Cloning for reproductive purposes and cloning for the purposes of biomedical research

OPINION
Cloning for reproductive purposes and cloning for the purposes of biomedical research
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Chair: Prof. Dr Drs h.c. Spiros Simitis
Jägerstraße 22/23 · D-10117 Berlin
Phone: +49/30/20370·242 · Fax: +49/30/20370·252
Email: kontakt@ethikrat.org
www.ethikrat.org

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A INTRODUCTION

Since the birth of Dolly the cloned sheep was reported in 1997, public interest has focused also on the possibility of producing human beings by cloning using the technique of nuclear transfer. Throughout the world, such projects and experiments are regarded as abhorrent. This disapproval is reflected in numerous legal texts and political initiatives aimed at prohibiting the cloning of human beings for reproductive purposes. In its declaration of 28 November 2002, the German National Ethics Council (NER) unanimously and without reservation rejected cloning for reproductive purposes. At the beginning of 2003, the Bundestag (the Lower House of the German Parliament) passed a resolution calling on the Federal Government to work together with France and other countries at the United Nations to secure a universal ban on the cloning of human beings, whether for reproduction or biomedical research. The resolution was supported by the argument that human cloning, in whatever form, constituted a violation of human dignity and should therefore be universally repudiated. The United Nations negotiations on a cloning convention were adjourned for a year in December 2003.

Even if a United Nations resolution is adopted in the foreseeable future, it will not put an end to the worldwide debate on cloning. Owing to major differences in the views of individual countries, starkly contrasting philosophies and divergent assessments by the researchers concerned, cloning will remain a vexed question in the fundamental ethical and political debate on the future of mankind. For this reason the NER decided to present an Opinion on cloning in which it attempts to address the essential facts and to give an impression of the wide spectrum of views existing on the subject.

Cloning is defined scientifically as the asexual reproduction of cells or organisms to yield genetically identical individuals. In the living world, asexual reproduction occurs mainly in single-celled organisms, in which two daughter cells arise from a
single mother cell. Plant cuttings too are products of asexual reproduction and hence clones. In the animal kingdom, offspring are produced almost exclusively by sexual reproduction: egg and sperm cells fuse after division and recombination of the genetic material and give rise to a genetically new individual. Monozygotic twins are considered to be a special case of cloning, although they develop from a fertilized ovum formed by sexual reproduction. One individual in a twin or multiple birth cannot be regarded as the offspring of the other(s).

Developmental biologists have wondered since the late nineteenth century whether complete organisms could be cloned in animal experiments. This project proved very difficult and was at first successfully achieved only by embryo splitting; cloning by cell nuclear transfer followed in amphibians in the 1960s and in mammals two decades later.

Dolly, the sheep “created” in 1996, was the first example of a clone obtained by transfer of a somatic cell nucleus from an adult mammal into an egg cell whose maternal nucleus had previously been removed. The aim of such research is either to propagate genetically identical high-performing livestock (e.g. cattle) or to create and clone genetically modified animals whose bodies can produce human-compatible biologically active substances (such as vaccines or important proteins) which, for example, when secreted in milk, can be used for therapeutic purposes.

With the application of nuclear transfer in various species of mammals, the possibility of cloning human beings moved a step closer owing to the biological similarity of these species to man. There has since been a wide-ranging debate on the technical feasibility of producing human beings in this way, as well as on the ethical and legal permissibility of relevant experiments and of the practical implementation of any successful techniques developed. The discussion about cloning comes to a head upon each media report of a declaration of intent or announcement that a cloned baby is to be created or is already on the way. The results allegedly achieved have not hitherto been demonstrated, let alone scientifically verified.

The reproductive cloning of human beings is universally rejected by the research community. Conversely, a vigorous debate is currently raging on the production and use of cloned human embryos for biomedical research intended not to give rise to a pregnancy but to yield embryonic stem cells for further research or therapeutic experimentation. A scientific journal reported for the first time in February 2004 that cloned human embryos had been created by nuclear transfer and that embryonic stem cells had been obtained from them.

The present Opinion discusses the biological possibilities and the ethical and constitutional aspects of human cloning both for reproductive purposes and for those of biomedical research. In addition, the legal situation in the Federal Republic of Germany is discussed and the provisions applicable in certain other countries, as well as international and supranational agreements, are reviewed.
B DEFINITIONS AND SCIENTIFIC BACKGROUND

1. Definitions

1.1. Cloning

Except where otherwise stated, the term “cloning” is always used in the following in relation to the human species and denotes the artificial production of a human organism genetically identical to another human being. The term “cloning” covers the technique of somatic cell nuclear transfer (SCNT) or cell nuclear replacement (CNR) – the “Dolly technique” – as well as the artificial division of an embryo formed from germ cells (embryo splitting). Both techniques are discussed below. For pragmatic purposes, genetic identity is equated with identity of the genome of the cell nucleus. Possible differences in the few genes occurring not in the nucleus but in the mitochondria (organelles responsible for energy metabolism) are disregarded. Differences resulting from somatic mutations arising during the course of life in the cells whose nuclei are transferred are also not taken into account.

