

Animal Experimentation and Animal Welfare in the Context of the European Union: Reflections on the Directive 2010/63/EU and Its Transposition in Italy

Ilja Richard Pavone*

ABSTRACT: Directive 2010/63/EU on the Protection of Animals used for Scientific Purposes – which replaces the former Directive 86/609/EEC – provides a common framework on animal testing in the European Union. Its adoption raised a fierce debate in European countries and in particular in Italy between opponents and supporters to experiments on animals. This paper, after an analysis of the content of the Directive, aims to analyse issues concerning its transposition in Italy, which took place through the Legislative Decree No. 26 of 4 March 2014.

KEYWORDS: Directive 2010/63/EU; Animal Experimentation; Animal Welfare; Legislative Decree No. 26/2014.

SUMMARY: 1. Introduction. – 2. The European Legal Framework. – 3. The Directive 2010/63/EU. – 4. The Regulation of Use of Non-Human Primates (NHPs) in the Directive 2010/63/EU. – 5. The Transposition of the Directive 2010/63/EU by Member States. – 6. The Case of Italy. – 7. Conclusions.

1. Introduction

Research on animals had and continues to have a fundamental role in scientific and medical developments and improves our comprehension of a multitude of human and animal diseases¹.

Animal models play a crucial role in fundamental medical research: progress in the fields of drug discovery, regenerative medicine and cancer research among others, are heavily dependent on *in vivo* models to validate *in vitro* observations². In fact, despite the growing interest for alternative and

* PhD, Researcher, Institute of Biomedical Technologies, Biolaw Unit, National Research Council, Rome. This essay has been subjected to a double blind peer review.

¹ A. GUERINI, *Experimenting with Human and Animals: From Galen to Animal Rights*, Baltimore, 2003, 137 ss., E.F. PAUL, J. PAUL, *Why Animal Experimentation Matters: The Use of Animals in Medical Research*, London, 2001, 4 ss.

² Animals in biomedical research are mainly used for basic research, translational research (research in which the aim is the improvement of human welfare, *i.e.* drug testing), research in which the aim is the improvement of human welfare and for education; see *e.g.* G. GENICOT, *Droit médical et biomedical*, Bruxelles, 2010, 763 ss., T. HARTUNG, *Toxicology for the Twenty-First Century*, in *Nature*, 460, 2009, 208 ss. According to the German Animal Welfare Act of 1998 (*Tierschutzgesetz*), experiments on animals are defined as, «Experimental procedures or treatments of animals, if these may be linked to pain, suffering or damage to these animals, or on the hereditary material, if these may be linked to pain, suffering or damage to the animals with modified hereditary material or the animals which bear these» (§ 7).

complementary methods, research is still strictly linked to “test *in vivo*”, considered as the reference model for a sure and predictive medicine³.

However, conventional rodent and large animal experiments raise ethical issues at the same time as animal welfare and animal rights issues⁴. In addition, the numbers related to animal experimentation are increasing, reaching an average of 912.000 animals in Italy, 12 million in European labs and 115 million worldwide. This data is highly underestimated because it does not take into account invertebrates, fetal and animals forms, or part of them, used or already suppressed⁵.

Indeed, it is necessary to reconcile, in a shared and balanced way, different goods, all of them worthy of protection, such as the advancement of human health and welfare, the promotion of scientific research on one side, and the reduction of animal suffering and the avoidance of useless and disproportionate pain to the animals on the other side.

The European Union (EU) tried to answer to the ethical concerns raised by animal research adopting Directive 2010/63/EU on the «Protection of Animals used for Scientific Purposes»⁶, which is the most relevant EU legislative act on this matter.

The Directive sets up more stringent requirements for the use of animals in biomedical research with the goal of improving their protection. The Directive aims to ensure the highest standard of care of animals used in biomedical research and has the final goal of the replacement of the use of animals in experimentation in line with the 3Rs (Replacement – use of non-animal methods; Reduction – methods which reduce the number of animals used; Refinement – methods which improve animal welfare), including the promotion of alternative methods.

In this paper, we will focus our attention on the main legal issues surrounding animal testing in the European Union. Particular attention will be paid to the positive and controversial aspects of Directive 2010/63/EU and to the major issues concerning its transposition in EU Member States, with particular attention to the case of Italy. This country was in fact the last one to transpose and implement the Directive after a heated debate in the Parliament, as well as in the civil society, between supporters and opponents to animal testing.

A focus will be devoted to the specific measures concerning the use of nonhuman primates (NHPs) set up in the Directive. As an introduction, we will briefly analyse the legal evolution in the EU context of the principle of animal welfare.

³ H. LA FOLLETTE, *Animal Experimentation in Biomedical Research*, in T.L. BEAUCHAMP AND R. FREY (eds), *The Oxford Handbook on Animal Ethics*, Oxford, 2011, 796 ss.

⁴ On the rising of animal rights and on the debate on animal testing, see L. BATTAGLIA, *Un’etica per il mondo vivente. Questioni di bioetica medica, ambientale, animale*, Roma, 2011; H. LA FOLLETTE, *Brute Science: Dilemmas of Animal Experimentation*, London, New York, 1997; V. MONAMY, *Animal Experimentation. A Guide to the Issues*, 2nd ed, Cambridge, 2009, B.G. NORTON, *The Preservation of the Species. The Value of Biological Diversity*, Princeton, 1986; T. REGAN, *The Case for Animal Rights*, in P. SINGER (ed.), *In Defense of Animals*, New York, 1985, 13 ss., P. SINGER, *Animal Liberation*, New York (1975, reprinted in 2002).

⁵ http://ec.europa.eu/environment/chemicals/lab_animals/home_en.htm (last visited 31/10/2015). For an analysis of the economic interests behind animal testing, D. LYONS, *The Politics of Animal Experimentation*, Basingstoke, 2013; M. KHUAN, *Sperimentazione animale e farmaci che ammalano*, 2010, 14 ss., available at the website of LAV, www.lav.it/download.php?t=files&id=4719 (last visited 31/10/2015).

⁶ Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the Protection of Animals used for Scientific Purposes, 2009 OJ (C 227), 51 (EU) [Directive for the Protection of Laboratory Animals].

2. The European Legal Framework

Animal welfare has become a priority of EU policies in the last decade. Provisions on animal welfare are therefore provided in primary (treaties) as well as in secondary (directives, regulations) legislations. Animal welfare relates to the general health and well-being of animals and covers a wide range of issues, from the care of family pets to concerns about exploitation and abuse.

The former European Community began to deal with the issue of animal welfare in the Eighties mainly within the harmonization process⁷, while nowadays the evolution in EU policies includes animal welfare within a broader framework encompassing social and economic issues. This development reveals the modification in attitudes in EU society with regard to the necessity of reducing unnecessary sufferings to animals⁸.

On 24 November 1986 the European Council of Ministers adopted Directive 86/609/EEC on «the Protection of Animals used for Experimental and other Scientific Purposes»⁹, whose aim was harmonizing national regulations in order to avoid distortion and unfair competition within the Community.

On 10 February 1987 the former European Community signed the Council of Europe Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes¹⁰.

The principle of animal welfare was however expressed for the first time by the Declaration 24 on the Welfare of Animal annexed to the Maastricht Treaty of 1992, which called upon EC institutions to «pay full regard to the welfare of animals» when drafting and implementing legislation¹¹.

The European Centre for the Validation of Alternative Methods (ECWAM), was then established in 1994 in order to specifically coordinate the validation of alternative test methods at the European

⁷ Actually the first directive concerning animal welfare dates back to 1974 when the former EEC enacted Council Directive 1974 (74/577/EEC) (stunning of animals before slaughter), 1974 O.J. (L 316), 10.

⁸ On the concept of animal welfare, V. CAPORALE *et al*, *Global Perspectives on Animal Welfare*, in *Rev. sci. tech. Off. int. Epiz.*, 24 (2), 2005, 567; R. CILIBERTI, *La tutela degli animali nella ricerca scientifica*, in *Argomenti di bioetica*, 2, 2007, 1.

⁹ Directive 86/609/EEC of the Council of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (86/609/EEC), 1986 OJ (L 358), 1 (CE). S LOUHIMIES, *Directive 86/609/EEC on the Protection of Animals used for Experimental and other Scientific Purposes*, in *Altern Lab Anim*, 2, 2002, 217 ss.

¹⁰ CETS No. 123. The treaty was opened for signature on 18 March 1986 and entered into force on 1st January 1991. The treaty has 22 Parties (*i.e.* France, Germany, Spain, United Kingdom). Italy did not sign the treaty. The relative instrument of accession by the former CE has been deposited on 30 April 1998. The Convention established a range of controls for all species used in animal testing, which was broadly equivalent to the 1986 Directive. The fundamental principle of the convention is the acceptance of the use of animals in experiments but also the reduction of that use by replacing experiments with alternative methods. The agreed purposes in the Convention are research on: (i) prevention of diseases; (ii) diagnosis and treatment of diseases, (iii) protection of environment, (iv) scientific research, (v) education and training, (vi) medico-legal investigations. The member states agreed that: (i) procedures using animals should be used only if no other method exists; (ii) alternatives to animal experimentation should be encouraged, (iii) procedures using less painful methods, fewest and less sensitive animals should be prioritized, (iv) systems to control animal experimentation and to avoid replication of experiments should be put in place. E.VERGES, *L'expérimentation animale et les droits européens*, in J.P. MARGUENAUD, O. DUBOS (eds.) *Les animaux et les droits européens*, Paris, 2009, 137 ss.

