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CHALLENGES IN REGULATING FARM ANIMAL CLONING

An assessment of regulatory approaches and the legal framework within the EU

Jennifer Gunning, Mette Hartlev & Christian Gamborg

PROJECT REPORT 13

DANISH CENTRE FOR BIOETHICS AND RISK ASSESSMENT

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Project report 13
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Challenges in regulating farm animal cloning:

An assessment of regulatory approaches and the legal framework within the EU

Report from the project Cloning in Public
A specific support action within the 6th framework programme, priority 5: Food quality and safety

Coordinator:
Danish Centre for Bioethics and Risk Assessment (CeBRA)
http://www.bioethics.kvl.dk

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1 Introduction

This report is the sixth deliverable from the project "CLONING IN PUBLIC; a specific support action within the sixth framework programme, Priority 5, Food quality and safety" (Contract no. 514059).

The overall aims of CLONING IN PUBLIC are: (a) to develop recommendations on European regulation of, and guidelines covering, research on farm animal cloning and its subsequent applications (e.g. in genetically modified animals for bio-reactors); and (b) to stimulate informed public debate across Europe on these issues in which key stakeholders, university students and members of the public participate. These aims are of equal importance. Clearly, they are also interrelated, because if regulations and guidelines are to serve their purpose, they must take public concerns into account. In addition, stimulating, informing and reporting public debate is part of the more general and long-term aim of improving communication between science, civil society and European authorities at different levels, and hence facilitating discussion, within Europe, of public affairs connected with science and technology.

The main objective of this report is to assess the legislative framework currently in place. Before any further action is taken at the European level, however, it must be decided whether existing EU legal instruments already provide sufficient control, and whether any further controls, if these are needed, would be better addressed at national level, through professional self-regulation or indeed by the action of market forces. The report presents the current regulatory situation. Adopting on a risk analysis approach and referring to a broader set of concerns (including, for example, worries about animal integrity), it asks whether there are gaps in the present legal framework. The report considers overall regulatory approaches to meet potential gaps, looking at regulatory aims (e.g. ensuring food safety), levels (e.g. national), models (e.g. prohibition) and related regulatory tools (e.g. statutory law). It takes into account both scientific and commercial developments, as well as public and stakeholder opinion.

An earlier version of this report was used as input to a legal and ethical aspects workshop in Prague, 23–25 November, 2005.[1] The workshop's objectives included identifying and discussing the considerations that recommendations on regulation and legislation must take into account and developing different scenarios of regulation that can form a basis of dialogue with stakeholders and the public. A *third* and final legal report will be prepared. This will be a synthesis of the present report and the first legal report as well as the legal-ethical workshop. It will contain recommendations on the regulation of farm animal cloning and serve as input to a concluding participatory conference of the CLONING IN PUBLIC project to be held in October 2006.

In this report the term "cloning" refers to *asexual reproduction* – or, more precisely, to the production of individuals with virtually identical genetic material by asexual reproduction. In recent debates, interest has centred on cloning by somatic cell nuclear

[1] See http://www.sl.kvl.dk/cloninginpublic/.

transfer (SCNT).[2] The term "farm animal" refers to farm animal species such as ruminants (e.g. cows, sheep), pigs and poultry (chicken, turkey). The term does *not* imply that an animal is kept or used in an agricultural setting or for agricultural purposes. Thus, the potential application of a cloned farm animal species may be in medicine (see the first technical report from the CLONING IN PUBLIC project, 2005). The report does not cover legislation applying exclusively to genetically modified animals. However, where legislation may reasonably be suspected of covering cloning *as well as* genetic modification, regulatory aspects of genetic modification are indirectly covered.

CLONING IN PUBLIC reports on the scientific, legal and ethical aspects of farm animal cloning are publicly available. All project reports, as well a list of project deliverables, presentations, work plans and workshops are available at the project website: http://www.sl.kvl.dk/cloninginpublic/

This report has been prepared by Dr Jennifer Gunning, Centre for Ethics, Law & Society, Cardiff Law School, Cardiff University, Dr. Mette Hartlev, Faculty of Law, University of Copenhagen and Dr. Christian Gamborg, the Danish Centre for Bioethics and Risk Assessment at the Royal Veterinary and Agricultural University. We would like to thank Paivi Männerkorpi, Kai Uwe Sprenger and Andrew Tommey from DG SANCO for helpful comments on and input to an earlier version of the report. We would also like to express our great thanks to Dr. Paul Robinson.

The picture on the front page of this report was downloaded from the Roslin Institute Image Library: http://www.roslin.ac.uk/imagelibrary/.

[2] For further explanation, see the CLONING IN PUBLIC report "The science and technology of farm animal cloning" available at http://www.sl.kvl.dk/cloninginpublic/.

2 Current EU legislation

Within the EU regulation can be introduced either in binding legal instruments (regulations, directives and decisions) or in non-binding instruments (recommendations and opinions), see Table 1.

Table 1. Regulation at the European level – regulatory modalities

Modality	Description
Regulation	The most directly applicable of the legal instruments since it takes immediate effect in the Member States and requires no further national legislation.
Directives	While binding on the Member States as to the objectives to be achieved, directives leave it up to each Member State how this will be done through national legislation. This can lead to inconsistencies between Member States as to the implementation and rigorousness of the legislation introduced.
Decision	An instrument whereby Community institutions give a ruling on a particular matter requiring Member States (or even an EU citizen) to refrain from taking a particular action or to confer rights. A decision differs from regulations and directives in that it is specific about those to whom it is addressed and is wholly binding on them.
Recommendations and Opinions	Non-binding instruments that encourage or allow lines of action to be proposed by institutions or advisory bodies without imposing any legal obligations. Such instruments may, however, form the basis of later binding legislation.

It should be borne in mind that the principle of subsidiarity is embedded in the Treaty establishing the European Community (Article 5). This limits the exercise of power by the EU by ensuring that matters should be left to the Member States at national level unless it is more appropriate for action to be taken at European level.

No specific, binding legal instrument has been passed on animal cloning in the EU, although, as was noted in the first legal report of this project, the issue does appear as part of a non-binding Opinion of the European Group on Ethics.[3] As was also noted in the first legal report, there is a body of binding legislation in the form of regulations and directives addressing issues such as food safety and animal health and welfare; these issues are the principal ones raised by farm animal cloning. Additionally, zootechnical legislation allows for free trade in breeding animals, and so it may be of relevance to cloned animals used for breeding purposes; animal identification legislation allows the tracking of farm animals. A collection of measures addressing genetically modified organisms would apply to cloned genetically modified animals. Consumer protection is largely dealt with in novel food and labelling regulations.

[3] Opinion of the group of advisers on the ethical implications of biotechnology to the European Commission. Ethical aspects of cloning techniques, 28 May 1997.

2.1 The Treaty on the Establishment of the European Community

According to Article 2 of the Treaty on the Establishment of the European Community (TEC) The Community shall have as its task to promote "…a harmonious, balanced and sustainable development of economic activities, a high level of employment and of social protection, equality between men and women, sustainable and non-inflationary growth, a high degree of competitiveness and convergence of economic performance, a high level of protection and improvement of the quality of the environment, the raising of the standard of living and quality of life, and economic and social cohesion and solidarity among Member States". The free movement of goods, services, persons and capital is an essential element of the internal market. This is reflected in a number of the more specific provisions in TEC – for example, those covering quantitative restrictions between Member States (Articles 28-31) and the common agricultural market (Articles 32-38). Protection and improvement of the environment are also of central concern (Articles 95 and 174-176), as is the protection of consumers (Articles 152-153).

2.2 Food safety and consumer protection legislation

If meat from SCNT-cloned animals were to reach the food market, questions about consumer protection and consumer rights would inevitably arise. The focus of consumer *protection* regulation is on the health and safety of the consumer. The concept of consumer *rights* is a broader: in addition to health and safety, it also covers the consumer's right to be informed and the right to self-determination or free choice. Suppose, for example, that meat from a SCNT-cloned cow could be detrimental to the health of human beings. That would have implications for both consumer safety and consumer rights. If, on the other hand, the meat were perfectly safe, only consumer rights would be relevant: the issue being whether the consumer has a right to be informed about the cow being cloned in order to be able to exercise a free choice.

There are a number of EU directives and regulations on consumer protection and the consumer's rights. None of these instruments specifically refers to animal cloning, but the instruments might have an impact on the marketing of food products from cloned animals. The most relevant and important legal sources are:

- Regulation (EC) No 258/97 concerning novel foods and novel food ingredients
- Regulation (EC) No 1139/98 concerning the compulsory labelling of certain foodstuffs produced from genetically modified organisms
- Regulation (EC) No178/2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority, and laying down procedures in matters of food safety
- Regulation (EC) No 1829/2003 on genetically modified food and feed
- Regulation (EC) No1830/2003 concerning the traceability and labelling of food and feed products produced from genetically modified organisms and amending Directive 2001/18/EC
- Regulation (EC) No 641/2004 giving detailed rules for the implementation of Regulation (EC) 1829/2003

- Recommendation 97/618/EC of 29 July 1997 concerning the scientific aspects and the presentation of information necessary to support applications for the placing on the market of novel foods and novel food ingredients, and the preparation of initial assessment reports under Regulation (EC) No 258/97 of the European Parliament and of the Council
- Recommendation 2004/787/EC on technical guidance for sampling and detection of genetically modified organisms and material produced from genetically modified organisms as or in products in the context of Regulation (EC) 1830/2003
- Directive 2000/13/EC on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs

Generally speaking, food regulation imposes general requirements on all kind of foods in Regulation EC No. 178/2002[4] and Directive 2000/13. As a supplement to general food regulation, the EU has issued more specific and stricter regulation regarding so-called "novel foods" and genetically modified food.

The focus in *general food regulation* is on safety requirements, risk management, traceability, and labelling and presentation of foodstuffs (i.e. risk communication).[5] Regulation EC No. 178/2002 takes a "farm to food" approach, aiming to afford a high level of protection to human life and health but also taking account of animal health and welfare, plant health and environmental protection. It also establishes consumer rights to safe food and accurate information. The identification of the origin of feed and food ingredients and food sources is considered to be of prime importance in consumer protection. The traceability provisions of the Regulation became applicable from January 2005. They require businesses to identify at least the immediate supplier of a product and the immediate subsequent recipient (with the exemption of retailers to consumers). Regulation EC No.178/2002 also established the European Food Agency. The responsibility of this body for risk assessment will be discussed below. The regulation does not require prior authorisation to be obtained before a food product is put on the market. In addition to general requirements regarding safety and traceability it introduces provisions protecting consumer interests in making informed choices and the consumer's right not to be mislead. Consequently, it could be argued on the basis of this regulation that consumers must be informed if the origin of a food product is a cloned animal if they are not to be misled and hence if they are able to exercise informed choice.[6]

Special food regulation provides more specific and stricter regulation of novel foods and genetically modified food. It is of particular interest to consider whether food products from cloned animals fall within the scope of this stricter regulation. With regard to *GMO food regulation*, it is dependent on whether a cloned animal could be

[4] Member States are required to adapt their existing food law principles and procedures in line with the regulation by 1 January 2007.

[5] In addition to Regulation (EC) No 178/2002 and Directive 2000/13/EC there are number of other pieces of general food legislation addressing issues such as food hygiene, food contaminants, systems for food control.

