The European Group on Ethics in Science and New Technologies to the European Commission

Ethical aspects of animal cloning for food supply

- Opinion No 23 -

- 16 January 2008 -

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ABSTRACT

Ethical aspects of animal cloning for food supply

In February 2007, following the announcement by the US Food and Drug Administration (FDA) concerning possible authorisation of food products derived from cloned cattle, pigs and goats on the market, President Barroso asked the European Group on Ethics of science and new technologies (EGE) to issue an Opinion on ethical implications of cloning animals for food supply.
At the same time, the European Food and Safety Agency (EFSA), was asked to produce an Opinion on food safety, animal health, and environmental implications of live cloned animals obtained through somatic cell nuclear transfer technique (SCNT), their offspring and the products obtained from them.

After several months of internal working meetings, expert hearings, a public consultation launched in the Europa web site (800 contributions received) and a round table with representatives from academia, industry, NGOs, civil society, International organisations and industry[1], on January 16, 2007, the EGE has adopted its latest Opinion on ***ethical aspects of animal cloning for food supply***. The Group is aware of the EFSA draft Opinion and the FDA Report published the day before the adoption of the Opinion.

Considering the current level of suffering and health problems of surrogate dams and animal clones, the EGE has doubts as to whether cloning animals for food supply is ethically justified. Whether this applies also to progeny is open to further scientific research.

At present, the EGE does not see convincing arguments to justify the production of food from clones and their offspring[2]. If in the future food products derived from cloned animals were to be introduced to the European market, the EGE recommends that the following requirements are met:

> *Food safety* - The safety of food products for human consumption as a pre-condition for their marketing must be guaranteed and scientific updates and follow up research into progeny should be carried out.

[1] http://ec.europa.eu/european_group_ethics/activities/index_en.htm

[2] The conclusion in this paragraph was dissented by K. Marczewski.

Animal welfare and health - In accordance with the Amsterdam Treaty (animals as sentient beings) and the Lisbon Treaty, additional requirements should be met in intensive animal breeding, with the aim of following the guidance on animal welfare provided by the World Organisation for Animal Health (OIE), e.g. the five freedoms: from hunger, thirst and malnutrition; from fear and distress; from physical and thermal discomfort; from pain, injury and disease; and to express normal patterns of behaviour.

Traceability - Current EU legislation on food regarding traceability of animals and their food products should be enforced. It should be ensured that EU legislation provides for the ability to identify individual animals where necessary.

Global trade - The import of cloned animals, their offspring and materials derived from cloned animals (e.g. semen and food products) should be conditional on proper documentation, in particular with regard to traceability provisions and animal welfare.

In addition the EGE recommends that:

Animal welfare - Further studies and analyses on long-term animal welfare and health implications for clones and their offspring, as well as more comparative analyses with other assisted and traditional reproductive technologies in animal farming, should be carried out for a proper assessment of this issue, in line with EFSA draft opinion. The Commission should take initiatives to prepare a Code of Conduct on responsible farm animal breeding, including animal cloning.

Farm animal biodiversity and sustainability – The Commission should take proper measures to preserve the genetic heritage of farm animal species, for example by funding projects that aim to preserve domesticated breeds in Europe and to promote sustainable agriculture.

Public participation - Public debates should be promoted on the impact of farm animal cloning on agriculture and environment, on societal impact of increasing meat consumption and rearing of bovines, as well as on the fair distribution of food resources. The Commission should take a pro-active role in promoting public discussion on the use of animal cloning, and its potential implications, by financing a number of *ad hoc* initiatives aimed at promoting public debate on the marketing of food products derived from animal cloning.

Public perception - The Commission should launch a thematic Eurobarometer survey and qualitative studies on animal cloning for food supply, in order to collect indicators on public perception concerning the introduction of such products to the food market as is being done in other countries.

Labelling – The EGE is aware of the technical difficulties of labelling products from offspring, nevertheless it recommends that the Commission takes the initiative to devise targeted procedures prior to the marketing of such food in the EU.

Intellectual property issues – It should be clarified whether the exclusion clauses in Directive 98/44/EC (Art. 6d) on patentability of biological inventions and the EPO rules (23 d) to animal cloning for food apply.

Global trade and consumer's freedom – The EGE is aware that import issues of food products derived from cloned animals, including compliance with World Trade Organisations provisions, may

complicate the market situation, however, the EGE recommends that the Commission takes initiatives to ensure consumers' freedom and rights.

Research - Further research is needed, in particular basic research on animal cloning, as well as impact on human health, animal welfare for farmed species other than those covered by EFSA. Similarly, further ethical, legal and social implications of animal cloning for food supply as well as qualitative studies on public perception should be carried out.

The EGE Opinion has been issued to Commission President Barroso on 16.01.2008, the Opinion is accessible at http://ec.europa.eu/european_group_ethics/index_en.htm

OPINION OF THE EUROPEAN GROUP ON ETHICS
IN SCIENCE AND NEW TECHNOLOGIES
TO THE EUROPEAN COMMISSION

No 23 **16.01.2008**

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ETHICS OF ANIMAL CLONING FOR FOOD SUPPLY

Reference: Request from President Barroso

Rapporteurs: I. de Beaufort, P. Puigdomenech-Rosell, J. Glasa

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THE EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES (EGE),

I. HAVING REGARD TO

Having regard to the Treaty on European Union, and in particular Article F. 2 of the Common Provisions and the annexed Declaration n° 24 on the Protection of Animals,

Having regard to The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) *Codex Alimentarius* of 1963 as a reference document for consumers, food producers, manufacturers and national food control agencies,

Having regard to Council Directive 77/504/EEC of 25 July 1977 on pure-bred breeding animals of the bovine species,

Having regard to Council Directive 86/609/EEC regarding the protection of animals used for experimental and other scientific purposes,

Having regard to the European Conventions of the Council of Europe for the protection of animals kept for farming purposes (1976-EST 87) and in particular the Protocol of Amendment thereto, and for the protection of vertebrate animals used for experimental or other scientific purposes (1986-EST 123),

Having regard to Council Directive 88/407/EEC, laying down the animal health requirements applicable to intra-community trade in and imports of and imports of, deep-frozen semen of domestic animals of the bovine species; amended by Council Directives 90/120/EEC, 90/425/EEC, 93/60/EEC, Decision 95/1/EEC,

Having regard to Council Directive 88/661/EEC of 19 December 1988 on the zootechnical standards applicable to breeding animals of the porcine species,

Having regard to Council Directive 89/361/EEC of 30 May 1989 concerning pure-bred breeding sheep and goats,

Having regard to Council Directive 89/556/EEC, on animal health conditions governing intra-Community trade in and importation from third countries of embryos of domestic animals of the bovine species,

Having regard to Directive 90/219/EEC of 23 April 1990 on the contained use of genetically modified microorganisms (OJEC L 117, 8 May 1990, pp. 1 *et seq.*, as amended) and Directive 98/81/EC, which amended it,

Having regard to Council Directive 90/220/EEC, regarding the deliberate release into the environment of genetically modified organisms, and Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms,

Having regard to Council Directive 90/427/EEC of 26 June 1990 on the zootechnical and genealogical conditions governing intra-Community trade in equidae,

Having regard to Council Directive 91/629/EEC and 91/630/EEC, laying down minimum standards for the protection of calves and of pigs,

Having regard to the United Nations Convention on Biodiversity of 6 June 1992, ratified by the European Union on 25 October 1993,

Having regard to Council Directive 94/28/EEC, Art. 4-7, laying down the principles relating to. the zootechnical and genealogical conditions applicable to imports from third

countries of animals, semen, ova and embryos which are covered by European Union Council Directives 77/504/EEC, 88/661/EEC, 89/361/EEC, 90/427/EEC and 91/174/EEC and by the European Community decisions implementing these Directives,

Having regard to the Protocol on protection and welfare of animals, annexed to the Amsterdam Treaty[1],

Having regard to the World Trade Organisation (WTO) Sanitary and Phyto-sanitary (SPS) agreements of 1995, in particular to Art. 5.1, 5.2 and 5.3 on health risk assessments,

Having regard to Regulation No 258/97/EC concerning novel foods and novel food ingredients,

Having regard to Council Directive 98/44/EC on the patentability of biological inventions, specifically Article 6 thereof,

Having regard to Council Directive 99/74/EEC, laying down minimum standards for the protection of laying hens,

Having regard to Directive 2000/13/EC, on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs,

Having regard to Directive 2001/18/EC of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC[2],

Having regard to the General Food Law, Regulation (EC) No 178/2002, for 'the protection of human life and health, taking account of, where appropriate, the protection of animal health and welfare, plant health and the environment',

Having regard to Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed[3],

[1] OJ C340, 10 November 1997
[2] OJEC L 106, 17 April 2001

Having regard to Regulation (EC) No 1830/2003 of 22 September 2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms and amending Directive 2001/18/EC[4],

Having regard to Regulation (EC) No 1946/2003 of 15 July 2003 on transboundary movements of genetically modified organisms[5],

Having regard to the Treaty of Lisbon, signed on 13 December 2007 and currently open for ratification,

Having regard to Article 6 of the Seventh Framework Programme (FP7, 2007-2013): "All the research activities carried out under the Seventh Framework Programme shall be carried out in compliance with fundamental ethical principles",

Having regard to the EGE Opinion Nr. 9 "Ethical Aspects of Cloning Techniques", published on 28 May 1997,

Having heard the rapporteurs I. de Beaufort, P. Puigdomenech-Rosell, J. Glasa

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[3] OJEU L 268, 18 October 2003
[4] OJEU L 268, 18 October 2003, pp. 24 *et seq.*
[5] OJEU L 287, 5 November 2003, pp. 1 *et seq.*

Whereas:

1. Preamble

Given that the issue of cloning animals for food supply is a new and complex topic, the Commission is considering it carefully in the context of the existing legal framework, bearing in mind food safety, the desire of consumers for information, animal health and welfare, and other relevant factors such as ethical considerations.

In February 2007, following the announcement by the US Food and Drug Administration (FDA) concerning possible authorisation of food products derived from cloned cattle, pigs and goats on the market, President Barroso asked the EGE to issue an Opinion on the ethical implications of cloning animals for food.

At the same time, the European Food and Safety Agency (EFSA[6]), was asked to produce an Opinion on food safety, animal health, and environmental implications of live cloned animals obtained through somatic cell nuclear transfer technique (SCNT), their offspring and the products obtained from them[7].

The EGE previously issued an Opinion on the ethics of animal cloning in 1997, but owing to the state of the art of the technology at that time, it did not address the ethics of animal cloning specifically for food supply. The present EGE Opinion complements and updates the previous one and is intended to be complementary to that of the EFSA. The ethical considerations in this Opinion will therefore refer to the use of animal cloning in breeding establishments in order to produce progeny that could enter the food chain.

[6] The European Food Safety Authority (EFSA) is the keystone European Union Agency on risk assessment regarding food and feed safety. EFSA provides independent scientific advice and communication on existing and emerging risks. http://www.efsa.eu.int

2. Scientific background to animal cloning

2.1. Definitions

The term "cloning" is applied to different activities in life sciences[8], but for the purposes of this Opinion the word “cloning” will refer to cloning by somatic cell nuclear transfer (SCNT) that allows scientists to create genetic replicas (clones) from adult animals that “share the same nuclear gene set” as another organism.[9]

Cloning: The word 'cloning' derives from the Greek word for 'twin' and was originally used in microbiology and in agriculture for the process of multiplying single organisms by means of asexual reproduction to create a population of identical individuals.

Embryo splitting involves the division of embryos at an early stage of development to produce two embryos, and usually can only be performed once or twice, achieving a maximum of four genetically identical organisms. Experiments on embryo splitting date back to 1891 with sea urchins and later on with salamanders (1902).

