of the 3Rs which are considered the guide of how much, how and why to use animals in research. The analysis of protocols submitted to Ceua's evaluation prior to the implementation of guidelines [21] legitimises the legal orientation of ethically reasoned technical projects, validating the expectation that bureaucracy will increase control over animal welfare and strengthen ethical issues. The official direction for filling out a standardised protocol, based on the legal system and in accordance with bioethics, run through the viability of the examination and monitoring by Ceua [25]. Concomitantly, it leads the researcher to reflect on the technical, ethical, social and legal conception of the project, aiming scientific rigor, consistency and suitability [10,15].



http://dx.doi.org/10.1590/1983-80422018264273

The analysis did not show great discrepancies between private and public institutions, even in the face of recognised specificities of conception and management [26]. The uniformity in the minimum items required to understand the procedures corroborates what has been verified by Fischer and collaborators [15] in a workshop that discussed successes and vicissitudes of the Ceua. According to the authors, the Ceua requested uniform online submission. The adjustments became constant due to the need to consider the peculiarities of each research as the guidelines for the elaboration of the protocol [21] had been previously standardised.

Enhancement of legal regulations has led to a more complete and targeted, though more complex, form. Many researchers consider this new model a bureaucratic and laborious hindrance that delays research. This interpretation can be taken as lawful if the purpose of the research is utilitarian, aiming only to reach academic degree, career improvement, financing, recognition or other motive that is not directly related to its scientific and social merit [12]. However, it is necessary to understand that the completion phase of the form is an excellent time to reflect on the study, contributing significantly to the education and training of young scientists.

According to Richmond [10], researchers' complaints about regulatory rigidity are inconsistent with their inherent flexibility, coupled with specialised judgments to determine the best research strategy, as well as rigour and transparency to promote health and environmental safety. The decision to use living beings as an experimental model can not be taken lightly and should be inserted as one more item of the project, since it adds numerous complex variables to the investigation, many of which are still incomprehensible by science. These aspects, which may compromise results [27], increase the responsibility of the researcher and add the maintenance of ideal conditions for a living system to the matter of scientific rigor in data collection.

The analyses of the protocols submitted before, during and after the implementation of the Law 11.794/2008 [21], which establishes procedures for the scientific use of animals, verified its effectiveness in reducing experimental studies, promoting a lower level of invasiveness and increasing the number of references to animal welfare. These results portray a reality prior to the the Resolução Normativa Concea (Normative Resolution Concea) 27/2015 [21], whose most complete guidelines highlight the integrity of the researcher and the Ceua's priority to the application of the 3Rs principle as well as welfare promotion in each step of the research. With this, the researcher must assume the responsibility of correctly filling out the protocol and, with technical and ethical elements, to refrain from responding in an exclusively bureaucratic way [25].

However, one must consider the vulnerability of the researcher in the system established and the social expectation that he or she is responsible in his/her behaviour. Even though this vulnerability is small when compared to that of animals, researchers' autonomy may be compromised if they don't have appropriate knowledge and question who would be responsible to help them to overcome this condition. In this context it is necessary to reflect on the limits between the inspecting and educational roles of Ceua and the research institution [15,16,25]. There is no doubt that the legislation promoted improvements, as can be attested by data from this and other research [15,16,25]. However, Ceua members have questioned whether the increase of bureaucracy and the pressure for legal compliance coupled with severe penalties have not gradually removed the bioethics of the Comissão de *É*tica no Uso de Animais (Ethical Commission on the Use of Animals - Ceua) [15].

Until then, aspects such as relevance and justification of the work were little explored by protocols, although they were considered important for the reflection of the researchers because they are strongly linked to social and scientific responsibility. The generalist elaboration of the document, focusing only on the scientific context, did not direct the researcher to consider the cost-benefit of the research, ignoring the 3R s principles and disregarding studies with a similar approach [21,25].

In this respect, Richmond [10] emphasises that the justification of the project should not only be convenient, but honest and reflective of analysis and suitability to the hypotheses. Kostomitsopoulos and Đurašević [4] also point out that the ethical justification of studies with animal experimentation is conditioned to humanitarian procedures, exemption from anthropocentric valorisation and responsibility with the moral obligation to reduce and replace the samples and refine their research. Thus, the team must ensure the success and scientific relevance of the project, presenting properly all steps of the protocol subsequent to the conscious and consistent decision of animal use.