1.2. Cloning for reproductive purposes and cloning for the purposes of biomedical research

Cloning for reproductive purposes ("reproductive" cloning') denotes a process ultimately directed towards bringing about a pregnancy and the birth of a genetically identical child.

Cloning for the purposes of biomedical research (also referred to as “therapeutic” or “experimental” cloning) signifies a process intended not to bring about a pregnancy but to produce a blastocyst (an embryonic stage) from which embryonic stem cells for research purposes or therapeutic experimentation can be obtained on about the fourth day.

Cloning for the purposes of biomedical research thus initially uses the same techniques as cloning for reproductive purposes. The aims of cloning for biomedical research purposes are to study the process of development of such structures with and without genetic defects and, in the more distant future, to obtain renewed cells or tissues for the treatment of, for example, degenerative conditions. Owing to their genetic identity, these cells are expected to be particularly immunocompatible with the nucleus donor, and hence unlikely to be rejected when transplanted.

1.3. Embryo

A human embryo is defined as the organism developing from a fertilized ovum (zygote) up to the completion of basic organ development at eight weeks. The embryonic stage begins with cleavage (division without growth) of the fertilized ovum. Multiple divisions give rise to the compact berry-like cluster of cells known as the morula, which consists of a number of blastomeres (cells resulting from cleavage divisions). Further cell divisions lead to the formation of the blastocyst, a hollow, fluid-filled cellular ball, in which trophoblast cells (responsible for implantation and subsequent nutrition) are distinguished from embryoblast cells (from which the subsequent entire body can develop). Development up to this stage can also take place in vitro. Monozygotic twins can arise even after uterine

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1 The graphic phrase “cloning-to-produce-children” is sometimes also used.

2 Research on genetic diseases in man by cloning for biomedical research purposes is proposed, for example, by Wilmut (2004): 415.

3 The term "pre-embryo" stems from the British discussion of embryo research in the 1980s and denotes the development of the fertilized human ovum up to the formation of the primitive streak at the beginning of the third week. It is also applied – for instance, in the Spanish law on assisted reproduction techniques – to the stage before uterine implantation. The term is not commonly used in the German debate.
implantation, which normally commences on the fifth or sixth day after fertilization. Whereas the shape of a pre-implantation human embryo is quite unlike that of a human being, in the weeks after implantation the embryo gradually assumes human form, which is clearly recognizable in the fetus at twelve weeks. Molecular genetic methods can show unambiguously whether any in vitro embryo belongs to the human species.

The term “embryo” is also used (although the legitimacy of this usage is sometimes disputed) where an organism has come into being otherwise than through the union of an ovum and a spermatozoon.

In the current German legislation, Section 8 of the Embryo Protection Law defines an embryo as “already” being “a fertilized human egg cell with the capacity for development from the moment of kariogamy on, as well as any totipotent cell taken from an embryo which, given the further conditions necessary therefor, is capable of dividing and developing into an individual”. According to Section 3 of the Stem Cell Law, an embryo is deemed to be “already any human totipotent cell which, given the further conditions necessary therefor, is capable of dividing and developing into an individual”.

### 1.4. Totipotency

Totipotency is initially defined as the capacity of a naturally created embryo to develop after implantation in the uterus and ultimately to be born. This capacity is also possessed by an embryo formed by extracorporeal fertilization of an ovum in vitro. In experimentally created entities produced, for example, by nuclear transfer, totipotency is the criterion used to decide whether they constitute embryos or other kinds of cellular constructs. In the language of classical embryology, a cell is totipotent if it has the same capacity for development as a zygote resulting from gametic fusion — that is, if it can divide and develop into an embryonic organism and its accompanying extra-embryonic nutrient tissues. In research on mouse embryonic stem cells, it has become customary to describe cells as totipotent if they are capable of differentiating into any type of cell belonging to an organism — including gametes (germ cells) — but lack the capacity to form a complete organism by themselves. The word “totipotency” is used here, as in the relevant German legislation, to denote the capacity of a single cell to develop into a complete organism.

The existence of totipotency at any given time in an experimentally produced entity can be neither verified nor refuted for the purposes of human cloning, because appropriate experiments in humans — namely, experimental pregnancies — are precluded for ethical reasons. Moreover, according to the legal definition in the Embryo Protection Law and the Stem Cell Law, the presence of totipotency depends on a cell’s capacity to divide and develop into an individual “given the further conditions necessary therefor”; this means that failure to demonstrate totipotency could always be explained by invoking the legal definition, on the grounds that an essential further condition was not satisfied.

In animal experiments, embryonic stem cells (ES cells), whether singly or in clusters, are regarded as non-totipotent because they do not form a trophoblast for the subsequent development of the essential surrounding nutrient tissue.

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6 A totipotent cell is defined as follows in the Opinion of the American President’s Council on Bioethics: “A cell with an unlimited developmental potential, such as the zygote and the cells of the very early embryo, each of which is capable of giving rise to (1) a complete adult organism and all of its tissues and organs, as well as (2) the fetal portion of the placenta” (The President’s Council on Bioethics 2002:55).

