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# Transgenesis and animals in research — an overview of animal welfare considerations

Currently, biological sciences are greatly influenced by the emergence of the techniques of molecular genetics. The use of these techniques may raise unique ethical and animal welfare issues, particularly in relation to the manipulation of the genome. The production of transgenic animals is one such manipulation and points to consider in any discussion of the welfare implications of using transgenic animals are summarized here.

**What are transgenic animals?**

It is possible to transfer a specific sequence of DNA into the genome of an animal. When the DNA encodes a specific gene, the manipulation is one of gene transfer. The transfer of a functional gene into the germline of subsequent generations may change the physiology of those animals in ways that are not always predictable. A number of strategies are being developed to enhance gene transfer, by carrying the DNA with various vectors such as modified retroviruses, adenoviruses or by DNA trapped in liposomes. The DNA is either injected into a dividing oocyte or incorporated into embryonic stem cells *in vitro,* which are subsequently fused with a normal early embryo.

The DNA sequence of a particular gene can be prepared so that the base sequence has been changed in a precise manner. Conditions can be created in which there is a reasonable probability that the new sequence will be inserted into the genome of an animal replacing the normal sequence and thus inactivating that gene. An animal with such an inactivated gene is referred to as a gene knockout animal.

It cannot be assumed that a single copy of a transgene resides in cells of the recipient animal. Subsequent breeding programmes to establish homozygous animals or defined genetic strains may have unique welfare implications as the generation of novel genetic strains requires increased vigilance in detecting unexpected phenotypes.

Since the 1960s, the use, or the ways of avoiding the potential misuse of molecular techniques have been viewed with some mistrust by the public and by certain sectors of the scientific community. It has been suggested that biotechnology may be opening Pandora's box with undesirable consequences. Transgenesis has been viewed in this way but perhaps not from an informed perspective. A number of points for discussion are summarised in the following sections.

**Is transgenesis unacceptable because it is unnatural?**

Normal breeding procedures include the generation of breeding lines from naturally occurring variants by the selection of preferred phenotypes. After the transfer of a transgene, there may be no obvious phenotype to use as a selective trait and in generating a strain, the important strategy may be to avoid unwanted traits. The co-selection of cryptic variants can occur in both natural breeding and transgenic programmes. It is worth considering the natural progression in which tissue and gene transfer has developed over the last 40 years (Table 1).

The seven categories in Table I illustrate the progressive refinement of the means by which physiological processes can be perturbed . The examples are of obvious clinical relevance and the refinement essentially covers attempts to increase the precision of the modification as the organs are replaced by tissues, then by cells and finally, by specific DNA. Similarly, any augmented function by the transplanted material changes from being under the control of the DNA of the donor cells to being under the control of the DNA of the recipient, with obvious advantages in circumventing the immune rejection of transplanted cells. The reason for describing this progression is to emphasize that transgenesis is not a unique process presenting unique ethical issues, but a step in a continuum of methods, used to influ-

## Contents ...

This issue contains the facts sheet on Occupational Health and Safety in the Animal House and Associated Laboratory Facilities. The facts sheet is also available as an offprint.