¹¹ The Maastricht Treaty (the Treaty on European Union), was signed on 7 February 1992 and entered into force on 1st November 1993.

level¹². An effect of the institution of the ECVAM has been the establishment, in each member State of the European Union, of «National Platforms for Alternative Methods» (IPAM in Italy), coordinated by the European Consensus of Platforms on Alternatives (ECOPA), which provides for the participation of industries, government bodies, research institutes and animal protection associations.

Another major milestone in the protection of animals was attained in 1997 with the adoption of the Amsterdam Treaty, in which animal welfare became part of primary legislation for the first time¹³. It included an Animal Welfare Protocol (No. 33), which was integral part of the Treaty, establishing legal duties within the EC Treaty to take care of animal welfare in basic domains of EU law and policy¹⁴. Before the adoption of the Protocol, the legal bases and obligations concerning animal welfare had been unclear. The Protocol clearly states that the welfare of animals, as 'sentient beings', should be taken into account when creating European laws¹⁵.

Since then, the EU adopted a *corpus* of secondary legislations for the protection of animal welfare in several areas through the legal instrument of the directive. For instance, Directive 98/58/EC covers the different aspects of the welfare of farmed animals¹⁶, while Directive 1999/22/EC relating to the keeping of wild animals in zoos¹⁷ has the goal to protect wild fauna and to conserve biodiversity by

¹² The legal basis of the establishment of ECWAW can be found in articles 7 and 21 of Directive 86/609/EEC. Article 7 (2) states that «an experiment should not be performed (on an animal), if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practically available». Article 23 affirms that «the Commission and Member States should encourage research into the development and validation of alternative techniques which could provide the same level of information as that obtained in experiments using animals, but which involve fewer animals or which entail less painful procedures, and shall take such other steps as they consider appropriate to encourage research in this field». In general terms, this statement is equivalent to the clauses of the NIH Revitalization Act which mandate replacement, reduction and refinement of animal use in publicly funded research in the United States. ECWAW was formally replaced in 2011 by the European Union Reference Laboratory for alternatives to animal testing (EURL ECVAM), http://ihcp.jrc.ec.europa.eu/our_labs/eurl-ecvam (last visited 31/10/2015).

¹³ The Treaty of Amsterdam (Amending the Treaty on the European Union, the Treaties Establishing the European Communities and Certain Related Acts) was adopted on 2 October 1997 and entered into force on 1st May 1999.

¹⁴ The Protocol reads as follows: «The High Contracting Parties, desiring to ensure improved protection and respect for the welfare of animals as sentient beings, have agreed upon the following provision, which shall be annexed to the Treaty establishing the European Community, in formulating and implementing the Community's agricultural, transport, internal market and research policies, the Community and the Member States shall pay full regard to the welfare requirements of animals, while respecting the legislative or administrative provisions and customs of the Member States relating in particular to religious rites, cultural traditions and regional heritage». D. BOWLES *et al.*, *Animal Welfare and the Treaty of Rome – Legal Analysis of the Protocol on Animal Welfare and Welfare Standards in the European Union*, in *J Env Law*, 12, 2000, 197 ss.

¹⁵ The recognition of animal rights had been already effectuated within UNESCO which adopted on 15 October 1978 the Universal Declaration of Animal Rights. The Declaration affirms that the animals – no longer considered as *res* – are entitled to a right to wellbeing and should not *inter alia* be ill-treated or subject to cruelty. See, e.g. M. BOWMAN, P. DAVIES, C. REDGWELL, *Lyster's International Wildlife Law*, Cambridge, 2nd ed., 2010, 26.

¹⁶ Directive 98/58/EC of the Council of 20 July 1998 concerning the protection of animals kept for farming purposes, 1998 OJ (L 221), 23. In addition to Council Decision 78/923/EEC concerning the conclusion of the European Convention for the protection of animals kept for farming purposes (1978 OJ, L 323, 12), the Union made this convention part of EU law.

¹⁷ Directive 1999/22/EC of the Council of 29 March 1999 relating to the Keeping of Wild Animals in Zoos, 1999 OJ (L 94), 24.

providing for the adoption of measures by Member States for the licensing and inspection of zoos in the EU, thereby strengthening the role of zoos in the conservation of biodiversity.

Specific issues are dealt with through EU directives and regulations on transport¹⁸, slaughter¹⁹ and the custody of some species of animals²⁰.

In 2006 the European Commission presented its first Action Plan on the Protection and Welfare of Animals, which mapped out the Commission's planned animal welfare initiatives for 2006-2010²¹.

It is with the entry into force of The Lisbon Treaty on the 1st December 2009 that the principle on animal welfare consolidated itself in the EU legal order. Indeed, this principle was inserted in Article 13 of the Treaty on the Functioning of the European Union – TFEU²². In particular, Article 13 has been included within the «Provisions having general application» of Title II of the TFEU, alongside the principles of equality between man and woman (Article 8), non discrimination (Article 10), environmental protection and sustainable development (Article 11). The duty of protection of animals has in this

¹⁸ Regulation of the Council (EC) No 1/2005 on the protection of animals during transport, 2005 OJ (L 3), 1.

¹⁹ Directive 93/119/EC of the Council of 22 December 1993 on the protection of animals at the time of slaughter or killing, 1993, OJ (L 340), 21 (CE), replaced by the Regulation of the Council (EC) No 1099/2009, of 1st January 2013, on the protection of animals at the time of killing, 2009 OJ L 303, 1.

²⁰ Directive of the Council 2008/119/EC laying down minimum standards for the protection of calves, 2009 OJ (L 10), 7; Directive of the Council 2008/120/EC laying down minimum standards for the protection of pigs, 2009 OJ (L 47), 5; Directive of the Council 1999/74/EC laying down minimum standards for the protection of laying hens, 1999 OJ (L 203), 53; Directive of the Council 2007/43/EC laying down minimum rules for the protection of chickens for meat production, 2007 OJ (L 183), 19.

²¹ The EU subsequently published a new Animal Welfare Strategy for 2012-2015 (the text is available at: http://ec.europa.eu/food/animal/welfare/actionplan/docs/aw_strategy_19012012_en.pdf; last visited 31/10/2015), which lays the foundation for improving welfare standards during that period and aims to ensure the same high standards are applied and enforced in all EU countries (European Union Strategy for the Protection and Welfare of Animals 2012-2015, Brussels, 15.2.2012, COM(2012) 6 final/2). The new strategy establishes Five Freedoms which all animals should enjoy: Freedom from Hunger and Thirst – by ready access to fresh water and a diet to maintain full health and vigor; Freedom from Discomfort – by providing an appropriate environment including shelter and comfortable resting area; Freedom from Pain, Injury or Disease – by prevention or rapid diagnosis and treatment; Freedom to Express Normal Behavior – by providing sufficient space, proper facilities and company of the animal's own kind; Freedom from Fear and Distress – by ensuring conditions and treatment which avoid mental suffering.

²² Consolidated Version of the Treaty on the Functioning of the European Union, May 9, 2008, 2008, O.J. (C115) 47, [hereinafter TFEU]. Article 13 – which draws on the Protocol on the protection and welfare of animals, and broadens its scope – states that «In formulating and implementing the Union's agriculture, fisheries, transport, internal market, research and technological development and space policies, the Union and the Member States shall, since animals are sentient beings, pay full regard to the welfare requirements of animals, while respecting the legislative or administrative provisions and customs of the Member States relating in particular to religious rites, cultural traditions and regional heritage». On the value of Title II of the Lisbon Treaty, see P. CRAIG, *The Treaty of Lisbon: Process, Architecture and Substance*, in *European Law Review*, 33, 2008, 137 ss., R. GEIGER, D.E. KHAN, M. KOTZUR, *Commentary on the TEU/TFEU*, Oxford, 2015, 111 ss; P. INGOLF, *The Treaty of Lisbon, Multilevel Constitutionalism in Action*, in *Colum. J. Eur. L* 15 (3), 2009, 349 ss.

way acquired a major visibility with respect to the past²³. Hence, as primary EU law, it now represents a fundamental precept of the European legal order²⁴.

The role of animals and their protection is declared as complementary to other objectives of social interest for the European Union, such as food security, food quality, environmental protection and environmental sustainability. Possible derogations to animal welfare are established in case of religious rites, cultural traditions and regional heritage; these areas may reduce the scope of animal protection. Therefore, animals are currently more protected not only by the secondary legislation, but also by an enlargement of the scope of Article 13. As in the former Amsterdam Protocol, animals are protected as sentient beings not only in the context of agriculture, transport, internal market and research, but now also in the political fields of technological development and space policies, while the fisheries section is also included²⁵. This leads to a more ethically sound legislative coverage regarding the use of animals, also in sensitive areas such as, for example, cloning of farm animals for food supply and animals in experiments²⁶.

Therefore, we can affirm that the Directive 2010/63/EU is only one piece in a wider policy developed by the European institutions in order to promote the highest level of animal welfare.

In the next paragraph, we will analyze in detail the content and scope of Directive 2010/63 with a focus on the most significant improvements compared to the former Directive 86/1986 as well as focusing on its most controversial points.

3.The Directive 2010/63/EU

3.1. General Description

The process of revision of the former Directive 86/609/EEC began in 2002 when the European Parliament invited the European Commission to prepare an updated draft directive, which would provide more stringent and more transparent measures in the sector of animal experimentation²⁷.

