

### Summary and conclusions

On 3<sup>rd</sup> December 2002 based on a parliamentary debate held in November 2002 the Folketing decided to encourage the government to appoint a preparatory committee to follow up on the Folketing's motion for the adjournment of 23<sup>rd</sup> May 1997 with a view to establishing rules for research in regard to animal cloning and accompanying technologies.

Cloning of animals means that a genetically identical<sup>5</sup> "copy" of another animal is created. Cloning can be done by two procedures that differ considerably in both method and application. **Embryo cloning** is a process where a recently formed embryo is divided into several embryos, which are implanted into a surrogate mother. The surrogate mother gives birth to genetically identical animals but in principle the full characteristics and appearance of the animals are unknown until the animals are born. **Cloning by somatic cell nuclear transfer (SCNT)** is based on a differentiated somatic cell from an animal. The nucleus from an animal cell is inserted into an egg cell from which the nucleus has been removed. Some time after the cell division has commenced the embryo is implanted into a surrogate mother. The animal born is genetically identical with (a clone of) the donor animal that provided the donor cell. By SCNT the existing animal and the "copy" do not necessarily look alike since it has been found that environmental factors will also influence the appearance of the animal.

Genetic modification means that the hereditary material of animals is altered artificially. It can happen either by inserting genetic material (transgene), which does not normally appear in

---

<sup>5</sup> A small part of the hereditary material is outside the nucleus of the cell. By cloning by somatic cell nuclear transfer (SCNT) not all the hereditary material from the donor cell will be transferred to the egg cell meaning that the donor animal and the "copy" (the clone) are not 100% genetically identical. For the remainder of the summary this is implied when the term "genetically identical" is used in association with SCNT.



the species in question, or by altering the genetic material normally present, e.g. by removing or copying genes or parts hereof. The insertion of new genetic material can be accomplished in several ways. If the precise localisation in the hereditary material is of little importance the transgene may be injected into a fertilized egg by a so-called microinjection whereafter the integration happens at random. If the exact localisation is important for example by deactivation of existing genes then it can be done in mice – and only in mice – by culturing embryonic stem cells, modifying these genetically in a test tube and inserting them in an embryo that is then implanted in a surrogate mother. This method is called embryonic stem cell transfection and the animals created are called knockout animals. In other species than mice such a targeted genetic modification and the ensuing knockout animals can only be accomplished by genetically modifying somatic cells, e.g. connective tissue cells, which are then cloned by SCNT.

In Denmark the legal regulation of cloning and genetic modification of animals is basically limited to what generally can be inferred from the Animal Welfare Act, the Animal Testing Act, and the Gene Technology Act. The only rule in the Animal Welfare Act specifically aimed at gene technology is a provision from which it appears that the Minister of Justice can establish rules on or prohibit the use of biotechnology, gene technology, etc. on animals yielding marketable produce in agriculture. Until now this provision has only been used in a proclamation on minimum requirements for protection of agricultural animals. Furthermore under a rule of the Gene Technology Act the Minister of the Environment has the possibility of appointing a body that at the Minister's request expresses an opinion on ethical questions covered by the act. So far this provision has not been utilized.

Thus the current legislation does not prevent cloning and genetic modification of animals from taking place. To the extent that cloning and genetic modification of animals happens for research and teaching purposes and the criteria set forth in the



Animal Testing Act are met it will be in accordance with this act that Animal Experimentation Directorate permits the activity. Denmark is a party to several common European protocols that may be relevant but none of these prevents Denmark from making legal regulations in this field. The committee has approached a number of other countries with a view to clarifying the state of the law there. None of the countries approached has specific legislation on cloning of animals while genetic modification of animals generally seems to be regulated by law abroad. In other words: the situation in Denmark is the same as abroad.

Genetically modified laboratory animals are used to a large extent in health research in Denmark as well as abroad, while cloning at present mostly is at a basic stage of research where the research primarily is focused on developing the actual cloning technique.

Studies of SCNT are necessary in order to make an effort to improve the technique and to evaluate the future applicability and value of it. It is a prerequisite for all further use of SCNT that the method is improved. Today, genetically modified animals into which genetically determined diseases are copied are already widely used as disease models. Knockout mice are an important element in this and by using SCNT it will be possible to inactivate genes in other species than mice in a routine manner.

Basic studies, including studies of the significance of the individual genes for the body's physiology, may in the long term have great importance for research breakthroughs in for instance the combating of disease. Today studies are carried out exclusively by genetic modification but SCNT would increase the possibilities of the basic studies since it will become possible to inactivate genes in other species than mice. The disease models and the basic studies both will contribute to furthering research and increase the potential of treatment of human beings.