Protocols have always detailed experimental model, sample handling and pharmaceutical drugs

used, reflecting the original Ceua conception focused on experimental studies with laboratory animals. Still, many commissions requested general data which were difficult to prove. This led Concea to standardise "accepted", "accepted with restriction" and "not accepted" drugs [10].

On the other hand, information on breeding and transport was neglected, with the sole responsibility being attributed to the vivarium, which allowed researchers to omit them. However, it has been shown that macro and microenvironment can significantly influence animal welfare [17,27], which, in addition to generating pain and suffering, may compromise the research results. This threatens the integrity of research as it disseminates incomplete or inconsistent data, which may lead to dubious or misleading interpretations and end up compromising the development of the research area [17] .

Asked about risks, researchers readily testified to their lack, probably in order to value the research. However, failure to identify risks previously precludes the creation of emergency mitigation measures [14]. Only reports of postoperative procedures are insufficient and it is necessary to encourage the preparation and validation of individual and accessible records for monitoring the animals.

Researchers often question subjectivity in identifying pain [15], in addition to the lack of efficient instruments to validate the animal welfare [17]. The DBCA understands that the absence of parameters to identify pain and discomfort does not justify ignoring them. It therefore encourages pilot studies for researchers and animals to adapt and abnormal physiological conditions are readily identified and mitigated.

The encouragement of alternative methods and the researcher's responsibility to seek information about them presented low adherence, even if experiments with animals on interventions with already validated alternatives are illegal [21]. Legislators have encouraged researchers to learn about innovations, adhere to their purposes and to indicate accurately the efficacy and safety of substance or product [21,28]. Richmond [10] warned that the use of alternative methods should aim to overcome the limits of the animal model and not be adopted for simple social convenience. He also stressed that new methods must be precisely described, consider the limitations of the findings and confirm negative animal tests.

The current term of responsibility is more complete, requiring the signature of all researchers, who must attest to know the Law 11.794 / 2008 [21] and its regulations, as well as being responsible for not duplicating the study for the lack of alternative methods and for training. This model assumes that adherence to the term is sufficient to safeguard the responsibility of other regulatory bodies [16]. Bioethical intervention, on the other hand, identifies an increase in the vulnerability of researchers, since they are conditioned to sign the term to validate the research, even if they do not have the knowledge attested.

However, it should be considered that understanding the content - broad and complex - is not guaranteed even if all available legislation is read. Collecting knowledge of the law without preparing the researcher regarding critical and responsible autonomy in situations of ethical conflict evidences the inoperability of some Ceua to foster bioethical paradigms. Therefore, if these commissions would change their behaviour in order to clarify the new paradigms, deficiencies in completing the form - attested in this study by the small reference to the 3Rs principle and the animal welfare - could be remedied.

This study observed a high number of protocols associated with undergraduate studies, which may compromise the social responsibility of publishing scientific findings, since, in this context, the use of animals seems to have fulfilled didactic and training functions. Although many of these protocols come from research groups that focus on scientific production, many are not effectively published. Thus, it is considered that the most appropriate at this stage of the training would probably be to work on the student's conception of research projects, biases, and aspects related to integrity by means of alternative methods or analysis of published articles' data. Then, in a later stage of professional maturation, after the student had assimilated such notions, one could allow the use of the animal as a biological model, since inserted in a situation reflected and planned according to the criteria in force.

The analysis of conditions imposed by scientific journals for the publication of animal research indicates a departure from co-responsibility for not clearly demanding researchers' ethical conduct, attributing this responsibility to the Ceua [14]. This limitation is legitimised by the volume of work, by the inexperience of human resources for follow-up and by the gratuitousness of the publication in the majority of the magazines. It adds to this the restriction of the space made available for publication, which makes it impossible a more complete reports of the real research conditions and biases.

In recent years, the collection of productivity, coupled with academic pressure and meritocracy, has been making the researcher vulnerable [2]. The utilitarian bias of the scientific publication adopted by many researchers and institutions has influenced the quality of texts, which must be demanded from researchers, financiers and editors, who must ensure good practice in the scientific environment and the delivery of reliable and reproducible results [9]. Publishing policies are tools for innovation and reflection on what is acceptable and what is not acceptable. Since instructions to the authors are the first instrument of communication between journal and researcher, they must carefully contemplate ethical determinations that confer integrity to the research [29].