Meanwhile, the EU Commission adopted a Recommendation on guidelines for the accommodation and care of animals used for experimental and other scientific purposes (18 June 2007)²⁸, which introduces guidelines for the accommodation and care of animals used for experimental and other scientific purposes. This Recommendation complements Annex III of Directive 2010/63/EU, which is based on provisions found therein, and sets down firm rules on requirements for accommodation

²³ For a wide and accurate exegesis of Article 13, see F.X. PRIOLLAUD, D. SIRITZKY, *Le Traité de Lisbonne: texte et commentaire*, Paris, 2008, 165 ss.

²⁴ On the legal values of the "Treaties" in EU Law, see D. CHALMERS, G. DAVIES, G. MONTI, *European Union Law: Cases and Materials*, Cambridge, 2010.

²⁵ The reference to space was included as a consequence of the utilization of animals in space activities. In fact, animals are still employed in space research (<http://history.nasa.gov/animals.html>; accessed 31/10/2015).

²⁶ D.RYLAND, A.NURSE, *Mainstreaming after Lisbon: Advancing Animal Welfare in the EU Internal Market*, in *Eur En Env'tl L Rew*, 22 (3), 2013, 101 ss.

²⁷ R. BINDER, E. LENGAUER, *The Current Revision of Directive 86/609/EEG from the Perspective of Animal Welfare Legislation*, in *Altex*, 23 (2006) 179 ss.; THOMAS G. KELCH, *Globalization and Animal Law: Comparative Law, International Law and International Trade*, New York, 2011, 155.

²⁸ Doc. number C(2007) 2525.

and care of experimental animals. It also aligns EU legislation with the revised Council of Europe guidelines (Appendix A of Convention ETS 123), on accommodation, and care of laboratory animals.

The Proposal for a Directive of the European Parliament and of the Council on the protection of animals used for scientific purposes was issued on 5 November 2008²⁹.

The legal instrument of the directive was preferred to the regulation because of its flexibility, that allows States a certain degree of discretion in adopting implementation measures at domestic level. In fact, by being binding «as to the results to be achieved» but leaving the Member States the choice of «forms and methods», the directive is by its nature very suitable for bringing about the necessary changes in national laws while respecting as far as possible the national legal systems, with their own conceptions and terminology³⁰. Not surprisingly, in the Declaration on Article 100a [95] of the then EEC Treaty annexed to the Single European Act (1986), the Member States already expressed their preference for directives as instruments of harmonization of laws above the use of regulations. Looking at the directive not as a means of limited intervention but rather as a new form of decision making, this typology of acts aims at restricting and directing the behavior of a subordinated body (the State) according to the orientations laid down by the hierarchically higher body (the EU)³¹.

This top down approach is clear in the Directive 2010/63/EU, which sets out non-negotiable principles established by the European institutions that Member States are obliged to respect, although within a margin of appreciation which safeguards domestic peculiarities.

The provisions of Directive 2010/63/EU – which replaces the former Directive 86/609/EEC – relate to the harmonization of the internal market in the field of breeding, supplying and use of animal and consequently Article 114 of the Treaty on the Functioning of the European Union (TFEU) (former Article 95 of the EC Treaty) was kept as the legal basis³². In fact, through the adoption of this Directive, the EU tried to maintain an equilibrium between research promotion, competitiveness of the EU and animal welfare within the internal market, in line with the principle of subsidiarity³³.

²⁹ EC Draft 15546/2008, COM(2008)543. The purpose of the draft Directive, as stated in its explanatory memorandum, was as follows: «Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes was adopted to harmonize practices in the area of animal experimentation in the EU. However, due to a variety of weaknesses in the current Directive, a number of Member States have established considerably more far reaching measures in their national implementation whereas others apply only minimum rules. The present uneven situation needs to be rectified to ensure that the objectives of the internal market are re-established. The current proposal aims at ensuring a level playing field, throughout the EU, for industry and the research community, at the same time strengthening the protection of animals still used in scientific procedures in line with the EC Treaty's Protocol on Animal Welfare. The proposal supports the Commission's overall strategy on animal experimentation, including enhanced promotion of the development, validation, acceptance and implementation of alternative methods and provides a solid basis for a full implementation of the principles of the Three Rs».

³⁰ S. PRECHAL, *Directive in EC Law*, Oxford, 2005, 4 ss.; J. SHAW, *Law of the European Union*, London, 3rd ed, 2000, 93 ss.

³¹ J. FAIRHURST, *Law of the European Union*, Harlow, 10th ed, 2014, 55; T. HARTLEY, *The Foundations of European Union Law: An Introduction to the Constitutional and Administrative Law of the European Union*, Oxford, 7th ed, 2010, 158 ss.

³² Art. 114, par. 1, of the TFEU states «[...] The European Parliament and the Council shall (...) adopt measures for the approximation of the provisions laid down by law, regulation or administrative action in Member States which have as their object the establishment and functioning of the internal market».

³³ Subsidiarity is a concept for the division of legislative powers at the lowest possible and efficient level. The principle is close to the principle of decentralization. Subsidiarity is outlined in Art. 5, Par. 2, of the TEU, as one

EU institutions felt the necessity to adopt a new directive on the protection of animals used for scientific purposes because of the failure of the former Directive 86/609/EEC³⁴ to reach its ultimate purpose, the approximation of legislations of Member States. Indeed, since the adoption of that Directive, disparities in Member States' rules on animal experimentation have increased instead of decreasing. Some countries adopted national implementing measures, assuring a higher level of protection of animals used for scientific purposes³⁵, while others decided to only apply the minimum standards established by Directive 86/609/EEC.

This lack of harmonization brought forward concerns for competitiveness resulting in market distortions and trade barriers. Accordingly, one of the goals of Directive 2010/63/EU is to provide more detailed rules, in order to diminish disparities in legislations across the EU in the treatment of animals used for scientific procedures and to ensure an appropriate functioning of the internal market.

Two other factors were however significant drivers of change: (1) growing interest in the public opinion on the issue of animal welfare³⁶; (2) availability of new scientific knowledge in respect to factors influencing animal welfare, as well as the capacity of animals to express pain, suffering distress, and lasting harm (Recital 6). In fact, in the last twenty years, the scientific basis on which the former Directive was established has changed considerably, thanks to an evolution of the techniques in the field of animal testing.

Indeed, the EU, in dealing with animal welfare has now taken into account ethical issues regarding the preoccupation of reducing suffering in animals, in addition to the "traditional" concerns related to the harmonization of the internal European market.

The general philosophy underlying the Directive is foreseen in Recital 10 whereas the EU recognizes the necessity to reach an equilibrium between two competing concerns (the necessity to replace the use of live animals in research and the fact that research on animals continues to be necessary to protect human and animal health and the environment).

of the EU's fundamental principles: «Under the principle of subsidiarity, in areas which do not fall within its exclusive competence, the Union shall act only if and insofar as the objectives of the proposed action cannot be sufficiently achieved by the Member States, either at central level or at regional and local level, but can rather, by reason of the scale or effects of the proposed action, be better achieved at Union level. The institutions of the Union shall apply the principle of subsidiarity as laid down in the Protocol on the application of the principles of subsidiarity and proportionality. National Parliaments shall ensure compliance with that principle in accordance with the procedure set out in that Protocol». On the subsidiarity principle, P. D. MARQUARDT, *Subsidiarity and Sovereignty in the European Union*, in *Fordham Int'l L.J.*, 18, 1994, 616 ss.; T. VAN DER BRINK, *The Substance of Subsidiarity: the Interpretation and Meaning of the Principle after Lisbon*, in M. TRYBUS, L. RUBINI (eds.), *The Treaty of Lisbon and the Future of European Union Law and Policy*, Cheltenham, 2012, 160 ss.

³⁴ O J L 358, 18.12.1996.

³⁵ Italy is one of these countries. In this regard, S. LOUHIMIES, *op. cit.*, 8 ss, O. ROHTE, *The Legal Regulations of the European Community on Animal Welfare in the Field of Agriculture and Research*, in *Dtsch Tierarztl Wochenschr*, 100(1), 1993, 19 ss.

³⁶ Opinions on the subject of animal use in research in the EU Countries continue to vary widely. They range from the view that any form of animal research is completely unjustifiable, to the belief that it is acceptable, provided it is carefully regulated to cause minimal suffering to the animals concerned, and is directed at alleviating human suffering or for the pursuit of knowledge that might in the long term achieve this end. I. RUHDEL, *Revision of the EU Directive 86/609/EEC: Results of the Internet Consultations of the European Commission*, in *Altex*, 24 (1), 2007, 415 ss.

With the ambition of conciliating these conflicting moral stands, the Directive aims to ensure the highest standard of protection of animals used in scientific research, while its ultimate goal is the definitive replacement of procedures on live animals for scientific and educational purposes (as soon as it will be scientifically possible to do so). According to EU institutions, biomedical research has reached the point where we can reasonably begin to envision a time when it could advance without causing harm to animals.

In line with this assumption, Recital 12 recognizes that animals have an intrinsic value which must be respected and affirms that the use of animals for scientific or educational purposes should be considered only in the absence of a non-animal alternative. However, the Directive recognizes the fundamental role of animals in research; in fact, it does not prohibit the use of animals in research, but highlights some key principles that must be respected.

3.2. Improvements with respect to the Former Directive 86/609

The new Directive presents significant improvements if its content is compared with that of the former 1986 Directive.

As to its scope, the range of animals under protection has been considerably increased, and now includes non-human vertebrates, (Cephalopods, Cyclostomes, Myxini) and foetal forms of mammals in the last trimester of foetal development (Article 3, (a), (i), (ii), b). Cephalopods, and foetal forms of mammals have been included in the 2010 Directive as there is scientific evidence of their ability to experience pain, suffering, distress and lasting harm (preamble, paras. 8-9).