Furthermore SCNT and embryo cloning may provide a basic knowledge of the characteristics of the fertilized egg and embryo as well as of the ensuing gestation including basic knowledge of malformations in common domestic animals. This may be of future importance to treatment of diseases both in humans and animals. Already today genetic modification makes it possible to develop animals for production of pharmaceuticals. However, to secure possibilities for development within this field technological improvements are important. New development within the field of SCNT may also lead to animals that would be able to provide organs for transplantation many years into the future. The same applies to the development of animals with certain characteristics for foodstuff purposes, e.g. for improving the quality of foodstuffs. Moreover embryo cloning and SCNT could lead to production of offspring from particularly valuable animals. However, traditional animal husbandry will be just as useful and considerably cheaper in by far the most cases. Recreation of extinct species and “copying” of people’s deceased pets is only possible through the use of SCNT.

Since the SCNT technique is not fully developed yet a large loss of embryos as well as an increased risk of miscarriage and malformation is seen by SCNT. Furthermore the method may cause a number of welfare problems for the surrogate animal that during gestation for example may suffer from dropsy. The relative inefficiency of the technique up till now means that a relatively high number of surrogate animals are required. An improved SCNT technique may mean an increased use of animals for testing because SCNT for example makes it possible to create disease models in other species than mice.

Genetic modification by microinjection or embryonic stem cell transfection does not in itself contain a risk of welfare problems for the animals; but in the animals that are used as disease models, or in other ways have been subjected to straining genetic modifications, strains of varying intensity may of course occur. It is characteristic of genetically modified animals that their genes



have been altered and that the alterations will be transmitted to their progeny. Consequently it is important that genetically modified animals are kept under controlled conditions.

The creation and use of cloned and genetically modified animals gives rise to ethical considerations. According to the committee there is first of all the animals' welfare to consider. Besides, there may be risks to the environment if genetically modified animals are released; and there may be hazards to human health if using the techniques leads to the development and spreading to humans of new disease carrying viruses. The committee attaches great importance to these concerns while remaining aware of other ethical considerations that are less clearly related to the traditional scientific way of thinking. These considerations are comprised by the committee under the concept of integrity. The integrity of animals may be infringed if their natural potentials are substantially reduced or shaped according to random human needs. The committee stresses that considerations on integrity should be included in the ethical evaluation but notes at the same time that the concept of integrity causes controversy and cultural conflict.

The use of biotechnology on animals does generally speaking not enjoy widespread support in the European population. The very use of technology to change animals and the other parts of nature is to many people something that in itself requires justification. The committee shares this view.

The committee thus finds that the use of biotechnological techniques on animals should not be allowed without further justification and ethical consideration. In the committee's opinion any use of biotechnology on animals including cloning and genetic modification must be evaluated based on a principle of proportionality. The committee finds that the negative consequences of the technology e.g. reduced animal welfare and increased risk of damage to the environment, should be weighed against the advantages that may be obtained by using



the technology such as new treatments of diseases in humans and animals.

Technically embryo cloning is further developed than SCNT to which many and substantial technical and biological problems are still connected. However, from the committees point of view it cannot be ruled out that the problems related to SCNT can be overcome with time, so that both types of cloning technique some day can be routinely used. Consequently the committee finds that the legislation should not distinguish between embryo cloning and SCNT.

In the committee's opinion it is at present not ethically and socially justifiable to apply cloning and genetic modification techniques to production of animals for production of foodstuffs and other agricultural products. In this context the committee particularly emphasises that the use of biotechnology on animals in this situation may be at the expense of the animals' welfare, integrity and health, without - in the committee's opinion - meeting essential needs. Furthermore the committee finds that by uncontrolled release of genetically modified animals there is a risk of contributing to the spread of infectious diseases in a hitherto unknown manner.

However, the committee sees possibilities in and finds it justifiable to use the mentioned technique in connection with research that may lead to important knowledge of diseases in humans and animals provided that, as till now, it is ensured by the Gene Technology Act that these animals do not come into contact with the external environment. In this connection it must be noted that biomedical research aimed at developing new methods of treatment of serious diseases in humans and animals depends to a large extent on these and other technological possibilities.

On this background the committee recommends as supplement to the existing legislation



- 
- > that specific rules for cloning and genetic modification of animals are set forth in Danish legislation, and
  - > that cloning and genetic modification of animals including import and breeding of such animals is permitted only if it serves an essential purpose.

By an essential purpose a majority of 10 of the committee's 11 members understands

- > basic research,
- > applied research aimed at improving health and environment,
- > creation and breeding of animals producing substances essentially benefiting health and environment, and
- > teaching at institutions of higher education and training of persons who are to carry out these techniques.

By an essential purpose one committee member understands

- > research concerning prevention and combating essential specific diseases in humans and animals,
- > production and breeding of animals producing biomedical substances for prevention and combating essential specific diseases in humans and animals, and
- > teaching at institutions of higher education and training of persons who are to carry out these techniques.