

Animals in research: a stony road

The implementation of the European Union directive on the use of animals in research into national laws is struggling

Marta Paterlini

During a national protest against vivisection in Italy on 20 April 2013, members of the pro-animal movement Fermare Green Hill (Stop Green Hill) forced their way into the Department of Biotechnology and Translational Medicine of the University of Milan, Italy, which also houses the Neuroscience Institute of the National Research Council. Outside, the police were trying to contain 400 protesters, who were screaming threatening slogans against the use of animals in research. Eventually, the researchers convinced the intruders not to free all the animals in the facility—many of which were being used as neurodegenerative disease models—but the activists tore apart all the identification cards on the cages, making it impossible to identify the animals left behind. The activists also set free 100 transgenic mice and a rabbit. The following day, scientists in Italy publicly protested in support of animal research and the University of Milan sued Fermare Green Hill. “Our animal models are treated according to European legislation,” commented Cecilia Gotti, a National Research Council researcher. “These people ruined years of research funded by national and European agencies.”

Scientists later discovered that Milan’s local authorities had been drafting a regulation for the protection and welfare of animals, with the potential to seriously limit research using animals within the city. Researchers wrote a public petition to the mayor asking him to withdraw the chapter concerning animal experimentation, which

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he eventually did. Whether the Milanese politicians who drafted the regulation were aware that they were in danger of violating existing European Union (EU) regulations, namely the update to the directive on the use of animals for scientific purposes, was unclear.

EU directive 2010/63/EU came into force on 9 November 2010, with the provision that EU member states would implement it into national law within 2 years. As of 1 January 2013, the directive has been formally applied across Europe. The new directive is considerably more prescriptive than its 1986 predecessor, specifying more explicitly what kind of experiments and procedures scientists are allowed to perform with animals. EU member states may pass neither more-restrictive nor less-restrictive new legislation, but more-stringent regulations already in force at the time the new directive was adopted may be maintained. As such, the aim of the new directive is to harmonize legislation across the 27 EU member states, which should make it easier for scientists to understand and work within the legal framework and regulations that govern research using animals.

The reality, however, is that different EU countries and research communities have dealt very differently with adopting the new directive. In Germany and the UK, scientists took part in discussions with the European Commission, the European Parliament and their national ministries and parliaments as soon as the first draft of the directive was published. “In Germany, scientists and research organizations have been very active communicating their concerns to members of parliament and the respective ministries ever since the EU directive

came into force back in 2010,” said Thomas Dantes, science officer at the Max Planck Society, Berlin, Germany. German law already sets high standards for experiments on vertebrate animals and was amended to implement the new EU regulations.

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In the UK, animal research is similarly subject to high standards of animal welfare. Although animal rights groups fear that the directive could reduce the stringency of regulation in the UK, experts claim these fears are unfounded. Rather, they argue that the EU directive recognizes the high standards of the UK animal research “as a benchmark”, according to Chris Magee, media and public affairs manager of the British non-profit organization Understanding Animal Research.

In other countries, things have not gone so smoothly. In Austria, for example, scientists were alarmed by an early government draft that appeared to be more restrictive than the EU directive. After a great deal of discussion, the Government eventually passed laws that were a translation of the EU directive, much to the relief of Austrian scientists. “Initially, politicians acted quite secretly, without consulting any of us, and it became a political conflict,” commented Jürgen Knoblich, deputy scientific director of the Institute of Molecular Biotechnology, Vienna, Austria.

In Italy, the situation is even worse. The implementation of the directive has been

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lost amid political crisis, and scientists have not been involved in drafting the proposed amendment to laws governing animal research. As a result, the Italian parliament has approved a bill with substantial restrictions that go beyond the requirements of the EU directive. Italian scientists fear that this will have detrimental effects on both biomedical research and animal welfare, as research might move to other countries with less stringent animal welfare regulations. "This may result in an infringement procedure and contravene directive 2010/63/EU itself", commented Dario Padovan, a biologist and coordinator of the scientific committee of Pro-Test Italia, a new non-profit organization set up to promote and explain animal research.

