Department for Environment Food & Rural Affairs

Farm Animal Genetic Resources Committee

FAnGR

Statement on cloning of farm animals

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Non-technical summary

- Cloning involves the removal of the nucleus from a somatic cell (any body tissue) of an animal and its transfer into an enucleated egg (an egg cell that has had its own nucleus removed) of a donor female of the same species. This is then stimulated to generate an embryo for transfer into a surrogate mother.

- As more than 99% of an animal's genes are contained within the DNA that is housed in the cell's nucleus (and identical in most cells throughout the body), embryos generated through cloning are essentially 'identical copies' of the animal providing the donor DNA.

- The remaining (<1%) genes are contained within the DNA of mitochondria, small organelles within the donor egg cell but outside of the nucleus. Some of these genes have a key role in controlling cell division and development of the early embryo.

- Current approaches for cloning farm animal species do not involve any genetic modification. The primary aim in using cloning is to reproduce an existing animal rather than to create one with novel DNA.

- Generally, progeny produced through cloning are completely normal and indistinguishable from naturally produced offspring. However, in past trials, some progeny have not developed normally, leading to significant welfare problems and premature death. This is likely due to a failure of 'mitochondrial genes' to function normally.

- Many of the original drivers for using cloning can now be achieved by using newer technologies such as genome wide selection and genome editing, but it could still have a key role in the conservation of rare breeds.

- Commercial cloning of bulls has been taking place on a regular basis in the USA, Argentina and Brazil to increase the number of high genetic merit animals providing semen for commercial use in both the home and overseas markets.

- There is currently no way of differentiating animals or animal products, including semen and embryos, deriving from either a healthy clone, its progeny or from those of conventionally bred animals.

- EU legislation regards foods and food ingredients derived from clones as novel foods. However, the European Commission and both the European Food Safety Authority and the UK Food Standards Agency all acknowledge that meat and milk from healthy clones and healthy offspring of clones is indistinguishable from, and as safe as that from, conventionally bred animals.

- The Committee believes that both UK and EU policy should be based on evidence, and as such does not consider that there is any scientific justification for treating the products of the healthy offspring of clones, including semen and embryos, any differently from conventionally bred animals with regard to the production of food.

Statement on cloning of farm animals

1. As part of its work plan the Committee considers that it may be helpful to set out its views on the cloning of farm animals.

2. The Committee recognises that science is continually evolving and that cloning is part of a continuum of developments in reproductive techniques including artificial insemination, embryo transfer, embryo splitting (which also occurs naturally in the creation of identical twins), *in vitro* fertilisation, blastomere nuclear transfer, and foetal and adult somatic cell nuclear transfer. This statement relates to cloning by somatic cell nuclear transfer (SCNT).

3. Cloning methods being used in farmed animals do NOT involve genetic modification: the intention with cloning is to reproduce an existing animal, rather than to create one with novel DNA that has not existed before.

4. SCNT has a lower success rate (*i.e.* fewer viable offspring per embryo transferred) compared with non-cloned embryo transfer and the process of cloning can in some instances produce animal welfare concerns in the resulting progeny, both probably due to dysregulation of mitochondrial genes. Risks relevant to this Committee's remit are those concerned with managing genetic diversity. The Committee recognises that the animal welfare consequences of new technologies must be considered carefully, and other bodies may wish to comment on issues such as welfare and consumer confidence.

5. Animals have the vast majority (>99%) of their DNA (containing its genes) in the cell nucleus and a minute fraction (<1%) in the mitochondria within cells but outside the nucleus. A cloned animal receives its mitochondrial DNA from the donor of the recipient egg, and the nuclear DNA from the donor of the somatic cell nucleus, and is therefore essentially an 'identical copy' of the animal providing the somatic cell. Both will be copies of DNA already existing in the population.