7 The legal definition is based on conditions that are not precisely defined: “Totipotency is the capacity of a cell to divide and develop into an individual given the further conditions necessary therefor.”

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4 Media reports on the early embryonic phase are sometimes misleadingly illustrated with representations of an embryo with recognizable human form in the second month. The National Ethics Council’s Opinion on genetic diagnosis before and during pregnancy (January 2003) includes information and illustrations on the course of early human development.

5 See Section C.
viable animal originating solely from ES cells can arise only from a cellular cluster and then only in the presence of other cells capable of forming a trophoblast. However, the conditions for this development are present in the genome, so that only the “further conditions necessary therefor” would need to be supplied artificially in order for this capacity too to be reactivated.

At least in animal experiments, totipotency can be achieved by experimental manipulation, one approach being modification of an individual cell before embryogenesis. In the “creation” of Dolly the sheep, for instance, a totipotent construct was formed from an udder cell after transplantation into an enucleated oocyte. Totipotency can also be reduced or prevented altogether by manipulation: one or more genes essential for subsequent implantation of the blastocyst created could already be blocked at the time of culturing of the donor cell or isolation of the cell nucleus for transfer. Such precautions, taken before production of the clone, would, it is hoped, preclude actual or potential totipotency in the resulting entity. In such a case, totipotency cannot be used as a reliable criterion, unaffected by external actions, of whether a human embryo exists in a practical situation. Hence the only remaining way to determine the totipotency or otherwise of experimentally created human constructs is argument by analogy: if experiments in a large number of animal species regularly lead to a demonstrably totipotent product – because a new individual was born – it can be inferred that human entities created by the same procedures would also be totipotent. Although the results of animal experiments cannot be totally extrapolated to man, the report published in February 2004 on the creation of cloned human embryos by nuclear transfer and the subsequent derivation of stem cells (see Section A 4.2) indicates that reasoning by analogy is a valid approach.

2. Cloning techniques and other methods of artificially producing blastocysts

Two main techniques proven in animal experiments are candidates for the application of cloning to man – namely, embryo splitting and nuclear transfer. In addition to these procedures, some other methods of artificially producing blastocysts that can be used for the derivation of stem cells are outlined below. However, these entities lack the property of genetic identity that is characteristic of a clone.

2.1. Embryo splitting

The technique of embryo splitting imitates the natural formation of monozygotic twins. Twins can arise through splitting of a morula or blastocyst. In animals, a morula can also be broken up by removing the primary zona pellucida and inserting the cells in groups into empty zones so as to produce multiples. In this way, a number of genetically identical embryos are obtained from a single embryo. This technique can be used in such species as the mouse, rat, rabbit, sheep, cow, pig and rhesus monkey. It would presumably be feasible in humans too. In animals, identical multiples can also be produced from ES cells: if mouse ES cells are injected into blastocysts from other mice treated to inhibit independent embryo development (tetraploidy), viable mice whose genome is identical to that of the ES cells develop. The defective (tetraploid) cells of the host blastocyst contribute solely to the extra-embryonic tissue responsible for implantation and subsequent nutrition.

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8 Nagy et al. (1990); Nagy et al. (1993); Wang et al. (1997); Eggan et al. (2001).
9 Such blocking is possible if the sequence and position of the relevant gene are known. Such interventions may well become feasible as more information becomes available on the human genome and its functions. With gametes, too, precautions could be taken to ensure that, whereas they can form blastocysts after fertilization, these will not be capable of further development.
10 Escribá et al. (2002).
11 Nagy et al. (1993); Eggan et al. (2001).
2.2. Cell nuclear transfer

For the technique of nuclear transfer, a receptor oocyte and the nucleus of a donor cell are required. The former provides the medium necessary for development, as an embryo can develop only if developmental factors that support and control the initial phases of development are present in the cytoplasm (cell sap) of the oocyte. The oocytes also contain components necessary for structuring the cell’s component parts up to the stage of blastocyst formation. The nucleus of the donor cell furnishes the genetic traits of the donor, with which or whom the clone is intended to be genetically identical.

The receptor cell consists of an oocyte from which the nucleus is removed, for example by aspiration with a micropipette. This makes the oocyte “genetically dumb”; the only genetic material remaining in it comprises a small number of genes present not in the genome of the nucleus but in the mitochondria. This means that the clone is, strictly speaking, not wholly genetically identical to the donor, unless the oocyte and the transferred cell nucleus are taken from the same (female) individual. This residual complement of genes from the receptor oocyte may be significant in some cloning applications, but is usually regarded as negligible in practice. The donor cell nucleus is fused with the enucleated oocyte, thus giving rise to a single-celled entity equivalent to an ovum fertilized by a spermatozoon. If this structure can be stimulated to divide spontaneously and to develop, it is a cloned embryo.