It should be emphasised that in the case of animal research, it is essential to link ethical conduct to the promotion of animal welfare. The data from this study demonstrate that Ceua's approval was more requested than that of the Comit*ês de É*tica em Pesquisa (Research Ethics Committees), probably because the law on animal research precedes the norm for studies involving humans. Still, and even after legal determination, studies such as Silla, Oliveira Sans and Molento [29] showed that only 10% of the journals analysed conditioned the publication to the approval of the research by evaluation bodies.

The results also showed that insufficient information is published both nationally and internationally. Just mentioning Ceua's approval and reporting conducting an experiment based on guideline or legislation does not provide enough elements to legitimise results and promote comparability and reproducibility. It is the responsibility of the researcher not only to conduct research with rigor and ethics, but also to convey correct and complete data so that they are incorporated into knowledge and effectively fulfil their social function [17,30].

It should be noted that none of the reviewed journals mentioned the possibility of disclosing losses and bias, reinforcing the culture consolidated by many researchers that methodological failures and negative results should not be part of technical, ethical and legal procedures of publication. Begley and Ellis [12] reiterate that the encouragement of some journals to deliver positive results - and in some cases the suggestion to remove original data in the publishing process - makes it unfeasible to expose the losses to subsequent investigators by allowing an inappropriate and sterile process to be repeated, delaying techno-scientific development.

Obviously, it should be considered that dissemination vehicles do not have access to the actual process of the research and should therefore rely on the integrity of the data presented by the researcher, who may decide to present more attractive results, omitting biases, in order to see his or her article accepted and meet academic demands. The data of this study attest the negligence of those surveyed in informing the actual experimental conditions in both national and international publications. It is clear that all conditions that can influence the model and, automatically, the results must be shared in full.

Integrity is an appropriate conduct, which enables the real interpretation of the data, making it possible to compare research and scientific advances. It was verified in great part of the analysed works that macro and microenvironment data were generalised, presented from standard texts. Such an exposition does not reinforce the presentation of straightforward studies that report previous environmental and handling conditions concomitant with interventions and all initiatives for refinement of the research.

It has been scientifically proven that the refinement of the environment promotes physiological and psychological stability, allowing low levels of animal welfare to be identified and eliminated [10,27]. For Braga [27], ignoring the influence of environmental conditions on the research results, as well as altering or omitting information during publication, constitutes scientific misconduct and lack of ethical commitment [14].

## Final considerations

The integrity of animal experiments must be based on the ethical principles of responsibility, honesty and impartiality, indispensable requirements for the researcher who has at his or her disposal a legal and administrative structure that leads him or her to a conscious, critical and sustainable reflection in the elaboration, execution and dissemination of the research. The results of this study indicate a predominance of the utilitarian vision of the research by some researchers, linked to bureaucratic demands, demonstrating the importance of reflecting, discussing and applying principles of bioethics.

Integral, true research that contributes to the consolidation and evolution of scientific knowledge must encompass scientific rigor at

all stages. In the case of the use of animals, it is necessary to go beyond reductionist conception to actually ensure their physical and mental integrity under the biological and ethical view. Researchers must assume social responsibility, linked to the quality and accuracy of the data and ethical responsibility, and not increase the vulnerability of the animals [17].

The framing of ethical and legal guidelines in the 3Rs principles calls for the responsibility of properly trained researchers. The reflection on why, what, how, when and how many animals to use should be disconnected from the logistic or monetary convenience an be instead the result of autonomous, critical, conscious, responsible and ethical decision. Russo [2] suggests that by incorporating responsibility as the value of science measurement, fraud will automatically be replaced by mutual compromise between society and science, in which the quality of the protocol and of the data disseminated will be the driving force of the research, not the quantity of publications.

Richmond [10] warns that instead of directing efforts to only reduce the number of animals used in research, it is also necessary to minimise their suffering, since narrowing the sample size does not necessarily mean that the pain is reduced. Therefore, it is necessary to apply the right test at the right time, based on complete information and not only on statistical projections dissociated from the living organism, whose underestimation may make future interpretations unfeasible. The author also suggests considering the number of animals killed during the experiment as an indicator of ethical and technical standards of refinement and scientific use of the data, embodying the ethics of care.