[6] Article 16 in Regulation (EC) 178/2000 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety.

defined as a GMO (see subsection 2.6 of this report). If this were the case, food products from cloned animals would need to comply with the rules and procedures laid down in the regulation (e.g. they would need prior authorisation based on a risk assessment and labelling).[7] The labelling provisions require the words "genetically modified" or "produced from genetically modified organism" to appear clearly on the product. Furthermore, it must also be made clear if a food product may give rise to ethical or religious concerns.[8] The *novel food regulation* also sets up a system of risk assessment and prior authorisation, as well as conditions for use and labelling requirements. It is, however, questionable whether food products from cloned animals would fall within the scope of novel food regulation. Regulation (EC) No 258/97 concerning novel foods and novel food ingredients applies to foods and food ingredients which have not been used for human consumption to a significant degree (before 15 May 1997) and which fall under certain categories, such as "food 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 use" (Article 1(e)). Food from cloned animals could fall under this provision, as food ingredients from cloned animals have not previously been used for human consumption. Article 1(f) must also be considered. It stipulates that "foods and food ingredients to which has been applied a production process not currently used, where that process gives rise to significant changes in the composition or structure of the foods or food ingredients which affect their nutritional value, metabolism, or level of undesirable substances" are covered by the regulation. SCNT would without doubt qualify as a "production process not currently used", but as there is no scientific evidence that the food products from SCNT-cloned animals would be significantly different as regards their nutritional value (etc.) (see section 3 of this report), it is doubtful whether cloned animals would fall under the scope of Regulation (EC) No. 258/97.

Labelling is especially important where consumer rights are concerned. Labelling regulations may allow people to exercise choice in moral matters related to animal cloning. In foods, labelling has three basic purposes: identification, information and marketing. It is a legal requirement that consumers are provided with clear, accurate, understandable information, so that they make an informed choice. Further, consumers make social, ethical and lifestyle statements through their choice of foods or brands. In view of this, it is not only essential nutritional information that is provided, but also details of production methods, origin and so on. The labelling requirements in special food regulation are more demanding and clear than the requirement on consumer information laid down in general food regulation.[9]

2.3 Animal welfare legislation

The EU has already enacted a number of binding instruments on animal protection, including the protection of farmed animals. These include:

[7] Articles 4-11 in Regulation (EC) No 1829/2003 on genetically modified food and feed.
[8] Article 13 (2) b in Regulation (EC) No 1829/2003 on genetically modified food and feed.
[9] Article 8 in Regulation (EC) No 258/97 concerning novel food and novel food ingredients and article 12-13 in Regulation (EC) No 1829/2003 on genetically modified food and feed.

- Directive 86/609/EEC of 24 Nov. 1986 on the protection of animals used for experimental and other scientific purposes
- Protocol on the protection and welfare of animals to the Treaty of Amsterdam amending the Treaty on European Union, the Treaties establishing the European Communities and certain related acts, signed on 2 October 1997
- Directive 98/58/EC concerning the protection of animals kept for farming purposes
- Decision 2003/584/EC concerning the conclusion of the Protocol of Amendment to the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes

Animal welfare concerns are also articulated in a protocol to the Treaty of Amsterdam stipulating that "In formulating and implementing the Community's agriculture, 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".[10]

At present the cloning of animals is performed exclusively on an experimental basis. The general aim of Directive 86/609 and Directive 2003/65 is to set up common standards for the protection of animals used for *experimental and other scientific purposes* in order to avoid barriers to free trade. The directives refer to the principles of proportionality and minimal harm, and they set minimum standards, for example, governing the acquisition of animals, their housing and care, and the authorisation and control of an establishment and its personnel. These rules also cover the cloning of animals as part of an experiment and the use of cloned animals for experimental purposes. According to Article 24, Directive 86/609 does not restrict the right of individual Member States to apply or adopt stricter measures for the protection of animals used in experiments or for the control and restriction of the use of animals for experiments.

Cloned animals may in the future also be used for *farming purposes*. Directive 98/58 defines general requirements for the protection of animals kept for farming purposes. These requirements relate to, for example, housing and care, personnel and breeding procedures. Paragraph 20 of the Annex to Directive 98/58 prohibits use of breeding procedures (natural or artificial) that cause or are likely to cause suffering or injury to animals. This provision could be relevant to the use of SNCT-cloning, as such cloning may be associated with a range of animal welfare-related problems – for example, high death rate for newborn cloned animals, high birth weight (birth weights double the normal are not unusual leading to caesarean section) and deformities. It would need to be demonstrated that the problems associated with animal cloning were significantly different from, or more severe than, those related to other animal breeding technologies to require the enacting of further regulation.

[10] Protocol on protection and welfare of animals to the Treaty of Amsterdam, amending the Treaty on European Union, The Treaties establishing the European Communities and the related Acts (1997).

2.4 Animal identification legislation

Animal identification is an important part of traceability in animal production. Identification is addressed in several regulations which apply to different farm animal types:

- Regulation (EC) No 1760/2000 on bovine animals
- Directive 92/102/EEC on porcine animals
- Regulation (EC) 21/2004 on ovine and caprine animals

Special means of identification might be required for cloned animals or their offspring.

2.5 Zootechnical legislation

Zootechnical legislation aims to promote free trade in breeding animals and their genetic material compatibly with the sustainability of breeding programs and preservation of genetic resources. Such legislation is relevant here, because the cloning of farm animals will, if it happens, have much to do with the improvement of livestock and the preservation of genetic resources. Elite cloned breeding animals will have high export value and will need to be included in herdbooks and breeding lines. EU zootechnical legislation is species-based. The relevant directives here are:[11]

- Directive 77/504/EEC on pure-bred breeding animals of the bovine species
- Directive 88/661/EEC on the zootechnical standards applicable to breeding animals of the porcine species
- Directive 89/361/EEC concerning pure-bred breeding sheep and goats
- Directive 90/427/EEC on the zootechnical and genealogical conditions governing intra-Community trade in equidae. In the case of equidae, cloning is likely to be of value only for high performance competition horses which are often geldings; these will never be food animals.

Member states are not allowed to restrict trade in, and acceptance of, the breeding of so-called “pure bred” breeding animals, i.e. animals where both parents and grandparents are entered in a herd-book. The regulation does not specifically address how to consider a SCNT-cloned copy of a pure-bred animal, and it can be questioned whether such an animal would fulfil the requirement of having parents (plural). If the clone had parents, it could be entered in a herd-book. This would mean that Member States are not allowed to restrict imports of SCNT-cloned animals or germinal products from SCNT-cloned animals within the scope of the regulation (breeding purposes).[12]

2.6 Legislation relevant to GMOs

EU regulation pertaining to genetically modified organisms covers a number of issues. These include: the contained use of GMOs, the deliberate release of GMOs into the environment, the identification and traceability of GMOs, and the use, labelling and

[11] See http://europa.eu.int/comm/food/animal/zootechnics/legislation_en.htm for current zootechnical directives.

[12] The accepted understanding in DG-SANCO is that clones can be entered in a herdbook.

traceability of genetically modified food. The purpose of EU regulation in this area is first and foremost to protect human health and the environment against adverse effects caused by the release of GMOs into the environment. The most important legal instruments here on cloned animals are:

- Directive 90/219/EEC on the contained use of genetically modified microorganisms, as amended by Directive 98/81/EC.
- Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms, repealing Council Directive 90/220/EEC13
- Regulation (EC) No 1476/94 on Genetic resources in agriculture
- Regulation (EC) No 1946/2003 on transboundary movements of genetically modified organisms

The relevant parts of the Directive 2001/18/EC are Article 2.2 and Annex IA, which define what is meant by a "genetically modified organism". Article 2 states:

> "For the purposes of this Directive:
> (1) "organism" means any biological entity capable of replication or of transferring genetic material;
> (2) "genetically 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 the techniques listed in Annex I A, part 1;
> (b) the techniques listed in Annex I A, part 2, are not considered to result in genetic modification;
> (3) "deliberate release" means any intentional introduction into the environment of a GMO or a combination of GMOs for which no specific containment measures are used to limit their contact with and to provide a high level of safety for the general population and the environment;
> (4) "placing on the market" means making available to third parties, whether in return for payment or free of charge"

Annex IA, in describing the relevant techniques, states:

> "TECHNIQUES REFERRED TO IN ARTICLE 2(2)
> PART 1
> Techniques of genetic modification referred to in Article 2(2)(a) are inter alia:
> (1) recombinant nucleic acid techniques involving the formation of new combinations of genetic material by the insertion of nucleic acid molecules produced by whatever means outside an organism, into any virus, bacterial plasmid or other vector system and their incorporation into a host organism in which they do not naturally occur but in which they are capable of continued propagation;

[13] Directive 90/219/EEC is based on article 130S of the Rome Treaty, Directive 2001/18/EC is based on article 95 on the Treaty Establishing the European Community.

(2) techniques involving the direct introduction into an organism of heritable material prepared outside the organism including micro-injection, macro-injection and micro-encapsulation;
(3) cell fusion (including protoplast fusion) or hybridisation techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not occur naturally."

Generally speaking, Directive 2001/18 covers the step moving from contained use to the deliberate release of GMOs, both as part of a scientific experimentation and pursuant to marketing. The deliberate release of SCNT-cloned animals (or products deriving from these animals) must comply with the rules and regulations laid down in Directive 2001/18. The general aim of this directive is to ensure that the laws, regulations and administrative provisions of the Member States are approximately the same, and to protect human health and the environment where there is deliberate release of GMOs into the environment or where GMOs are placed on the market as products or product ingredients within the Community. The directive requires authorisation for the deliberate release of GMOs into the environment or the market; it introduces formal rules regarding, for example, risk assessment, scientific evidence and labelling, as well as the procedures to be followed by national authorities and the European Commission.

If genetic modification technology is used in connection with SCNT, the cloned animal will be a genetically modified organism and will therefore be covered by existing GMO regulation. However, it is also necessary to consider whether SCNT in itself involves genetic modification. If that is the case, all SCNT-cloned animals will fall under the scope of the GMO regulation. In connection with Article 2(2) in Directive 2001/18 there is disagreement among the scientific experts as to whether the use of SCNT in itself involves "alteration" of genetic material (see section 3 of the present report). Accordingly, it is not possible, on the basis of science, to say whether SCNT-cloned animals are GMOs. In addition to the scientific uncertainty, the wording of the directive also gives rise to uncertainty. Article 2(2) stipulates that within the terms of its definition of a GMO (see above), genetic modification will occur (among other things) through use of the techniques listed in Annex IA, Part 1. Now, among the techniques listed in Annex IA is the "…direct introduction into an organism of heritable material prepared outside the organism including micro-injection, macro-injection and micro-encapsulation". This description covers SCNT. Consequently it supports an interpretation favouring the definition of SCNT-cloned animals as GMOs even if no "alteration" of genetic material has taken place. However, the interpretation is also questionable, as the wording of Article 2(2) explicitly mentions "alteration" of genetic material which is most naturally understood as requiring change or amendment. This interpretation is also supported by the other two examples of techniques listed in Annex IA, Part 1, both of which refer to "new combinations of genetic material". However, any interpretation here needs to reflect the fact that the GMO legislation is intended to apply where *foreign* DNA is introduced into an organism.

If SCNT-cloned animals are covered by the GMO regulation, they will fall under either Directive 90/219 or Directive 2001/18, depending on the situation that arises. If SCNT-cloning techniques or SCNT-cloned animals are used in animal experimentation in "contained circumstances", they will fall under Directive 90/219 on contained use. The

purpose of the directive is to protect human health and the environment in connection with the contained used of GMOs.

If SCNT-cloned animals are not covered by the GMO regulation there are no special rules covering their contained use in experimentation or their deliberate release into the environment (for a further discussion, see subsection 4.5 of this report).

2.7 Intellectual property rights

Intellectual property rights could also have on impact on animal cloning. The European Patent Convention 1973 (EPC) and Directive 98/44/EC on the legal protection of biotechnological inventions (hereafter the Biotechnology Directive) regulate patents on biotechnological inventions. The directive aims to harmonise existing international conventions and requirements on the patentability of biotechnological inventions across Member States.

The Biotechnology Directive sets out requirements determining when an invention can be patented, but it does not control the utilisation of inventions. Such utilisation is a decision for national authorities, considering health, safety and environmental concerns. Equally, there may be other laws prohibiting the production or use of a biotechnological invention.