However, the Directive makes no reference to bird embryos, like for instance chicken embryos, which are commonly used in developmental biology, gene expression analysis and loss/gain of function experiments. Chicken embryos are therefore exempted from the scope of the Directive, despite their capacity to experience suffering³⁷.

The Directive centres on the 3R's System (Recitals 10-13; Articles 4, 13), a widely accepted ethical framework for conducting scientific experiments using animals humanely, namely the replacement of animal studies by other methods, the reduction of the number of animals and the refinement of the ways in which animals are used³⁸. The 1986 Directive, instead, contained no direct reference to the 3R's, although it requested the use of alternative methodologies if available, the use of the minimum number of animals through which it is possible to obtain the established scientific goals, the housing and the maintenance of the animals at the highest levels and the reduction, where possible, of pain, suffering and anxiety³⁹.

³⁷ See H. RASHIDI, V. SOTTILE, *The Chick Embryo: Hatching a Model For Contemporary Biomedical Research*, in *Bioethics*, 31 (4), 2009, 45 ss.

³⁸ The 3 R System has been formulated by William Russell and Rex Burch. It represents two of the more contentious issues in animal based research, teaching and testing: the numbers of animals being used, and the pain and suffering being experienced by these animals. W. M. S. RUSSELL, R. L. BURCH, *The Principles of Humane Experimental Technique*, (London, 1959). More in general, on 3Rs implementation in clinical practice, A. ROGIER, *ECOPA: The European Consensus on Three Rs Alternatives*, in *Altern Lab Anim.*, 32, 2004, 349.

³⁹ For example, Article 7(3) stated that: «In a choice between experiments, those which use the minimum number of animals, involve animals with the lowest degree of neurophysiological sensitivity, cause the least pain, suffering, distress or lasting harm and which are most likely to provide satisfactory results shall be selected».

The duty to replace, reduce and refine the use of animals in scientific procedures is deeply embedded in EU policies. In fact, this principle is set up in the Directive 98/8/CE on biocides⁴⁰, the Directive 1999/45/CE on dangerous preparations⁴¹, the 7th amendment to the Directive 76/768/CEE on cosmetics⁴².

The Directive has provided that competent authority carrying out project evaluation at the national level (which must be appointed by each Member State) must evaluate compliance of each application for project authorisation with the requirement for replacement, reduction and refinement (Article 38, par. 2b)⁴³.

Replacement is defined as ensuring that «wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals shall be used instead of a procedure» that involves animals. In this regard, the Directive establishes that Member States shall ensure the use of a scientifically satisfactory method or testing strategy not entailing the use of live animals. In this regard, we must underline that currently there is a consensus in the scientific community on the necessity to promote alternative methods that do not imply the use living organism⁴⁴. In an Opinion on alternative methodologies, the Italian National Bioethics Committee affirmed in the Introduction that «it is advisable to limit animal testing to what is strictly necessary, reducing their number and controlling suffering and harm, and it expresses the hope for a development of the research and the application of alternative methodologies»⁴⁵. However, some of its members sustained that «alternative methodologies should be intended not as substitutive but as a complementary method to animal

⁴⁰ Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, 1998 OJ (L 123) 14.

⁴¹ Directive 1999/45/CE of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labeling of dangerous preparations, 2000 OJ (L 200) 1.

⁴² Directive 2003/15/EC of the European Parliament and of the Council of 27 February 2003 amending Council Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products, 2003 OJ (L 66) 26.

⁴³ In addition, Member States shall contribute to the development and validation of 3Rs (Art 47(1)) including the nomination of qualified laboratories for validation studies (Art 47(2)) and a single contact point to provide advice on suitability of methods proposed for validation (Art 47(5)) nomination of qualified laboratories for validation studies (Art 47(2)) and a single contact point to provide advice on suitability of methods proposed for validation (Art 47(5)); ensure the dissemination of information on the 3Rs (Art. 47 (4)).

⁴⁴ Examples of relative replacement include computer modelling, recourse to human volunteers, e.g. non-invasive imaging studies, *in vitro* methodologies using established humans or animals; see <https://ecvam.jrc.ec.europa.eu/> (last visited 31/10/2015). Gruber and Hartung provided a description of these alternatives and discussed about the advantages associated (F.P. GRUBER, T. HARTUNG, *Alternatives to Animal Experimentation in Basic Research*, in *ALTEX*, 21, 2004, 1 ss.).

⁴⁵ Opinion of the Italian National Bioethics Committee of 18 December 2009, *Alternative Methodologies, Ethics Committees and Conscientious Objection to Animal Testing*, available online at http://www.palazzochigi.it/bioetica/eng/pdf/alternative_methodologies_rivisto_2.pdf (last visited 31/10/2015). This document, in the view of balancing the existing different values, paid particular attention to the issue of animal welfare and recognized the principled of the respect of the intimate and personal belief of the scientists, that do have a right to Conscientious objection to animal testing, according to Law n. 413 of 12th of October 1993. This law allows, scientists, students, doctors or the staff of the health service, to refuse their co-operation in industrial, medical or university animal experiments for ethical reasons.

testing»⁴⁶. The clinical practice showed, in effect, the existence of complementary methods (research on this typology of methods takes 70% of the activity of a laboratory), that could at least reduce the number of animals used in research⁴⁷.

Reduction is defined as reducing animal numbers to as few as possible «without compromising the objectives of the project». It refers to methods which minimise animal use and enable researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same number of animals, thereby reducing future use of animals, the Directive establishes by requiring that an animal experiment should not be performed when an alternative method exists, and by encouraging the development and validation of alternative methods to replace animal testing⁴⁸.

Refinement is defined as minimizing or eliminating «possible pain, suffering, distress or lasting harm to the animals». The phrase – pain, suffering, distress, or harm – is used frequently in the Directive to describe the potential negative effects of experimental procedures.

Another element of novelty of Directive 2010/63 is represented by the attention it pays to the protection of biodiversity (in accordance with the principles enshrined in the UN Convention on Biological Diversity of 1992). In fact, the use of endangered species must be allowed only under special circumstances (Article 7).

Another main element of change is related to the significant increase in minimum, binding house and care requirements (Article 22, Annex II)⁴⁹.

The revised Directive makes it compulsory to carry out ethical evaluations and requires that animal research projects be subject to authorization. All research projects using animals need a prior authorisation from the competent authority (Article 36). The project evaluation is a critical part of the whole authorisation process (Article 38); the competent authority shall verify that the project meets some basic criteria established in Article 38, let. (a), (b), (c), of the Directive (the justification of the project from a scientific or educational point of view, the requirement from a law, the justification of the use of animals for the purpose of the project). In addition, the competent authority shall evaluate the goals of the project and its predicted scientific benefits or educational value, the compliance of the project with the 3R requirements and shall carry out a harm-benefit analysis – which must take into account ethical considerations – to assess whether the harm to the animals in terms of suffering, pain and distress is justified by the expected outcome and may ultimately benefit human beings, animals or the environment. The evaluation process is carried out in an impartial manner (and may therefore integrate the opinion of independent parties) and must be transparent.

Also breeders, suppliers and users are requested to obtain an authorization (Section I, Articles 20-33) and are subject to periodical inspections to verify compliance with the requirements of the Directive

⁴⁶ *Ivi*, at 6.

⁴⁷ For instance, several studies on the efficiency of alternative methodologies to the Draize eye test have been carried out; M.P. VINARDELL, M. MITJANS, *Alternative Methods for Eye and Skin Irritation Tests: An Overview*, in *Journal of Pharmaceutical Sciences*, 2008, 97, 46 ss., S.L. WILSON, M. AHEHARNE, A. HOPKINSON, *An Overview of Current Techniques for Ocular Toxicity Testing*, in *Toxicology*, 2015, 327, 32 ss.

⁴⁸ I. RUHDEL, *Guidance on determining Indispensability and balancing Potential Benefits of Animal Experiments with Costs to the Animals with Specific Consideration of EU Directive 2010/63/EU*, in *ALTEX*, 2, 2012, 219 ss.

⁴⁹ On this topic, E. ALLEVA, A. VITALE, *We urgently need more Data to improve the Lives of Laboratory Animals*, in *Nature*, 2000, 116 ss.

(Section II, Articles 34-35). To this aim, each breeder, supplier and user is also required to establish an «animal welfare body» which plays the role of essentially fostering a climate of care. Animal welfare bodies are supposed to advise the staff on animal welfare; implement the Three Rs; establish and review facility operations and processes; monitor the development and outcome of projects; and provide advice on plans to adopt animals out at the conclusion of research projects (Articles 26-27)⁵⁰. Other novelties in relation to the 1986 Directive concern end of life issues for animals. Death as an endpoint of a procedure should be avoided (Article 13, para. 3) and neuromuscular blocking agents cannot be used without anaesthesia or analgesia. In addition, their use requires a scientific justification.

A classification of severity of procedures has been introduced (Article 15) and it is an important tool to help focus the implementation of refinement and to assist in reporting the application of the 3Rs. The procedures in this article have been classified in four groups: mild; moderate; severe; non recovery⁵¹.

The innovation is represented by the ban of very severe procedures which are long lasting and cannot be ameliorated. In fact, two thresholds have been established (lower and upper). The lower threshold is exceeded if the animals may experience a level of pain, suffering or distress equivalent to, or higher than that caused by the introduction of a needle⁵². The upper threshold is exceeded if the animals may experience severe pain, suffering or distress, which is likely to be long-lasting and cannot be ameliorated.