The lack of technology to reduce, replace and refine should not be seen as an obstacle, but as a possibility of investment and multidisciplinary action in the creation of more sophisticated, efficient and fast means to achieve direct and necessary application responses such as:

- technology to homogenise the sample and reduce the need for replications involving genetic interference and monitoring, environmental control and statistical processing;
- technology to refine the breeding environment, promoting less manipulation of animals with microchipping and filming;
- protocols and biomarkers to identify low levels of animal welfare BEA pain signals;
- validation of environmental enrichment techniques for specific interventions;
- instantaneous and effective mitigating measures and more efficient drugs for each animal species;
- simulators and alternative methods;
- education through compulsory and optional courses of bioethics, lectures, seminars, disciplines, acting in different sectors of society and increase of Ceua's visibility ;
- creation of a public database for disclosure of errors.

Obviously, the technical limitations of the current system, both in terms of institutions and vehicles for scientific dissemination, go beyond the field of activity of the researcher. This professional is placed in a condition of vulnerability in the conflict between responding responsibly to ethical and legal demands, which he or she may not know to the satisfaction, or responding to bureaucratic and academic demands, often conditioning the effectiveness of the researcher's professional practice.

It is necessary to emphasise that although the responsibility is of all the involved in the project, the researchers must be aware of the activities subject to regulations, seeking to obtain adequate formation on the matter. They need to understand and follow the rules of project design and execution with merit and disclose the complete data [10]. Failure to comply with the approved protocol and the inability to follow institutional or legal recommendations for the care of animals are considered a serious type of misconduct [31]. Padua and Guilhem [3] refer to the sharing of responsibilities between scientists and society in general, whose cooperative work must establish standards of conduct without prejudice to science or researchers, as well as co-operative and corrective sanctions.

Cases of misconduct have increased the number of policies on integrity in research. Bioethics is inserted in this context, subsidising the educational and formative role of the Ceua [15,25] and stimulating the adoption of the new parameters of research in education and scientific practice [1,3,4]. Richmond [10] points out that changing paradigms, processes and technologies in all countries seeking technical excellence and innovation demands new skills, costs and time, and it is fundamental to look for ways to reduce bottlenecks that may affect research.

However, the author also warns that often the data may be limited and inadequate instead

of necessarily invalid. Although regulatory bodies present practical obstacles, only through transparency and dialogue will these issues be resolved in a consensual and fair manner for all. While integrity education in research is the responsibility of institutions, the articulation with development agencies and publishers is necessary and urgent.

It should be noted that Shinkai [30] reinforced the direct responsibility of journals, considering editorial staff, reviewers, authors and readers, about the quality and suitability of the research. It is imperative that studies submitted to publication prove adherence to scientific, ethical, social and political standards, thus promoting self-criticism regarding the relevance of the research. In this context, it should also be considered that journals and academic institutions do not have the autonomy to waive or change federal norms, and are often also vulnerable to the idiosyncrasies of the models adopted in the country to classify scientific production.

The information obtained in this work also showed that the topic of integrity in research needs to be more discussed in institutions. It is also necessary that researchers and professors be able to design and implement more efficient procedures to consolidate new ethical paradigms regarding the use of animals [25]. However, for Russo [2], the commissions established at these institutions to discuss integrity in research will be insufficient if students, scientists, editors, jurists and society do not discuss scientific responsibility. The complexity of the issue in the face of increasing dissemination of scientific information demands investments in technology, qualification of human resources and high level education with early academic training and continuing education, in which the understanding of conceptions and paradigms will consolidate the culture of ethics and integrity in research [3].

Bioethics generated and consolidated the Ceua, aiming through its processes to ensure animal welfare in experiments. However, the legal regulations have established bureaucratic procedures that prescribe legal and administrative sanctions, without, however, promoting the deepening of bioethical reflection and practice. Associated with this situation, the replacement of Ceua members by new participants who did not experience the pre-legislation period, has made possible the vulnerability of all actors involved in animal use in the biomedical context. In this moment of transition, it is necessary to strengthen the bioethical reflection in the formation and guide the researchers to the dialogue with other sectors of the society.

The decision to use animals for research should be the result of a critical reflection based on common ethical values, and experimental planning, interventions, data analysis and dissemination of results should be carried out in a responsible and thorough manner to justify its use in order to meet an ethically valid necessity.