6. Cloning has a potential role in conserving rare breeds that would otherwise be at risk of extinction following a disease outbreak, or in the case of a severe decline in a population. These boosted populations could then continue using conventional breeding to multiply further. Genetic diversity of these breeds could also be increased by breeding from clones of unrelated castrated males, or unrelated females unable to breed successfully unaided. However, in those species in which embryo transfer is effective, the cryopreservation of embryos, ova and semen are more desirable methods to be used for conserving rare breeds, as combined they conserve all the DNA (nuclear and mitochondrial) of the breeds in question

7. There is a theoretical benefit that by reproducing "copies" of desirable animals, it is possible to allow more farmers to access animals of high genetic merit (for improving food production, food quality, disease resistance *etc*.) more quickly. However, the cost and the success rates make this commercially unfeasible in the EU at present.

8. In the past cloning would also have been a necessary step to allow implementation of approaches such as genome editing that could be used to overcome challenges presented by inherited diseases in small populations. However, the Committee notes that recent advances in highly targeted genome editing approaches mean that cloning is no longer a necessary step to achieve this.

9. While it was initially suggested that desirable attributes (*e.g.* resistance to disease, improved productivity, lower greenhouse gas emissions) could be spread more rapidly and more widely with the use of cloning, recent developments in genomics have allowed the introduction of new approaches such as Genome Wide Selection which offer an alternative method for improving such traits within populations relatively quickly, whilst also maintaining a good level of genetic diversity. As such they also offer the potential for greater levels of overall improvement over time and, unlike cloning, rely on traditional animal breeding technologies.

10. The Committee understands that commercial cloning has been taking place on a regular basis, particularly in the USA, Argentina and Brazil. In these countries there are currently no regulations restricting legal export of healthy clones, their offspring, semen or embryos, or products derived from clones or their offspring, and there is no labelling requirement to allow additional controls in importing countries. At the same time, since there is currently no way of differentiating animals or animal products deriving from a healthy clone or the offspring of a healthy clone, it would be impossible to ensure full traceability.

11. The Committee notes that substantial work has been carried out by the European Commission and by the European Food Safety Authority (EFSA) on food safety in relation to cloning, while the Food Standards Agency (FSA) is responsible for food safety in the UK. All bodies share a similar view that the current evidence suggests that meat and milk from healthy clones and healthy offspring of clones is as safe as that from conventionally bred animals.

12. The Committee notes that EU legislation regards foods and food ingredients derived from clones as novel foods which must be assessed and approved at EU level before they can be placed on the market. Legislation on novel foods is the subject of current EU negotiations, including discussion of future applicability to foods and food ingredients derived from clones. This legislation does not cover trade in cloned animals or semen, ova, embryos or offspring from clones.

13. The Committee does not consider that there is any scientific reason for treating the healthy offspring of clones differently from other animals with regard to the production of food. This applies to both the first and subsequent generations of offspring. The Committee recognises that clones themselves have been achieved by novel procedures and there is a case for subjecting them to special scrutiny, but this case does not apply where healthy clones produce healthy offspring through conventional breeding practices, including artificial insemination and embryo transfer.

14. The Committee believes that UK and EU policy should be based on evidence, should take account of benefits as well as risks, and should be proportionate to the risks. It should also be enforceable. In these respects, the Committee considers that cloning can offer benefits and that from a scientific viewpoint, restrictions on the offspring of healthy clones and products from those offspring would be disproportionate and currently unenforceable especially in relation to imported products.

Notes

1. The Farm Animal Genetic Resources Committee provides technical advice to Defra and Devolved Administrations on matters relating to the conservation and sustainable use of farm animal genetic resources.

2. The first viable cloned farm animal from an adult somatic cell was Dolly the sheep, born in the UK in July 1996. Since then, cloning techniques based on using adult cells have developed, although it remains a young technology. Cloning is expensive and is likely to remain confined to niche uses in agriculture for many years to come. The farm livestock most likely to be cloned are high value cattle and pigs. There are very few cloned cattle and pigs relative to the size of the world's cattle and pig populations. There are only a small number of elite bulls in the world and it is mainly these that are being commercially cloned.