Cloning by somatic cell nuclear transfer (SCNT) involves replacing an egg’s nucleus with the nucleus of an adult cell (or that derived from an embryo or foetus) to be cloned, and then activating the egg’s further development without fertilisation. The egg genetically re-programmes the transferred nucleus, enabling it to develop directly into a whole new organism.

2.2. Historical background

In nature, the normal reproductive process in bacteria and in the simpler animals may be considered a form of cloning. Amoebas are single-celled protozoa which reproduce by binary fission, resulting in two offspring with identical genes. In more complex animals, cloning occurs when a fertilised egg splits to give identical twins. In the case of humans these are

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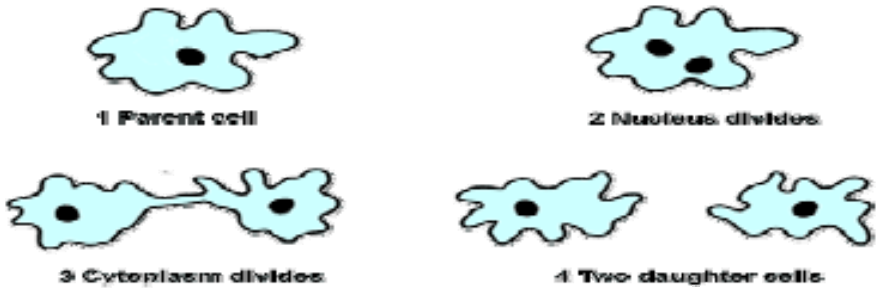
[7] Animal species covered: Captive large ruminants (cattle); Captive small ruminants (goats, sheep); Pigs; Oviparous animals (birds, chicken).

[8] For example, molecular cloning involves different techniques to multiply DNA sequences either in-vitro or in vivo, related to recombinant DNA techniques. Cellular cloning is the process of isolating single cells in culture and propagating them in order to obtain a cell population. It is the basic procedure for produceingclonal cell lines, for example for the production of monoclonal antibodies.

[9] In their phenotype there seem to be differences due epigenetic effects influencing gene expression. "Epigenetics" aims to describe the inheritance of information on the basis of gene expression in contrast to "Genetics", which aims to describe the inheritance of information on the basis of DNA sequence.

homozygous twins. This natural phenomenon has been studied over a long period of time, and biologists have started to develop techniques to induce or reproduce the cloning of living organisms.

Examples of natural cloning



Contrary to the general perception, cloning is not a new technology. The first experiments of nuclear transfer with amphibians (*Rana pipiens* and *Xenopus laevis*) were performed in the United States and Britain during the 1950s to study the irreversibility of the modification of genetic material of differentiated cells from adult animals (1952, cloning of tadpoles). Cloning experiments were then performed in amphibians in the 1960s (fish were cloned in 1963), in sheep in the 1980s, in monkeys in the 1990s, and in a range of animal species during the last 10 years (from primates, to cattle, to swine in the early 2000's).

During the last decade (1997-2007) only non-primate mammals were reported to be cloned. Most recently, in 2007 a US-based research group reported the creation of several embryos cloned from an adult rhesus monkey[10].

Table 1. Domestic animal species cloned so far:

Year of first cloning	Species
1963	Carp
1996	Sheep
1998	Cow, Mouse
2000	Pig, Goat
2002	Rat, Rabbit
2003	Mule, Horse
2004	Cat
2005	Dog
2006	Ferret

[10] The Independent, 12 November 2007, http://news.independent.co.uk/sci_tech/article3152325.ece

2.3. Somatic cell nuclear transfer (SCNT)

At present, the most commonly used technique for animal cloning is Somatic Cell Nuclear Transfer (SCNT). SCNT can be achieved via three main steps:

1) ***enucleation of an oocyte***, performed mechanically by fixing the oocyte and aspirating the nucleus by using a sharp glass pipette.
2) ***transfer of the nucleus*** from the donor cell[11] into the fertilized enucleated oocyte[12]; most commonly, the somatic cell's nucleus is injected under the zona pellucida of the egg cell by using a micro-manipulator and a microscope. To induce membrane fusion of the two cells, a short electrical impulse is applied.
3) ***activation and reprogramming of the reconstructed embryo***. In order to kick start development, reprogramming of the donor nucleus is needed; this seems to happen via factors present in the recipient's cytoplasm, but the exact mechanisms are still unknown. A necessary step in this process is to mimic the cellular conditions after physiological fertilisation[13].

When the cloned embryo resulting from SCNT starts to develop it is transferred to a surrogate mother, which carries out the pregnancy. The transfer to the surrogate mother is species specific, both in terms of timing and procedure. In some species, like pigs, the transfer has to be done by surgical procedures, and it is usually carried out one day after the nuclear injection and embryo activation (a single one-cell stage). In other species, like cattle, transfer can be done without surgical procedure, and embryos are usually transferred at a later stage, one week after embryo reconstruction[14]. So far, around a dozen animal species have been cloned via SCNT. Animal clones that are relevant for the food market include sheep, goats, bovines and pigs.

As the commercial interest in cloning farm animals has grown, the cloning technique has been refined and success rates are improving. A step in this process is the establishment of alternative and simplified procedures for the production of cloned animals. For example, in

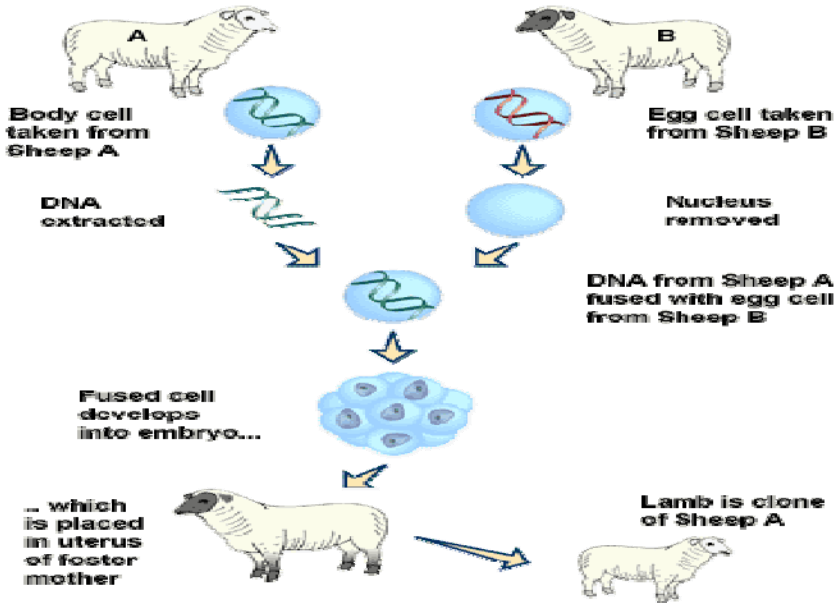
[11] *Donor somatic cells* can now be derived from a variety of different tissues. Interestingly, some tissues seem to be more suitable for SCNT than others, giving higher rates of pregnancy and live births, the reason thereof still being unclear. At present, cloned offspring has been born from a dozen of differentiated donor cells, out of roughly 200 existing cell types.

[12] *Recipient oocytes* are often obtained from slaughterhouses (as for cows, pigs, sometimes sheep), so that material is abundant even if of lower quality, and extremely inexpensive. They are cultured in vitro and treated with hormones for a variable length of time before they can differentiate and be used for SCNT.

[13] Some of these conditions include: increase of the intra-cellular calcium, which usually follows the penetration of the spermatozoa, and subsequent decrease of the maturation promoting factor (MPF). Both conditions can be artificially achieved by treating the reconstructed embryo after SCNT briefly with a chemical agent to block protein synthesis, or by applying a brief electrical shock.

order to reduce the need for expensive equipment such as micromanipulators for nuclear transfer, scientists have recently discovered so called 'handmade' cloning[15]. This nuclear transfer technology might also make the techniques available to less developed countries, where it would not otherwise be possible to implement it successfully.

Figure 2 Scheme of the Cloning technique



2.4. Dolly

The attention of the general public was attracted when the birth of the first cloned mammal, Dolly, was announced in 1996. Its embryo was derived from cells that had been taken from the udder of a 6-year old Finn Dorset ewe and cultured for several weeks in the laboratory. These cells were then fused with unfertilised eggs from which the genetic material had been removed and then successfully implanted in a surrogate mother sheep[16]. *Dolly*'s birth provided a revolutionary method of producing animals identical to an adult one[17].

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[14] In cattle, initially 1-4 embryos were transferred, but nowadays there is a tendency towards single transfer, to avoid problems with multiple pregnancies.

[15] Vajta G. "Handmade cloning: the future way of nuclear transfer? Trends Biotech, 25:250-253 (2007)

[16] Biologists cultured 276 of these reconstructed eggs for 6 days in temporary recipients. Twenty-nine of the eggs that appeared to have developed normally up until the blastocyst stage were implanted into surrogate Scottish Blackface ewes.

[17] The innovatiove feature of the nuclear transfer technique (NTT) was the use of unfertilised eggs and their fusion with a cell that contained the genetic endowment of only one organism.

After the successful experiment that produced *Dolly*, several laboratories[18] began to work on applications of animal cloning using somatic cell nuclear transfer. Biologists successively cloned other animals, such as goats and cattle (see Revel, 2000:43-59). In 1997, the cloning of a transgenic lamb (*Polly*) cloned from cells engineered with a marker gene and a human gene[19] was announced. In this way, the genetic modification of a lamb was combined with the techniques of cloning, thereby generating animals that produce a new protein.

2.4.1. Biological implications

Contrary to the common perception, a number of biological factors contradict to the claim that clones are carbon copies of their ancestors:

1) The mitochondrial DNA comes from the egg and is therefore different from that in the cells of the donor of the nucleus;

2) Gene expression depends not only on the sequence of naked DNA, but also on DNA modifications, chromatin structure and the presence of small RNAs. These mechanisms are the basis of epigenetic mechanisms and it is not known how they are reprogrammed in the cloned embryo;

3) The whole new organism develops from a single cell that multiplies several million times giving origin to multiple organs and allowing for spontaneous DNA mutations in single somatic cells and phenotypical differences;

4) Several organs including the immune system and the brain are not fully developed at the embryonal stage, hence clones may have multiple differences from their nucleus donor.

2.5. Animal health and welfare problems related to cloning

As already stated, cloning is not a new technology, but it still has relatively low efficiency and leads to high perinatal and postnatal disease and mortality of cloned organisms. Animal health

[18] "In cloning procedures generally, nuclei are extracted from cultured cells that might have come originally from an embryo, a foetus or an adult organism. The nuclei are inserted into egg cells which have had their original nucleus removed, a process called nuclear transfer. In the initial work at the Roslin Institute, the egg cells along with their transplanted nuclei were then implanted directly into a foster mother, where they developed and, in the case of Dolly, resulted in a viable offspring." (http://www.sciam.com/explorations/090297clone/beardsley.html).

[19] Human clotting factor IX (see: http://www.sciencemag.org/cgi/content/abstract/278/5346/2130)

and welfare issues are therefore extremely important when assessing the implications of this technology and its industrial use in terms of both efficacy and safety.

2.5.1 Animal health

The mechanical stress exercised on the donor egg cell and in vitro conditions for the embryonic culture are critical aspects of the cloning techniques. A high degree of technical skill and quality equipments are needed, otherwise the 'quality' (viability, health) of the clones, as well as the overall SCNT efficacy are compromised.

In cattle, at day 50 post transfer, pregnancy rates can be as high as 65% (and therefore similar to other assisted reproduction technologies), but a continual loss is observed up to delivery, leading to a live birth efficiency as low as 13% (a value, which is highly laboratory dependent). After birth, around 20% of calves don't survive the first 24h, and an additional 15% die before weaning.

Animal cloning induces several complications with regard to the pregnancy and developmental anomalies appear at both in vitro and in vivo phases (Table 2). Those comprise for example, missing embryo development, increased foetal loss, placenta inadequacy, abnormal placenta and foetus size, increase in the average abortion rate.
For the cloned animals, following abnormalities are observed with varying frequencies: an increased weight; malformations and reduced viability at birth; respiratory problems; enlarged foetal liver; epidermal haemorrhages; kidney abnormalities etc.