The Biotechnology Directive does provide some clarification on the patentability of inventions involving animals. It reiterates that plants are patentable, but that plant varieties – which can be legally determined – are not. When it comes to animals, there is no legal definition of an animal variety. Animal varieties are not patentable, but inventions relating to animals are patentable if the technical feasibility of the invention is not confined to a particular animal variety. This has important implications for genetically modified animals. Genes are patentable, not as such, but only in connection with a particular inventive step and a proven industrial application. The Administrative Council of the European Patent Office decided in 1999 that genetically modified plants and animals are patentable. It is worth noting that the directive explicitly extends the patentability of a process like cloning to all plant and animal varieties.

In the Biotechnology Directive it is stated that human cloning cannot be the subject matter of a patent. This limit reflects the wish of the European legislature to exclude inventions whose commercial exploitation would be contrary to public order and morality. However, no explicit mention of animal cloning is made in the directive. Since animal cloning is not explicitly included in the directive, the implication *could* be that animal cloning is patentable. Certainly, the patent authorities have previously accepted patents on GM animals such as Onco mouse. However, since the listing in the directive of non-patentable procedures and products is not exhaustive, it is possible that the patenting of a cloned animal would be considered contrary to public order and morality. And as a cloned animal is a copy of an existing animal, it could be difficult to fulfil the invention requirement (even if the techniques and procedures involved in the cloning are patentable).[14]

[14] See Laurie, G. 2003. Intellectual property protection of biotechnological inventions and related materials. Innogen working paper 4 for a discussion of this, and other biotech intellectual property right court cases.

To summarise, there is some uncertainty, at international and EU level, about the ownership and patentability both of the basic processes of animal cloning through SCNT, the patentability of the animals created thereby, and the patentability of derived products. The Biotechnology Directive (98/44/EC), while stating that human cloning cannot be the subject matter of a patent, is silent about animal cloning. There is a non-exhaustive list of unpatentable processes which may suggest, by omission, that animal cloning can be subject to patenting. However, since the listing of non-patentable procedures and products in the directive is not exhaustive, it remains possible that the patenting of a cloned animal would be considered contrary to public order and morality. In addition, the question remains whether the invention criterion would be satisfied by cloned animals.

3 Risk assessment

Farm animal cloning, like other animal biotechnologies, raises concerns about the potential hazards both of the technology and the products deriving from it. In essence, with cloned farm animals, this breaks down into risks to animal health and welfare and to food safety. So far few studies of the risks of farm animal cloning have been published. Those that have focus mainly on the composition of products (milk and meat) from cloned animals or their off-spring, and on the physical effects that SCNT-technology has on the physical welfare of the animals. Farm animal cloning has been related to high pre- and perinatal mortality, and cloning efficiency is certainly low at present. It has not been established to what extent these problems are the result of in vitro culture or the epigenetic and reprogramming effects of cloning. There is the possible risk that large numbers of clones of one individual might leave those clones more susceptible to disease. From the food safety point of view it needs to be established that food products from cloned animals or their offspring are as safe as those from normally bred animals.

The Codex Alimentarius Commission (CAC) of the UN Food and Agriculture Organisation (FAO) and The World Health Organization of the United Nations (WHO) produces a Procedural Manual in which the hazards associated with foods are addressed. Conduct of risk analysis is guided by general decisions of the CAC, including: (1) the Statements of Principle Relating to the Role of Food Safety and Risk Assessment,[15] (2) the Working Principles for Risk Analysis[16] and (3) the Principles for the Risk Analysis of Foods Derived from Modern Biotechnology,[17] all of which were adopted in 2003. These principles divide risk analysis into three elements: risk assessment, risk management and risk communication. For food derived from biotechnology the Working Principles require:

> the assessment of a whole food or component thereof relative to the appropriate conventional counterpart
> a) taking into account both intended and unintended effects
> b) identifying new or altered hazards
> c) identifying changes, relevant to human health, in key nutrients.

That is, a full comparative compositional analysis must be made of, in this case, food from cloned animals and their non-cloned counterparts. The risk assessment should be based on scientific, multidisciplinary investigation and use data from a variety of sources such as the developer of the product, the scientific and technical literature, independent scientists, regulatory agencies and international bodies.

Risk management is required to be proportional to the risk and includes such measures as appropriate food labelling, marketing and post-market monitoring. Where scientific uncertainties exist as to risk the precautionary principle may be applied as part of risk management. Risk communication requires transparency of process and appropriate consultation with experts, policy makers and the public at large.

[15] Codex Alimentarius Procedural Manual; Thirteenth Edition.
[16] http://www.fao.org/docrep/meeting/006/y9259e.htm
[17] CAC/GL 44-2003 – but this is silent as to whether it applies to cloned animals.

The appropriate EU risk assessment mechanisms are set out under Regulation EC 178/2002. Firstly, three of the five principal objectives of the European Food Safety Authority (EFSA) are issues of risk assessment. These are:

- To assess the risk of, and as appropriate, propose risk-related factors for specific groups of regulated substances, following notification procedures and time schedules defined by legislation (e.g. food additives, food flavourings and feed additives, including medicinal products, pesticides, GMOs and novel food).
- To monitor specific risk factors and diseases and provide scientific opinions on tests and other tools to control these diseases (e.g. the geographical BSE risk assessment or the monitoring of zoonoses or other food-borne zoonotic agents.
- To apply and promote new and harmonized scientific approaches and methodologies for hazard and risk assessment for food and feed.

The EFSA's risk assessments are carried out by its Scientific Committee, which is assisted in its work by eight specialist Scientific Panels. None of these panels is specifically set up to assess animal cloning, but there are panels on GMOs, on biological hazards and on animal health and welfare.

Secondly, following the adoption of Regulation EC 178/2002, a regulatory committee called the Standing Committee on the Food Chain and Animal Health (SCFCAH) was set up "to assist the European Commission in the development of food safety measures at all stages of the food chain". This committee is responsible for scrutinising and proposing any necessary regulatory amendments in formal Opinions which can be formally adopted by the Commission.

The methodology of risk assessment has been addressed by Rudenko et al.[18] and, more recently, by Kelly.[19] Rudenko et al. promote a two-pronged assessment methodology. First, they describe a Critical Biological Systems Approach (CBSA) designed to identify any subtle hazards which may lead to phenotypic variability, disruption in immune function or alterations in metabolism which may affect milk or meat composition. It is recommended in this approach that cloned animals are monitored from the postnatal period through all developmental stages to adulthood, using detailed blood and urine analysis of a large number of biological markers and parameters. The second approach is that of Compositional Analysis (CA), in which the products from cloned animals are compared with those of matched non-cloned animals. Kelly also recommends that molecular analysis should be included in a safety analysis of transgenic animals. Both authors agree that the two-pronged approach should have as its basis the twin hypotheses that:

a) a healthy animal is likely to produce safe food products;

b) food from healthy clones and their progeny that is not materially different from the conventional counterpart is safe.

[18] Rudenko, L et al. (2004), Food consumption risks associated with animal clones: what should be investigated? *Cloning Stem Cells,* vol. 6 (2), pp. 79-93

[19] Kelly, L. (2005), *Rev. sci. tech Off. Int. Epiz.*, vol. 24(1), pp. 61-74

3.1 Risks in the food chain – current knowledge

Critical Biological Systems Approach
It is generally agreed that cloned animals that are obviously unhealthy or display signs of deformity would not be considered fit to enter the food chain and therefore pose no risk. From the paper published by Rudenko et al. it would appear that there is very little data in the literature which could be used to inform a CBSA analysis, and there appear to be no published CBSA results.

Compositional Analysis Approach
In the US, where companies are ready to put products from cloned livestock on the market, the FDA has charged its Centre for Veterinary Medicine to evaluate food safety, animal health and environmental aspects of animal cloning. The FDA has imposed a moratorium on the marketing of food products until the risk assessment is complete.[20] The interim findings on food safety are:

> The current weight of evidence suggests that there are no biological reasons, either based on underlying scientific assumptions or empirical studies, to indicate that consumption of edible products from clones of cattle, pigs, sheep or goats poses a greater risk than consumption of those products from their non-clone counterparts. The level of certainty is highest for bovine clones, followed in decreasing order of certainty, by porcine, caprine, and ovine clones. Edible products from the progeny of healthy clones are likely as safe to eat as similar products from the progeny of non-clone animals, based on underlying biological assumptions, compelling evidence from the mouse model system, and limited data in the species evaluated. The one study of the composition of milk from bovine clones does not indicate any food safety concerns. The level of confidence that may be placed in these conclusions could be increased by additional data, particularly with respect to composition of edible products.[21]

The final report is still awaited, but it is widely anticipated that it will present a similar conclusion.

More recently groups from the University of Connecticut and a number of institutions in Japan have reported on a comparative analysis comparing over 100 parameters in the composition of meat and milk from beef and dairy cattle derived from cloned animals and breed-matched controls.[22] Their conclusion was:

> …that most parameters of the composition of meat and milk from somatic animal clones were not significantly different from those of their genetically matched comparators or industry breed comparators, and that all parameters examined in this

[20] http://www.fda.gov/bbs/topics/NEWS/2003/NEW00968.html
[21] http://www.fda.gov/cvm/Documents/CLRAES.pdf
[22] Tian, X.C., Kubota, C. et al (2005), Meat and milk compositions of bovine clones. *PNAS*, vol. 102, no. 18, pp. 6261-66

study were within the normal range of beef and dairy products approved for human consumption.

However, the researchers emphasise that the study was conducted as a pilot study with a relatively small number of clones derived from a single genetic source from each breed. It is suggested that more conclusive studies with large numbers of clones from different genetic backgrounds will be needed to increase confidence in the safety of such products. Walsh et al.[23] came to a similar conclusion looking at cloned dairy cows, but again the numbers are small.

Little work in the literature assesses the safety of the progeny of cloned farm animals. The publications that do attempt this[24,25] suggest that the progeny of cloned animals are unlikely to inherit any epigenetic disturbances resulting from their cloned parents. In model animals this appears to hold true even when the cloned animals have abnormal phenotypes.[26] It is believed that gametogenesis resets the epigenetic signals for gene expression so that offspring do not inherit epigenetic disturbances from their cloned parents.

3.2 Risks in other applications – current knowledge

Cloned farm animals could be used as *bio-reactors*. However, the risk of introducing new diseases (zoonoses) into humans when animals are used as medicine factories generates a serious need for these biological compounds to be thoroughly tested before commercialisation.

When it comes to *xenotransplantation*, use of nonhuman primates as donors has largely been ruled out owing to problems with raising them, welfare problems affecting the animals (e.g. isolation of the infants), and a suspected higher risk of transferring diseases from the donor to the human recipient. For example, it has been shown that endogenous retroviruses can be produced by porcine cell lines and infect human cell lines. A porcine lymphotropic herpesvirus has been identified. The risks associated with this virus and possible ways of excluding it from potential donor animals are as yet unquantified.

3.3 Risk assessment – gaps and uncertainties

It is clear that risk assessment, in the case of cloned animals and their progeny, remains at an early stage, and such studies as have been completed have been on relatively low numbers of animals. Some ongoing studies have yet to publish, and in Europe results are awaited from a programme of risk assessment of products derived from farm animal

[23] Walsh, M.K. et al. (2003), Comparison of milk produced by cows cloned by nuclear transfer with milk from non-cloned cows. *Cloning Stem Cells*, vol. 5(3), pp. 213-219

[24] Martin, M., Adams, C., Wiseman, B. (2004), Pre-weaning performance and health of pigs born to cloned (fetal cell derived) swine versus non-cloned swine. *Theriogenology* vol. 62(1-2), pp. 113-22

[25] Mir, B. Et al. (2005), Progeny of somatic cell nuclear transfer (SCNT) pig clones are phenotypically similar to non-cloned pigs. *Cloning Stem Cells* vol. 7(2), pp.119-25

[26] Shimozawa, N. et al. (2002), Abnormalities in cloned mice are not transmitted to the progeny. *Genesis* vol. 34(3), pp. 203-7

cloning that is being carried out by INRA in France. The INRA programme involves 77 adult cattle clones from 5 different genotypes. It also, at this stage, involves 12 offspring from clones and combines the CBSA and CA approaches. Nonetheless, the number of cases studied remains small, and it may be difficult to limit uncertainty in the absence of a larger number of cases. As the results of more risk assessment studies become available it may be possible to analyse their results, but plainly this will depend on the extent to which they investigate comparable parameters. Domestic animals do not normally produce toxins in edible tissues; therefore in non-transgenic cloned animals it is unclear what hazards should be looked for. Moreover, if the results of different studies are to be combined, there needs to be some form of consensus as to which biological parameters are likely to be indicative of a food hazard. Even in non-cloned animals, product composition, such as fatty acid composition of milk or meat, can be altered by external factors such as dietary intake.