It is quite positive that the Directive provided rehoming of animals involved in experimentations (Article 19). In this regard, the Directive establishes that Member States may assure that animals are rehomed or returned to a suitable habitat or husbandry appropriate to the species, provided that the state of the health of the animal allows it and that there is no danger to public health (*i.e.* the animal has been infected with a virus during the experiment).

⁵⁰ On the establishment of animal ethics committees in Italy, see M. MARTINI, S. PENCO, I. BALDELLI, B. BIOLATTI, R. CILIBERTI, *An ethics for the living world: operation methods of Animal Ethics Committees in Italy*, in *Ann Ist Super Sanità*, 51, 2015, 244 ss.

⁵¹ Mild procedures cause short-term mild pain, suffering or distress and/or minor changes in well-being or condition. They can include anaesthesia; non-invasive imaging; short-term social isolation; taking a blood sample; and superficial surgical procedures. Moderate procedures cause short-term moderate pain, suffering or distress or long-lasting moderate pain, suffering or distress. They can result in moderate impairment in well-being or condition. Examples include surgery under general anaesthetic; tumour induction; a modified diet; and evoking an escape or avoidance response without allowing the animal to escape the stimulus. Severe procedures cause severe pain, suffering or distress or long-lasting moderate pain, suffering or distress. They can cause severe impairment in well-being of condition. Examples include any test where death is the end-point or fatalities are expected; testing a device that could cause pain/death if it were to fail; inescapable electric shocks; or forced swim tests. See *EU Expert working group on severity classification of scientific procedures performed on animals* (Conducted in support of the revision of Directive 86/609/EEC on the protection of animals used for scientific purposes), Final Report, Brussels, July 2009, available on line at: http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf (last visited 31/10/2015).

⁵² The same wording is present in the CoE Resolution (ETS 123) «The use of animals for other research purposes, for example, on nutrition and feeding, when they may experience a level of pain, suffering or distress equivalent to, or higher than, that caused by the introduction of a needle (for example, blood sampling, deprivation of food».

Another important transition concerns the ban of the use of animals caught in the wild if belonging to an endangered species. The Directive requires that only animals of second or older generations be used, subject to transitional periods, to avoid taking animals from the wild and exhausting wild populations.

Particular attention is also paid in the Directive to issues related to education, training and competence (Article 23, para. 2)⁵³. The goal of this disposition is to harmonize education programmes across the Member States, and to allow free movement of those engaged in laboratories that carry out experiments on animals across the EU States.

3.3. Controversial elements

The Directive has been the object of critiques by all sides involved in animal experimentation (animal welfare groups, scientists and enterprises); it determined a delay in the transposition of the Directive in the domestic legal order by some States (one of these is Italy).

In fact, the drafters of the Directive have been forced to find a balance between the different interests involved (protection of animal welfare as well as of scientific research) and one element that clearly emerges from a single reading of the Directive is its nature of compromise. It never states clearly prohibitions of certain practices but always foresees exceptions, using the term «shall» instead of «must». For instance, with reference to the endangered species, on the one hand it prohibits the use of some specimens of endangered species⁵⁴, but, on the other hand, it allows their use if some conditions are respected (one of this is the existence of scientific justification to the effect that the purpose of the procedure cannot be achieved by the use of species other than those listed in Annex A of the Directive).

Also with reference to the issue of the use of non-human primates (NHPs), which is highly controversial due to their genetic proximity to human beings, the Directive uses an ambiguous terminology. Article 8 of the Directive affirms that non-human primates «shall not be used in procedures», with some exceptions: the research is performed with a view of avoiding, preventing, diagnosing or treating debilitating or potentially life-threatening clinical conditions in human beings and there is scientific justification to the effect that the purpose of the procedure cannot be achieved by the use of species other than non-human primates (Article 8, let. *a*, *b*). In fact, Recital 17 of the Directive recognizes that the use of non-primates in scientific procedures is still necessary in biomedical research. The same scheme (composed of a principle and, at the same time, exception clauses) has been used with reference to animals taken from the wild (Article 9), animals bred for use in procedures (Article 10), as well as stray and feral animals of domestic species (Article 11). In all these cases the Directive states that “competent authorities may grant exemptions”.

⁵³ Specimens of endangered species are listed in Annex A to the Council Regulation (EC) No 338/97 of 9 December 1996. These include, for instance, Goeldi's Marmoset, Lemurs, Mortlock flying-fox, Pemba flying-fox, Red spider monkey, Woolly spider monkey Tartiers.

⁵⁴ See Consensus Document, *National Competent Authorities for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes. A working document on the development of a common education and training framework to fulfill the requirements under the Directive*, available online at http://ec.europa.eu/environment/chemicals/lab_animals/pdf/Endorsed_E-T.pdf (last visited 31/10/2015).

Another controversial element is related to the use and re-use of animals. Article 16 of the Directive states that an animal already used in one or more procedures may be used in a new procedure provided that the actual severity of the previous procedures was «mild» or «moderate» and that the further procedure is classified as «mild», «moderate» or «non recovery»⁵⁵. The reuse of an animal is meant to reduce the total number of animals upon which experiments are carried out, in line with the 3Rs.

However, according to animal welfare groups, this disposition establishes that there is no limit to the number of procedures an animal will be obliged to endure, provided these procedures are classified as mild or moderate.

We will analyze in the next paragraph how research on non-human primates, probably the most debated and contended issue concerning animal testing, has been dealt with by the Directive. We will see how the negotiations on the Directive have been influenced by this topic, which determined a compromise between the positions of the different participants involved, but which eventually satisfied none of the actors involved.

4. Regulation of Use of Non-Human Primates (NHPs) in the Directive 2010/63/EU

4.1. The use of NHPs in Research

Every year, more than 10.000 non-human primates are used in the experimental procedures in the European Union. Testing is mainly carried out on Macaques, Marmosets, Vervets and Baboons⁵⁶. If compared to the other species of mammals employed in research (*i.e.* dogs, mice, rabbits) their number is quite low. The animals utilised in biomedical research in the EU are mostly rodents (95%) and less than one percent (about 0.30%) of all animals needed for medical discovery are nonhuman primates⁵⁷. However, despite the statistical data showing the low number of experiments performed on NHPs, this issue has been a topic of special concern during the negotiation process of the Directive.

In fact, the admissibility of research on NHPs is still debated under an ethical and scientific viewpoint⁵⁸. The use of NHPs constitutes a particular concern and uncertainty primarily because of their

⁵⁵ «Re-use» is a term to indicate the subsequent use of an animal which has already completed a procedure (or series of procedures/techniques) for a particular scientific purpose. In this regards, see, *e.g.*, National Competent Authorities for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes. *Working document on specific articles in Directive 2010/63/EU* adopted in Brussels, 6-7 October 2011, available at http://ec.europa.eu/environment/chemicals/lab_animals/pdf/Consensus_document.pdf (last visited 31/10/2015).

⁵⁶ These species are not included in the list of endangered species under the Convention on International Trade of Endangered Species (CITES).

⁵⁷ Seventh Report from the Commission to the Council and the European Parliament on the Statistics on the number of animals used for experimental and other scientific purposes in the member states of the European Union. The Report provides an overview on the number of animals used in the EU in for experimental and other scientific purposes. This report is available at COM(2013)859/final, http://ec.europa.eu/environment/chemicals/lab_animals/transposition_en.htm (last visited 31/10/2015).

⁵⁸ Testing on NHPs began in the 1920s, and there was a resurgence in the 1950s with the space program and the development of an anti polio vaccine and again in the 1980s when it seemed like chimpanzees were prom-

evolutionary proximity to human beings and to the risk of transmission of diseases from animal to human being⁵⁹. However, their genetic similarities to humans are precisely what make them particularly suitable candidates for experiments carried out within research programmes on immune based diseases (multiple sclerosis), neuro-degenerative disorders (Parkinson, Alzheimer), infectious diseases (HIV, malaria, Hepatitis, Ebola)⁶⁰. Their utilization in research is driven by the “high-fidelity” notion, according to which NHPs are likely to be better models than mice and rats for studying human diseases.

The debate surrounding the use of NHPs in biomedical research within the European institutions had its starting point in the declaration of the Steering Committee of the European Commission of 2002⁶¹. It highlighted the continuing necessity, at least for the near future, of the use of NHPs in biomedical research⁶².

Since then, several publications have been produced arguing under an ethical and scientific viewpoint the necessity to replace the use of non-human primates in biomedical research⁶³. The discussion on the admissibility of biomedical research on NHPs has determined a legislative change towards restrictive regulations in some EU countries: the Netherlands, as well as Belgium, enacted laws banning great ape research⁶⁴.

ising subjects for AIDS research. J. LUY, *Ethical and Legal Aspects of Animal Experiments on Non-Human Primates*, in *Dtsch Tierarztl Wochenschr*, 114 (3), 2007, 81 ss.

⁵⁹ Arguments for phasing out research on NHPs are based mainly on ethical and scientific concerns, which rely upon a Pathocentric position – primates, due to their genetic similarities to the human being and their ability to feel pain and suffering, should be granted a moral consideration. For these reasons, animal welfare groups retain that impeding intensive research on all NHPs should be the priority. The essential element of the discussion is on the availability of alternative methods to replace the use of non-human primates. K.M. CONLIN, A.N. ROWAN, *The Case for Phasing Out Experiments on Animals*, in *Hastings Center Report*, 42 (6), 2012. For a discussion on the rights of non-human primates, see C.M. MAZZONI, *La questione del diritto degli animali*, in S. RODOTÀ, P. ZATTI (eds.) *Trattato di biodiritto. La questione animale*, Milano, 2012, 281 ss.