2.3. Other techniques

In animal experiments, blastocysts and embryonic stem cells are also produced by methods other than somatic cell nuclear transfer. For instance, one research group reports the activation of unfertilized oocytes of non-human primates (in which a diploid, largely homozygotic cell arises by fusion of the haploid nucleus of the second polar body with that of the oocyte), which then developed to the blastocyst stage (parthenogenesis, or “virgin procreation”). Stem cells with characteristic properties of ES cells, which differentiated in vitro into various cell types, were derived from the blastocysts. According to the authors, their results might be a potential alternative to human cloning for the purposes of biomedical research, although these blastocysts are not genetically identical to the oocyte donor. However, the derivation of stem cells from unfertilized human oocytes would not permit the production of stem cells for male patients.

It is known from animal experiments that, in mammals, parthenogenetically activated oocytes as such are not capable of development. Although they may form blastocysts, the trophoblast is smaller than normal. The blastocysts may implant and begin to differentiate like an embryo, but the resulting pregnancy soon ends in spontaneous abortion. Yet the possibility of using parthenogenetically created blastocysts to obtain stem cells for therapeutic purposes cannot be ruled out.

Another group of workers, working with long-term cultures of mouse embryonic stem cells, succeeded in producing oocyte-like cells from both female and male stem cells. Blastocyst-like structures sometimes arose from these oocyte-like cells in culture without fertilization.

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12 For instance, there is some debate as to whether proteins coded for by mitochondrial DNA might cause an immune reaction in the nucleus donor after a cell or tissue transplant.

13 Fusion can be effected by, for example, electrical stimulation after the nucleus has been injected into the empty oocyte with a micropipette.

14 Cibelli et al. (2002).
15 Vrana et al. (2003).
16 Holden (2002).
17 Hübner et al. (2003).
18 The cells showed the markers characteristic of gametes in the experiments reported so far. However, it is not yet proven whether they are in fact functional germ cells.
A recent paper also reports the successful ripening\textsuperscript{19} of sperm-like\textsuperscript{20} cells from mouse embryonic stem cells and their use for the fertilization of mouse oocytes. The resulting embryos developed into blastocysts.\textsuperscript{21}

3. Success rates in the cloning of mammals

3.1. Reprogramming of cell nuclei

For successful creation of an embryo by nuclear transfer, the cell nucleus to be cloned must be suitably prepared. A growing cell, which becomes increasingly specialized in the course of somatic development, progressively diverges from the original state of the fertilized egg cell. Its DNA is then modified, for example, by attached methyl groups. Although these leave the information content of the genetic material unchanged, they regulate how this information is read and determine which genes in which cells are inactive and which are active.\textsuperscript{22} The spectrum of cellular RNA and proteins changes correspondingly. For nuclear transfer, all functional states must be returned (reprogrammed) to that typical of the fertilized egg cell. The closer the cell whose nucleus is transplanted into the egg cell is to the embryonic state, the more successful the cloning process will be: the best results in animal experiments are obtained with nuclei from embryonic cells and embryonic stem cells, as well as from cells obtained from gamete-producing tissues (testicles or ovaries). The reprogramming of somatic cell nuclei is very seldom successful, and it was precisely the success of cloning after nuclear transfer from a sheep udder cell that made the report of the birth of Dolly in 1997 so sensational. For this reason, particular attention must be devoted to the factors whereby reprogramming of a somatic cell nucleus can be achieved.

3.2. Success rate of cloning techniques using nuclear transfer

A number of studies – which, however, lack statistical significance – have been conducted on the success rate of reproductive cloning in various mammal species. These show major fluctuations depending on species, the tissue from which the donor cell nucleus was obtained, and other factors. Offspring are born on average in no more than 4% of cases of nuclear transfer to an oocyte.

The success rate – i.e. the yield of born animals – is higher in all species once the blastocyst stage has been reached. However, the range of success rates reported is very wide and manifestly also dependent on the precise details of the techniques used, so that a definitive judgement is not yet possible. The results of cloning after blastocyst implantation would appear to be quite good in cattle (the success rate in some cases exceeding 50%, referred to blastocysts), appreciably poorer in sheep and goats (around 10%) and particularly bad in mice, rats, rabbits, pigs, cats, horses and mules (a few per cent at most). To date, it has proved totally impossible to clone dogs and monkeys by somatic nuclear transfer.

3.3. Health status and vitality of clones

In addition to the large number of clones lost by abortion and others born with severe deformations, a few physically vital clones have been obtained in animal experiments and even brought to maturity and reproduction. In these cases, the clones’ offspring seem to have developed normally.

\textsuperscript{19} Toyooka et al. (2003).
\textsuperscript{20} See footnote 18.
\textsuperscript{21} Geijsen et al. (2004).
\textsuperscript{22} Individual genes are labelled (“imprinted”) according to their paternal or maternal origin. The second X-chromosome is inactivated in female individuals. Chromatin – the form in which DNA is packaged in chromosomes – may be present in different functional states. The histone proteins surrounding the chromosome may also be modified.
Yet it is disputed whether the clones’ vitality and life expectancy come close to those of naturally produced individuals. Many clones exhibit “large offspring syndrome”, while conditions associated with premature ageing and other manifestations of wear and tear have been observed in others. Clones may tend to inherit severe somatic mutations from their donor individuals. Furthermore, many reprogramming errors seem to have effects that persist into adulthood. Finally, a clone may “assume” the biological age of the donor if this is manifested at cell nucleus level (e.g. in telomere length\textsuperscript{23}). Insufficient research has yet been carried out to determine whether undamaged mammal clones are at all possible. At any rate, Dolly the sheep developed severe arthritis at the age of six years. Externally vital cloned cattle have not yet been observed for long enough for a final judgement to be possible. On the basis of their experience with mouse clones, some workers believe that wholly undamaged clones can exist. They consider it more probable that embryonic stem cells can be produced from cloned embryos, because the vital cells would multiply preferentially in stem cell cultures with their large number of cycles of division; moreover, these cells would not need to possess all the functions required for the development of a fully functioning organism.