3.4 Consequences for risk management measures

Risk management must be proportionate to risk and therefore would appear to require sound scientific underpinning. Hence, while scientific uncertainties exist, it would seem appropriate to invoke the precautionary principle. This is adumbrated in the Treaty of Maastricht, specified in Article 7 of Regulation EC/178/2002, and expounded in a Communication from the Commission.[27] Recourse to the precautionary principle is, officially, a central plank of EU policy, and the Commission takes the precautionary principle to belong in the general framework of risk analysis and of risk management in particular. The Communication is clear about the importance of distinguishing between reliance on the precautionary principle and the search for zero risk which is unlikely to be found in reality. In the US, the FDA has invoked the precautionary principle in imposing a moratorium on the introduction to the market of products from cloned animals. Although the EU may find it attractive to take the same action in the current circumstances, existing novel foods legislation probably makes a moratorium unnecessary. In looking at measures which may result from reliance on the precautionary principle, the communication from Commission concludes that "The decision to do nothing may be a response in its own right" and that "Recourse to the precautionary principle does not necessarily mean adopting final instruments designed to produce legal effects, which are subject to judicial review".[28] Whatever decision is taken, it will be a political decision based on the level of risk "acceptable" to the society on which the risk is imposed.

If, as expected, the publication of the FDA's final report on the risks associated with products from cloned animals finds substantial equivalence with products from non-cloned animals, the American moratorium is likely to be lifted and these products may enter the US food market. This would put pressure on the EU to allow trade. However, the Sanitary and Phytosanitary Measures Agreement (SPS) of the World Trade Organization (WTO) allows countries to act on trade to protect human, animal or plant life or health.[29] The SPS allows countries to set their own standards for food safety, but these regulations must be based on science. Member countries are referred to

[27] Communication from the Commission on the Precautionary Principle COMM (2000) February 2000.
[28] Ibid.
[29] The WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement).

international standards (in this case the FAO/WHO Codex Alimentarius Commission), but they may use measures which result in higher standards if there is scientific justification. They can also apply the precautionary principle where there is scientific uncertainty, but only as a temporary measure (SPS Agreement, Article 5.7). It is clear that if there is already a sufficient body of evidence that food products from cloned animals are safe, the EU will not be justified in preventing their importation.

Finally, there remains a key issue about how far risk assessment should go. Should it consider the offspring of cloned animals? This question is related to the issue of substantial equivalence.[30] Such equivalence involves comparison of the composition of the food (or feed) component under review with an existing food or feed (component) already consumed safely by humans or animals. If the component of food/feed is not found to differ, in respect of nutritional or anti-nutritional components, from its conventional counterpart, it is considered substantially equivalent. At the outset – e.g. when the evaluation was used in relation to genetically modified food – it was thought that if a genetically modified food was substantially equivalent to its traditional counterpart, a risk assessment would be unnecessary. However, since then it has been questioned whether showing that a food or feed component is chemically similar to its natural counterpart is adequate evidence that it is safe for human consumption.[31] The US relies more strongly (albeit less and less) on this evaluative approach than the EU. The European regulatory authorities now place far more emphasis on identifying any unintended consequences. Classifying a novel food as substantially equivalent to an existing, safe food no longer shows a risk assessment to be superfluous. Efforts are being made to improve testing methods for composition, toxicity and allergenicity. Thus, in contrast with the US situation, in the EU substantial equivalence guides or informs further safety assessments. In the US, scientific studies have not been able to show substantial differences. Hence, under US legislation, it may even be against the law to label products, because such labelling would refer to a non-existent difference (see section 4 of this report).

A “narrow” and a “wider” notion of risk assessment can be distinguished. The narrow sense applies to the standard approach, with risks being defined scientifically. In the wider sense, however, a broader range of risks are brought in to reflect the risk perceptions of the lay person. Studies have shown that ordinary people do not have the same perception of risk as scientists. Moreover, their choices are made with regard to scope of examination, time horizon, type of hazard and concerns addressed. The concept of risk is not unambiguous. Thus the factors that one chooses to take into account, the methodologies chosen to assess their relevance, and likelihood and the overall evaluation of what is an acceptable risk, are based on underlying value judgments that reflect the ethical perspective of the risk evaluator. At an expert workshop on the legal and ethical aspects in Prague, 2005 the most important of these choices were identified as:

[30] “Substantial equivalence embodies the concept that if a new food or food component is found to be substantially equivalent to an existing food or food component, it can be treated in the same manner with respect to safety (i.e., the food or food component can be concluded to be as safe as the conventional food or food component)” (Joint FAO/WHO Biotechnology and Food Safety Report, 1996, p. 4)

[31] See e.g. Millstone, et al. (1999) 'Beyond Substantial Equivalence', *Nature*, October 7.

- What specific biological compounds should be examined from the multitude of possibilities?
- For how long a time period should the risk assessment aim?
- For how many generations of animals should the risk assessment aim?
- How should scientific uncertainty be dealt with?
- Should risks to animal health only be discussed in relation to animals ready to enter the market-place or also encompass the large number of animals that may never make it so far due to the inefficiency of the technology?
- Should risk assessments focus on concerns about biological risks related to human health, animal welfare and the environment, or should they encompass a broader range of notions such as risks to social structures or animal integrity?

Clearly, these choices, which potentially affect the outcome of a risk assessment, need to be stated in a transparent way, along with the results of the risk assessment.

3.5 Conclusions

Within the EU a wide range of legislative measures exist under which the regulation of farm animal cloning could fall. However, apart from National legislation in Norway and Denmark, these measures do not address farm animal cloning *per se*.[32] Where transgenic animals are cloned, these will fall under existing GMO legislation, but only because they are genetically modified, not because they are cloned. Where cloned animals are created and reared in an experimental setting they are protected by the relevant animal protection laws. EU food law does not yet specifically address products from cloned animals or their offspring, but it includes the mechanisms to do so. Regulation (EC) No 258/97, Regulation (EC) No 178/2002 and Regulation (EC) No 1829/2003 require the implementation of proper risk assessment, including invocation of the precautionary principle if appropriate, before having recourse to further regulation.

From this examination of the current state of risk assessment of products from cloned farm animals and their progeny it is apparent that the studies completed so far only involve small numbers of animals, and that scientific uncertainty persists. However, for healthy cloned animals that are not genetically modified the potential hazards to human health are probably both small and, for their normally conceived progeny, undetectable. The outcome of the FDA risk assessment is likely to result in products from cloned animals arriving on the market. Although European research made the breakthrough in animal cloning, and particularly farm animal cloning, most state-of-the-art research is now taking place outside Europe, and the likelihood is that cloned animals and their products will enter Europe from elsewhere before European-made products are available. While the WTO allows countries to restrict trade to protect human, animal or plant life or health and set their own standards on food safety, these assessments must

[32] See Section 5.1, 5.2 and 6.4 in this report and Section 4.1 in the first legal report of CLONING IN PUBLIC: *Farm Animal Cloning: The Current Legislative Framework*, available at http://www.sl.kvl.dk/cloninginpublic for a more detailed description of the Danish and Norwegian laws.

be scientifically based. In this context the precautionary principle can be invoked, but only as a temporary measure.

4 Possible gaps in the current legal framework – from a risk perspective

4.1 Food safety – novel food and product safety

Owing to the low efficiency of farm animal cloning at present (with 5-10% of implanted embryos growing to adulthood), the cost of cloning is so high that the technology is only likely to be used to produce high-value breeding stock whose natural offspring, if they are food animals, will go into the food market.[33] However, possible entry into the market of food products from cloned animals cannot be excluded, so it is appropriate that risk assessments are taking place both with respect to cloned animals and their progeny. So far these risk assessments have been principally based on compositional analysis and small numbers of animals. If the FDA were to conclude that products from cloned animals could safely be allowed onto the market, the EU may need to proceed to a more regulatory approach to risk management. This would need to be done largely through adjustments to novel food and labelling regulations. In this connection it might, from a food safety perspective, be problematic if foodstuffs from cloned animals are not covered by the regulation on novel food and/or genetically modified food. As there remains uncertainty with regard to the potential risks associated with these food products, it could be argued that there should be a system of risk assessment and prior authorisation comparable to the system that governs novel and genetically modified foods. Decisions would also need to be made about the acceptability of importing cloned breeding stock and the concomitant need to make changes to the existing zootechnical directives.

An appropriate starting point from which to consider cloning laws may be the Novel Ingredients Regulation 258/97/EC[34]. This regulation requires the official review and approval of all novel ingredients to ensure that novel foods are safe when consumed in foreseeable quantities. It also requires novel ingredients to be non-misleadingly presented and nutritionally comparable when used as replacements for conventional products. The regulation applies to novel foods introduced into the EU from 15 May 1997. It is not retrospective, and it does not apply to food additives, flavourings or extraction solvents.

Six categories of food or ingredient are deemed to be novel if they have not previously been used to a significant degree for human consumption within the EU before 15 May 1997. For present purposes four of these categories are relevant. These are:

c) Food ingredients with a new or intentionally modified primary molecular structure.
d) Foods and food ingredients consisting of, or isolated from, micro-organisms, fungi or algae.
e) Foods and food ingredients consisting of, or isolated from, plants and food ingredients isolated from animals, except for foods and food ingredients

[33] In this section, only food applications are considered.
[34] OJ L43 14/02/97 came into force 15 May 1997

obtained by traditional propagating or breeding practices and having a history of safe food use.

f) Foods and food ingredients prepared in a production process not currently used, where that process gives rise to significant changes in the composition or structure of the foods, or food ingredients, which affect their nutritional value, metabolism or level of undesirable substances.

Where cloning is concerned, (e) and (f) are likely to be the most relevant of these categories. Category (e) concerns food ingredients obtained from animals not obtained by traditional breeding practices. This would include food ingredients derived from cloned animals but not those derived from their normally bred offspring. Category (f) addresses production processes and this might be considered to include foods such as humanised milk from cloned GMO animals. These regulations may need to be amended slightly so as to expressly include cloning technology and its resulting food products. A specific piece of legislation on the labelling requirements would also need to be enacted.

Food safety falls under Regulation EC No. 178/2002, but pharmaceuticals (and cosmetics, and nutraceuticals and so on) derived from products derived from cloned animals must also be considered. If it is determined in the interests of the public (e.g. out of respect for the right of individuals to choose the kinds of technology involved in food production) that traceability systems must be implemented for products derived from cloned animals within the food chain, it will be necessary to identify and track every product/ingredient derived from a cloned animal from source to consumption.

To meet consumer interests it may be necessary in law to differentiate and then legislate for the various ways in which cloning technology may impact on food consumption:

- Consumption of cloned animals such as meat and fish.
- Animal products of cloned animals (e.g. milk, eggs).
- Product ingredients (e.g. cheese as an ingredient rather than as such).
- Processing aids, additives, flavourings and similar products derived from cloned animals/their by-products.
- Enzymes/bacteria from cloned animals/their by-products used in food production, which may or may not be present in the final product.
- The use of products derived from cloned animals or technology in food supplements and fortified foods (nutraceuticals).
- Animal feed derived from products derived from cloned animals for animals entering the human food chain.
- Animal products/ingredients/feed derived from animals fed with animal feed derived from a cloned source.
- Cloned animal products intended for consumption by pet animals.
- Cloned animals/their by-products as raw materials for fertiliser, compost or similar products used in food production.