*The data presented in this research were sampled during the development of a master's thesis entitled "Animal welfare as a parameter for the evaluation of integrity in research", defended in the Programa de Pós-Graduação em Bioética da Pontifícia Universidade Católica do Paraná (Post-Graduate Program in Bioethics of the Pontifical Catholic University of Paraná), approved on 25 February 2016. We are grateful to the agência Fundação Araucária (Araucária Foundation agency) for the scholarship grant agreement 11/2013, the trainee Mariane Londero, the scientific initiation student Marina Kobai Farias and the master student Lilian Quintana Jankoski for their assistance in data collection.*

## Referências

1. Vasconcelos S. Integridade e conduta responsável na pesquisa: grandes desafios. Pesqui Fapesp [Internet]. 2012 [acesso 20 ago 2017];(200):58-9. Disponível: https://bit.ly/2QtQ5St
2. Russo M. Ética e integridade na ciência: da responsabilidade do cientista à responsabilidade coletiva. Estud Av [Internet]. 2014 [acesso 20 ago 2017];28(80):189-98. Disponível: https://bit.ly/2y0ZdHL
3. Pádua GCC, Guilhem D. Integridade científica e pesquisa em saúde no Brasil: revisão da literatura. Rev. bioét. (Impr.) [Internet]. 2015 [acesso 20 ago 2017];23(1):124-38. Disponível: https://bit.ly/2qz8wJU
4. Kostomitsopoulos NG, Đurašević SF. The ethical justification for the use of animals in biomedical research. Arch Biol Sci [Internet]. 2010 [acesso 20 ago 2017];62(3):781-7. Disponível: https://bit.ly/2RH1v5q
5. Santos LHL. Sobre a integridade ética da pesquisa. São Paulo: Fapesp [Internet]. 2011 [acesso 20 ago 2017]. (Texto de trabalho). Disponível: https://bit.ly/2znzj13