Epigenetic changes in reprogramming of the donor's nucleus in SCNT have been implicated in causing many of these anomalies. Much of the ongoing research in this rapidly expanding field is focused on gathering and understanding data in prospective observation studies in cloned animals during their lifetime.

The mentioned phenotypic abnormalities are documented in the first generation (F0) of cloned animals (i.e. in the clones themselves), while their offspring (F1) seems to be apparently healthy. The available data, however, are still limited to allow at present any definitive conclusions. Due to the long life cycle of the most of the farm animals in question,

the data and information gathering in order to respond to the questions regarding the SCNT cloned animals' health may require a longer period of time than the one analysed so far.
The EFSA Opinion will provide a more detailed analysis of the animal health implications of SCNT based upon the actually available data.

Table 2. Abnormalities correlated with SCNT

Short-term abnormalities	These abnormalities include decreased rate of growth and chromosomal abnormalities. This usually leads to early embryonal death, within the first few weeks of gestation.
Other abnormalities	Abnormalities can be observed later during gestation or even after birth. The major cause of such abnormalities is thought to be of epigenetic origin and can be correlated with inadequate reprogramming of the donor DNA.
Large offspring syndrome[20] (LOS)	LOS comprises a large number of symptoms, often manifested as increased birth weight of offspring, due to foetal overgrowth and prolonged gestation. Also due to LOS, most of deliveries in cattle are performed via caesarean section. Following problems are related to LOS: placental abnormalities, stillbirth, malformations of several organs (liver, brain, uro-genital tract), immune dysfunction, infections. The pathological picture can vary considerably from case to case and among different species.
Post-natal Mortality	Postnatal mortality is observed in a biphasic modality: early neonatal mortality, usually within one week after birth, or later in life up to 6 months of age. In the first group, death is usually due to cardiovascular failure, whereas in the second group the majority of cases are related to immuno-deficiencies and / or liver failure. After six months of age, if the animal reaches adulthood, it is usually as healthy as control, non-cloned animals

2.5.2. Animal welfare

The animal health problems related to SCNT cloning techniques (see 2.4.1. for details) pose multiple and questions from the point of view of the animal welfare. When considering those questions, the welfare of the clones themselves (F0 generation), of their "surrogate mothers", as well as of the next generations of the clones' progeny (F1, F2 and subsequent) should be taken into account, together with existing knowledge gaps in this area.
The EFSA draft Opinion provides a detailed analysis of the animal welfare implications of SCNT based on the actually available data.

2.6 Potential applications of animal cloning for the food supply

After 10 years of research activity the main planned application of animal cloning for food production today is the propagation of a desirable genotype: individuals of high genetic merit, improved traits such as an increase in productivity, animal health and/or the quality of food products. In this sense, cloning is seen as a way of ensuring a continuum supply of genetic material from elite animals to be used in breeding programmes for farm animals. Thus, the

[20] The term used to describe some of these developmental anomalies is 'large offspring syndrome" (LOS).

animals to be cloned would be those having traits of interest for farming, such as resistance to diseases, or characteristics of interest for food production, such as quantity of milk, quality of meat or others.

Animal cloning is therefore seen as representing a further technological process for animal breeding, in which reproduction occurs in an asexual manner and which allows the propagation of desired traits more quickly than through standard mating schemes. At present a range of breeding techniques is employed in animal farming, including: artificial insemination (AI), in vitro fertilization (IVF) and embryo splitting. SCNT may have an impact on classical farm animal breeding because it would be possible to duplicate animals with high genetic value to increase their number of offspring (e.g. increasing the number of valid males for artificial insemination etc.).

Table 3. Current Animal Breeding techniques

Artificial insemination (AI)	Studies of AI for cattle breeding began as early as the 1900's. By the 1940's it had become a routine procedure. It allows mating between high quality livestock without the physical presence of the bull. The bull's semen is collected, frozen and shipped worldwide, where female animals are inseminated. Nowadays AI represents nearly 75% of all inseminations for cattle breeding and up to 85% for swine breeding. Breeders keep accurate records in order to avoid inbreeding problems.
In Vitro Fertilisation (IVF)	IVF is employed in farm animal breeding in order to allow embryo selection and to increase productivity.
Embryo splitting	Each good quality embryo can be dissected by means of a stereoscopic microscope and a fine glass needle (or a razor) to give rise to twins. Using this procedure a 1.5 fold increase in productivity can be achieved, even in less developed countries, as the technology involved is not particularly complex.
Animal cloning for breeding purpose	The extremely high fidelity in reproducing a particular genotype achieved by cloning could lead to 'tailor-made' strains of livestock. Biotechnology companies claim that the major potential benefit of cloning is the possibility of building up a herd of animals for breeding that will create genetically determined populations. Cloning of animals for mating would make it possible to respond more quickly than in traditional mating programmes to the needs of both animal breeding and the food industry. However, the relevance of SCNT to the long-term future applications for farm animal breeding and food production in Europe still needs to be explored.

The potential of cloning for animal breeding programmes has been boosted by the improvement in the efficacy of the technology involved. In fact, when Dolly was created the success rate was around 2%; now it is 10-20% in cattle, although the data are highly species-dependent. As for other ART used in animal breeding programmes, the post-natal success rate of cloning generally remains quite low, regardless of the methodology used. In some cases, the low success rate - combined with the fact that cloned animals sometimes differ from the original animal due to epigenetic effects, plus the high final cost of the technology - may

make the possible applications of animal cloning in food and animal breeding industry a very complex issue, and cloning might become unattractive from an economic point of view.

Frozen semen from cattle is sold widely in the EU for artificial insemination purposes, and some companies in the US already offer semen from cloned bulls[21], envisaging a rapid expansion of the market for cloned livestock from the US to the EU if this is commercialized.

This would suggest that the cloned animals have a low probability of entering the food chain by themselves, and that only their progeny may be used for food production. Offspring from cloned cattle and pigs are currently used for research purposes only, but may be ready to enter the food chain soon if this technique is commercialized; the same applies to food products, such as milk, meat and derivatives, obtained from the offspring of clones.

The estimated timeline for the commercialization of food products derived from cloned animals has been indicated for the USA and foresees the commercialization of food products from cloned animals within a couple of years from now (see table 4 below).

Table 4. Indicative timetable for the commercialization of food products derived from cloned animals[22]

2005 → 2010:	Semen and offspring from cloned cattle, and milk, meat and derivatives from offspring of cloned cattle; Semen and offspring from cloned pigs, and pig meat and derivatives from offspring of cloned pigs.
2010 → 2015:	Cloned cattle and milk, beef and derivatives from cloned cattle; Cloned pigs, pig meat and derivatives from cloned pigs.

If authorised by the FDA (or EFSA in the EU), it may be hypothesised that it will take at least 3-5 years before food from the offspring of clones becomes available to the consumer (earlier for swine, later for bovines). In the dairy industry, most clones will be breeding bulls used for semen collection.

According to EU experts, no cloned animals have yet reached the food chain in Europe and no projects have yet been established to use bovine clones (or their products) for the food supply industry. However, an accurate forecast for the EU is still very difficult to make at present. The EFSA Opinion may provide some significant information on this question.

[21] http://www.timesonline.co.uk/tol/life_and_style/food_and_drink/article1264944.ece
[22] 'Dolly for dinner? Assessing commercial and regulatory trends in cloned livestock.', Suk J. et al., Nature Biotechnology, 25(1), 2007.

2.7 Long-term future applications of animal cloning

In the long run, the cloning of farm animals could be combined with genetic modifications so as to have livestock with specific characteristics, for example, genetic resistance to specific diseases (bovine BSE, mastitis, brucellosis, tropical diseases etc.) or producing food products of higher value than natural ones, so-called "nutraceuticals", such as low-lactose milk, kappa casein rich milk, better beef from myostatin TG cattle etc. In this way, cloning - in combination with transgenesis[23] - may be a potentially rich source of edible products for biomedical purposes (e.g. production of proteins, such as milk proteins, to be used for therapeutic purposes at lower cost, or providing a source of organs or tissue for xenotransplantation).

In Europe, the most promising application still appears to be cloning for biomedical purpose, such as the production of animal models for biomedical purposes (e.g. research in the field of Alzheimer's disease[24], models to improve the understanding of embryogenesis, bioreactors etc.) or as sources of organs for transplantation. This use of animal cloning, however, entails completely different aspects that need to be considered from the legal and ethical points of view, and so it is not addressed in this Opinion (see EGE Opinion on Cloning[25]).

2.8. Safety and risk assessment of cloning for food

To date, there has been no comprehensive scientific risk assessment at EU level on the use of products from cloned animals or their offspring (e.g. meat and milk, semen, and embryos). EFSA is to produce a risk assessment that will cover food safety, human and animal health, animal welfare and the environmental implications that may flow from this use of biotechnology. The EFSA Opinion, due to be published in early 2008, will cover both cloned animals and their offspring.

2.8.1 Report by the US Food and Drug Administration (FDA) on the health of cloned animals and safety of their food products

[23] As transgenic clones, the clones are derived from donor cells containing exogenous DNA inserted by molecular biology techniques, they are subjected to risk assessments specific to the inserted construct, its insertion site, and its subsequent expression.

[24] Vajta lab, Population Genetics and Embryology, Institute of Genetics and Biotechnology, Faculty of Agricultural Sciences, University of Aarhus, DK-8830 Tjele, Denmark; Institute of Human Genetics, University of Aarhus, DK-8000 Aarhus, Denmark.

[25] http://ec.europa.eu/european_group_ethics/docs/opinion9_en.pdf

The US agency responsible for food safety (FDA) carried out a risk assessment of cloned animals (cattle, swine, sheep and goats), their offspring and their food products[26]. The Opinion of the FDA has been adopted on January 15, 2008.

The FDA attempted first of all to identify hazards and risks on the basis of the available data and consideration of the biological processes involved in cloning. In order to analyse the potential risks associated with food derived from animal clones and their progeny, the FDA asked whether such food posed any additional risk relative to that arising from sexually-derived animals or other kinds of 'conventional' animals[27].

According to the FDA draft report, as cloning is a relatively new technology, available data are still limited[28,29]. Data-set size will therefore increase in the near future, making risk assessment more and more significant[30].

Because no additional genes are inserted, the FDA has concluded that the main hazard to which clones are exposed is that arising from incomplete or inappropriate nuclear reprogramming of the genetic information from the donor somatic nucleus (e.g. epigenetic effects[31]). This would explain the low "success rate" of cloning, death, metabolic derangements, or other the perinatal difficulties observed in some newborn clones, or occasional examples of altered metabolic pathways in very young animals. Those clones exhibiting the above malformation will be excluded from the market; food hazard may remain for those clones that have apparently normal functions, but with sub-clinical physiological

[26] http://www.fda.gov/bbs/topics/NEWS/2006/NEW01541.html
[27] In this context, 'conventional animals' were defined as 'animals derived by any reproductive means other than SCNT', thus comprising other ARTs such as artificial insemination and IVF.
[28] Hazards and risks are being identified, as well as the degree to which existing data (and their pool size) address questions of food safety.
[29] At present, most of the research studies on animal cloning report on the success rates of this biotechnology from various donor cell sources and culture conditions; they also report on the frequency of abnormalities and other problems such as the large offspring syndrome (LOS), the nature and frequency of developmental defects.
[30] The question arises as to whether enough data have been collected to draw confident conclusions regarding food products derived from animal clones. It is true that the cloning technology has not yet generated large, statistically strong datasets on clones. In this sense, one observation made by the FDA concerning Developmental Study was that the data on the health of livestock clones were consistent across species, even if some anomalies appear to be species-specific. For example, although LOS seems to be more prevalent in cattle and sheep, surviving animals overcame initial anomalies and became "healthy and normal." According to the FDA, such consistency increases the value of even small datasets (e.g. goats), and contributes to the judgments regarding the health of these clones and their suitability as food sources. In addition, the FDA evaluated other reports on the composition of meat and milk from clones and their progeny.
[31] Epigenetics describes stable alterations in gene expression potentials that arise during development and cell proliferation, or alterations in DNA function without alterations in DNA sequence.

anomalies[32]. However, these effects are not transmitted to the offspring of the healthy animals that are those used for reproduction, as it is supposed that characteristics of an epigenetic nature are in general not transmitted to the descendance.