Pharmaceuticals (together with cosmetics, nutraceuticals and similar products) derived from products derived from cloned animals will also have to be considered. There is often a more complex consumer attitude to medicinal and quasi-medicinal products, and it is more likely to be accepted that science can improve such products. As there is a

higher degree of consumer acceptance, the pressure for labelling seems less intense than it is in connection with food applications.

Experience from the GM debate indicates that public concern may raise the following questions:

- Would the supply chain have to separate "cloned" and "non-cloned" products, in a way similar to that in which it separates "GM" or "Non-GM"?
- Who would take responsibility for auditing supply chains and enforcing contractual warranties for product origin, particularly if DNA levels are undetectable?
- Would catering establishments be exempt from any requirement to label?
- Should food producers be responsible under civil liability laws for any adverse effect, or should this burden fall upon cloning companies and their insurers?
- Should DNA derived from cloned animals be detectable in the final product if labelling is to be necessary? Ingredients for labelling are usually defined as substances used in manufacture and still present in final product. However, non-detectable GMOs also need to be labelled following the latest reforms.
- Can science accurately detect cloned genes in the offspring?

4.2 Traceability – animal identification legislation

If it is determined, in the interests of the public (e.g. out of respect for the right of individuals to choose the kinds of technology involved in food production), that traceability systems must be implemented for products derived from cloned animals within the food chain, it will be necessary to identify and track every product/ingredient derived from a cloned animal from source to consumption. A European, and possibly more widely international, Animal Identification/Tracking system similar to that introduced in response to FMD and BSE in EC Regulation 1760/00 (which establishes a system for identifying and registering bovine animals and regarding the labelling of beef and beef products) and EC Regulation 21/2004 (which governs the identification of sheep and goats) would be needed. Such registers could, for instance, be expanded to include information on whether an animal was cloned or was the offspring of a cloned animal. In addition, according to EC Regulation 178/2002, the supply chain would require a network of audits and testing to ensure compliance, together with a series of product warranties and legal indemnities. This would create a heavy and costly burden on both industry and officers of Member States tasked with enforcement and prosecution. This cost can be seen either as an additional economic burden on the use of the technology, or as an inherent part of the production method. In the latter case, it must be factored in when the economic feasibility of cloning applications is considered.

Given that cloned animals may parent offspring, it may also be worth considering in advance whether any traceability system would be required to track generations, and whether the consumer would seek some kind of assured ancestry. For example, consumers may demand a classification or labelling scheme for food products enabling them to differentiate between a product derived from a first generation clone and products from the natural offspring of a cloned animal. Alternatively, it might be

sufficient to state that cloning technology was involved in the production of the product somewhere along the line.

4.3 Experiences with GM labelling

GM labelling has been at the centre of the European labelling controversy for the last decade. It is the only relevant comparator here; nonetheless it may not turn out to be appropriate for cloned animal products. More distantly related are the labelling requirements for irradiated foodstuffs.[35] Laws on genetic modification date from 1990. Since then a complex series of laws has developed in which labelling requirements have been repeatedly amended. Previously the rules required labelling only if the modified DNA was present in the final product. However, in 2004 GM laws changed substantially. The current rules (summarised in Table 2 below) are:

- Foods *from* GMOs must be labelled regardless of whether the modified DNA is present in the final product (this applies even to highly refined soya and maize oil).
- No labelling is required on products produced *with* a GMO (such as a processing aid or a GM enzyme/protein (e.g. the GM bacteria used to produce chymosin for the manufacture of cheese).
- Adventitious contamination up to 0.9% by EU-approved GM is permitted
- Adventitious contamination up to 0.5% by GMOs with a positive safety assessment is permitted even if they have not been formally approved.[36]
- Catering establishments are obliged to label GM foods, and to train staff to answer questions on their GM policy.
- Animal feed derived from GMOs must be labelled regardless of DNA presence.
- However, farmers are not required to inform consumers whether animals have been reared on GM or non-GM feed.
- There is no right for consumers to be informed whether an animal has been treated with GM medicinal products.
- There is a harmonised Community framework for tracing and identifying food/feed derived from GMOs at all stages of the food chain. This relies on paper-based records and has been criticised as providing opportunities for fraud. The system is based on unique identifier codes.

[35] Labelling of irradiated foodstuff is another example of EU labelling requirements, Directive 1999/2/EC on the approximation of the laws of the Member States concerning foods and food ingredients treated with ionising radiation.

[36] This expires after 3 years from introduction. In exchange for this Parliament won concessions on co-existence with agreement that "operators should avoid the unintended presence of GMOs in other products" with obligations on Member States to gather information and develop guidelines on co-existence.

Table 2. GM food and labelling rules

GM	Defined as "food"?	Labelled as GM?
Ingredients	Yes	Yes
Additives	Yes	Yes
Flavourings	Yes	Yes
Processing aids	No	No
Products (milk, meat, eggs etc.) from animals fed GM fodder	Yes	No

Whilst GM laws may be an obvious starting point from which to develop cloning laws, this approach is likely to be resisted by the food industry. The industry has lobbied strongly against various GM reforms. It was particularly unhappy about labelling regardless of detectability (a case in point being highly refined soya/maize oils).

European food law is a combination of horizontal legislation (which affects all foods) and vertical legislation (which is product-specific or technique specific). Thus labelling and hygiene requirements are horizontal; chocolate and honey regulations are vertical. It may be necessary to amend or repeal certain existing horizontal instruments to meet ethical concerns. Most food laws are directives requiring implementation in national law. However, the most recent GM laws to have been introduced by the EU have been regulations, which are directly and immediately applicable in Member States.

There are several options on cloning labelling. These include:

- The use of individual prefixes "cloned…." in the list ingredients.
- The use of statements such as "May contain ingredients derived from animal produced using cloning technology".
- Labelling of all products provided DNA derived from cloned animals is present in the final product. (This is an unlikely course of action because of problems of detection.)
- Labelling of all products regardless of whether the DNA derived from cloned animals is detectable.
- "Clone-free" labelling. Would it be more desirable (easier, more effective) to label 100% traditionally bred or born animals, rather than introduce a generation scheme for offspring?

Another option is to use a certification mark for cloned animals, with products derived from such sources bearing a mark of wholesomeness – provided that such a difference in quality is present. Such mark should be backed by regular testing to ensure products are analytically indistinguishable from conventionally produced equivalents.

Would the categories "organic" and "farm assured" and similar such categories necessarily exclude cloned sources? Instinctively, they should: most people would consider GM soy in an organic product a contradiction.

Product liability laws may be relevant here. Directive 99/34/EEC extended product liability laws to primary agricultural products. Liability under the directive is strict, so no fault is required. This many have an affect on the insurance risk of products derived from cloned animals. However, there are a number of defences available to producers, including that of "development risks". This means that if adverse effects of consuming products derived from cloned animals were only proven after expiry of the 10-year limitation period, consumers may be denied compensation for damage.

4.4 Animal breeding

Zootechnical legislation
There is likely to be intra-community and external trade in cloned breeding animals. The EU would need to decide on the acceptability of introducing cloned animals, say, from the US, into European breeding lines, and whether the clone of a pure-bred animal is equivalent to a pure-bred animal. This would need to be addressed through decisions attached to the relevant zootechnical base directives.

The Cartagena protocol may be relevant here. If there is any possible adverse effect on biological diversity, or on human health, trans-boundary protection may be needed. For GMOs there is a system for notifying and exchanging information on GMO exports to third-party countries, and specific procedures govern the way exporters and importers must notify the Biosafety Clearing House set up by the Cartagena protocol.

4.5 Release into the environment

As mentioned previously (see subsection 2.6 of this report) there appears to be some uncertainty as to whether cloned farm animals would fall under Directive 2001/18.[37] As also has already been pointed out, the purpose of EU regulation in this area is first and foremost to protect human health and the environment from adverse effects caused by the escape of genetically modified DNA into the environment. Directive 2001/18 on the deliberate release into the environment of genetically modified organisms**t** is a total harmonisation directive pursuant to Article 95 of the Treaty Establishing the European Community.[38] The relevant parts of the directive are Article 2.2 and Annex IA, as these define what is meant by a genetically modified organism.

[37] Directive 2001/18/EC of the European Parliament and of the Council on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC.

[38] Consolidated version of the Treaty Establishing the European Community, Article 95, 4: "If, after the adoption by the Council or by the Commission of a harmonisation measure, a Member State deems it necessary to maintain national provisions on grounds of major needs referred to in Article 30, or relating to the protection of the environment or the working environment, it shall notify the Commission of these provisions as well as the grounds for maintaining them." *Official Journal C 325 of 24 December 2002*

Clearly transgenic clones would fall within the terms of the directive. However, there has been uncertainty as to whether non-transgenic clones would be included. The usual interpretation is that cloned animals are exempt from the directive. If animal clones were to fall under the directive, suitable general regulation of imports at the national level may not be possible. The directive already regulates all questions on approval for marketing, including the import of GMOs, using risk assessments focusing on health and the environment. Moreover, greater practical difficulties may arise, as it is not possible to ascertain as such whether the animal in question is cloned or not. In addition, there is a widespread view that the level of advancement of cloning today is relatively low in relation to cloned farm production animals or companion animals. Consequently, it may thought that regulation of import is not relevant at present.

If non-transgenic clones were included, it would need to be decided whether they fell into the definition under Annex IA(2),[39] because the nuclear DNA, which is heritable material, is prepared outside the organism (if an egg can be called that) and is introduced by micro-injection. It might also fall under the definition given in Annex IA(3). While SCNT does not form new combinations of genetic material through the fusion of two cells, nuclear DNA from a somatic cell forms a new association with the mitochondrial DNA in the enucleated egg cell in which it is placed. Both types of DNA are heritable, and the method by which they are brought together is not natural.

It is necessary, then, to establish, perhaps through judicial review, what was intended by the legislators. While they use similar biological technologies, there is a striking difference between GMOs and non-transgenic clones, since GMOs have additional genes, often from other species, inserted into their DNA, whereas non-transgenic clones have a normal genotype. GMOs may therefore pose an environmental hazard, whereas non-transgenic clones would be expected to have the same environmental interactions as their normally bred counterparts.

4.6 Conclusions

It is difficult to identify genuine gaps in the present legal framework until further information is available from risk assessment and from subsequent discussions had by the relevant experts seconded to the Commission. If it is discovered that non-transgenic cloned animals and their products are substantially equivalent to animals already in commercial production, such animals may be covered by much of the existing legislation. If, however, it is decided that there are sufficient differences, the legal framework will need to be amended specifically to include non-transgenic cloned animals.

[39] See Section 2.6.

5 Possible gaps in the current legal framework – other concerns

Risks to human health and the environment posed by animal cloning obviously raise concerns that need to be addressed. However, in addition to scientific uncertainty there remains uncertainty about the acceptability of products from cloned animals. That acceptability may be linked to a number of other important concerns such as animal welfare, animal integrity, consumers' rights and, more generally, an interest in promoting the basic values underpinning the EU (e.g. sustainability, biodiversity) and in promoting the precautionary principle). This approach is, for example, articulated in Recital 19 to EC Regulation No 78/2002 which declares:

> It is recognised that scientific risk assessment alone cannot, in some cases, provide all the information on which a risk management decision should be based, and that other factors relevant to the matter under consideration should legitimately be taken into account including societal, economic, traditional, ethical and environmental factors and the feasibility of controls.

5.1 Animal health and welfare

Studies of the effects of cloning on animals – effects on the embryos while in vitro, the development of the embryo in the uterus of the surrogate mother, and the animal's postnatal development – show that the technology has a substantial health and welfare impact. The success rate of cloning, measured as the proportion of healthy animals born, is still somewhere around 5-10%, depending on the species.[40] Few of the cloned embryos develop into viable embryos that can be transferred to a uterus. Of these only few are born, and of these many experience welfare problems. The welfare problems here are usually collected under the heading Large Offspring Syndrome (LOS). This encompasses, among other things, an unacceptably high level of losses during early and late pregnancy, stillbirths, early postnatal deaths, short lifespan, obesity and malformations. The causes of LOS are still poorly understood, and much research effort is going into understanding the reasons behind the low efficiency of the technology. This research is driven by the ambition to make cloning a viable economical alternative to other kinds of animal reproduction.

