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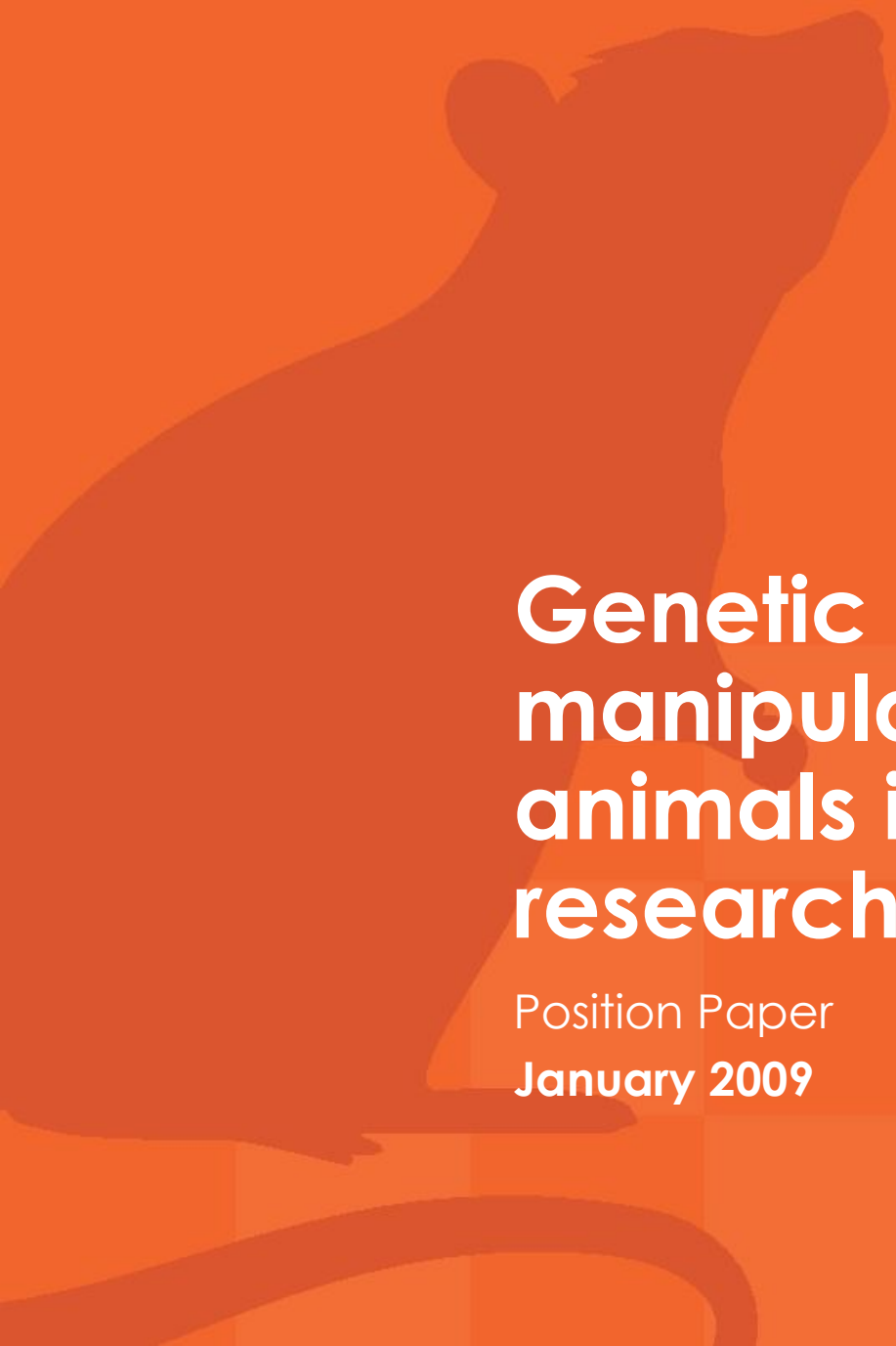

Genetic manipulation of animals in research

Position Paper

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The situation today

Genetic manipulation involves the deliberate modification of the genome - the material responsible for inherited characteristics. There are specific welfare concerns associated with genetic modification of animals. The crossing of boundaries between species and the interference with the genetic integrity of animals has also evoked strong moral objections.