The FDA could not identify any toxicological hazard of concern for human consumers and, although they stated that additional data from other sets of animals would be useful in increasing confidence in food safety, the weight of evidence at this time is sufficient for the agency to draw the conclusions it has set out in its Draft Risk Assessment with reasonable certainty.

Table 5. FDA study datasets

Source	Animals	Number	Group	Analysis
Cyagra	Cattle	67 clones 83 controls	1) Neonatal 2) 1-6 months 3)Up to 18 months	1) clinical chemistry and hematology 2) veterinary examination
Viagen	Swine	7 clones 15 controls	50 days to 6 months	Veterinary examination Composition of meat
		4 clones 3 controls	For fertility tests	Semen analysis, breeding capacity
		F1 progeny: 402 clones 300 controls	Development up to ca. 6 months	Abnormalities and weight at birth, physiology tests Veterinary examination
Analysis was not performed in a double blind manner.				

2.9 Biodiversity, epidemics.

Some have advocated that the multiplication of bioengineered gene pools, in a repetitive number through cloning, could interact with mechanisms of population genetics and may seriously damage biodiversity[33] and favour the consolidation of specific allelic frequencies at a population level[34]. It may therefore have a negative impact on adaptive mechanisms[35] of the species and significant social and economic consequences for rural areas, agricultural

[32] The preliminary FDA draft described the analysis of the composition of meat (from bovine and swine clones) and milk (from bovine clones) products from F0 generation. The above analysis has not shown any biologically relevant difference with the control animals, or food commonly consumed from these species on a daily basis. Another dataset on the progeny (F1) of swine clones also indicated that the composition of meat from those animals does not differ from that of traditionally bred animals (see Table 6).

[33] An example in agriculture: the 1845 Irish potato famine was due to genetic uniformity of potato plants. (http://www.centerforfoodsafety.org/pubs/fact%20sheet.pdf)

[34] The possibility of continuously recombining genetic data allows adaptive processes. The primary source of genetic variations in living beings is random genetic mutation and during cell division. The first one creates new genetic information that will be naturally selected over time, the second one reshuffles the random genetic changes created by mutations.

trade and public perception[36]. In the long run it may cause the affirmation of specific allelic frequencies, which may lead to epidemics due to the spread of breeds sensitive to a disease that may rapidly propagate. It may be a way to reduce diversity in species that are already suffering from a reduction of their genetic base. Therefore, cloning may cause an increase in pathogenic gene frequencies at a population level or the loss of adaptive capacities.

Countering the arguments above, some have advocated that cloning cannot affect the incidence of given genes at population or species level owing to the limited number of cloned animals, and that cloning could be a useful tool to breed animals with specific gene lineage, such as cattle that are resistant to diseases or to specific environments[37].

2.10. Farm animal cloning at international level

The first labs involved in mammal SCNT were in the USA, UK and Japan. However, over the last decade, and in particular between 1997 and 2003, SCNT research began to be carried out in different regions of the globe. At present, more than 160 laboratories in about 37 countries are working on SCNT. Most of the resources are directed towards livestock cloning (around 75% of cases), whereas less than 30% of the work is directed at laboratory animals. Cattle are most efficiently cloned by SCNT, which is practised in around 80 laboratories (50% of total cloning labs) in 24 countries.

European Union

At present, there are very few institutes working on the cloning of large animals, and fewer still that have an economic interest in doing so (mainly for racehorses and other lucrative business, less for the food industry *per se*). In the EU there are currently roughly 120 cattle clones[38]: in France (ca. 80), Germany (ca. 30) and Italy (ca. 10).

Japan

Japan is the country with probably the highest number of cloned animals. Since the first cloned calves born in 1990, some 1 242 cloned bovine animals have been manufactured in Japan to date (status as of end March 2007). As regards the cloning of pigs for biomedical research purposes, the first third-generation pig was born in August 2007 at Meiji University

[35] http://blog.greenparty.ca/en/node/461
[36] http://www.soilassociation.org/
[37] http://www.kirinholdings.co.jp/english/ir/news_release0601.html
[38] Data from Agrobiogen (Germany). http://www.agrobiogen.com/

in Tokyo[39]. Reaching the fourth generation of clones has significant implications for the breeding and reproduction of valuable large cloned animals, such as racehorses and mating bulls.

United States of America (USA)

So far the USA is the country in which most of the companies have been established with the aim of animal cloning for the food industry. The FDA report was based on a large population of cloned animals derived from two such companies: ViaGen[40] and Cyagra[41]. There are currently between 1 000 and 2 000 cloned cattle in the USA.

Argentina

The first cloned calf was born in Argentina in summer 2002. Argentina then began to actively invest in the cloning of large animals. Some of the US-based livestock cloning companies opened branches in South America, especially Argentina and Brazil.

China

Cloning research has been developing in China since the 1990's. The first company specialising in SCNT was founded in 2001 and its focus is mainly on the cloning of domestic animals. At the moment, China seems to represent a possible market for cloned livestock, as the first cloned calves of Australian origin were sold to China in early 2002. Chinese experts advocated a use of SCNT for the preservation of endangered species, such as the giant panda.

[39] The pig is an important model in biomedical research, particularly for therapeutic purposes for diseases such as diabetes and transplantation of the pancreatic Langerhans islets.
[40] http://www.viagen.com/en/our-services/cloning/
[41] http://www.cyagra.com/index.htm

3. LEGAL ASPECTS

The framework of EU legislation on animal breeding, animal health and welfare and food is applicable to any future technologies on animals, such as animal cloning (SCNT). Most EU legislation may be applicable to animal cloning under specific circumstances, as there is currently no dedicated regulation on food products derived from cloned animals or animal cloning as such in the EU.

EU legislation on animals for food production requires EU competence in the following sectors:

1. **Internal market for foodstuffs**: National laws hinder the free movement of foodstuffs and create unfair competition, thereby directly affecting the functioning of the internal market.
2. **Food safety and consumer health protection**: In order to protect public health, certain foods are subject to a safety assessment via a Community procedure before being marketed in the EU (harmonised safety approach at EU level). Labelling measures are also desirable, in order for the consumer to make an informed choice.
3. **Animal welfare and health**: protection of animal health and welfare is an animal husbandry requirement in the EU.
4. **Zootechnics:** regulation of the breeding aspects of animal husbandry.

Other relevant regulatory aspects to be taken into account include: 1) National legislation on cloning (EU Member States); (2) International trade agreements, (3) Intellectual Property Rights (IPR).

3.1 EU Regulatory Framework.

The **EU Treaty** lays down a number of principles (which are properly reflected in the European Charter of Fundamental Rights[42]) that may apply to animal cloning for food production, namely:

[42] Charter of Fundamental Rights: 'Conscious of its spiritual and moral heritage, the Union is founded on the indivisible, universal values of human dignity, freedom, equality and solidarity; it is based on the principles of democracy and the rule of law. It places the individual at the heart of its activities, by establishing the citizenship of the Union and by creating an area of freedom, security and justice.' (…) It seeks to promote balanced and

> Article 14 (‘**Free movement of goods, persons, services and capital’);** Article 94 (‘EU legislation for the approximation of such legislation of the Member States as **directly affects the establishment or functioning of the common market**.’) Article 95 (‘The Commission, in its proposals, concerning **health, safety, environmental protection and consumer protection**, will take as a **base a high level of protection**, taking account in particular of any **new development based on scientific facts.)**

The Additional Protocol to the Amsterdam Treaty also states that EU Member States desire to ensure improved protection and respect for the welfare of ‘animals as *sentient beings*' and that

> "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."

3.1.1 EU food regulations

Regulation (EC) **N° 178/2002** lays down the **general principles of EU food law**[43] with regard to protection of human life and health and the protection of consumers' interests, taking account of, where appropriate, the protection of animal health and welfare, plant health and the environment. It entails in particular an obligation on operators to place on the market only food for which they have an assurance of safety. According to the above Regulation, food that complies with Community provisions governing food safety shall be deemed to be safe insofar as the aspects covered by specific Community provisions are concerned[44]. The general principles and provisions of food law apply to all foods, including food derived from clones and their offspring.

EU Directive 2000/13/EC on the **labelling of food products** lays down rules for the labelling of foodstuffs to enable European consumers to obtain comprehensive information on the content and the composition of food products. Labelling helps consumers make an informed

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sustainable development and ensures free movement of persons, goods, services and capital, and the freedom of establishment.

[43] General Food Law (Regulation 178/2002): Objectives: High level of protection of human life and health and the protection of consumers' interests, including fair practices in food trade, taking account of, where appropriate, the protection of animal health and welfare, plant health and the environment; Free movement of Food; International standards taken into consideration; Science based decisions-making. In some cases other legitimate factors need to be taken into account: e.g. societal, economic, traditional, ethical and environmental factors and the feasibility of controls.

choice when purchasing their foodstuffs. Under the terms of the above Directive, it is not necessary to label a production technique or process 'as such', e.g. a cloning technique, used in the production of the foodstuff.

Regulation (EC) No 258/97 on **novel foods and novel food ingredients** covers food that was not used to a significant degree for human consumption before 15 May 1997, and inter alia falls into category (e) of Article 1(2):

> *foods and food ingredients consisting of or isolated from plants and food ingredients isolated from animals, except for foods and food ingredients obtained by traditional propagating or breeding practices and having a history of safe food use.*

Regulation (EC) No 258/97 may cover **animal food products** (e.g. meat, milk) produced from a clone, but not food products derived from offspring of clones, since offspring are reproduced in a 'conventional' way[45] (i.e. using a traditional breeding technique).

Regulation (EC) No 258/97 also states that, in order to protect public health, novel foods are subject to a safety assessment and authorisation under a Community procedure before they are placed on the market (EFSA). Additional specific labelling for novel foods may be required in a case where a novel food or food ingredient is no longer equivalent to an existing food or food ingredient. The comparison, based on a scientific assessment, must have regard to the accepted limits of natural variations for characteristics of food.

GMO legislation would apply *only if* the cloning technique were to be combined with genetic modification. Whilst cloned animals are not necessarily genetically modified, one of the reasons for using cloned animals may be the rapid extension of inserted genetic material.

Directive 2001/18/EC regulates the deliberate release into the environment of **genetically modified organisms** and therefore has environmental and human health protection purposes as stated under Article 1 of the Directive[46]. According to Directive 2001/18/EC[47], 'genetically

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[44] When there are no specific provisions at Community level, food products have to conform to national food law of the Member States in whose territory they are marketed (see also the Art. 28 and 30 of the EU Treaty).

[45] EFSA will clarify in its Opinion the applicability of EC/258/97 provisions to products from clones and offspring.

[46] In accordance with the **precautionary principle,** the objective of this Directive is to approximate the laws, regulations and administrative provisions of the Member States and to protect human health and the environment when: 1) carrying out the deliberate release into the environment of genetically modified organisms for any other purposes than placing on the market within the Community, 2) placing on the market genetically modified organisms as or in products within the Community.

modified organism' (GMO) means an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination. Within the terms of this definition, a genetic modification occurs at least through the use of one of the techniques listed in Annex I A of the above Directive[48].

EU legislation on GMOs (Directive 2001/18/EC, Regulations (EC) 1829/2003 and 1830/2003[49]) therefore seem not to be applicable to cloning techniques unless SCNT is combined with genetic modification[50]. The applicability of this legal framework will need to be explored on a case-by-case basis as regards the technique used to produce the clones.