In assessing whether gaps in the present legal framework exist that might lead to a failure to address concerns about the cloning of farm animals, it is necessary to determine the extent, if any, to which cloned animals are significantly different from traditionally bred animals. Here it is important to appreciate that much farm animal reproduction is now highly technical, involving *inter alia* semen collection, artificial insemination, superovulation, embryo retrieval by uterine lavage, in vitro fertilisation, embryo transfer and delivery by caesarean section. In addition, and rather importantly, cloning by embryo splitting and blastomere nuclear transfer (BNT) has been in use for

[40] Horse, for example, has proved difficult to clone - with one example being 400 eggs to produce the foal Paris-Texas; a clone of the stock stallion Quidam de Revel recently imported to Denmark.

decades.[41] A number of the reproductive technologies used in commercial livestock breeding have adverse effects on animal welfare in that they may cause pain and distress or require the animal to be killed. The present legal framework would appear to cover the use of these reproductive technologies in commercial livestock production, and the resulting livestock enter the food market with little or no difficulty. Many of the adverse effects associated with in vitro technologies also affect animals produced by SCNT-cloning. Hence uncertainty persists about whether such problems are due to SCNT-cloning per se or the linked reproductive technology. Further scientific research is therefore needed to determine whether a specific aspect of cloning requires exceptional animal protection measures to protect the animals involved. Since unhealthy or deformed animals will be excluded from the food chain, they do not need to be considered in any food safety risk assessment.

New ground rules for EU action on animal welfare were established by the Treaty of Amsterdam (1999) in a special Protocol on the Protection and Welfare of Animals. The protocol defines the limits of EU competence to legislate. At a national level, taking the example of the first animal cloning legislation within EU Member States, the Danish legislation involves balancing the purpose of using animal cloning against foreseeable animal welfare problems. In studies made in preparation for the law, animal welfare is viewed as a reason for restricting animal cloning. In Directive 98/58/EC, which concerns the protection of animals kept for farming purposes, cloning technology is not presented as unique in giving rise to animal welfare problems; such problems are also encountered within conventional breeding and livestock production. Here, a certain degree of animal suffering and other welfare problems are broadly accepted. The question is at what point animal welfare problems within cloning become unacceptable. The Danish law assumes that ethically problematic consequences of the technology can be justified by "substantial" benefits to society brought by the technology. It does not explicitly define what these benefits are, but health and the environment are mentioned several times.[42]

5.2 Animal integrity

Another type of concern is animal integrity. This was raised in connection with the Danish legislation on farm animal cloning. Integrity can be defined in a number of ways, but here it implies that more is at stake than animal welfare: that is, integrity demands that we ask whether animal cloning technology conflicts with what is considered permissible human utilisation of animals, regardless of reduced welfare or not. The question is about the extent to which it is acceptable to violate the animal's "integrity" or hamper its natural "expression". In many cases, appeal to animal integrity is made when the use of the animal is seen as "wrong" but cannot be argued against from, say, the perspective of health or welfare. The integrity of an animal can be violated without the animal feeling any pain or experiencing reduced welfare in some other way (Ministry of Science, Technology and Innovation, 2003). Violations of the

[41] Animal Cloning and the Production of Food Products, Proceedings from a workshop sponsored by the Pew Initiative on Food and Biotechnology and the Center for Veterinary Medicine of the US Food and Drug Administration, September 2002

[42] Cloning of animals for the purpose of increased production within agriculture or cloning of sports or companion animals seem excluded from the Danish legislation.

integrity of an animal do not imply that we, as humans, are at risk, or that our aesthetic sense of what is natural is challenged. When integrity is violated, the animal is affected beyond welfare in a way which many people find troubling. Thus the notion of integrity tries to capture the sentiment that we should leave animals as "natural beings", i.e. not as treat them as a product of human ingenuity. Thus, although there may appear to be no welfare-based objections to the use of a technique, there might be a concern which has been articulated in FAWC 1998 cloning report as "… an attitude […] which condones the moulding of animals to humankind's uses, irrespective of their own nature and welfare" – a concern that the cloned animal is being treated as a manufactured being. Animal integrity is not addressed in EU regulation, but it was, as has just been mentioned, raised in the Danish debate preceding the Danish cloning legislation.

5.3 Consumer rights

From a consumers' rights perspective, it might considered that there is a legal gap if foodstuff from cloned animals is covered neither by the regulation of novel food nor the regulation of genetically modified food and hence requires more specific labelling requirements. General food law (Regulation (EC) No 178/2002) explicitly mentions the consumer's right to make informed choices, but it is questionable if this provides the consumer with a right to receive specific information when food products derive from cloned animals.

5.4 Free trade

As stated above in subsection 2.5, zootechnical legislation aims to promote free trade in breeding animals and their genetic material compatibly with the sustainability of breeding programs and preservation of genetic resources. Some of the barriers to regulating cloning, the products derived from cloned animals and animal biotechnology are institutional or economic. Too tight a regulatory framework may hinder commercialisation and reduce competitiveness. Too loose a framework may conflict with views on animal welfare, food safety, and other issues. Moreover, it might be difficult to distinguish the offspring of cloned animals from natural offspring. As a representative from the European Biotech Industry pointed out at the expert workshop in Prague, different kinds of regulation in different areas, countries and regions will present a serious obstacle to the industrial development of the technology. From the perspective of the industry shared or standardized legislation is much to be preferred over a multitude of different regulation systems – even though a standardized solution might need to be more stringent than some of the differentiated systems.

Differences between Member States and international laws on products derived from cloned animals, could impede the free movement of cloning-related goods, and this could lead to problems of unfair competition. This might cause problems:[43]

- where products permitted in one Member State should be able to move freely within the EU

[43] See also section 4.4. and section 5.6.

- where products are imported into Europe from Non-Member States (particularly the US) and Europe adopts a different approach from the main international producers
- where products permitted in Europe are exported internationally to countries with different standards/requirements

5.5 Public concern

In Europe it would seem that Europeans are more concerned about biotechnology applied to food than biotechnology applied to healthcare. A Eurobarometer survey in 2005[44] reported that 54% of those interviewed considered that food from GMOs is dangerous; only 14% disagreed. On the other hand, another survey carried out at the same time[45] found that the majority would accept the cloning of animals such as monkeys or pigs for research into human diseases provided that it was highly regulated and controlled (35%) or only used in exceptional circumstances (22%), while 8% found it acceptable in all circumstances and 31% found it wholly unacceptable. Cloned animals used for these purposes would have to be transgenic. It is not clear what the public reaction would be to products from cloned, non-transgenic animals. The foci of the public's concerns – both as citizens and consumers – *might* include:[46]

- Loss of genetic diversity – the selection of certain attributes, may ignore the advantages of other breeding lines
- General concern about human cloning implications – see the Norwegian law
- Unknown complications – selectively breeding into animals of genetic faults which will affect the food chain in future decades
- The inbreeding of cloned breeding lines
- The "What's in it for me?" approach – it is necessary to show the consumer (and not just the shareholder) the benefits of cloning
- Distribution of the costs of traceability within the industry, since these costs could damage small producers
- The potential for fraud being high if labelling is required regardless of detectability.

These concerns touch upon a mix of legal, cultural and ethical issues. To deal with cultural and ethical barriers it is necessary to have effective dialogue between the public and policy makers, and between the public and the scientific community. In such a communication it is important to recognise that there are quite different views both on cloning as such and ethically acceptable/important uses of farm animal cloning.

[44] Special Eurobarometer 224/Wave 63.1 *Europeans Science and Technology*, Jan-Feb 2005
[45] Special Eurobarometer 225/Wave 63.1 *Social Values of Science and Technology*, Jan-Feb 2005
[46] Cf. the report "Public perceptions of farm animal cloning in Europe" from the CLONING IN PUBLIC project. The report concludes that the existing knowledge about the Europeans perception of farm animal cloning is limited due to a lack of qualitative and quantitative studies focusing on this specific issue.

5.6 Consequences for future regulation

EU regulation imposes a rather complex regulatory framework on animal cloning. However, some uncertainty and possible gaps remain. With regard to the question of *consumers' right to information* (labelling and so on) it seems advisable to address the issues in Community law. It is more questionable whether the issue of *animal integrity* should be addressed in EU regulation or whether it would be better to leave regulation to Member States. EU regulation recognises that Member States may have a certain "margin of appreciation". This happens, for example, when EU regulation takes the form of "minimum directives" stipulating minimum of requirements which may be supplemented by stronger national requirements.

On farm animal cloning technologies, two fundamentally opposed views exist: (1) that all farm animal cloning and animal products derived from cloned animals should be accepted; and (2) that no farm animal cloning and products derived from cloned animals should be accepted. Compromise positions – such as allowing some specific cloning techniques, or permitting cloning for some purposes (e.g. scientific research), for some applications (e.g. medical), or for some end products (e.g. pharmaceuticals) – are open to attack from both sides. Avoidance of the two extremes may mean coming closer to ordinary people, who rarely hold one of the two extreme views. Happily, this would mean that the public and decision makers do not become alienated. In effect, most countries have adopted pragmatic, compromise solutions when regulating the procedure of cloning and clone products.

Some countries approach regulation through the end uses of cloning-derived *products*. An example of this is the US, which regulates by product regulation through the FDA. Other countries regulate the *process* of farm animal cloning. So far, only two European countries do this. But regulation is most often achieved through existing animal welfare/protection legislation which does not specifically address animal cloning. Thus, although EU regulation controls the use of animals for research, there is no regulatory framework for cloning in livestock production. Where direct farm animal cloning legislation has been passed, as it has in Norway, the legislation in question only applies to the production of cloned animals. Imports of cloned animals or products are not covered, owing to worries about free trade. The following analysis of the regulatory framework currently covering the free movement of goods and food products – a framework that might apply to products from cloned animals – illustrates how certain issues might be handled.

There is a European principle (derived from the French *Cassis de Dijon* case in 1979) that, in general, a food product lawfully produced and marketed in one Member State should be marketable in other Member States unless it can be proved that this would present a threat to public health.

This principle originates from the Treaty of Rome provisions to abolish trade barriers. These provisions were contained in the original Articles 30-36, which became Articles 28-30 in the consolidated version of the Treaty. Article 28 prohibits quantitative restrictions on imports (and measures having equivalent effect). Article 29 provides such a prohibition between Member States. Article 30 permits such restrictions in

certain situations. However, this must not amount to arbitrary discrimination or a disguised restriction on trade.

The case law and the Treaty establish that, for a Member State to refuse entry of a cloned product from a fellow Member State, it would be necessary to establish justification on grounds of either public morality, public policy, public security, the protection of health and life of humans, animals or plants, or the protection of industrial and commercial property.

Naturally, European law also applies to products imported from Non-Member States, so international producers would have to meet any cloning and labelling requirements adopted within the EU. Labelling of products derived from cloned animals or containing products from cloned animals is not covered by the current labelling rules. Labelling may still be considered relevant (compare the GMO issue) on the grounds that consumers have a right to information and free choice. Current regulation does not address the present uncertainties about animal cloning. This could be the cause of trade wars – indeed this has already happened with hormone treated meat and GMOs. It will be necessary to take advice and cooperate with the WTO, the World Health Organisation (WHO), the FAO, and the Codex Alimentarius Commission. Particular attention will need to be given to the The WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) and The WTO Agreement on Technical Barriers to Trade (the "TBT Agreement").

5.7 Conclusions

The EU has adopted a scientific and risk-based approach to food. Once it has been established whether products derived from cloned animals can enter the food chain as safe nutritional equivalents of conventional products, attention *could* therefore turn to the practicalities of labelling, traceability and consumer information. In law it may be necessary to differentiate, and then legislate for, the various food types derived from cloning technology. Pharmaceuticals (and cosmetics, nutraceuticals, and so on) derived from products derived from transgenic and cloned animals will also have to be considered. If they are determined to be in the interests of consumer information or safety, traceability systems must be implemented for products derived from cloned animals within the food chain, and it is a legal requirement that consumers are provided with clear, accurate, understandable information so that they can make an informed choice of product. However, this is by no means a given order of events, as other ethical concerns, relating to products derived from cloned animals and the food chain, which cannot be assessed from a hazard perspective, might arise.