Laboratory use of genetically modified (GM) animals continues to increase dramatically. Within the EU, statistical comparison of figures of GM animal use is not available, but where GM animals are listed by member states they are generally increasing. For example, in Sweden a recent 27,000 increase in the number of mice used is attributed to increase in genetic modification[1] and in the UK GM animals now count for one quarter of all procedures[2] .

In the field of biotechnology the pace of scientific development often outstrips meaningful ethical debate and Eurogroup is extremely concerned about the ethical and welfare implications of the use of biotechnology techniques on animals.

Welfare concerns of genetic modification

Ethical and welfare concerns that apply to the production and use of GM animals include the following:

- There are specific procedures associated with genetic modification that can be painful, such as surgical embryo transfer of manipulated embryos into recipient mice.
- Genetic modification can affect animals' characteristics in ways that cause suffering. Effects of modification can also be difficult to predict.

[1] Commission of the European Communities (2003) Third 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 (data for 1999) CEC, Brussels.
[2] Home Office (2003) Statistics of Scientific Procedures on Living Animals -Great Britain 2002: The Stationary Office, London.

- The technology is inherently inefficient and wasteful of animals' lives. Large numbers are required in both the creation and maintenance of GM lines.
- GM animals are increasingly viewed by scientists as biological tools rather than sentient animals with intrinsic value and the capacity to experience pain, suffering and distress.
- Many GM animals are 'born to suffer'; since genetically modified disease models may well experience pain, suffering and distress.
- The demand for the production of transgenic animals seems set to increase, even though the general aspiration is to reduce the numbers of animals used in research and testing.

Welfare concerns of mutagenesis

Similarly to GM animals, the use of mutant animals is also rising. Mutant animals either carry a naturally occurring genetic mutation, or result from the application of mutagenic compounds or radiation. Very similar concerns exist for the welfare of mutant animals as for GM animals in that the genetic mutation can have deleterious effects on welfare. When mutants are produced artificially, huge numbers of animals can be used to obtain animals of 'scientific interest', which is a cause for added concern.

Welfare concerns of cloning

Cloned animals are created via a process called nuclear transfer; where the nucleus of an egg is replaced with cell material derived from another animal or animal embryo. The types of animals cloned using nuclear transfer now include sheep, mice, bovines, horses, cats and goats. In the laboratory, the technique is often employed to create animals with specific genetic changes. Outside of research the technology is thought to have some potential in stock breeding. Nuclear transfer raises a number of issues with respect to animal welfare:

- Due to the inefficiency of the technology, a considerable number of animals are used in order to produce the cloned animals.
- A large proportion of animals produced by this technology have died shortly after birth as a result of physiological problems and other abnormalities.
- Many cloned livestock animals are overgrown at the time of birth, which can make birth difficult or necessitate caesarean section delivery.
- The long-term effects of nuclear transfer cloning on animal welfare are unknown. However, there is now evidence that cloned mice have a significantly reduced life-span in comparison with non-cloned controls and that all animal clones are more likely to suffer from a range of abnormalities, including tumours, liver disease, pneumonia and disorders of the immune system.

Reasons for the application of biotechnology to animals

The variety of potential applications for genetic modification is growing, along with the species to which they are applied. GM, mutant and cloned animals are employed in science and industry for a variety of purposes, including to provide:

- Models for basic fundamental research to understand gene function.
- Models of human or animal disease.
- Bioreactors to produce therapeutic proteins in milk or blood.
- Sources of tissues or organs for xenotransplantation.
- Livestock with improved production traits and improved disease resistance.
- Better subjects for vaccine and toxicity testing.

Xenotransplantation

The ethical acceptability of xenotransplantation (the transplantation of animal organs or tissues into humans) is open to question. The justification of animal use in solid organ transplantation development is particularly debatable since even if it does become a viable treatment option it is likely to be rapidly replaced by artificial organs (which would not require the use of immunosupressants in patients) in the long term.

There are particular welfare concerns with research linked to the development of xenotransplantation:

- Use of pigs as organ sources
    - There is potential wastage of animals in the process of developing animals to provide the organs. For example the creation of GM pigs who are genetically altered to produce less of an immune response in humans often involves a cloning step and, as already discussed, cloning is highly inefficient.
    - The quality of life for animals to be used as sources for organs and other tissues may be poor. For example source organ pigs are often housed in pathogen free environments that may be relatively barren and hence do not provide for their complex behavioural and social needs.