Genetically modified foods or food ingredients may be exempt from the requirements of Regulation 258/97 as they are separately covered by Regulation 1829/2003 on genetically modified food and feed.

3.1.2 Other existing relevant EU legislation: zootechnics, animal welfare, animal health

The **breeding aspects** of animal cloning are covered by Community legislation on **zootechnics** (Directives 77/504/EEC, 88/661/EEC, 89/361/EEC, 90/427EEC, 94/28/EC), which has as its aim the need to avoid trade restrictions for purebred animals.

Zootechnical rules have harmonised the EU marketing and **import of animals, semen, ova and embryos** whether they have been bred by natural mating or produced using biotechnological techniques such as artificial insemination, embryo transfer, in-vitro-fertilisation or SCNT. The relevant provisions are the following:

> "Member States shall ensure that the following shall not be prohibited, restricted or impeded on zootechnical grounds: 1) intra-Community trade in pure-bred breeding animals of the bovine species, 2) intra-Community trade in the semen and embryos of pure-bred breeding animals of the bovine species (…) intra-Community trade in bulls used for artificial insemination". (Directive 77/504/EEC, Article 2)

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[47] Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms; Scope: Article 2

[48] Regulations (EC) No 1829/2003 and 1830/2003 refer to the definition of GMO laid down in Directive 2001/18/EC.

[49] Directive 2001/18/EC on the deliberate release of GMOs into the environment and Regulations 1829/2003 on GM food and feed and 1830/2003 on labelling and traceability of GMOs.

[50] The above Directive would therefore apply to animal cloning if manipulation of the gene sequence of the cloned animal were to be carried out.

Some EU regulations are designed to regulate specific animal species, for example Dir. 88/661/EEC concerns swine species, Dir. 89/361/EEC sheep and goats, and Dir. 90/427 equidae.

Council Directive 94/28/EC amending Directive 77/504/EEC: Articles 4 – 7 inclusive refer to the import of animals, semen, ova and embryos respectively:

> "To be imported, the (animals, semen, ova) embryos referred to in Article 1 must: 1) come from an animal which is entered or registered in a herd book or register kept by an authority shown on one of the lists referred to in Article 3 (1); 2) be accompanied by a pedigree and zootechnical certificate to be drawn up in accordance with the procedure laid down in Article 12.

Trade in food products or animal farming is therefore already regulated at EU level.

Animal welfare aspects are covered by the Council of Europe's *European Conventions on the Protection of Animals*[51] and several Council Directives. Council Directive 98/58, in particular, deals with the protection of animals kept for farming purposes, and states that natural, artificial breeding or other breeding procedures which cause, or are likely to cause, suffering or injury to any of the animals concerned must not be practised.

The more recent Council Directive 1999/74/EC[52] defines the minimum welfare criteria and addresses alternative forms of rearing for laying hens, such as free range and enriched environment to allow animals a more natural behaviour[53].

In the case of cattle and pig rearing, Council Directives 91/629/EEC and 91/630/EEC opened the debate about the most appropriate farming techniques to achieve better health and welfare results to improve the quality of the meat; as a consequence, sow stalls were banned and other

[51] http://ec.europa.eu/food/animal/welfare/references/farmspc/jour323_en.pdf
Article 1:" This Convention shall apply to the keeping, care and housing of animals, and in particular to animals in modern intensive stock-farming systems".

[52] 1999/74/EC of 19 July 1999 laying down minimum standards for the protection of laying hens.

[53] Since then, investments have been increasing for research into the correlation between hen farming methodology, animal welfare and public health. Simultaneously, the market quota of 'free range' eggs has been increasing steadily in many EU countries, showing European consumers' interest in welfare friendly food products, as reported by two Eurobarometers surveys on "Consumers attitudes towards welfare friendly products" in 2005 and 2006 http://ec.europa.eu/food/animal/welfare/euro_barometer25_en.pdf

measures were adopted[54], such as investing in research to find alternative solutions to castration of piglets.

EU **animal health** rules are applicable to intra-Community trade in and imports of live animals, semen, ova and embryos, irrespective of whether they have been bred by natural mating or produced using biotechnological techniques such as artificial insemination, embryo transfer, and *in vitro* fertilisation.

Moreover, the framework of the present EU legislation on animal health is also applicable to the movement of live animals and their products resulting from future technologies such as SCNT.

Council Directive 89/556/EEC of 25 September 1989 on animal health conditions governing intra-Community trade in and importation from third countries of embryos of domestic animals of the bovine species and Council Directive 88/407/EEC of 14 June 1988 laying down the animal health requirements applicable to intra-Community trade in and imports of semen of domestic bovine species regulate the import of **bovine** semen and embryos[55], subject to the exceptions set out in Article 1(2) of Directive 89/556/EEC: "This Directive shall not apply to embryos derived by transfer of nuclei". However, to date, no EU Member States have taken action on this exclusion area, and therefore harmonised EU rules apply[56].

In addition, there are numerous directives and decisions laying down animal health requirements relating to the movement of semen, ova and embryos of other animal species, but none of the other pieces of legislation include any such exception. Cloned embryos from animal species other than bovines are therefore covered by EU animal health legislation.

The legal framework that regulates **animal cloning for research** purposes is Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes. The scope of that Directive is determined by the likelihood of an animal being subject to pain, suffering, distress or lasting harm, including any course of action intended, or liable, to result in the birth of an animal in any such condition.

[54] 91/629/EC and 91/630/EC of 19 November 1991 laying down minimum standards for the protection of cattle and pigs.
[55] For bovine embryos derived by transfer of nuclei, which are excluded from the scope of Directive 89/556/EEC [OJ L 302, 19.10.89, p.1], Member States are allowed to set national import conditions.

> Article 2 (d) 'experiment' means any use of an animal for experimental or other scientific purposes which may cause it pain, suffering, distress or lasting harm, including any course of action intended, or liable, to result in the birth of an animal in any such condition,…"[57]

The Council of Europe Convention ETS 123, on the same subject, was adopted in 1986. The Community is a party to this Convention, with Directive 86/609/EEC as the implementing instrument. With reference to genetically altered animals, the Parties to the Convention agreed to interpret the Convention as follows:

> (1) For the purpose of the Convention, Parties understand the expression "animals carrying harmful genetic modifications" as referring to genetically engineered animals and mutant animals capable of producing as a consequence offspring likely to suffer significantly.
> (2) Generating a transgenic strain is considered as constituting a procedure under Article 1, sub-paragraph 2 c.
> (3) The breeding of animals carrying harmful genetic modifications may be considered on certain conditions to be determined by each Party as a procedure under Article 1, sub-paragraph 2 c. Such procedure must be carried out in accordance with the Convention.
> (4) If the breeding of animals carrying harmful genetic modifications is not considered to be a procedure, Articles 14, 15 and 16 shall apply. [58]

3.2 National legislation in the EU Member States

Denmark is the only EU Member State that has specific legislation on cloning and genetic modification of animals. The law was passed in Denmark in June 2005 (Act no. 550 of 24 June 2005) and it allowed the cloning and genetic modification of vertebrate animals after approval from the Animal Research Inspectorate (§ 1) for:

- Basic research (studies of biological mechanisms)
- Applied research aiming at considerable improvement of health or environment.
- Breeding of animals producing substances of considerable benefit to health and the environment or
- Teaching and education at universities and similar or other teaching at the same level and teaching of persons who are dealing with cloning and gene modification.

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[56] There are plans for an amendment to Council Directive 89/556/EEC in the near future to close this gap.
57 Council Directive 86/609/EEC of 24 November, OJ L 358, 18.12.1986, p. 1–28 -http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31986L0609:EN:NOT

According to Danish law, the Animal Experiments Inspectorate may refuse approval if the cloning, the gene modification or the use of cloned or genetically modified vertebrates is not evaluated to be of *considerable* benefit. The same applies to breeding of cloned and genetically modified animals used for experiments. Animal cloning is therefore not allowed if the expected benefit deriving therefore is not relevant[59]. The Animal Experiments Inspectorate will authorise cloning practice on a case-by-case basis and take the decision for approval following an assessment based, inter alia, on scientific issues, animal welfare, integrity of the cloned animals, environmental risks compared to the benefits of such technology, etc.

Possible cloning applications, which are subject to approval, include the use of this animal biotechnology for the production of human proteins (therapeutic use, e.g. producing milk with a special composition), but not animals with special characteristics for food production purposes (meat aimed at a special market). The law is silent about the import of cloned animals and products derived from them.

3.3 World Trade Organisation (WTO), GATT and SPS agreements

The World Trade Organisation (WTO) has developed a multilateral system of trade to lower customs and trade barriers, and abolish discrimination in international trade. WTO agreements are the legal ground rules for international commerce which were negotiated and signed by a large majority of the world's trading nations and ratified by their parliaments. The General Agreement on Tariffs and Trade (GATT) and the Sanitary and Phyto Sanitary (SPS) agreement include measures that might be relevant for trade of food products resulting from animal cloning.

Since 1995 (after the Uruguay Round of the General Agreement on Tariffs and Trade -GATT) an agreement entered into force regarding food safety, animal and plant health. Aspects covered by the agreement include measures related to food contamination, pests and pesticides and labeling. As a consequence, individual WTO Member States' policies regarding the blocking of food imports are restricted to specific situations, and no WTO Member State can endorse safeguard measures or a ban against a specific trade product (including food)

[58] http://www.coe.int/t/e/legal_affairs/legal_co-operation/biological_safety,_use_of_animals/laboratory_animals/Res%20interpretation.asp#TopOfPage

unless it has carried out a relevant risk assessment and provides evidence to support a trade restriction.

Under the WTO SPS agreement, the application of quarantine policies for safety reasons is regarded as a 'technical barrier to trade' to the detriment of foreign competitors. According to the SPS agreement, if there is no scientific evidence proving a product to be a threat to human health and the environment, its marketing must be authorized. It is up to the individual member countries of the WTO to demonstrate that a product is dangerous before its trade can be prevented, even if it is impossible to accurately predict all damage posed by all products.

Articles 5.1 and 5.2 of the SPS agreement state

> "Members shall ensure that their sanitary or phytosanitary measures are based on an assessment, as appropriate to the circumstances, of the risks to human, animal or plant life or health, taking into account risk assessment techniques developed by the relevant international organizations" and "In the assessment of risks, Members shall take into account available scientific evidence; relevant processes and production methods; relevant inspection, sampling and testing methods; prevalence of specific diseases or pests; existence of pest- or disease-free areas; relevant ecological and environmental conditions; and quarantine or other treatment".

Article 5.3 addresses the manner in which risk assessments may be interpreted:

> "In assessing the risk to animal or plant life or health and determining the measure to be applied for achieving the appropriate level of sanitary or phytosanitary protection from such risk, Members shall take into account as relevant economic factors: the potential damage in terms of loss of production or sales in the event of the entry, establishment or spread of a pest or disease; the costs of control or eradication in the territory of the importing Member; and the relative cost-effectiveness of alternative approaches to limiting risks."

The import/export of food products derived from animal cloning will be subject to WTO provisions on trade and barriers to global trade.

3.4 WHO-FAO *Codex Alimentarius*

The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) have encouraged food-related scientific and technological research, as well as discussion, to raise awareness about food safety, hygiene and related issues at

[59] The Animal Experiment Inspectorate is not in possession of sufficient knowledge to make the evaluation; it may obtain the opinion of a competent authority institution or the like before making the decision.

international level. In 1963 they created the Codex Alimentarius[60] as a reference document for consumers, food producers, manufacturers and national food control agencies. Since then, the Codex Alimentarius has enabled the formulation and harmonization of food standards and has ensured the protection of public health and fair practices in the food trade through the global implementation of such standards worldwide.