4. Human cloning

As late as in April 2003, some scientists still considered that the “Dolly technique” might not be applicable in humans. Results obtained with rhesus monkeys suggest that, in non-human primates, enucleation of the receptor oocyte also removes components essential to further cell division and development.\textsuperscript{24} Hence the assumption that, in man, cloning for reproductive purposes would be impossible and cloning for biomedical research purposes extremely difficult.

In February 2004, however, as stated earlier, the creation of cloned human embryos by cell nuclear transfer was reported for the first time in a scientific journal.\textsuperscript{25}

4.1. Cloning for reproductive purposes

It is as yet unclear whether successful human cloning for reproductive purposes is feasible. The reprogramming errors unavoidable in cloning are so numerous and so randomly distributed that control or correction of their effects appears impossible, at least for the foreseeable future. According to the current state of our knowledge, any attempt actually to clone human beings for reproductive purposes would carry an extremely high risk of severe health impairment, malformations, deformities, serious pathological syndromes and drastically reduced life expectancy in the clones.

4.2. Cloning for the purposes of biomedical research

A multi-stage procedure is necessary for the creation of cells or tissues potentially usable to treat, for example, degenerative diseases. After nuclear transfer and formation of a blastocyst, ES cell lines are produced from its inner cell mass. The ES cells are differentiated in vitro into the desired cell type and transferred to the recipient. The entire process has hitherto been conducted in animal experiments only in a very small number of cases: haematogenic stem cells and dopamine-forming nerve cells were produced and transplanted into the mice from which the donor cell nuclei originated.\textsuperscript{26} On average some

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\textsuperscript{23} Telomeres are short segments of DNA at the ends of the chromosomes, which become shorter upon each cell division and ultimately disappear. No further cell division is then possible.

\textsuperscript{24} Simerly et al. (2003).

\textsuperscript{25} Hwang et al. (2004).

\textsuperscript{26} Rideout et al. (2002). The treated mice, which were unable to develop an immune response owing to a genetic defect, formed immune-defence
60 oocytes were consumed for the production of one ES cell line after nuclear transfer in the mouse.27

The experiments mentioned earlier, on the cloning of human embryos, required a total of 242 oocytes from 16 women. Nuclei from cumulus cells28 of the relevant oocyte donors were transferred to 176 enucleated oocytes (autologous nuclear transfer).29 Thirty blastocysts developed; the inner cell mass was successfully extracted from 20 of them and a stem cell line was finally derived from just one of these 20.

Owing to the high demand for human egg cells, attempts have been made to use non-human oocytes as receptor cells. According to one report, the transfer of human cell nuclei into enucleated rabbit oocytes yielded blastocysts from which cells with some of the properties of ES cells were successfully extracted.29

However, more interest was aroused by the paper mentioned in Section 2.3, in which it was shown that oocyte-like cells could be generated in vitro from mouse ES cells.30 If the oocyte-like cells obtained in this way could be used as receptor cells in nuclear transfer and the procedure were also possible with human stem cells, oocytes harvested direct from donors’ bodies would no longer be necessary for human cloning.

5. Outstanding issues

It has not yet been established whether cells and tissues obtained from the transfer of somatic cell nuclei into enucleated oocytes, once transferred to a receptor, function correctly and also integrate into the tissue structure during the course of their subsequent development. Whereas some workers consider this possible, others take the view that this is the wrong approach to the production of cells capable of regeneration, and opt instead to use embryonic stem cell lines derived from embryos resulting from the fertilization of egg cells (e.g. excess embryos left over from extracorporeal fertilization). Still others hold that correctly functioning cells can be obtained by selection from embryonic stem cell lines irrespective of how they were produced. Again, owing to the higher probability of tumour formation with embryonic stem cells, some experts consider the use of adult stem cells to be the best research strategy.

In the view of many scientists, the fundamental issues should, at least initially, be investigated by animal experiments prior to any attempt with human cells.

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27 Wakayama et al. (2001).
28 Cells which surround and nourish the oocytes during maturation.
29 Since the oocytes and cell nuclei originated from the same women, the possibility of parthenogenetic activation cannot be completely ruled out. However, this is considered unlikely owing to the presence of heterozygotic chromosomes and the expression of genes labelled according to paternal and maternal origin.
30 Chen et al. (2003).
31 Hübner et al. (2003).
C CURRENT LEGAL SITUATION

1. In Germany

The undisputed aim of the German Embryo Protection Law (ESchG) passed in 1990 was to prohibit human cloning in all its forms, and moreover to make the ban subject to penal sanctions. However, experts disagree on whether the existing provisions satisfy the strict requirements of Article 103(2) of the Basic Law on the specificity of criminal-law prohibitions. The following highly condensed account of the legal situation outlines the differing positions on certain points to be found in the literature.