⁶⁰ See, Working Group Report chaired by Sir David Weatherall, *The Use of Non-Human Primates in Research*, 2006, 200 ss., available at www.acmedsci.ac.uk/download.php?f=file&i=17171 (last visited 31/10/2015). Twelve of the seventeen diseases listed by the World Health Organisation (WHO) under the program to fight epidemics and pandemics require the use of non-primates during the development, production or testing of the related vaccines and medicines (www.who.org, last visited 31/10/2015).

⁶¹ European Commission, Health & Consumer Protection Directorate-general. The Need for Non-Human Primates in Biomedical Research. Statement of the Scientific Steering Committee, 4-5 April 2002, http://ec.europa.eu/food/fs/sc/ssc/out253_en.pdf (last visited 31/10/2015). The 1986 Directive contained few specific provisions relating to the use of NHPs. Art. 18, par. 3, Requested an individual identification of each nonhuman primate.

⁶² The same conclusions have been reached in a report published in December 2006 by a working group made of independent experts chaired by Sir David Weatherall on «The use of non-human primates in research» (the s.c. “Weatherall Report”): report available at <http://royalsociety.org/policy/publications/2006/weatherall-report/> (last visited 31/10/2015).

⁶³ See, for instance, J. BAILEY, *Non-Human Primates in Medical Research and Drug Development: a Critical Review*, in *Biogenic Amines*, 35, 2005, 192 ss.

⁶⁴ See A. GILLESPIE, *Conservation, Biodiversity and International Law*, Cheltenham, 2011, 251; A. KNIGHT, *The Beginning of the End for Chimpanzees Experiments*, in *Philos Ethics Humanit Med*, 3, 2008, 16 ss.; C. SAUCIER-BOUFFORD, *The Legal Rights of Great Apes*, in *The Global Guide to Animal Protection*, 235-236 (Andrew Linzey ed., 2013). The Belgian law however has foreseen an exemption clause: «[An] exemption is only granted in exceptional circumstances and only if the experiment is aimed at research to maintain the species in question or

In September 2007, the European Parliament adopted a declaration⁶⁵ calling for restrictions on the use of Great Apes and wild caught monkeys as well as phasing out the use of all non-human primates with alternatives (para. 6). This change of position had been determined by the pressure that animal welfare groups placed on European institutions in order to ban research on NHPs. In fact, this declaration had been proposed by the Animal Defenders International (ADI) and the National Anti-Vivisection Society. The European Parliament asked to the European Commission to provide a study on the alternatives to the use of NHPs in research and testing

In 2008, an independent scientific committee appointed by the Direction-general "Environment" of the European Commission⁶⁶, approved a scientific opinion on the possibility to replace the use of non-human primates in biomedical research. After a deep analysis of scientific evidence available in literature, the committee concluded that valid alternatives – that would allow the stop of the use of primates in basic or applied research or in the development or testing of new drugs – did not exist⁶⁷. Therefore, the European Commission, in its answer to the European Parliament affirmed that, given the current status of knowledge, a complete ban on the use of NHPs in biomedical research was not possible.

The dispute is not, however, exhausted neither at European nor at global level. In the United States a Great Apes Protection Act was adopted on 17 April 2008 and in a Report issued in 2011 by the Committee on the Use of Chimpanzees in Biomedical and Behavioral Research, it was affirmed that: «most current use of chimpanzees for biomedical research is *unnecessary*»⁶⁸.

The dispositions of the Directive concerning NHPs, as we will see in the next paragraph, avoid to take a position in favor or against biomedical research on non-human primates. In fact, after declaring general principles of intent with regard to the use of NHPs, all the dispositions provide for exception clauses that in fact allow – under strict circumstances – research on NHPs, not setting therefore restriction on their use.

4.2. The ambivalent regulation of research on NHPs in the Directive 2010/63/EU

Rules on NHPs in the Directive 2010/63/EU are included in Articles 7-11. In this regard, it is worth underlining that the Directive has provided for a double standard of protection, according to the spe-

biomedical objectives of essential importance to the species concerned if the species concerned is the only one that appears to be suitable for that objective».

⁶⁵ European Parliament. Written Declaration on Primates in Scientific Experiments 2004/2009 Pursuant to Rule 116 of the Rules of Procedure by Jens Holm, Rebecca Harms, John Bowis, Martine Roure and Mojca Drčar Murko on Primates in Scientific Experiments, 6 September 2007, http://ec.europa.eu/environment/chemicals/lab_animals/pdf/declaration_nhp_en.pdf (last visited 31/10/2015).

⁶⁶ European Commission, Health & Consumer Protection Directorate-general, Scientific Committee on Health and Environmental Risks – SCHER. The Need for Non-Human Primates in Biomedical Research, Production and Testing of Products and Devices, 2009, http://ec.europa.eu/environment/chemicals/lab_animals/pdf/scher_o_110.pdf (last visited 31/10/2015).

⁶⁷ J. BAILEY, K. TAYLOR, *The SCHER Report on Non-Human Primate Research - biased and deeply flawed*, in *Altern Lab Anim*, 37 (4), 2009, 427 ss.

⁶⁸ Committee on the Use of Chimpanzees in Biomedical and Behavioral Research, *Chimpanzees in Biomedical and Behavioral Research: Assessing the Necessity* (Washington, D.C., 2011, 6). See J. KANH, *Raising the Bar: The Implications of the IOM Report on the Use of Chimpanzees in Research*, in *Hastings Center Report*, 42 (6), 2012.

cies used in an experimental procedures. The drafters of the Directive followed the biological distinction between the family of great anthropoids apes, which comprises (in addition to humans), bonobos, chimpanzees, gorillas and orang-utans and primates outside the family of great apes, such as the five existing species of baboons (Guinea or Western baboon, *Papio papio*; Olive baboon, *Papio anubis*; Yellow baboon, *Papio cynocephalus*; Hamadryas or Sacred baboon, *Papio hamadryas*; Chacma baboon, *Papio ursinus*). This distinction is based upon a hierarchical standpoint, stating that the comparable interests of anthropoid apes are higher than those of other primates.

Following this position, experiments on Great Apes – considered as the closest species to human beings (Recital 18) – have been *de facto* prohibited («great apes shall not be used in procedures»), though with a safeguard clause (Article 55). It establishes that where a Member State has scientifically justifiable grounds on the essentiality of the use of non-human primates (*i.e.* an epidemic requesting their use), it may adopt provisional measures authorizing their use previous, transmission to the European Commission of the necessary information in order that it could take a decision on the merit within 30 days after it received a State communication⁶⁹.

Specifically, for NHPs, the aim is to restrict and limit their use to translational or applied research which must be with a view to the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions in human beings (Recital 17). In fact, NHPs shall not be used in procedures, with the exception of those procedures meeting the following conditions: there is a scientific justification that the purpose of the procedure cannot be achieved by the use of other species; the studies are aimed at the preservation of the species; the procedure is undertaken with a view to the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions.

A «debilitating clinical condition» for the purpose of the Directive means a reduction in a person's normal physical or psychological ability to function. Although this definition is open to various interpretations (narrow or wide)⁷⁰, the «life-threatening and debilitating» clause represents a welcome limitation on certain research which is not strictly necessary to the improvement of human health. Indeed, the majority of experiments on NHPs are not conducted for research into curing serious human diseases; 66% are pre-clinical safety assessments of new drugs (pharmacokinetic profiling, acute dose toxicology, repeat dose toxicology).

The same wording is present in the report issued in 2011 by the US Institute of Medicine. Among the criteria listed by the report in order to justify research on chimpanzees, the research in question must significantly slow or prevent important advancements to prevent, control, and/or treat life-threatening or debilitating conditions.

The Directive further requires scientific justification that no other species can be used and that the procedure upon NHPs must be undertaken.

⁶⁹ The use of Great Apes should only be allowed in research: aimed at the preservation of those species; in relation to conditions endangering human life (malaria, hepatitis C, respiratory syncytial infection); in the case of an unexpected outbreak of a life-threatening or debilitating disease in human beings; no other species or alternative method could suffice for the aims of the procedure.

⁷⁰ T. HARTUNG, *Comparative Analysis of the Revised Directive 2010/63/EU for the Protection of Laboratory Animals with its Predecessor 86/609/EEC*, in *Altex*, 27, 2011, 299 ss.

Article 10 and Annex II cover the supply of primates; Member States shall ensure that non-human primates may only be used in procedures where they are the offspring (F2) of non-human primates which have been bred in captivity (F1) or sourced from self-sustained colonies. The Commission shall conduct a feasibility study by 2017, which shall include an animal and welfare assessment.

Reliance on F1 or F2 colonies represent two ways of reducing capture of animals from the wild. F2 colonies mean that first generation born in captivity is only used for reproduction and cannot be used for research purposes. It implies therefore the killing of first generation surplus males which could neither be used for reproduction purposes nor can they be used for research.

Self-sustaining colonies are closed colonies, where retired breeders (F0 or F1) are replaced by animals bred in the colonies. There is no replenishment from the wild. All purpose-bred animals, including F1, can be used for research. It requires exchange of breeders between colonies from time to time to maintain genetic diversity. This approach does not create the problem of surplus males and achieves the objective of limiting capture of wild primates for reproduction⁷¹.

Identification requirements for each primate have been extended with respect to the former Directive, requesting now, in addition to the registration of the primate, each animal to have a lifetime personal history record.