The Codex Alimentarius also has relevance for the international food trade. Thus, the WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) and the Agreement on Technical Barriers to Trade (TBT Agreement) have encouraged the international harmonization of food standards. Codex Alimentarius standards have become the benchmarks for national food measures and regulations, and their evaluation within the legal parameters of the WTO Agreements.

The latest report of the Ad Hoc Intergovernmental Task Force on Food Derived from Biotechnology (September 2007[61]) pointed out at the guidelines for risk assessment when comparing recombinant-DNA animals with their conventional counterparts in order to identify new or altered hazards in the new animals. A key element in such analysis is to take as a reference animals with a history of safe use. However, the established guidelines do not apply to cloning. As the mandate of the work was discussed, the work was limited to genetic modification and cloning was seen as an assisting technique for genetic modification.

3.5 Intellectual Property (IP) regulation

As a general rule, under Article 52 of the European Patent Convention, patents can be granted to any invention which is new, is susceptible of industrial application and involves an inventive step. Exceptions can be made in the case of specific classes of inventions that cannot be patented, namely for methods of treatment (for both diagnostic and surgery), plant or animal varieties and essential biological processes for their production and, lastly, for inventions contrary to 'ordre public' and/or morality. For biotechnological processes, which cloning could be interpreted to be, rules 23b, c and d apply[62], opening the possibility of

[60] http://www.codexalimentarius.net/web/index_en.jsp
[61] http://www.codexalimentarius.net/web/archives.jsp?lang=en
[62] Rule 23b…(2) "Biotechnological inventions" are inventions which concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used. (3) "Biological material" means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system.; Rule 23c Biotechnological inventions shall also be patentable

patenting, if cloning were not to fall into the categories described in Article 53(a) and, in particular, in "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".

According to Rule 23d (d) of the European Patents Convention, patents shall not be granted to 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[63]. This is also stated in Directive 98/44/EC on the legal protection of biotechnological inventions where it is also indicated that "inventions shall be considered unpatentable where their commercial exploitation would be contrary to *ordre public* or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation". Directive EC/98/44, specifically Article 6, states:

> 1. Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; 2. On the basis of paragraph 1, the following, in particular, shall be considered unpatentable: (…) (d) 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.

This last condition may be interpreted to mean that animal cloning is not acceptable for public order and morality if it involves animal suffering and is not carried out for medical purposes. The question remains as to whether the arguments in support of animal cloning for food can be categorized as a substantial medical benefit and whether cloning can be regarded as a modification of the animal gene identity.

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if they concern: (a) biological material which is isolated from its natural environment or produced by means of a technical process even if it previously occurred in nature; (b) plants or animals if the technical feasibility of the invention is not confined to a particular plant or animal variety; a microbiological or other technical process, or a product obtained by means of such a process other than a plant or animal variety.; Rule 23d Under Article 53(a), European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following: (a) processes for cloning human beings; (b) processes for modifying the germ line genetic identity of human beings; (c) uses of human embryos for industrial or commercial purposes; (d) 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.

[63] EPO: *Rule 23d"*Exceptions to patentability Under Article 53(a), European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following: (a) processes for cloning human beings; (b) processes for modifying the germ line genetic identity of human beings; (c) uses of human embryos for industrial or commercial purposes; (d) 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." (http://www.european-patent-office.org/legal/epc/pdf/epc_2006_v5_bm_en.pdf)

Article 27 (3)(b) of the TRIPS Agreement (WTO) provides that animals other than micro-organisms, and essentially biological processes for the production of animals other than non-biological and microbiological processes, may be excluded from patentability. The European Patent Convention recognizes this in rules 23b and 23c.

4. Ethical issues

Animal cloning for food supply involves a number of specific ethical concerns that come to play when decisions are to be made concerning the application of SCNT cloning technologies in breeding establishments for farm animals.

These ethical concerns are related to a broad spectrum of decisions with regard to (see also Table 6):

a) cloned animals and their offspring (e.g. use of animals for humans' purposes; animal health; animal welfare; "animal integrity");
b) human beings (e.g. human health and wellbeing; food safety; bio-safety; possibility of misuse – in humans ('slippery slope arguments'));
c) environment (e.g. biodiversity; environmental pollution and degradation; environmental sustainability);
d) human society at large (e.g. social desirability, social acceptance; consumers' rights; justice issues – local, regional, global; intellectual property rights).

Table 6 Ethical concerns in animal cloning for food supply

Concerns for the cloned animals (and for their offspring)	**Concerns for humans**	**Concerns for the environment**	**Concerns for the society**
Using the animals for humans' purposes	Human health and wellbeing (including food safety and food security)	Biodiversity Biosafety	Public perception Social desirability Social acceptance Consumers' rights
Animal health Animal welfare		Environmental sustainability	Justice issues (local, regional, global) Intellectual property rights
Animal "integrity" ("animal rights"?)	Misuse in humans ('slippery slope' concerns)	Pollution, degradation	Industrialisation of agriculture Sustainability of agriculture

It should be pointed out, however, ethical issues outlined here are just part of a complex framework of ethical concerns connected with modern agriculture[64], and some advocated that animals do not have a moral status and can be instrumentally used for human purposes[65].

[64] The ethical issues connected with the use of advanced (bio)technologies in agriculture will be analysed in the following EGE Opinion.

[65] See: Animal Rights & Human Morality by Bernard E. Rollin (**Prometheus Books.** September 30, 2006)

4.1 The moral status of animals

Historically, the moral status that people attributed to the animals (or believed the animals somehow possess), and especially to the domesticated and later on to the farmed ones, has mainly evolved along two lines: either animals were seen as a mere objects possessed by their owners and available to them for any purpose the owner might wanted to used them, or the animals were given various degrees of respect. These attitudes were influenced strongly by cultural and religious traditions.

More recently philosophers have defended the moral status of animals in a number of theories arguing that an animal is a moral subject as it is: (a) able to feel pleasure and pain[66], (b) subject-of-a-life[67], an element of biodiversity[68] etc.

The first theory comes back to the philosophy of Bentham and Mill[69], and has been advocated more recently, inter alia, by Peter Singer. According to his theory, actions causing pain in sentient animals are morally unacceptable, since animals are considered moral subjects – Need quote-. Therefore, if cloning affects animal welfare and health, then this use of biotechnology is ethically problematic[70].

Another theory advocates that animals have a moral value in themselves as 'subjects-of-life' (intrinsic value argument) and states that both human and non-human beings are (analogously) moral entities because of their sentient capacities. The corollary of this argument is the non-instrumentalisation of animals for human purposes.

A number of philosophers have opposed animal bioengineering on the basis of categorical arguments (animals' intrinsic value[71], or integrity[72], or telos[73]). They argued that, as we

[66] Singer P. (1985) *In Defence of Animals* N.Y.: Blackwell; Singer P. (1990) *Animal Liberation* N.Y.: Avon Books; Suzuki D. & Knudson P. (1987) *Genethics, the ethics of engineering life* Stoddart Publishing Co. Toronto
[67] Regan T. (1983) *The Case for Animal Rights* Berkeley California.: University of California Press
[68] Norton B. (1986) *Why preserve natural Variety*? Princeton University Press Princeton
[69] Jeremy Bentham, *The Introduction to the Principles of Morals and Legislation*, edited by J. H. Burns and H. L. A. Hart, London: Athline Press, 1970. Many of John Stuart Mill's works are relevant, especially his *Utilitarianism* and *On Liberty*.
[70] Rollin B. (1998) *The Unheeded Cry. Animal Consciousness Animal Pain and Science.* Oxford University Press
[71] Dol et al. (1999) *Recognizing the intrinsic value of animals* Van Gorcum & Comp. Assen
[72] Van den Bos et al. (1997) *Animal Consciousness and Animal Ethics* Van Gorcum & Comp. Assen

attribute a moral value to human beings, we ought to extend this ethical concern to other animal species[74] and oppose animal biotechnology (transgenic animals and cloning in particular, but also other GM of animals for breeding purposes – blind chickens, for example). Other theories have advocated the possible use of animals in animal biotechnology under specific conditions where animal pain is minimised and authorised in well justified circumstances[75] on an assessment based on the 3Rs (Reduction, Refinement and Replacement) principle and on the five freedoms as defined by the World Organisation for Animal Health (OIE): freedom from (1) hunger, thirst and malnutrition; (2) fear and distress; (3) physical and thermal discomfort; (4) pain, injury and disease; and (5) to express normal patterns of behaviour.

4.2 Sustainability and animal farming

In the age of globalization, national boundaries tend to diminish in importance because each country is largely interconnected with, and interdependent on, many others through economic and political links. In the area of farming, several kinds of methods can be observed worldwide, and such typologies often depend on the scale of farmed rural areas.

Whereas in several countries agriculture is characterized by very large farming areas which belong to a few farmers, in Europe the average size of farming properties is much smaller and they belong to a large number of farmers. It is only natural that farming processes have been developing differently on different continents. In several countries, agriculture has generally been employed on a large scale and using automated means of production; on the EU side, family-based properties have tended to follow a more traditional type of farming and on a smaller scale (Small and Medium-sized Enterprises). Apart from any economic considerations in terms of costs and revenues, this development is likely to remain on different tracks.

According to a recent FAO report[76] (2007), cattle breeds currently make up 22% of the world's recorded mammalian livestock breeds, and human kind relies upon 14 species of livestock in total for 90% of its animal food production. Most probably, there are three

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[73] Rollin B. (1989) *The Frankestein Syndrome. Ethical and Social Issues in the Genetic Engineering of Animals* Cambridge Cambridge University Press. Rollin B. (1998) On telos and genetic engineering in Holland and Jonson (eds.) *Animal Biotechnology and Ethics* Chapman and Hall London 1998:162

[74] Naess A. (1984) In defence of deep ecology *Environmental Ethics* 6(3):265-270

[75] Fincham J.R. & Ravez J.J. (1991) *Genetically Engineered Organisms: Risks and Benefits* University of Toronto Press. Toronto-Buffalo; Fox. M. (1992) *Superpigs and Wondercorm* Lyons & Bufford N.Y.; Kaiser M. Wellin S. eds. (1995) *Ethical Aspects of Modern Biotechnology* Centre for Research Ethics Goeteborg;

countries in the world that would initially use animal cloning for food supply: they are Argentina, USA, and China.

Consequently, a discussion on the ethics of animal cloning for food cannot be restricted to economic or legal considerations alone. Other factors related to sustainable agriculture are just as important (e.g. human responsibility towards the environment and future generations – intergenerational justice and ecology). Sustainable farming is indeed an important focal concept. It involves many dimensions, including human health, safety, animal welfare, environmental concerns, biodiversity and global justice. It does not contain or add anything that is not covered by these dimensions; it combines them. The above concerns will be addressed in the next Opinion of the EGE, including issues related to the ethics of industrialized agriculture at EU and international level.

Another concern that has been put forward during the discussion on cloning relates to the potential use of animal cloning as a tool to develop SCNT and then to open the door for possible use of the technology with human beings (the "slippery slope" argument).

4.3 Religious considerations

To a great extent, the relationship between mankind and animals varies according to the religious views of the society involved. Generally speaking, humans' attitude to animals varies considerably between Western to Eastern cultures. Eastern - predominantly Hindu or Buddhist - cultures tend to have a greater respect for animals and their protection due to their belief in reincarnation and in recognizing the divine in all living forms. Western cultures tend to view animals as instrumental to human wellbeing and necessities, provided that such necessities do not cause pain to animals.

4.4 Public perception and public acceptance

A survey conducted in the US by the International Food Information Council in 2005 reflected that 34% of respondents would be likely to buy food products from cloned animals if the FDA determined them to be safe to eat (compared to 64% against). Accordingly, public perception of animal cloning is likely to play a major role in its development and its

[76] http://www.fao.org/newsroom/en/news/2007/1000598/index.html

commercial prospects. This perception may vary greatly between countries, including between EU Member States.