The proposed amendment includes a ban on breeding dogs, cats and non-human primates in Italy for research; a ban on the use of dogs, cats and non-human primates for purposes other than health research; a requirement that experiments using animals for health research have the explicit approval of the Ministry of Health; a ban on research that does not use anaesthesia or analgesia, unless the objective of a study is to test these effects; and a ban on the use of animals for studies of addiction, xenotransplantation and training, except for in higher education for vets and physicians. Animal right activists are pleased by the proposed changes. "The Italian legislation represents a big revolution and an innovative act in favour of lab animals," commented Michela Kuan, a nutritionist and a member of the animal-rights group Lega Anti Vivisezione in Rome. "For those who do not believe in animal models," she continued, "this will be a great opportunity to push for alternative methods to achieve a total replacement of animals in research."

How Brussels will react to the proposed changes to Italian law is unclear, especially as other EU countries are also

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behind in implementing the directive. "The [European] Commission will in due course assess the situation for all member states concerning transposition of this directive following the normal process and consider [...] launching an investigation, which may result in an infringement procedure," said Joseph Hennon, a spokesman for the European Commission's Directorate General Environment. "Once directive 2010/63/EU has been transposed in a majority of member states, the Commission will conduct an assessment of compliance and completeness of the transposition with the directive, as is the case with all new EU legislation. Action will be taken or not depending on the results of the study."

"The EU directive is a workable compromise between political pressure and scientific need, and it found a sort of consensus within the scientific community," said Stefan Treue, director of the German Primate Centre, Göttingen, Germany, "but there is still room for interpretation. I expect court cases and confusion at the national level. But the main issues I see are the large increase in bureaucratic requirements that are of no benefit for the animals and the lack of a clear set of rules if an application for an animal experiment is not decided about in a timely manner." Indeed, scientists fear that bureaucracy will lead to paralysis: university departments wishing to undertake research must apply to university central offices, which must then apply to local authorities, which send a decision back to universities, which then decide whether to approve or refuse a department's application, thereby increasing the time it takes to get permission to start work.

Because other countries have less restrictive laws on the use of animals in research, the fear is that research in Europe will become less competitive. "The promised advantage—that unified laws will bring more transparency to animal experimentation throughout Europe—is hard to see. Rather, one sees a very complicated process of translation into the languages of member states and consideration of national laws and interests as well. [On the whole] I think it is potentially damaging to medical research," said Richard Moriggl, director of the Ludwig Boltzmann Institute for Cancer Research in Vienna, Austria. Dantes also sees potential for trouble with translating the directive, pointing out that its inherent flexibility might lead to

it being translated in ways that are more or less friendly to science.

Anna Olsson, who coordinates the Laboratory of Animal Science research group at the Institute of Molecular and Cell Biology in Porto, Portugal, believes that the new legislation is generally a step forward. "It does not require impossible things. In countries with already advanced legislation, such as the UK or Sweden, there is no increase of demand. Science is a collaborative matter and it's good to operate under the same legislation, after all." But others are not so certain. "If the original goal was to harmonize, I think they achieved the opposite," Knoblich said. "Bureaucracy from Brussels is affecting us badly. Thousands of hours [spent translating the directive] means a lot of wasted time and little thinking. How should we compete with the USA and Asia now? We should think globally. I foresee that many young scientists will be forced to go abroad."

David Smith, former president of the Federation of European Laboratory Animal Science Associations, Ipswich, UK, is not so concerned: "This is a fear, but it's not realistic to claim a brain drain." He believes that solid projects will continue to be appropriately funded and approved.

An increased bureaucratic burden and a loss of competitiveness are not the only criticisms European scientists have levelled against the new rules. A pillar of directive 2010/63/EU is the implementation of the 3Rs, replacement, refinement and reduction in the use of animals in research, first proposed in 1959 [1]. "The [European] Commission's ultimate goal is to replace all animal use for scientific purposes," Hennon said. "However, the Commission understands that not all scientific questions asked today can be answered solely through testing with non-animal methods; therefore, we accept that animals are still needed today for research and testing. The new directive plays a pivotal role in boosting the development, validation and uptake of alternative approaches. EURL ECVAM [European Union Reference Laboratory for Alternatives to Animal Testing] is of the firm belief that by endeavouring to understand the basic mechanisms underlying the toxicity of chemicals, we can take a rational approach to designing systems that integrate cell-based assays and computational models for predicting toxicity, to replace animal tests that simply try to recreate a disease outcome."