6. World Conferences on Research Integrity. Singapore statement on research integrity [Internet]. 22 set 2010 [acesso 20 ago 2017]. Disponível: https://bit.ly/2PRLqZC
7. Conselho Nacional de Desenvolvimento Científico e Tecnológico. Diretrizes [Internet]. 2011 [acesso 20 ago 2017]. Disponível: https://bit.ly/2MZN4H6
8. Heyde CJ. NABR's misinformation cripples animal welfare and scientific integrity. AWI Quarterly [Internet]. 2002 [acesso 28 out 2013];(51)3:14-15. Disponível: http://bit.ly/2cMb0j9
9. Academia Brasileira de Ciências. Rigor e integridade na condução da pesquisa científica: guia de recomendações de práticas responsáveis [Internet]. 2013 [acesso 20 ago 2017]. Disponível: https://bit.ly/2pww2XK
10. Richmond J. Refinement, reduction, and replacement of animal use for regulatory testing: future improvements and implementation within the regulatory framework. Ilar J [Internet]. 2002 [acesso 20 ago 2017];43(Supl 1):S63-8. Disponível: https://bit.ly/2z0kTUh
11. Open Science Collaboration. Estimating the reproducibility of psychological science. Science [Internet]. 2015 [acesso 20 ago 2017];349(6251):aac4716. Disponível: https://bit.ly/221S3Jz
12. Begley CG, Ellis LM. Drug development: raise standards for preclinical cancer research. Nature [Internet]. 2012 [acesso 20 ago 2017];483(7391):531-3. Disponível: https://bit.ly/2PfD56p
13. Baker M. 1,500 scientists lift the lid on reproducibility. Nature [Internet]. 2016 [acesso 20 ago 2017];533(7604):452-4. Disponível: https://bit.ly/2JP2GNp
14. Fischer ML, Oliveira GMD. Ética no uso de animais: a experiência do Comitê de Ética no Uso de Animais da Pontifícia Universidade Católica do Paraná. Estud Biol [Internet]. 2012 [acesso 20 ago 2017];34(83):247-60. Disponível: https://bit.ly/2AT4an8
15. Fischer ML, Oliveira GMD, Malheiro A, Feijó AGS, Molinaro E, Casais-e-Silva LL *et al*. Regimento e protocolo. Estud Biol [Internet]. 2014 [acesso 20 ago 2017];36(Supl 1):1-12. Disponível: https://bit.ly/2DaXulG
16. Fischer ML, Prado AMR, Oliveira GMD, Tolazzi AL, Passerino ASM, Zotz R *et al*. Concepção, implementação e consolidação do Comitê de Ética no Uso de Animais da PUCPR. Estud Biol [Internet]. 2014 [acesso 20 ago 2017]; 36(Supl 1):247-60. Disponível: https://bit.ly/2Ost1lf
17. Fischer ML, Aguero WP, Rodrigues GS, Simão-Silva DP, Moser AM. Enriquecimento ambiental como princípio ético nas pesquisas com animais. Rev. bioet. (Impr.) [Internet]. 2016 [acesso 20 ago 2017];24(3):532-41. Disponível: https://bit.ly/2SXtMGf
18. Fischer ML, Librelato RF, Cordeiro AL, Adami ER. A percepção da dor como parâmetro de status moral em animais não humanos. Conexão Ciênc [Internet]. 2016 [acesso 20 ago 2017];11(2):31-41. Disponível: https://bit.ly/2PfEtpD
19. Broom DM, Fraser AF. Comportamento e bem-estar de animais domésticos. 4ª ed. Barueri: Manole; 2010.
20. Russel WMS, Burch RL. The principles of humane experimental technique [Internet]. Special ed. London: UFAW; 1992 [acesso 20 ago 2017]. Disponível: https://bit.ly/2ATy6zk
21. Brasil. Ministério da Ciência, Tecnologia, Inovações e Comunicações. Normativas do Concea para produção, manutenção ou utilização de animais em atividades de ensino ou pesquisa científica [Internet]. 3ª ed. Brasília: Concea; 2016 [acesso 20 ago 2017]. Disponível: https://bit.ly/2OJRIuq
22. Brasil. Ministério da Educação. Plataforma Sucupira [Internet]. Brasília: Capes; 2014 [acesso 20 ago 2017]. Disponível: https://bit.ly/1KCtInH
23. Associação Médica Mundial. Declaração de Helsinque da Assembleia Médica Mundial (WMA) [Internet]. Helsinki: WMA; 1964 [acesso 20 ago 2017]. Disponível: https://bit.ly/2MP2H4A
24. Conselho Nacional de Saúde. Resolução CNS nº 466, de 12 de dezembro de 2012. Aprova diretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos [Internet]. Diário Oficial da União. Brasília; nº 12, p. 59, 13 jun 2013 [acesso 20 ago 2017]. Disponível: https://bit.ly/20ZpTyq
25. Zuanon ÁCA, Benjamin LA, Fonseca CC. Contribuições para a adoção de uma cultura de divulgação, valorização e de respeito aos comitês e, ou, comissões de ética no uso de animais. Rev Ceres [Internet]. 2014 [acesso 20 ago 2017];61(Supl 1):757-63. Disponível: https://bit.ly/2SWKK7N
26. Bittencourt HR, Viali L, Rodrigues ACM, Casartelli AO. Mudanças nos pesos do CPC e seu impacto nos resultados de avaliação em universidades federais e privadas. Avaliação [Internet]. 2010 [acesso 20 ago 2017];15(3):147-66. Disponível: https://bit.ly/2DwMPmg
27. Braga LMGM. O animal como um modelo experimental: noções básicas de genética, sanidade, alojamento e manutenção de animais de laboratório. In: Feijó AGS, Braga LMGM, Pitrez PMC, organizadores. Animais na pesquisa e no ensino: aspectos éticos e técnicos [Internet]. Porto Alegre: EdiPUCRS; 2010 [acesso 20 ago 2017]. p. 171-86. Disponível: https://bit.ly/2OxmqGj
28. Presgrave OAF. Alternativas para animais de laboratório: do animal ao computador [Internet]. Rio de Janeiro: Fiocruz; 2002 [acesso 20 ago 2017]. Disponível: https://bit.ly/2zIanjM
29. Silla VC, de Oliveira Sans EC, Molento CF. An estimation of the extent of animal use in research in Brazil, as determined by bibliographic sampling from journals published in the State of Paraná. Altern Lab Anim [Internet]. 2010 [acesso 20 ago 2017];38(1):29-37. Disponível: https://bit.ly/2SV5Pzr
30. Shinkai RS. Integridade na pesquisa e ética na publicação. Sci Med [Internet]. 2011 [acesso 20 ago 2017];21(1):2-3. Disponível: https://bit.ly/2Qvc9My

31. InterAcademy Council. Responsible conduct in the global research enterprise: a policy report [Internet]. Amsterdam: IAC; 2012 [acesso 23 out 2018]. Disponível: https://bit.ly/2qBZtbd

**Participation of the Authors**

Marta Luciane Fischer analysed, interpreted and discussed the data and organised the results. Gabriela Santos Rodrigues tabulated the data. Both authors conceived the project, collected data and wrote the article.

Recebido: 24.5.2017
Revisado: 22.3.2018
Aprovado: 24.3.2018