Since 1991 the Eurobarometer surveys have examined the attitudes of the European public. However, no specific public surveys have yet been conducted on the social perception of animal cloning for food supply. Knowledge in the EU about the public perception of animal cloning is very limited[77]. According to the available data, there is public acceptance for cloning as a research tool in biomedicine (e.g. bio-pharming), but not for its application in agriculture. From the available data it seems that European citizens differentiate between medical and agricultural applications and are most sceptical towards biotechnology when it is applied to animal rearing or food production. Public concerns about cloning tend to be primarily human-related (food safety; socioeconomic effects, consumer choice) and less often zoocentric (animal welfare and integrity). At the present time it seems that the public is not fully informed about the uses and implications of cloning. Taking into account the precedents of GM food, public interest would be likely to intensify as products came closer to marketing.

Under the 6th Framework Programme, the Commission has supported a project entitled "Cloning in public", a specific support action project co-ordinated by the Danish Centre for Bioethics and Risk Assessment (CeBRA, DK). The project had two main objectives: 1) to stimulate informed public debate across Europe on farm animal cloning and to ensure public participation in the formation of European policies and regulation; 2) to make recommendations on regulation and guidelines concerning research and applications of farm animal cloning. The argument for this project was that 'Whether a decision is made to rely on existing regulation or to introduce new, specifically targeted legislation, concerns about both free trade and social acceptability in Europe will have to be negotiated[78].

4.5 The consumer's right to know, free choice and labelling

Once food safety risks are ruled out, a possible concern would be a requirement for consumer information and product labelling, either confined 'only' to clones and products derived from

[77] Earlier research indicates that public acceptance of animal biotechnology is closely related to the perceived usefulness of the applications suggested. Consequently, research and biomedical applications seem to be more acceptable to the public than agricultural applications which are regarded more negatively. See (a) Eurobarometer EB 52.1, 1999; (b) The report CLONING IN PUBLIC: Public perceptions of farm animal cloning in Europe (August 2005); and (c) Lassen, J, Gjerris, M & Sandøe, P (2005): After Dolly – ethical limits to the use of biotechnology on farm animals. *Theriogenology* (Submitted).

[78] http://www.sl.kvl.dk/cloninginpublic/

them, and/or on offspring and their products. Since a clone and its derived products cannot effectively be distinguished from another animal, a labelling policy would have to be associated with some sort of trace-back or integrity preservation systems. Currently, beef meat must be traceable. Animal semen and embryos are also already traceable. However, for other processed products, the control of labelling could present difficulties, in particular for offspring[79].

From a technical point of view, the "analytical" traceability entails two different issues: (1) the analytical identification of clones/offspring and derived products and (2) the authentication of traceability schemes for individual animals and derived products (not limited to clones, but generalised). Traceability schemes for animals are already enhanced through the use of Electronic Identification/Radio frequency identification of animals up to the slaughterhouse, and this may be further improved through the use of molecular markers (see also 2.4.2).

[79] An open question regarding the definition of offspring would be: For how many generations would the offspring of clones have to be labelled?

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The aim of farm animal breeding is to select animals that have genetic characteristics such as disease resistance or quality features that are of interest to farmers. Cloning of vertebrates via SCNT is a recently developed technology which is used in biomedical research and animal breeding, and can also be used for the production of' food, such as meat and dairy products. The cloning technology may also be used for the reproduction of animals, which are of high value to their owners, such as race horses and pet animals, as well as for the conservation of endangered species.

Animal cloning for food supply, however, opens a wide range of safety, legal, ethical and societal concerns, as well as political concerns of various kinds (e.g. global trade). Some of these concerns are being analysed by the EFSA, in particular those related to the scientific aspects of food safety and animal welfare.

5.1 Scope of the opinion

The EGE has issued an Opinion on the ethics of animal cloning in 1997, but given the state of the art of the technology at that time it did not address the ethics of animal cloning specifically for food supply. This EGE Opinion updates the previous one and is intended to complement that of EFSA. The ethical considerations in this Opinion will therefore refer to the use of animal cloning in animal breeding in order to produce progeny that could enter the food chain.

The EGE is aware that the experience in animal cloning could be used in the development of genetically modified animals (genetic modifications to produce nutraceuticals, bio-pharming or prevention of animal diseases in farm breeding, or increasing the added value of food products from cloned animals and their offspring) or in the development of cloning techniques as such[80]. However, these issues, while acknowledged as relevant and deserving further analysis with regard to their scientific, ethical, legal and social implications, are not the subject of this EGE Opinion. In line with the EFSA report, and with the request from

[80] As far as the potential use of SCNT on human beings for reproductive purposes, the Group reaffirms its opposition to such practices.

President Barroso, this Opinion is limited to the use of animal cloning without genetic modification.

5.2 Arguments on animal cloning for food

The major arguments advocated *in favour* of animal cloning for food are economic ones, namely, inter alia, to keep up European competition vis-à-vis third countries on the free market; to facilitate industrial development; to improve food production and quality, while lowering prices for consumers, as happens in the case of other intensive farm practices. Some have therefore advocated cloning as a possible development towards standardised, cheaper food production, particularly meat, which would then be affordable by a larger proportion of the population. Others have argued that cloning may be a useful tool to accelerate the breeding of animals with specific genetic lineage, such as cattle resistant to diseases or adverse conditions[81], or that it might have proven positive effects on human and animal health like, for instance in conjunction with transgenesis[82].

Arguments against this use of animal biotechnology, on the other hand, articulate concerns that are based on human health and safety, animal health and welfare, animal integrity, biodiversity, the risk of epidemics, social and economic effects on rural areas, agricultural trade (see Chapters 2 and 4 of this Opinion). Others have pointed to the danger that animals are valued only as far as their instrumental use to human kind and identified the risk that an increased use of cloning might eventually facilitate human reproductive cloning.

The Group is aware that there are differing viewpoints on the moral acceptability of using animals in modern farming and is aware that there are some very strongly held views against the instrumental use of animals for human purposes regardless of positive consequences this might have for humans. The Group therefore recognises that, for some people, animal cloning for food supply is an ethically unacceptable practice, whatever conditions are required.

The EGE wishes to emphasise that embarking on cloning for food supply means opening up a new dimension in the general context of breeding that is not merely technical, and which for some people may create a moral unease that cannot be simply dismissed.

[81] These last two arguments, however, cover uses of animal cloning other than that addressed in this Opinion.
[82] See paragraph 2.7 of this Opinion.

5.3 Food safety

The EGE has neither the competence nor the authority to assess risks related to food safety. Nevertheless, the decision on the levels of risks to individuals and society that are acceptable raises ethical issues. The scientific risk assessment of food safety of products derived from animal clones and/or their offspring falls within the remit of the EFSA (EFSA Opinion and its subsequent updating) and the Group bases itself on that. EFSA's draft Opinion states that (1) measures restricting animal cloning for food purposes can not be justified on food safety grounds, (2) "the available data for risk assessment are limited" and (3) there are uncertainties in their assessment[83]. The EGE underlines the importance of guaranteeing the safety of food products for human consumption as a pre-condition for their marketing and stresses the importance of scientific updates and follow up research into progeny.

5.4 Animal welfare and health

In the Amsterdam Treaty animals are recognized as 'sentient' beings[84] and, therefore, while meat production is important in the human diet, and the slaughter of animals a necessity, it should always be clear that the way in which we treat animals should be in accordance with the already existing animals welfare and health standards required in EU legislation (see 3.1.2 of this Opinion). However, in addition to these standards, the Group believes that additional requirements should also be taken in intensive animal breeding, in particular the guidance in animal welfare provided by the World Organisation for Animal Health (OIE[85]), namely the five freedoms already mentioned in paragraph 4.1 of this Opinion; freedom: from hunger, thirst and malnutrition; from fear and distress; from physical and thermal discomfort; from pain, injury and disease; and to express normal patterns of behaviour.

Infringements of the above criteria would need to be balanced by important benefits to human beings. The EGE has however doubts whether infringements of these standards can be justified by the benefits obtained by current procedures in cloning animals for food production.

[83] See EFSA draft Opinion, Conclusions chapter, p.30.
[84] This notion is also stated in the Lisbon Treaty, currently under ratification, and which is extended to all technological developments (B specific amendements).
[85] www.oie.int

In addition, according to information provided by EFSA, the Group noted a lack of data[86] on the long-term animal welfare and health implications of clones and their offspring[87], due to the current limited use of the technology. Further studies and analyses on long-term animal welfare and health implications for clones and their offspring, as well as more comparative analyses with other assisted and traditional reproductive technologies in animal farming, are needed for a proper assessment of this issue.

However, the Group is concerned that intensive breeding techniques may adversely affect animal welfare and that a review of current practices should be conducted at European level. For this reason the Group suggests that the Commission takes initiatives to prepare a Code of Conduct on responsible farm animal breeding, including animal cloning.

5.5 Farm animal biodiversity and sustainability

Although the Group acknowledges that cloning could be used to maintain certain rare animal breeds among farm animal species[88], the intensive industrial use of cloning applied to highly prevalent animal races might ultimately reduce diversity and affect their global distribution. Recent reports have highlighted the danger that the use of a limited number of breeding lines in intensive animal farming may affect the biodiversity of farm animals (see Chapter 2.7.3 of this Opinion) and create inbreeding problems.

While the Group is also aware that the use of animal cloning in animal husbandry would be difficult to extend on a global level[89], it nevertheless advocates the need to protect biodiversity and limit inbreeding in farm animals stocks as far as possible, in order – among other things – to avoid the risk of global epidemics. In that respect, the Group recommends the EC to take proper measures to preserve the genetic heritage of animal species[90], for example by funding projects that aim to preserve domesticated species and breeds in Europe.
The Group is concerned about the global impact of increasing meat consumption on the environment as cloning of farm animals could be another step in increasing such impact.

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[86] See EFSA draft Opinion, Conclusions chapter, p.30.
[87] Similar considerations apply to the existence of data on other assisted reproduction technologies (ART) in animal breeding.
[88] Cattles (*Bos bovis*) is a species and there are around 1.2 billions individuals worldwide, falling into about a thousand breeds, or races, see 2.7.3.
[89] By David Fraser, ftp://ftp.fao.org/docrep/fao/009/a0158e/a0158e00.pdf
[90] From the EGE Opinion Nr.3 on the Ethical implication of Biotechnology: "Biodiversity … with ratification of the UN Convention on Biological Diversity, the Community would be well advised to start considering the matter with view to clarifying what it understands the concept to mean in practical terms".

5.6 Societal aspects

5.6.1 Public participation

The Group realises that, while cloning is only one step, and so far a relatively marginal one in the process of industrialization of agriculture and globalisation, it is of the utmost importance, in terms of global justice and environmental impact, that a debate be held concerning the issues underlying and accompanying this global development. The Group therefore underlines the importance of a public debate on the concept of biotechnologies in modern agriculture, the environmental and societal impact of increasing meat consumption and rearing of bovines, as well as the fair distribution of food resources and the need to promote sustainable agriculture at EU level and worldwide.

In order to be able to exercise its freedom of choice, the public also needs to be adequately informed, and public debate should therefore be promoted.

The Group therefore invites the Commission to take a pro-active role in promoting public discussion on this use of animal cloning, and its potential implications, by financing a number of ad hoc initiatives at Member State and pan-European level aimed at promoting public debate on the marketing of food products derived from animal cloning. Relevant stakeholders (media, industry, policymakers, NGOs and the scientific community) should participate in this effort in a pro-active manner and communicate reliable information about the work done. Transparency at all decision making levels (both at private and institutional level) is essential because a constructive public debate can only take place if based on reciprocal trust and in full knowledge of factual data.