In the view of the drafters of the Directive, its dispositions, if correctly implemented, can represent a step in the direction of the complete replacement of NHPs with alternative methods. Based on the scientific evidence available today, however, it is very unlikely that primates will completely be replaced in the foreseeable future by other animals or tests on cells grown in the laboratory. In our opinion, the only attainable goal – at least for the immediate future – is the reduction of the number of NHPs used in research⁷² and the refinement of practices in order to improve the welfare of NHPs⁷³.

5. The transposition of the Directive 2010/63/EU by Member States

Member States are obliged under Article 288, Paragraph 3, of the TFEU, to achieve the result established by a directive. The entire process by which obligations under Article 288 are fulfilled can be labelled by the term «implementation»⁷⁴. This process can be divided into a number of separate stages, depending on the duties upon States.

The first stage of the implementation process requests the transposition of the directive into domestic legislation through the adoption of general measures of legislative nature. The transposition of Di-

⁷¹ See the Report of the Scientific Committee on Animal Health and Animal Welfare, *The Welfare on Non-Human Primates used in Research*, 17 December 2002, 46 ss., available at http://ec.europa.eu/food/fs/sc/scah/out83_en.pdf (last visited 31/10/2015).

⁷² A.A. LACKNER, R.S. VEASEY, *Current Concepts in AIDS Pathogenesis: Insights from the SIV/macaque Model*, in *Annu Rev Med*, 58, 2007, 461 ss. See more at <http://www.avert.org/hiv-animal-testing.htm#sthash.JDmslJlc.dpuf> (last visited 31/10/2015); K. VAN ROMPAY, *Antiretroviral Drug Studies in Non Human Primates: a Valid Animal Model for Innovative Drug Efficacy and Pathogenesis Experiments*, in *AIDS Rev*, 7 (2), 2005, 67 ss.; K. VAN ROMPAY, *The Use of Non Human Primate Models of HIV Infection for the Evaluation of Antiviral Strategies*, in *AIDS Res Hum Retroviruses*, 7(2), 2012, 16 ss.

⁷³ In this regard, H.M. BUCHANAN-SMITH, *Refinement of the Use of Non-Human Primates in Scientific Research. Part I: the Influence of Humans*, in *Animal Welfare*, 15, 2006, 203 ss.

⁷⁴ S. PRECHAL, *op. cit.*, 4.

rective 2010/63 – completed by all 28 EU Member States only on 22 April 2015 – requested a number of measures and the set up of institutions and bodies by the Commission as well as by Member States. Member States had to establish a national inspections system (Article 35), National committees for the protection of animals used for scientific purposes (Article 49) and to appoint competent authorities (Article 59).

The second and third stage of the implementation process are referred to as «application» and «enforcement».

We can therefore classify EU Member States in three categories. Some countries such as Denmark, Estonia, Finland, Germany, Ireland, France, Portugal, have already adopted a legislation *ad hoc* and decrees and ordinances and have communicated to the European Commission the text of those provisions according to Article 61 of the Directive⁷⁵. Therefore, the three stages of the implementation process have been fulfilled.

The United Kingdom was one of the first countries to implement the Directive, despite some of its provisions being now or going further than previous legislation. In United Kingdom, the use of animals in experiments and testing is regulated under «The Animals (Scientific Procedures) Act 1986 Amendment Regulations 2012». In line with the Directive 2010/63, the Bill foresees a strict license process for breeders, suppliers and users of animals, based on a three strand system of control (Articles 7-9) (individual license, project license, establishment license). In fact, before starting any experimentation on animals, an *ad hoc* license must be provided to each individual performing research on animals, to the program of work and to the establishment where the research is supposed to be carried out⁷⁶.

Article 2 of the new Directive allows Member States to retain national provisions in force on 9 November 2010 that give more extensive protection to animals than those set out in the new Directive so long as they are not used to inhibit the free market. UK has retained special protection for dogs, cats and horses as well as non-human primates and has retained all the higher UK standards in every case where it will ensure better animal welfare. A second group of States (Netherlands, Poland and Romania) have enacted legislations *ad hoc* but they did not apply yet the national measures transposing the Directive. Finally, Italy is the only EU country that – as we will analyze in the next paragraph – concluded the “transposition” phase with a huge amount of delay.

6. The case of Italy

If the transposition of the Directive into domestic legislations was quite easy for countries such as the UK, in Italy the situation is quite different. In fact, the implementation of the Directive raised a fierce

⁷⁵ For instance, Directive 2010/63/EU was transposed into Irish law by the European Union (Protection of Animals Used for Scientific Purposes) Regulations 2012 [S.I. No. 543 of 2012]. The Irish Medical Board (IMB) has been appointed at the competent body for the implementation of the Directive. Among its tasks, the IBM grants authorizations: (a) to research projects involving the use of animals; (b) to breeders and suppliers of animals. As to Germany, it was transposed by the *Verordnung zur Ablösung der Versuchstiermeldeverordnung und zur Änderung tierschutzrechtlicher Vorschriften* (VersTierMeldVEV k.a.Abk.) V. v. 12.12.2013 BGBl. I S. 4145 (Nr. 72); Geltung ab 18.12.2013.

⁷⁶ The revised legislation was adopted on 18 December 2012 and came into force on 1st January 2013. On the legislation in the United Kingdom concerning animal experimentation, see E. JACKSON, *Medical Law: Text, Cases and Materials*, 3rd ed, 2013, Oxford, 446.

debate in the Italian scientific community and in the public opinion on the legitimacy of animal testing⁷⁷. As a consequence of the irreconcilable positions between supporters and opponents of animal testing, Italy is the only EU country that have failed to satisfy the Directive within 2014, contravening its duty to enact the necessary measures within the specified time. In this regard, according to a consolidated jurisprudence of the European Court of Justice, the State cannot plead practical, financial or administrative questions as a justification of its non-compliance with obligations established by the EU Treaty⁷⁸. This delay comported the beginning of an infringement proceeding by the European Commission against Italy, on 23 January 2014 in conformity with Article 258 of the TFEU⁷⁹.

Animal experimentation was regulated in Italy by the Legislative Decree 116/92⁸⁰ (which abrogated Law 12 June 924/193⁸¹). Eventually, on 28 August 2013, the Italian Parliament adopted Law No. 96, the national law of transposition of the EU Directive⁸². Article 13 of Law No. 96 – then reproduced by the Legislative Decree No. 26 of 4 March 2014⁸³ – is the “apple of discord” because, according to some scientists, its content would limit in an excessive manner the freedom of scientific research⁸⁴.

The different paragraphs of Article 13 of the above mentioned law contain a severe restriction to some kinds of research: the breeding or use of cats, dogs and non-human primates and specimens of species in danger of extinction for basic research is forbidden (art. 13, let. *b, g*); animals of any nature previously employed in procedures classified as of ‘moderate’ severity ‘mild’ or ‘non-recovery’ within

⁷⁷ A European Citizen’s Initiative (ECI), named “Stop Vivisection”, was launched in 2012, according to Article 10(1)(c) of Regulation No. 211/2011/EU on the Citizens’ Initiative and it gathered 1.17 million signatures. The petition was submitted to the European Commission on 3 March 2015, asking the abrogation of the Directive. The text of the petition is available at <http://ec.europa.eu/citizens-initiative/public/initiatives/finalised/details/2012/000007> (last visited 31/10/2015). However, the European Commission, with a statement of 3 June 2015, decided not to support this initiative (<http://ec.europa.eu/transparency/regdoc/rep/3/2015/IT/3-2015-3773-IT-F1-1.PDF>, last visited 31/10/2015).

⁷⁸ See, e.g. Case 301/81 Commission v. Belgium [1983] ECR 467; Case 136/85 Commission v. Italy [1987] ECR 479.

⁷⁹ See “Infringement Cases”, *European Commission asks Court to impose financial penalties on Italy*, http://ec.europa.eu/environment/legal/law/press_en.htm (last visited 31/10/2015).

⁸⁰ Decreto legislativo 27 gennaio 1992 n. 116, «Attuazione della direttiva n. 86/609/CEE in materia di protezione degli animali utilizzati a fini sperimentali o altri fini scientifici», in *Gazzetta Ufficiale* n. 40 del 18-21992 – Suppl. Ordinario n. 33). See A. MANCIOTTO, A. VITALE, *Legislazione e cura degli animali sperimentali: situazione attuale e prospettive future*, Istituto Superiore di Sanità, Rapporti ISTISAN 07/16 Roma, 2007; Gruppo di lavoro sulle attività e i rischi lavorativi nella ricerca scientifica con modelli animali, *Manuale per la gestione integrata degli stabulari. Principi e indicazioni per la protezione degli animali e la sicurezza dei lavoratori*, in *Consiglio Nazionale delle Ricerche. Quaderni de “la ricerca scientifica”*, 117, 2012, 17 ss.

⁸¹ Legge 12 giugno 1931, n. 924, concernente provvedimenti per la protezione degli animali, in *Gazzetta Ufficiale*, Serie generale, n. 180 del 6 agosto 1931.

⁸² Legge di delegazione europea 2013, n. 96, in the *Gazzetta Ufficiale*, Serie generale n. 194, 20 agosto 2013, into force since 4 September 2013. On the problems concerning the implementation of the Directive in Italy, see editorial *Italian Biomedical Research under Fire* (December 2013) vol. 16, num. 21, *Nature Neuroscience*, <http://www.nature.com/neuro/journal/v16/n12/pdf/nn.3595.pdf> (last visited 31/10/2015); R. FORASTIERO, *The Legal Protection of Animals Used for Scientific Purposes: Reflections on the Implementation of Directive 2010/63/EU in Italy*, in *Studi sull’integrazione europea*, 3, 2014, 565 ss.