- Use of animals in associated research

  The procedures used can be highly invasive and involve substantial amounts of suffering, e.g. to the primates used as test recipients of pig organs who undergo transplantation surgery, often in combination with severe anti-rejection drug regimes. The use of primates in any experiment, especially ones involving substantial suffering, is always going to be of huge welfare and ethical concern, but when the likelihood of end success is debatable that concern is magnified.

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Relevant legislation

Genetic modification

There are two types of legislation relevant to genetic modification:

- Regulation of animal experiments relating to their creation and use – Council Directive 86/609/EEC,1986 regarding the protection of animals used for experimental and other scientific purposes, and Convention ETS 123, 1986 for the protection of animals used for experimental and other purposes (both are under revision).
- Regulation on the contained use and deliberate release of GM organisms - Directive 2001/18/EC, 2001 on the deliberate release into the environment of genetically modified organisms (this repealed Directive 90/220).

Neither Convention ETS 123 nor Directive 86/609/EEC make specific reference to the welfare of GM animals. ETS 123 covers all aspects of animal use in research, including fundamental research, but it is not legally binding, whereas 86/609 is legally binding on EU Member States but covers only those animals used in experiments for safety testing and protection of the environment. In addition, 86/609 is designed only to promote harmonisation of laboratory animal conditions within industry between EU member states, and not to promote animal welfare or the furtherance of best practice and application of the three Rs.

The Deliberative Release Directive 2001/18/EC covers aspects concerning the release of a GM organism in the environment, risk assessments, traceability and labelling etc. It does not cover the welfare of released GM organisms.

Xenotransplantation

The Committee of Ministers of the Council of Europe has adopted a recommendation to its Member States on xenotransplantation, underlining the need to keep patients fully informed and calling for the establishment of world-wide agreements and monitoring

procedures. The Council of Europe has also agreed guidelines on Xenotransplantation. These include that primates should not be used as source animals for organs and requirements for research and source animals to comply with Directive 86/609.

Patenting

The European Patent Office (EPO) began to receive patenting applications for transgenic animals in the 1980s. The case of the 'Harvard Oncomouse', filed in 1984, has been a long runner and continues to be a controversial test case in this area. This case has demonstrated that transgenic animal production processes, together with gene sequences for particular applications, may be patented according to certain conditions. This is in accordance with Directive 98/44/EC, 1998 on the legal protection of biotechnological inventions.

However, throughout the case there have been numerous arguments put by third parties before the Opposition Division to the proprietor as to patentability. For example, Article 4 of the Directive of the European Parliament and of the council of 6th July 1998 on the legal protection of biotechnological inventions (98/44/EC), generally known as the Biotech Directive, prohibits the patenting of animal varieties. It was eventually established that GM animals did not themselves constitute animal varieties and are not therefore excluded from patentability under this Article. Further, Article 6 prohibits the patenting of inventions which run counter to public order or morality, including 'processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes'. Here it was decided that the benefits of the Oncomouse outweighed the risks and so patentability still stood.

The "patenting" of genetically modified, or transgenic, animals is also mentioned under the Convention on the Grant of European Patents, which established the EPO and to which all EU Member States are signatories. The Convention on Biological Diversity, also has some points of relevance, as one of the conventions main goals is to ensure the fair and equitable sharing of the benefits from the use of genetic resources.

Action needed

- Policies, guidelines and legislation must be developed to ensure that biotechnology techniques are only applied to animals where there is very strong justification and that the use, suffering, and wastage, of all the animals involved is minimised. More specifically policies must clearly state that biotechnology should not be used for the following purposes:
    - creation of any genetically modified animal whose suffering will not, or cannot, be alleviated;
    - cloning or genetically modifying animals to improve agricultural production traits;

    - creating cloned or GM animals for use as companions, or for other trivial purposes, e.g. the glowing rabbit who was created as a "work of art";
    - propagating a 'check-list' approach to the species it is possible to genetically modify and/or clone.
- Greater consideration must be given to an animal's capacity for suffering, the likelihood of suffering occurring and how that suffering will be alleviated before GM animals are made.

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