Scientists themselves remain sceptical. “What needs to be clearly appreciated is that replacement—the third R—will never be possible without serious detriment for biomedical research, since pathologies changes over time,” said Roberto Caminiti, professor of physiology at the Sapienza University in Rome, Italy, and chairman of the Committee on Animals in Research (CARE) for the Federation of European Neuroscience Societies, Brussels, Belgium. “The European philosophy of replacing animals is hypocritical. As I have already broadly commented, I can testify to the increasing interest among the younger generation in the integrative study of brain function. At the same time, I stress the dramatic negative consequences that a severe limitation or ban on the use of non-human primates will have on education in a discipline that currently places Europe at the forefront of modern research in neuroscience” [2].

Treue said, “I strongly believe that it is impossible to replace models of complex pathologies in the foreseeable future. The only alternative would be to use humans,

but that is not ethically acceptable. The FDA [US Food and Drug Administration] recently approved an HIV vaccine for safety trials in humans, and experiments with monkeys and mice have given hope that an effective vaccination may be possible. Research using a relative of the virus, which affects monkeys, SIV, has helped scientists to understand why HIV is so deadly and how this disease can be effectively treated. Let’s face it, cell culture is not enough. You need animals for the benefit of patients.”

Sarah Wolfensohn, former head of veterinary services at Oxford University, UK, and now a consultant for Seventeen Eighty Nine, an independent consultancy for animal health and welfare, commented that, “there is still much we can do on the R that stands for refinement; that is, [we can maximize] animal welfare [by refining] husbandry and experimental procedures so that they are less painful and distressful for the animals: the provision of bedding and the type of environment, the promotion of tiny things that are good for the animals’

quality of life, such as the way you handle the syringe, for instance.” Wolfensohn added that the new directive also introduces the important concept of animal suffering and the accumulative level of pain that was not included in previous legislation.

The implementation of directive 2010/63/EU has also given the scientific community in Europe pause to reflect on their approach to and communication of the importance of animals to research. Many researchers who work with animals are not comfortable talking about their research with the public or politicians, but there is an increasing realization that they should start to do so. “The moment animal experimentation is criminalized the matter becomes political, not scientific any more. Public opinion is misinformed and has access to one version [of the facts] only, if scientists fail to gain more public space. Scientists should gain space instead of locking ourselves in an ivory tower. Media are manipulative,” said Moriggl.

Caminiti is similarly concerned: “Animal right activists from all over Europe have a

strong influence on Brussels, whereas we do not have any spokesman in Europe. The scientific world is dormant, never ready to fight, not able to create a stable movement. It is complex to help people understand that transgenic mice are useful, so we should definitely work hard on communication, where we have failed so far."

Bernard Rollin, professor of philosophy, animal sciences, and biomedical sciences at Colorado State University, Fort Collins, CO, USA, said, "Public concern is strong and not negotiable. Scientists are stupid when they refuse to say that animal research does not have ethical issues. Then, other people will speak instead of them. Scientists are narrower and narrower and do not have an overview any more, and they fail to speak to normal people. It's time for science to talk to society." Indeed, politicians often follow public opinion, so it is the public who have to be convinced of the need for using animals in biomedical research."

Wolfensohn noted, "It is important to show and share with people the fact that

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animal welfare is a priority, not only in politicians' agendas, but within research institutes as well." She cited the example of the University of Leicester, Leicester, UK, which at the inauguration of its new animal research facility last year opened the doors to the media. "The general public does not have [any] idea what is going on in a laboratory, they cannot see it. In most cases animal facilities are not open, not only for security reason, but also because they do not have the authority to do so. I must say that heads of departments can be excellent researchers but bad administrators and bad science promoters."

Italian scientists might well have begun to tune into society. On 8 June 2013, researchers staged a series of protests across the country to draw attention to what they say is an increasingly negative attitude about science based on misinformation. The events—collectively called Italy United for Correct Scientific Information—were partly in response to the attack on the University of Milan in April. On 19 September 2013, hundreds of scientists protested in Rome against the proposed new law. Also a handful of politicians took part in the rally, organized by Pro-Test Italia. The remaining politicians will take time to hear the message about the importance of animals to research

coming from the public rather than the scientific community, but unless scientists can achieve that level of public support and understanding, both science and society are set to lose.

CONFLICT OF INTEREST

The author declares that she has no conflict of interest.

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