Current EU regulation on animal cloning focuses on application. Cloning as a technique is not in itself covered by EU regulation. The case for regulating cloning as such could be based on fundamental societal values, concerns about animal integrity, or on other "public" concerns (see Article 30 in the Treaty Establishing the European Community).[47] Ethical considerations are normally raised at the national level. Less

[47] Treaty establishing the European Community, Article 30: " The provisions of Articles 28 and 29 shall not preclude prohibitions or restrictions on imports, exports or goods in transit justified on grounds of public morality, public policy or public security; the protection of health and life of humans, animals or

often they appear at the EU level – for example, when the aim is to find common standards at EU level of what is "ethically acceptable".

In some EU directives, reference is specifically made to national ethical principles. Recital 9 in Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms explicitly declares that it is of particular importance to respect ethical principles recognised in the Member States, and that Member States are allowed to take such principles into consideration when GMOs are deliberately released or placed on the market as or in products. Directive 98/44/EC on the legal protection of biotechnological inventions also mentions the need to refer to moral and ethical principles recognised in a Member State to supplement the standard legal examinations under patent law (recital 39). Accordingly EU legislation leaves room for the application of EU rules within the framework of national ethical principles.

plants; the protection of national treasures possessing artistic, historic or archaeological value; or the protection of industrial and commercial property. Such prohibitions or restrictions shall not, however, constitute a means of arbitrary discrimination or a disguised restriction on trade between Member States."

6 Regulation designed to meet the gaps

6.1 Regulatory models and tools

In general, regulations are mechanisms through which concerns are "translated" into practice. There are several forms of *societal* regulation, as is shown in Table 3.

Table 3. Forms of societal regulation

Regulation	Description
Market mechanisms	In this perspective alone, whether food based on farm animal cloning is to be found in supermarkets, pets are to be cloned or biomedical applications are to be developed and sold, will depend on the demand of consumers and whether it is profitable for producers and retailers to develop and produce these goods. These mechanisms are part of the drive for scientific advance and development, and technological innovation.
Professional standards	This is a well-known regulation method within the medical profession (and other professions), where, for example, internal guidelines determine acceptable procedures, research and applications. In addition, committees may form part of this regulatory approach.
Constant negotiation on a case-by-case basis	These agreements can be made on a number of levels, ranging from granting approval to a private company, broader agreements made between an industrial sector as a whole and the relevant agency.
Statutory law	In this type of law, regulations in rules and provisions are based on special authority. In a democratic society special procedures govern the ways in which statutory law can be made. Using statutory law may well be a signal of (a) vital concerns and interests at play, (b) a special need for the protection of citizens against potential hazards, (c) the need to safeguard fundamental, societal values, or (d) a wish to create legitimacy of applications of specific technologies where these are greeted with initial scepticism by the public. Finally, it needs to be considered if regulating through statutory law gives rise to disadvantages or carries costs exceeding the perceived benefits of such a form regulation.

The first three forms of regulation are examples of self-regulation. Here, stakeholders regulate the area. By contrast statutory law depends on political, either national and/or supra-national (e.g. EC) control. Within the European region, self-governance is promoted as an efficient and non-bureaucratic form of regulation and as a value in itself. However, there are also a number of problems. One of the drawbacks of regulating entirely through market mechanisms is the possible lack of transparency to users and consumers and the risk of allowing stronger parties gain an upper hand. Regulation predominantly through professional standards may lead to excessive deference to the profession in question, and to a lack of due consideration for the concerns of consumers and citizens. A risk associated with the case-by-case approach is that of losing sight of long-term interests and benefits for society as a whole.

The order of the types of societal regulation presented above is reflected in the way technologies and applications of biotechnology are regulated. In many cases, regulation may begin within the research communities. For example, embryonic stem cells are not

market-regulated; they are controlled by ad hoc regulation, standards, law, and so on. Generally speaking, the influence of international regulation, especially EU regulation, on national regulation has increased substantially: this can be seen, for example, in Directive 98/44/EC on the legal protection of biotechnological inventions, and in Directive 2001/18/EC on the deliberate release into the environment of genetically modified organisms. To an ever greater extent, EU regulation has focused on issues relating to the market and the free movement of goods. To an ever smaller extent, such regulation has focused on non-economic values – values which, however, are now being expressed in the Treaty Establishing the European Union.[48]

Where statutory law is concerned, an important precondition of creating efficient regulation is to be sure of what one is aiming at, what is considered permissible and what will not be accepted. With modern biotechnology it is often difficult to clearly foresee positive and negative developments and the ramifications of the technology. There are two main avenues here: one is *detailed regulation*, specifying prohibitions and restrictions. The other is *framework regulation*, where greater specificity can be achieved once the benefits and risks of a new technology are known. Detailed regulation may be more precise. Framework regulation promises greater flexibility. Uncertainty can be handled in different ways. One way is to set up intermediary prohibitions or other restrictions on research and its applications in order to avoid possible unforeseen consequences until more is known – at which point regulatory practices can be amended. Another way is to adopt a wait-and-see approach, in which framework regulation can be a quick and efficient way for the authorities to change regulation if negative consequences unexpectedly follow. Obviously, however, if a clear position is discernible – if, for example, animal cloning is seen as undesirable in any event – one might as well prohibit such activities. Moreover, depending on the strength of such undesirability, substantial sanctions in the case of breaches of the ban may be effective.

These forms of societal regulation are in practice combined in a number of ways and are given various weightings. In order to get a better grip on these forms of regulation in relation to farm animal cloning, we shall now describe three scenarios.

In the European context, the control of activities relating to animal cloning could be addressed at three different levels: European legislation, national legislation or through a laissez faire approach with control through codes of practice or international trade agreements and market forces. For any of these controls to work, there must be consensus that the type or level of regulation being proposed is the most appropriate.

6.2 Regulating complexity

Under the Treaty establishing the European Community, the European Commission has the “right of initiative”, which means that it is responsible for drawing up new proposals for legislation to put before the European Parliament and Council. Action will be taken at EU level only if the Commission believes that a problem cannot be solved more efficiently by national, regional or local action.

[48] Treaty on European Union (consolidated text). *Official Journal C 325 of 24 December 2002*

National regulation may be introduced as a result of either external or internal drivers. The former may take the form of a European directive and result in statutory legislation; the latter, following from the recommendations of an advisory body or public pressure, may also result in new statutory legislation or an amendment to existing statute law, or involve a less binding form of regulation such as the introduction of a code of practice. Whatever the driver, before embarking on new regulation, it is advisable for policy makers to bear in mind the Principles of Good Regulation[49]. Although these apply explicitly in the UK, such principles are likely to be applied by policy makers elsewhere. Table 4 summarises the five principles of good regulation.

Table 4. Principles of good regulation, suggested by the UK Better Regulation Task Force

Principle	Description
Proportionate	Regulators should only intervene when necessary. Remedies should be appropriate to the risk posed, and costs identified and minimised. Laws require enforcement and this can be punitive or educational.
Accountable	Regulators must be able to justify decisions, and be subject to public scrutiny. Proposals for regulation should be subject to consultation and regulators and enforcers should establish clear standards and criteria.
Consistent	Government rules and standards must be joined up and implemented fairly. New regulations should take account of other existing or proposed regulations whether of national, EU or international origin.
Transparent	Regulators should be open, and keep regulations simple and user friendly. The need for regulation should be clearly defined and effectively communicated. Stakeholders should be given sufficient information and ample time to respond to any consultation. Those being regulated should be made aware of their obligations, with law and best practice clearly distinguished. The consequences of non-compliance should be made clear.
Targeted	Regulation should focus on the problem, minimise side effects, and not be all-embracing. In preference a "goals-based" approach should be adopted with regulators and regulated given flexibility in deciding how to meet clear unambiguous targets. Enforcers should focus primarily on those whose activities give rise to the most serious risks.

The EC uses a number of tools and processes to ensure that regulation is used only when necessary and that the burdens they impose are proportionate with their aims. These include: (1) withdrawal or modification of pending legislative proposals, (2) measures to simplify existing legislation, and (3) better quality of new Commission proposals through the systematic use of impact assessment and public consultation in the development of new policy proposals.[50]

It is clear that there should be some form of public consultation before any decisions about regulation are made. If the issue is so serious that existing regulations are

[49] Published in 1998 and revised in 2000. The Principles of Good Regulation, UK Better Regulation Task Force

[50] http://europa.eu.int/comm/enterprise/regulation/better_regulation/index_en.htm

considered insufficient and only a statutory approach is appropriate, policy makers will need to take account of any implications such legislation might have not only for enforcement but also for economic impact. Above all there must be common understanding as to what the regulation is intended to achieve.

If it is considered that statute law is the only way forward then different options are available. The most restrictive option is to enact prohibitionary legislation with penalties for failure to comply. Another option is to enact detailed legislation taking account of all aspects of the technology, prohibiting certain activities and allowing others. This may give rise to problems for the future in a rapidly advancing area of biotechnology. A third option is to enact framework legislation which is mainly permissive (although some activities may still be prohibited with penalties for infringement), but with regulation carried out through licensing activities by a regulatory body. The regulatory body would draw up and enforce a code of practice as part of the licensing procedure, and this code could be revised periodically in the light of experience. All forms of legislation should be subject to review.

The regulatory body can use various forms of regulation depending on its nature. A purely administrative body, such as an environmental protection agency, can make "administrative regulations" which are legally binding standards. Issuing of guidelines or recommendations is also a possibility here. Such guidelines provide of course just that – guidance. As such they are not legally binding, although in reality they are often seen as binding because they are issued by a public authority. A different situation arises where the regulatory body is an independent committee or board, since recommendations or codes of conduct are less binding in character. A special licensing system can also be put into place. An example would be a system in which it is necessary to obtain a license to clone specific animals. (Similar systems operate in many countries in relation to animal experimentation.) Another example is a license allowing specific companies and research institutions to clone animals.

To date only two European countries have enacted legislation on animal cloning: Denmark and Norway. In other European countries the regulation of animal cloning is indirect, relying on existing laws on animal protection or animal biotechnology. Institutional research ethics committees also play a non-statutory role. The willingness to introduce legislation restricting animal cloning will depend in part on its potential economic impact. Countries with a large animal production industry will not wish to become uncompetitive as a result of the improvement of livestock through cloning in countries outside Europe. Cloning may be the most effective way of reproducing transgenic animals that are important to the pharmaceutical industry. Public concerns can be exercised through choice promoted by labelling regulations.

A third option, and one not relying on common EU cloning legislation, would be to adopt a laissez faire approach to regulation. In this approach no direct action would be taken to control animal cloning. Reliance would be placed on existing control mechanisms and regulation would be allowed to evolve though professional codes of practice, international trade agreements and patent law, together with public pressure and market forces. This is very much the position in the US, where federal legislation cannot be used to prohibit an activity such as animal cloning. However, government

pressure can be brought to bear by restricting the availability of federal funds for research, as can be seen in the US government's attitude to human embryonic stem cell research. Individual States in the US can enact state legislation, but on an issue such as animal cloning, particularly in those States where animal production is an important part of the economy, this is unlikely. Animal welfare issues at the research level are the responsibility of Institutional Review Boards. New products arising from animal cloning would be regulated by the FDA. Parallel mechanisms already exist in Europe.

As was demonstrated in our first legal report, if the laissez faire approach were to be applied in Europe, it would operate on the back of a broad swathe of existing regulation, and this would provide some control of animal cloning at both the national and EU levels. Finally, it should be emphasised that the three scenarios described are not necessarily mutually exclusive.