3. Birds cannot currently be cloned. Furthermore, the different structure of their ova mean that cryopreservation of ova for breed preservation purposes is not feasible. However, recent developments in the isolation, cryopreservation and transfer of progenitor germ cells (PGCs) from very early embryos, which during development differentiate into those responsible for the production of ova and sperm, offers an exciting new method for breed preservation of rare poultry.

4. During the natural process of cell division the chromosomes, made up of DNA, are copied, with one copy going to each daughter cell. While there are 'proof-reading' processes in place to maximise the probability that an exact copy is produced, occasionally mistakes (naturally occurring 'mutations') do occur. Such mutations may involve something as small as a single base substitution within the individual gene (a 'single nucleotide polymorphism' or SNP) and can alter the structure of the individual gene products coded for by that specific gene, increasing or decreasing their biological activity within the body.

5. The accumulation of such mutations over time creates so called 'allelic variations' (polymorphisms) of individual genes across the whole genome, and this gives rise to genetic diversity within all animal populations. These polymorphisms underlie variation in performance, disease resistance *etc.* within breeding populations.

6. Genome Wide Selection involves identifying SNPs along the whole genome of individual animals, associating variation in each one with attributes of interest (*e.g.* carcass composition, meat quality, disease resistance, milk yield *etc.*) and then selecting animals to be parents of the next generation based on the most desirable SNPs.

7. The main risks from cloning relate to ensuring that: animal welfare requirements are met; any differences between clones and conventionally bred animals are understood and addressed; high level use could result in higher inbreeding and reduced levels of genetic variation in populations which could undermine biodiversity and progress using conventional selective breeding approaches; and that consumer confidence is maintained. Of particular note are:

- the welfare of donors, recipients and clones themselves should be an important consideration, but there are no welfare issues for offspring of healthy clones separate from those that already apply to other animals produced through conventional breeding;

- Breed Societies and breeders need to be alert to the need to take steps to minimise inbreeding and to ensure sufficient diversity within breeds to ensure their future 'genetic health'. Diversity is the basis of breed improvement and, other than improved dissemination of a few elite animals, cloning cannot contribute to the continuous process of breed improvement through selection;
- consumer confidence is of course important, but is for others to address. It depends on openness and honesty; in this context, the extent to which cloned animals, their first generation offspring, and subsequent generation offspring have already been widely dispersed must be taken into account. The reality is that there is no way of testing animals or their products, including semen or eggs, to determine if they are clones or are derived from clones. Nor is it possible to identify animal products from all animals in the EU or outside the EU which may have a cloned animal in their ancestry.

8. In January 2008, the US Food and Drug Administration published a risk assessment of animal cloning, which is available at www.fda.gov/cvm/cloning.htm.

9. In July 2008, the European Food Safety Authority (EFSA) published its opinion on animal cloning, which is available at http://www.efsa.europa.eu/en/scdocs/scdoc/767.htm. This was subsequently up-dated by statements in:

2009 (http://www.efsa.europa.eu/en/efsajournal/pub/319r.htm),
2010 (http://www.efsa.europa.eu/en/efsajournal/pub/1784.htm), and
2012 (http://www.efsa.europa.eu/en/efsajournal/doc/2794.pdf).

These reports clearly conclude that there is no indication of any difference for food safety of meat or milk of clones and their progeny compared with conventionally bred animals.

10. In December 2013 the EU produced draft proposals for (i) a Directive on the cloning of animals of the bovine, porcine, ovine, caprine and equine species kept and reproduced for farming purposes: (http://ec.europa.eu/food/food/biotechnology/novelfood/documents/proposal_2013-0433-cod_en.pdf) and (ii) for a Directive on the placing on the market of food from animal clones: (http://ec.europa.eu/food/food/biotechnology/novelfood/documents/cloning-2013-0433_app_en.pdf).
The first of these prohibits the use of cloning or import of animal clones of 'animals kept and reproduced for farming purposes' while the second prohibits the placing on the market of food from animal clones, including that imported from outside of the EU.

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