1.1. Prohibition of cloning under Section 6(1) of the Embryo Protection Law

1.1.1. Foundation

The primary legal foundation of the cloning ban is Section 6(1) of the Embryo Protection Law, which provides that anyone “who artificially causes a human embryo with the same genetic information as another embryo, a fetus, a human being or a deceased person to come into being” shall be liable to penal sanctions. With regard to modern cloning techniques, two possible violations of this provision call for closer examination. Firstly, does a human embryo within the meaning of the Law actually come into being in the cloning situation, and, secondly, does the clone have the “same genetic information”? The two questions must be answered separately for embryo splitting on the one hand and nuclear transfer (the “Dolly technique”) on the other.

1.1.2. Presence of the same genetic information

In the case of embryo splitting, the genetic information is identical, as the separated cells or divided blastocyst comprise cells or cellular clusters from the same human organism.

The situation with the nuclear transfer method differs in that, owing to the mitochondrial genes contained in the enucleated oocyte, 0.01–0.02% of the total genome does not coincide with the genetic information contained in the transplanted nucleus, at least if the enucleated oocyte and the transferred cell nucleus do not originate from the same (female) individual. For this reason, a few authors consider that the element of the “same” genetic information pursuant to Section 6(1) of the Embryo Protection Law is lacking. However, the overwhelming body of jurisprudence agrees with general usage in deeming this degree of identical genetic information to be perfectly legitimately described by the word “same”, so that this element is regarded as present in the case of the nuclear transfer method too.32 It is indeed true that the “same” genetic information would no longer be present if the somatic cell nucleus were substantially modified in its genetic structure prior to transfer into the enucleated oocyte; Section 6 of the Embryo Protection Law would then be inapplicable.

32 According to recent estimates, the human genome contains some 25,000 genes. Exactly 37 by no means unimportant genes (0.15%) are located outside the cell nucleus in the “mitochondria”; as a rule, these are transmitted only in the maternal line with the cytoplasm of the egg cell and hence do not originate from the transferred nucleus in cloning by the “Dolly technique”. Expressed in terms of “genetic letters”, the proportion of the total information accounted for by the mitochondrial DNA is 0.005% (16,600 out of approximately 3.2 billion). By comparison, the difference between two unrelated persons of the same sex is about 0.1% (approximately 3 million out of 3.2 billion letters). Disregarding the very small proportion of mitochondrial DNA, a clone is said to be “genetically identical” if the genome of the nucleus, and hence in practice most of the genes, are copied identically. In highly exceptional situations, however, the ascription of the term “genetically identical” in cloning by cell nuclear transfer could conceivably be of doubtful validity owing to substantial differences between the donor of the cell nucleus and the clone – for instance, (i) manipulation (e.g. “knock-out”) of an important gene before cell nuclear transfer, or (2) the presence of genetic mutations in the mitochondrial genome of the cell nucleus donor. A number of diseases are due to mutations in mitochondrially coded genes. Since the clone does not include the mutation, it does not fall ill and therefore differs substantially from the “original”, notwithstanding a high degree of quantitative agreement in the genetic information.
not be understood purely chronologically in the sense of “before the time in question”, but should be interpreted in the sense of “also”, so that any egg cell capable of development, and hence also a fertilized egg cell from the moment of karyogamy on, is covered. However, an egg cell could, according to this view, also attain a stage of development corresponding to the post-fertilization stage by nuclear transplantation. Another interpretative element adduced here is the comprehensive prohibition of cloning considered to be the intention of the legislation.

1.2. Prohibition of cloning under Section 2(1) of the Embryo Protection Law

Embryo splitting also contravenes Section 2(1) of the Embryo Protection Law, which includes a prohibition on the use of an embryo for a purpose other than that of its preservation. The splitting process is a use which can hardly be imagined as serving the purpose of preserving the embryo that undergoes it.

In addition, Section 2(1) of the Embryo Protection Law can be applied to non-reproductive cloning if an embryo formed by splitting is consumed for biomedical purposes.

However, nuclear transfer is covered by Section 2(1) of the Embryo Protection Law only if it is assumed that the entity created by that technique is an embryo within the meaning of the Law. As in the case of Section 6(1) of the Embryo Protection Law (see Section 1.1.3. above), the result once again depends on the disputed question of interpretation involved in the definition of an embryo.