In deciding which of the scenarios to pursue, consideration need to be given as to why regulation of animal cloning could be needed. There would appear to be a number of different values and concerns at play, including:[51]

- Consumer protection
- Consumer choice
- Economic development
- Innovation
- Product safety
- Public health and new medical applications
- Animal protection
- Other ethical concerns

6.3 The EU-level regulatory approach

Consensus on an EU ban on animal cloning would be difficult to achieve. Public opinion on the issue is not clear cut, particularly as the technology has applications ranging from livestock improvement, providing animal models for medical research, "pharming", providing humanized organs for xenotransplantation and the production of specialized foods such as humanized milk for infants. Several factors may play a role in any decision about how to regulate. Regulation could target the purpose of the technology or the technology itself, but it is difficult to pinpoint the boundaries here. If regulation were to target the technology, it would be important to see the technology in context, since animals cloned for research or medical use are likely to be genetically manipulated as well and will include farmed as well as laboratory species. Given this, it may be more appropriate for legislation reflecting a "moral" view of applications to be prepared at the national level by individual countries.

EU legislation could present an obstacle to national standards. For example, the Danish Act on animal cloning does not address imports of cloned and genetically modified animals, because national restrictions on GM animals are prohibited. In other words, a strong national desire for a ban on animal cloning and cloned animals cannot be fully

[51] Cf. the CLONING IN PUBLIC report: Ethics and farm animal cloning: Risks, values and conflicts.

met with domestic laws because of the overall EU regulation. There is no reason, however, why the EU could not take a moral stance with regard to research funding: it could withhold funding from animal cloning research in the same way as it refuses funds for therapeutic cloning research. In principle this would not prevent animal cloning research from being funded by national or other organisations.

If the EU were to ban animal cloning (or even just farm animal cloning) from a moral standpoint, it would follow that it should not allow imports of products from cloned animals from other countries. This would put the EU in a difficult position with regard to international trade agreements and the WTO, since moral grounds for embargoes on goods or products from other countries are prohibited.

The EU may wish to regulate animal cloning on the grounds of safety, or in the interest of allowing individuals to choose not to purchase products which they believe to have been produced through an unethical process. It is unlikely that cloned animals will come into the human food chain, since they will be created to provide elite sires for livestock improvement and it will be their naturally created offspring which will provide food products. So far, the progeny of cloned animals have proved to be perfectly normal. Clone-associated phenotypes appear to be the result of epigenetic, rather than genetic, errors which are not transmitted to the next generation.[52] At this relatively early stage in the technology there has been relatively little research on food safety, but such research as there has been seems to indicate that food products from cloned livestock are compositionally equivalent to those from naturally produced animals.[53,54] Some products, such as specialized milk products, could come from genetically modified cloned animals. However, as subsection 2.1 of this report explains, Europe already has mechanisms and regulations for dealing with such products. These may need some adjustment and the European Food Agency should perhaps investigate whether special measures need to be introduced to regulate products coming from cloned animals or their progeny. Consideration may also need to be given at the European level to the tracking of cloned animals and embryos.

Animal protection is another potential reason for introducing further regulation. The EU already has a number of binding instruments on animal protection, including the protection of farmed animals. These are described in subsection 2.3 of this report. Thus to make a case for new forms of regulation it would be necessary to show that the animal protection needs associated with animal cloning are significantly different from, or more severe than, those created by other animal technologies.

6.4 The National level regulatory approach

As already explained, a raft of regulations enacted at EU level indirectly addresses the issues raised by animal cloning. These have a direct impact at national level on the Member States, since EU countries either have to implement regulations or introduce

[52] Epigenetics is the study of heritable changes in gene function that occur without a change in the sequence of nuclear DNA.

[53] Wells D. N., 2005, Animal Cloning: problems and prospects. *Rev. sci. tech. Off. Int. Epiz*, 24(1), pp 251-264

[54] Animal Cloning and the Production of Food Products: perspectives from the food chain. 2002, FDA

national legislation in line with the directives. Most Member States will have applicable animal protection legislation, although the new Member States will need to bring existing legislation in to line with the relevant directives.

With regard to product safety issues, again, existing EU measures already require Member States to act in various ways to ensure food safety and consumer choice. Any additions to these measures designed to deal with products derived from cloned animals or their progeny are probably best introduced at EU level.

Finally, there is the issue of other ethical concerns. Individual countries may, as a result of public consultation, decide that animal cloning is a moral issue – and then seek to prohibit such activity or restrict it to certain applications. As was described in the first legal report, such action has been taken by Norway, a member of the European Economic Area (EEA), and Denmark. Danish law restricts animal cloning to research purposes. The question of import has been discussed in the Danish Parliament, and during the legislative process it was promised that administrative rules would be issued requiring prior authorisation and restricting import to cloned animals used for research purposes. However, so far no rules have been issued and the law is, thus, silent on the import of both cloned animals as such and products from cloned animals. Norwegian law also restricts animal cloning to research purposes. Its principal aim is to prevent human cloning, and it is silent both on the import of cloned animals and imports of their products. WTO agreements apply at both the national and European level, so individual countries will probably be reluctant to enact legislation which is likely to be challenged in the international courts. Within the EU and the EEA internal market provisions require freedom of movement of goods, although, within the EEA, agriculture and fisheries are included in the WTO agreements only to a very limited extent. In principle this allows Member States to import products derived from cloned animals or their progeny from fellow Member States unless a risk can be scientifically demonstrated, as was the case with BSE and meat products from the UK.

6.5 The Laissez faire regulatory approach

Within Europe, largely as a result of the issues raised by genetic modification, a comprehensive set of regulations covering animal protection and product safety is already in force. These regulations may well address most of the public concerns about animal cloning. Risk assessments are currently underway in Europe and the US. In the US companies are ready to put products from cloned livestock on the market. The FDA has imposed a moratorium on the marketing of food products until the risk assessment being undertaken by its Centre for Veterinary Medicine to evaluate food safety, animal health and environmental aspects of animal cloning is complete.[55] Interims findings suggest that "there are no biological reasons, either based on underlying scientific assumptions or empirical studies, to indicate that consumption of edible products from clones of cattle, pigs, sheep or goats poses a greater risk than consumption of those products from their non-clone counterparts."[56]

[55] http://www.fda.gov/bbs/topics/NEWS/2003/NEW00968.html

[56] FDA. Animal Cloning: A Risk Assessment. DRAFT Executive Summary. Available at: http://www.fda.gov/cvm/Documents/CLRAES.doc

Since the US seems to be further advanced in risk assessment, it may be wise for the EU to delay taking action until the FDA risk assessment is complete. In this way inappropriate or unnecessary regulation could be avoided. An assessment could then be made as to whether any adjustment to existing legislation is necessary, or whether new legislation required.

6.6 Conclusions

In our previous legal report,[57] and in the first section of the present report, we have mapped current legislation with a bearing on animal cloning. This mapping exercise involved the examination of legislation on animal cloning as such, animal welfare, animal experimentation, GMOs, environmental law, food safety, consumer rights, trade and intellectual property rights at EU and national level. It can be seen, then, that we distinguish animal cloning legislation as such (e.g. the relevant Danish legislation) from legislation *affecting* animal cloning (e.g. Council Directive 98/589).

In assessing regulatory approaches to potential gaps in the legal framework it is necessary to address challenges that may arise from changes to the current regulatory framework. These challenges include identifying the aims of further regulation (such as ensuring food safety) and choosing appropriate regulatory responses. Such responses involve finding the level of regulation (such as EU directives), deciding upon a regulatory model (such as a rule model), and finally, determining the appropriate regulatory tool (such as binding administrative rules). Currently a host of different aims seem to characterise the regulation of farm animal cloning. At one end of the spectrum, there are the aims of ensuring public health and food safety, protecting the environment, securing animal protection and welfare. At the other end, there are the aims of meeting other public concerns, ensuring that the individual can make his or her own moral assessment and exercise free choice, and sustaining general norms of society. Between these ends lie more or less specific socio-economic concerns about matters such as free trade.

[57] Farm Animal Cloning: The Current Legislative Framework. A review describing the existing law, and its practical application within and beyond the EU. http://www.sl.kvl.dk/cloninginpublic.

7 Conclusions

To date, no binding legal instrument on animal cloning as such has been introduced in the EU. Thus, at present, a rather complex, indirect regulatory framework governs animal cloning at EU level. This framework is characterised by a certain amount of uncertainty and possible gaps.

With regard to product safety issues, existing EU measures already require Member States to act to ensure food safety and consumer choice. Any specific additions to these measures designed to apply to products derived from cloned animals or their progeny are probably best introduced at EU level. The first legal report from this project describes in detail the existing national regulatory framework within Europe.

Regulation (EC) No 258/97, Regulation (EC) No 178/2002 and Regulation (EC) No 1829/2003, together with Directive 2001/18, require the implementation of proper risk assessment, including application of the precautionary principle if appropriate, before recourse to further regulation. In looking at measures which may result from reliance on the precautionary principle, the communication from the Commission concludes that the "decision to do nothing may be a response in its own right", and that recourse "to the precautionary principle does not necessarily mean adopting final instruments designed to produce legal effects, which are subject to judicial review".[58] Whatever decision is taken here will be a political decision based on the level of risk that is deemed "acceptable" by the society on which the risk is imposed. Given this it is important to ask how far risk assessments should go.

The EU food laws designed to protect public health and safety are rigorous. They do not yet specifically address products from cloned animals or their offspring, but they incorporate mechanisms to do so. Examination of the current state of risk assessment of products from cloned farm animals and their progeny reveals that the studies completed so far only involve small numbers of animals, and that scientific uncertainty still exists. While the WTO allows countries to act on trade to protect human, animal or plant life or health and set their own standards of food safety, it insists that national policies of this kind are scientifically based. This means that the precautionary principle can be invoked, but only as a temporary measure.

Transgenic animals that are cloned will be caught under existing GMO legislation, but this will be because they are genetically modified, not because they are cloned. Where cloned animals are created and reared in an experimental setting they are protected by animal protection laws. There appears to be some uncertainty as to whether cloned farm animals would fall under Directive 2001/18. The usual interpretation here is that cloned animals are exempt from the directive. If non-transgenic clones were covered by the directive, it would need to be decided whether they satisfied the definition given in Annex IA(2) or that given in Annex IA(3). Ultimately here, it needs to be established, perhaps by judicial review, what was intended by the legislators.

[58] Communication from the Commission on the precautionary principle /* COM/2000/0001 final */

EU legislation allows EU rules to be applied within the framework of national ethical principles. Individual countries may, as a result of public consultation, decide that animal cloning is a moral issue and then either prohibit such activity or restrict it to certain applications. As was observed in the first legal report, such action has been taken by Norway[59] and Denmark.[60] Danish law restricts animal cloning to research purposes. Under it, a licence will be required for the import of cloned animals, which, again, can only be used for research. Danish law is silent on the import of products from cloned animals. Consensus across the EU on aspects other than risks to human health and the environment does not seem likely. Countries with an important livestock industry are likely to want to take advantage of the latest technological advances in livestock improvement, and the powerful pharmaceutical sector is likely to support the cloning of animals for the production of therapeutic substances. A moratorium on farm animal cloning on moral grounds is out of the question, because that would contravene international trade regulations. It would, however, be permitted on grounds of scientific uncertainty about safety, although any argument of this sort would, of course, collapse if risk assessments found no substantial risk. Finally, the Commission may choose, for moral reasons, not to support research into farm animal cloning.

In conclusion, it is difficult to identify genuine gaps in the present legal framework until further information is available from risk assessments and from subsequent discussion by the relevant experts seconded to the Commission. If non-transgenic cloned animals and their products are found to be substantially equivalent to animals already in commercial production, they may be covered by much of the existing legislation. If, on the other hand, it is decided that there is no such equivalence, and if there is public concern about issues other than risks to human health and the environment (e.g. about animal integrity and consumer choice), the legal framework will need to be amended specifically to cover non-transgenic cloned animals.

[59] Act No 22 of May 7 2004 amending Act No 38 of April 2 1993

[60] Lov om kloning og genmodificering af dyr m.v. af 14. Juni 2005 [Animal cloning and genetic modification Act of 14 June 2005

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