⁸³ Decreto Legislativo 4 marzo 2014, n. 26, Attuazione della direttiva 2010/63/UE sulla protezione degli animali utilizzati a fini scientifici, in the *Gazzetta Ufficiale* n. 64, 14 marzo 2014. The Decree – that entered into force on 10 July 2014 – eventually completed the process of transposition of the Directive by Italy.

⁸⁴ See, for instance, C. PETRINI, *From the Law of European Delegation to the Legislative Decree on Experiments with Animals: Consequences for Biomedical Research*, in *Clin Ter.*, 165 (5), 2015, 373 ss.

the meaning of Article 16 of Directive 2010/63/EU cannot be re-used (art. 13, lect. e); anaesthesia or analgesic agents must be applied during any procedure in which the animal may experience some pain, except in cases where anaesthesia or analgesia are the subject of the study (art. 13, lect. d); the use of genetically modified animals is limited. Art. 13, lect. e states that the generation of genetically modified animals, such as rodents, will need to take into account the «potential risks to human health, animal welfare and the environment».

According to a document of the Italian Bioethics Committee, the restrictions provided by Law No. 96 will have a negative impact on biomedical research in Italy and these norms constitute a clear violation of the Directive, which prohibits member States from introducing more restrictive rules⁸⁵. For instance, the ban on breeding on the national territory of dogs, cats, NHPs will hinder research in the framework of the European research and it will inevitably determine the importation of animals, with certain discomfort for the same animals and additional costs for research.

It is worth noting that, in some aspects, the Law goes even further than the Directive, for instance dealing with xenotransplantation (XT) (art. 13, f), even if the Directive makes no mention to this kind of transplants⁸⁶. Xenotransplantations are a new frontier of research, despite still raising several ethical and scientific concerns⁸⁷. The intention of scientists carrying out research on this technique is to fill and bridge the gap between people waiting for a transplant and the scarcity of available organs⁸⁸. However the first attempts were all largely unsuccessful, due to an inability to overcome hyperacute rejection and raised concerns as to the potential risk associated with the transmission of a virus or retrovirus from animal to human with its unpredictable consequences⁸⁹.

Given this hazard, research has now been focusing on xenotransplantation of cells and tissues, which is less problematic under an ethical and scientific point of view. A paper, published by a team of sci-

⁸⁵ See Comitato Nazionale per la Bioetica, *In merito ad alcuni problemi bioetici sollevati dalla Legge 6 agosto 2013, n. 96, art. 13 Criteri di delega al Governo per il recepimento della Direttiva 2010/63/UE del Parlamento europeo e del Consiglio, del 22 settembre 2010*, 24 January 2014, «Risposta al quesito posto al Comitato Nazionale per la Bioetica dalla Senatrice Prof. Elena Cattaneo», available at http://www.governo.it/bioetica/pdf/Legge_6_agosto_2013_n.96_testo.pdf (last visited 31/10/2014).

⁸⁶ On the ethical issues surrounding xenotransplantations, M. JORQUI-AZORFA, C. M. ROMEO CASABONA, *Some Ethical Aspects of Xenotransplantation in Light of the Proposed European Directive on the Protection of Animals used for Scientific Purpose*, in *Transplant Proc*, 42 (6), 2010, 2122 ss.

⁸⁷ Attempts to transplant kidneys and livers from chimpanzees and baboons, and hearts from chimpanzees, baboons, pigs and sheep into humans have been practised since 1992 when the first genetically modified pig, destined to transplant was created. See E. ANCONA, *Lo xenotrapianto come nuova frontiera in medicina*, in Atti del Convegno, Roma, CNR, 2-3 maggio 2000, *Animali e piante transgenici: implicazioni bioetiche*, Roma, 2001, 67 ss.; P. SOBBRIO, *Xenotransplantation and Human Rights*, in R. BIN, S. LORENZON, N. LUCCHI (eds.), *Biotech Innovations and Fundamental Rights*, Dordrecht, 2012, 207 ss.

⁸⁸ The Council of Europe defined transplantation as «transplant from animal to human of organs, tissues or living cells of animal origin». See, *Report on the State of Art in the Field of Xenotransplantation*, Strasbourg, 21 February 2003, CDBI/CDSP-XENO (2003) 1, available at [http://www.coe.int/t/dg3/healthbioethic/activities/06_xenotransplantation_en/XENO\(2003\)1_SAR.pdf](http://www.coe.int/t/dg3/healthbioethic/activities/06_xenotransplantation_en/XENO(2003)1_SAR.pdf) (last visited 31/10/2015). See also M. WESCHKA, *Xenotransplantation*, in (J. TAUPITZ, M. WESCHKA eds), *Chimeras and Hybrids in Comparative, European and International Research. Scientific, Ethical, Philosophical and Legal Aspects*, Dordrecht, 2009, 98 ss.

⁸⁹ L. CHAPMAN, *Xenotransplantation: Benefits and Risks*, in *Emerging Infectious Diseases*, 7, 2001, 545 ss.

entists in *The Lancet*, showed the positive impact that this innovative sector of research can have on the improvement of transplantations from man to man⁹⁰.

The issue at stake is that art. 13, lect. (f), of Law No. 96/2013, provided a narrow definition of xenotransplantation, limited to the transplant of one or more organs from animal to human (animals of different species), thereby also banning transplant of cells and tissues.

The ban on xenotransplantation will have, according to some scientists, a negative impact on the patients in the sectors of man to man transplantation, oncologic and immunologic research. In fact, clinical data shows that 50% of the patients reject the implanted organ (i.e. the kidney) within 15 years due to the donor antibodies⁹¹. Through the research on xenotransplantation scientists can learn how to contrast the rejection process. Strategies aimed at prolonging the survival of an animal that received a transplant can help to improve life expectancy of humans⁹².

In conclusion, the choice of the Italian legislator to adopt more stringent national disposition with the goal of protecting the welfare of the animals, is evidently not coherent with some rules of the Directive 2010/63.

7. Conclusions

The Directive 2010/63/EU – despite the criticism received by the different stakeholders involved in animal experimentation – too permissive for animal welfare groups⁹³, too restrictive for most scientists – is the result of a long and complex debate between different and irreconcilable positions and reflects, therefore, an acceptable political compromise.

In this regard, it is worth mentioning that many scientists worldwide agree on the necessity of experiments on animals for the medical progress. However, unnecessary experiments should be avoided and – as underlined by an editorial published on *Nature* – particular attention should be paid to the end of life issues of animals used in research⁹⁴. In fact, while the debate is mainly focused on what happens to the animals while they are alive, most of the laboratory animals are killed at the end of an experiment. Therefore, animal euthanasia should «reflect the most humane options available».

As to the alternative methods, there is a general consensus that they should be promoted, and in this regard, the Directive clearly established that experiments on animals should not be carried out, if alternative methods would originate equally valid outcomes. The Draize eye test, for instance, is a clear example of research that can be successfully substituted by alternative methodologies.

The central issue is therefore to distinguish between two categories of experiments: on the one hand, research which is unavoidable for the improvement of human health and the cure of severe

⁹⁰ R. BOTTINO, M. TRUCCO *et al.*, *Clinical Xenotransplantation: the Next Medical Revolution?*, in *The Lancet*, 379, 2012, 672 ss.

⁹¹ See research conducted by scientists at Stanford University on the rate of rejection of transplanted organs, available online at <http://scopeblog.stanford.edu/2012/11/01/the-mystery-surrounding-lung-transplant-survival-rates/> (last visited 31/10/2015).

⁹² A. D'APICE, *Kidney Xenotransplantation*, in *Kidney International*, 85, 2014, 265 ss.

⁹³ See for instance, the critical stance of the Lega antivivisezione (LAV) on the Directive 2010/63/EU at <http://www.lav.it/leggi/sperimentazione-vivisezione> (last visited 31/10/2015).

⁹⁴ See Editorial, *Fish have Feelings too. Our Obligations to keep the Suffering of Laboratory Animals to a Minimum – both in Line and in Death – does not apply only to Mammals*, in *Nature*, February 2014.

diseases (*i.e.* HIV/AIDS, Ebola, tumours and neurodegenerative diseases such as Amyotrophic Lateral Sclerosis or Multiple Sclerosis), which are justified under a scientific and an ethical point of view; on the other hand, research irrelevant, unnecessary, even hazardous to human health and which have little or no predictive value or application to human medicine. This kind of research is generated by the incapacity of the scientist, or by the will to produce several scientific papers, also in violation of international standards on research integrity⁹⁵. Therefore, the strict control and ethical review mechanisms proposed by the Directive are the most effective mechanisms to prevent unnecessary and unjustified pain and suffering for animals through unnecessary and unjustified pain.

In conclusion, we argue that experimenting on animals is acceptable if (and only if) suffering is minimized in all experiments, and human benefits gained could not be obtained by using other methods. In sum, the Directive reached its goal to harmonize the legislation of Member States at the highest level, impeding to single Member States to promote stricter laws aimed at protecting animals in experimentation, (with the exception of Italy as we have widely highlighted). Despite the problems which arose with reference to its transposition, through this Directive the European Union is again taking a leading role in research and development for new non-animal tests and technologies, by introducing a series of measures that represent a fair balance between the different exigencies of protection of animal welfare and of the advancement of science and research.

⁹⁵ See *e.g.* the Singapore Statement on Research Integrity, adopted on 22 September 2010 within the 2nd World Conference on Research Integrity, which requests researchers «to adhere to regulations and policies related to research» (Article 2).