1.3. Prohibition of cloning by nuclear transfer under Section 5(1) of the Embryo Protection Law?

Since Section 5(1) of the Embryo Protection Law bans the artificial modification of the genetic information contained in a
human germ line cell, the question arises whether cloning by nuclear transfer constitutes an infringement of this prohibition. Germ line cells are defined in Section 8(3) of the Embryo Protection Law as all cells that lead in a cell line from the fertilized egg cell to the egg and sperm cells of the human individual originating from it, as well as the egg cell from the insertion or penetration of the sperm cell up to the completion of fertilization as represented by karyogamy. Here, both the enucleated oocyte and the donor cell must be considered. At least in the case where the cell whose nucleus is transferred to the enucleated oocyte is not a germ line cell, Section 5(1) of the Embryo Protection Law cannot be invoked to justify a prohibition of cloning. As to the designated receptor egg cell, the prohibition of artificial modification of human germ line cells cannot be deemed to have been infringed, because this egg cell is not used for fertilization (see Section 5(4) No. 1 of the Embryo Protection Law). The nuclear transfer procedure in fact substitutes for fertilization.

1.4. Interim conclusion

It follows from the foregoing that, whereas in Germany the Embryo Protection Law unequivocally prohibits the cloning of human organisms by the technique of embryo splitting, the same cannot be said for the nuclear transfer method, although there is no doubt that the original intention of the relevant legislation was a comprehensive ban on cloning.

2. In Europe

The first relevant European instrument is the Council of Europe’s Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine of 4 April 1997, which took effect on 1 December 1999. The Additional Protocol on the Prohibition of Cloning Human Beings of 12 January 1998 (which came into force on 1 March 2001) is based on this Convention. Article 1.1 of the Additional Protocol provides as follows: “Any intervention seeking to create a human being genetically identical to another human being, whether living or dead, is prohibited.” For this purpose, according to the legal definition given in Article 1.2, possession of the “same nuclear gene set” as another living organism suffices to constitute genetic identity, so that the mitochondrial genes of the enucleated oocyte are irrelevant. In addition, Article 18 of the Convention prohibits the creation of human embryos for research purposes.

Since the Federal Republic has not hitherto acceded to the 1997 Convention and the Additional Protocol is open only to states that have signed the basic convention, neither of these European documents has legal force in Germany. Even in the event of accession, the legal situation described in Section 1 above would not immediately change. This is because the agreements leave the interpretation of the terms “human organism” and “human embryos” to the individual contracting states. Hence the Netherlands, for example, in signing the cloning protocol, declared that it interpreted the term “human being” in Article 1 as referring solely to born human beings.

The above considerations on the Convention apply also to the relevant provisions of the European directive on the legal protection of biotechnological inventions (98/44/EC) and the draft law transposing it into German law, which is currently before Parliament, in so far as “processes for cloning human beings” are described both in Article 6(2) of the directive and, in the same words, in Section 2(2) of the draft, as being contrary to ordre public and contra bonos mores.

Finally, the “Charter of Fundamental Rights of the European Union” of December 2000 contains a prohibition on reproductive cloning and eugenic practices (fourth indent of
A UN General Assembly resolution would not directly modify the legal situation in individual states, but would nevertheless have considerable political significance.

4. The situation in other countries

4.1. Cloning for reproductive purposes

Most countries either have, or are preparing, an explicit legal prohibition of human cloning for reproductive purposes. Cloning for reproductive purposes is legally prohibited in, for example, Austria, Denmark, Finland, Italy, Norway, Sweden, Switzerland, the United Kingdom, Australia, India, Japan, Singapore, South Korea, Argentina, and Brazil, as well as in certain American States (for example, Arkansas, California, Iowa, Michigan, New Jersey, North Dakota, Rhode Island, and South Dakota). A bill providing for a ban on all cloning in every State of the Union was introduced in Congress at the beginning of 2003, but has not so far been passed. In France, cloning for reproductive purposes is prohibited by the Bioethics Law adopted by the National Assembly and the Senate in July 2004.

In Israel, cloning for reproductive purposes was initially prohibited until the beginning of 2004; the relevant law was renewed in March 2004 and bans cloning for reproductive purposes for a further five years. There is also a legal moratorium in Russia.

In addition, a number of states, some of which have no specific legislation on reproductive cloning, have signed and ratified not only the Council of Europe’s Convention on Human Rights and Biomedicine but also the Additional Protocol on the Prohibition of Cloning Human Beings – namely, Croatia, Cyprus, Czech Republic, Estonia, Georgia, Greece, Hungary, Lithuania, Moldova, Portugal, Romania, Slovakia, Slovenia, and Spain. The following countries have signed but not yet ratified the Convention and the Additional Protocol: Finland, France,
Iceland, Italy, Latvia, Luxembourg, Netherlands, Norway, Poland, Sweden, Switzerland, Turkey and the Former Yugoslav Republic of Macedonia.

4.2. Cloning for the purposes of biomedical research

A number of different approaches to the regulation of cloning for the purposes of biomedical research can be distinguished, mainly reflecting differing views on the permissibility of research on human embryos.

4.2.1. Statutory permissibility

Cloning for the purposes of biomedical research is legally permitted in some countries. In the United Kingdom, embryos may be produced for research purposes, and the technique of nuclear transfer is also allowed. Research on embryos is confined to the first 14 days of development and each research project must be approved by the Human Fertilisation and Embryology Authority (HFEA). The production of embryos and cloning for the purposes of biomedical research are also subject to HFEA licensing. The HFEA granted the first licence for cloning for biomedical research purposes in August 2004.