5.6.2 Public perception

The Group acknowledges that the "food philosophy" of individuals and countries (i.e. their views on the role and importance of food, the cultural and social traditions associated with it, and the related views on the production processes for the different ingredients) varies considerably within Europe and worldwide. The Group also acknowledges that European citizens have different perceptions and (religious) beliefs as regards the consumption of meat or other products derived from cloned animals and/or their progeny[91]. However, there are no

[91] In this respect the consumption of milk from cloned animals may probably have a different impact on public perception than consumption of meat from clones.

definitive indicators as yet on the public perception of animal cloning for food supply and food products derived from cloned animals and their offspring. The Group therefore recommends that the Commission launch a thematic Eurobarometer survey on animal cloning for food supply, in order to collect indicators on public perception on the introduction of such products on to the food market as is being done in other countries[92].

5.7 Traceability and labelling

Traceability and labelling raise many issues, which can be related to the well-known precautionary principle, and are relevant to safety concerns, economic fairness, fairness in the burden of proof as well as to the earlier discussed issues of consumer freedom. In addition to this, it also raises issues of conditions of liability.

As far as the labelling of food products derived from animal cloning is concerned, the Group is of the opinion that consumer freedom can only be achieved when consumers have sufficient information to be able to choose the kind of products they want. In order to protect consumer freedom of choice, the Group asks for the enforcement of current EU legislation on food regarding traceability of animals and their food products (e.g. Directive 2000/13/EC)[93]. However, the Group is aware of the technical difficulties and costs of labelling products from offspring (information on ancestors), and calls on the Commission to devise targeted procedures (e.g. positive labelling of meat) prior to the marketing of such food in the EU[94].

5.8 Intellectual property issues

So far, patenting in animal cloning is limited to nuclear transfer techniques. The Group is concerned that patents might be extended to specific genes or to animals, and that this would lead to a monopoly/concentration of the resources that are important for breeding.

The Group also advocates further clarification, inter alia, through research, on the applicability of the exclusion clauses in Directive 98/44/EC (Art. 6) and the EPO rules (23 d) to animal cloning for food supply[95].

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[92] http://www.ap-foodtechnology.com/news/ng.asp?n=82108-farm-bill-cfs-cloning

[93] See Chapter 3.1.1 of this Opinion.

[94] The Group is aware that additionally to technical difficulties, additional costs to consumers will arise in consequence of the implementation of a broad labelling system.

[95] EPO: *Rule 23d "*Exceptions to patentability Under Article 53(a), European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following: (a) processes for cloning human beings; (b) processes for modifying the germ line genetic identity of human beings; (c) uses of human

5.9 Global trade

EU rules require the respect of animal welfare and animal ethics in breeding programmes. On the other hand, WTO agreements are based on the requirement that only scientifically documented risks to human health or to the environment can legitimately be used as a reason to limit free trade. If meat from cloned animals is to be marketed in third countries, it could be exported to the EU. This presents a dilemma between free trade considerations on the one hand and ethical concerns regarding the cloning of animals on the other. Resolving this political dilemma is not easy. On the one hand, ethical considerations, including animal welfare, are seen as crucial – also in terms of public perception – while on the other hand import issues, including WTO compliance, may complicate the market situation[96].

The Group acknowledges the complexity of the issue, but points out that there are already some examples of specific requirements in the EU covering the import of meat and food products from third countries, for example as regards the import of meat containing hormones. The Group therefore considers that the import of cloned animals, their offspring and materials derived from cloned animals (e.g. semen and food products, as described in 3.1 and 3.3) should be conditional on the documentation as indicated in this Opinion, in particular with regard to traceability provisions and animal welfare.

The Group notes the statement in the preamble and in Article 2 to the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) that members should not be prevented from adopting or enforcing measures necessary to protect animal health, subject to the requirement that these measures are not applied in a manner which would constitute a means of arbitrary or unjustifiable discrimination between members. It also notes Article 5(7) of the Agreement relating to risk assessment. There is not enough scientific evidence on cloned animals and their offspring, and the Group believes that research is required as described in the EFSA report.

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embryos for industrial or commercial purposes; (d) 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."
(http://www.european-patent-office.org/legal/epc/pdf/epc_2006_v5_bm_en.pdf)

[96] For further considerations, please see: *Challenges in regulating farm animal cloning. Recommendations from the project 'Cloning in public',* J. Gunning, M. Hartlev, C. Gambrog et al., Danish Centre for Bioethics and Risk assessment (2006).

5.10 Conclusions

The Group is aware of the EFSA draft scientific findings and recommendations on food safety, animal health and welfare and environmental impact, as well as the indications of current gaps in knowledge about animal welfare and health of animal clones and their offspring. The group is also aware on the results of the FDA report published the day before the adoption of this Opinion.

Considering the current level of suffering and health problems of surrogate dams and animal clones, the Group has doubts as to whether cloning for food is justified. Whether this applies also to the offspring is open to further scientific research.

At present, the EGE does not see convincing arguments to justify the production of food from clones and their offspring[97]. If in the future food products derived from cloned animals were to be introduced to the European market, the EGE recommends that the following requirements are met:

> *Food safety* - The safety of food products for human consumption as a pre-condition for their marketing must be guaranteed and scientific updates and follow up research into progeny should be carried out.
>
> *Animal welfare and health* - In accordance with the Amsterdam Treaty (animals as sentient beings) and the Lisbon Treaty, additional requirements should be met in intensive animal breeding, with the aim of following the guidance on animal welfare provided by the World Organisation for Animal Health (OIE), e.g. the five freedoms: from hunger, thirst and malnutrition; from fear and distress; from physical and thermal discomfort; from pain, injury and disease; and to express normal patterns of behaviour.
>
> *Traceability* - Current EU legislation on food regarding traceability of animals and their food products should be enforced. It should be ensured that EU legislation provides for the ability to identify individual animals where necessary.
>
> *Global trade* - The import of cloned animals, their offspring and materials derived from cloned animals (e.g. semen and food products) should be conditional on proper documentation, in particular with regard to traceability provisions and animal welfare.

In addition the EGE recommends that:

Animal welfare - Further studies and analyses on long-term animal welfare and health implications for clones and their offspring, as well as more comparative analyses with other assisted and traditional reproductive technologies in animal farming, should be carried out for a proper assessment of this issue, in line with EFSA draft opinion. The Commission should take initiatives to prepare a Code of Conduct on responsible farm animal breeding, including animal cloning.

Farm animal biodiversity and sustainability – The Commission should take proper measures to preserve the genetic heritage of farm animal species, for example by funding projects that aim to preserve domesticated breeds in Europe and to promote sustainable agriculture.

Public participation - Public debates should be promoted on the impact of farm animal cloning on agriculture and environment, on societal impact of increasing meat consumption and rearing of bovines, as well as on the fair distribution of food resources. The Commission should take a pro-active role in promoting public discussion on the use of animal cloning, and its potential implications, by financing a number of *ad hoc* initiatives aimed at promoting public debate on the marketing of food products derived from animal cloning.

Public perception - The Commission should launch a thematic Eurobarometer survey and qualitative studies on animal cloning for food supply, in order to collect indicators on public perception concerning the introduction of such products to the food market as is being done in other countries.

Labelling – The EGE is aware of the technical difficulties of labelling products from offspring, nevertheless it recommends that the Commission takes the initiative to devise targeted procedures prior to the marketing of such food in the EU.

Intellectual property issues – It should be clarified whether the exclusion clauses in Directive 98/44/EC (Art. 6d) on patentability of biological inventions and the EPO rules (23 d) to animal cloning for food apply.

Global trade and consumer's freedom – The EGE is aware that import issues of food products derived from cloned animals, including compliance with World Trade Organisations provisions, may complicate the market situation, however, the EGE recommends that the Commission takes initiatives to ensure consumers' freedom and rights.

Research - Further research is needed, in particular basic research on animal cloning, as well as impact on human health, animal welfare for farmed species other than those covered by EFSA. Similarly, further ethical, legal and social implications of animal cloning for food supply as well as qualitative studies on public perception should be carried out.

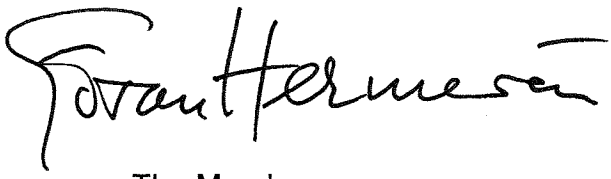
[97] The conclusion in this paragraph was dissented by K. Marczewski.

5.11 The need for revision of this Opinion

Since further research is needed and cloning technologies are constantly improving, this Opinion could be reconsidered, and possibly revised, in the light of new scientific data and societal considerations.

The European Group on Ethics in Science and New Technologies

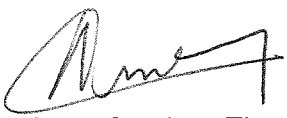
The Chairperson: Göran Hermerén



The Members:

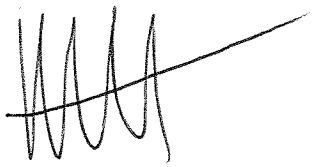
Emmanuel Agius

Francesco Busnelli Diana Banati



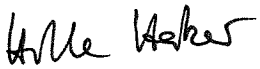
Anne Cambon-Thomsen

Rafael Capurro



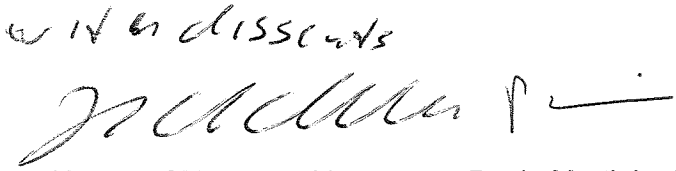
Inez de Beaufort

Jozef Glasa



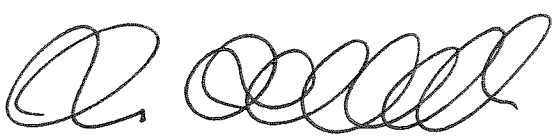
Hille Haker

Julian Kinderlerer

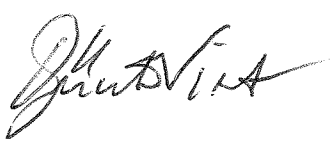


Krzysztof Marczewski Paula Martinho Da Silva

Linda Nielsen



Pere Puigdomenech-Rosell



Günter Virt

Krzysztof Marczewski
Member of EGE

In full respect for different ethical preferences of other EGE members I can not agree with following sentences of our opinion Nr 23 in the conclusion part:

"Considering the current level of suffering and health problems of surrogate dams and animal clones, the Group has doubts as to whether cloning for food is justified" and "At present, the Group does not see convincing reasons for the production of food from clones and their offspring".

The reasons for my disagreement are very probable, partially already mentioned in the opinion, numerous benefits for humans, connected with animal cloning for food supply. Therefore I am not seeing convincing ethical reasons for unnecessary delaying in introducing this technique and its products in to the European Food Market.

I expect in long time perspective positive impact on both economy (growth impulse) and ecology (restoring of biodiversity). I believe also that cloning of animals for breeding will have as consequence beneficial effects on both human health and animal welfare. The problem of obesity and type 2 diabetes connected with consumption of to feat meat, possible could be partially solved with introducing better quality meat from selected animals. Current argument for possible benefits for animals health is killing of thousands cattle because of BSE and now birds due to avian influenza, probably unnecessary by selected races.

But the most important cause of my disagreement is the need to protect the right to informed free choice of consumers which is for me close connected with the dignity of human beings. I suppose that probably only the minority of European will at present buy food based on cloned animals but the protection of the minority rights is a mile stone of democracy.

For me as physician, if currently in EU are not prohibited or seriously limited the traditional forms of breeding (e.g. *foie gras*) detrimental to the welfare of thousands of animals and very probably not specially healthy for humans and what's more if the cultivation of tobacco are not only tolerated but also supported which is at sure connected with suffering and death of millions of people, including the involuntary passive smokers, the arguments expressing doubts because of possible affected welfare of few cattle and pigs are not convincing. Especially if the veterinary problems connected with cloned animals are comparable with other already accepted techniques of artificial reproductions.

If we decide that the protection of people and animals are more important than the consumer's right to free choice we should, without doubts, begin from absolutely ban for tobacco.