In Belgium, a law that implicitly permits cloning for the purposes of biomedical research was passed in 2003: the creation of embryos for research purposes is permissible if no excess embryos are available for the research project concerned. Cloning for the purposes of biomedical research is also legally permissible in Israel, Singapore and certain American States, such as California, Massachusetts, New Jersey and Rhode Island.

The Swedish Parliament is currently discussing a draft law on stem cell research that also provides for the limited sanctioning of cloning for the purposes of biomedical research. Japan is at present preparing guidelines for the creation and use of human embryos for research purposes; the production of cloned embryos is also to be allowed.

4.2.2. No statutory regulation

Other countries and territories have no specific legislation on cloning for the purposes of biomedical research; the procedure is regarded as permissible there. This is the case, for example, in Luxembourg and most American States.

In some countries that have signed and ratified the Council of Europe’s Convention on Human Rights and Biomedicine and the Additional Protocol on the Prohibition of Cloning Human Beings, it has not yet been established whether cloning for the purposes of biomedical research is also prohibited under the Convention. The reason for this uncertainty is that, whereas the Convention bans the creation of human embryos for research purposes, it leaves the definition of an embryo to the contracting states. The Additional Protocol also leaves open the question of the point in time from which a genetically identical “human organism” is deemed to exist. The Swedish Research Council, for example, while regarding cloning for biomedical research as permissible, considers it incompatible with the Convention on Human Rights and Biomedicine, which Sweden has signed but not yet ratified. The same ambiguous stance is exhibited by countries such as Greece and Portugal.

4.2.3. Statutory prohibition

Cloning for the purposes of biomedical research is prohibited by law in, for instance, Austria, Italy, Norway, Spain, Australia and Switzerland. The Bioethics Law recently passed in France
also prohibits cloning for the purposes of biomedical research. A law banning cloning of any kind has been in force in Canada since April 2004; it is to be reviewed after three years.

The Dutch Embryo Law of 2002 prohibits the creation of human embryos for research purposes; however, this ban may be set aside within five years by decree. It is thus a moratorium rather than a prohibition. The Law is considered also to apply to somatic nuclear transfer.

In Ireland, there is no explicit prohibition of cloning; the extent of the rights of unborn children laid down in the Constitution has not been established in relation to cloning. The Irish Council on Bioethics presumes that, in the event of judicial proceedings, embryo research or cloning would be declared unlawful.

In Finland, the production of embryos for research purposes is prohibited by law; however, it is questionable whether nuclear transfer gives rise to an embryo within the meaning of the relevant law.

In the USA, cloning for the purposes of biomedical research is prohibited in some States, such as Arkansas, Iowa, Michigan and North Dakota. Relevant laws are still in preparation in a number of other States (e.g. Alabama, Connecticut, Florida, Texas and Wisconsin).

D CLONING FOR REPRODUCTIVE PURPOSES: ETHICAL AND CONSTITUTIONAL ASSESSMENTS

1. Position statement

The National Ethics Council (NER) unanimously declares itself in favour of a worldwide ban on the cloning of human beings for reproductive purposes and of a clarification of the German legal situation in the form of a criminal-law prohibition. The NER also unanimously holds that the cloning of human beings for reproductive purposes must be rejected not only in the present state of science and research, but also absolutely.

2. Arguments

A number of arguments can be adduced in favour of prohibition; however, these are assessed differently by individual members of the National Ethics Council, who also attribute differing levels of importance to them.

1. In cloning for reproductive purposes, the clone’s genetic endowment is deliberately laid down by third parties in such a way as to be identical with that of a living or deceased human being. Reproductive cloning is thus irreconcilable with the self-conception and fundamental values of a society based on respect for the non-disposability of every individual.

2. If the aim of reproductive cloning is to produce human beings conforming to the ideas and expectations of their “producers”, however variable the objectives, the result will be an instrumentalization incompatible with respect for human dignity.
3. Cloning for reproductive purposes seeks to use the ability to copy existing genomes in order to endow human beings with specific genetic characteristics regarded as desirable. This is tantamount to an attempt to promote and implement a form of positive eugenics.

4. By virtue of the deliberate specification of genetic endowment, cloning for reproductive purposes violates the principle of respect for the free unfolding of the personality and of individual self-determination. These must be safeguarded even before the exercise of self-determination becomes possible.

5. Reproductive cloning also violates the human dignity of the cloned person.

6. Reproductive cloning runs counter to the view of how human individuals should come into being that is inherent in man’s conception of himself.

7. Reproductive cloning disrupts generational and family structures that have hitherto been regarded as self-evident, so that relationships of vital importance for social identification are blurred.

8. The use of reproductive cloning, even for the treatment of infertility, is inconsistent with the medical treatment contract.

9. Cloning experiments, at least under current scientific conditions, consume large numbers of oocytes, the harvesting of which poses a health risk to their donors. There is also a risk of instrumentalization and commercialization irreconcilable with women’s dignity and self-determination.

10. As animal experiments have shown, reproductive cloning entails a high risk of severe pathology and malformations in the clone. In the event of pregnancies, too, a high abortion rate is likely, resulting in serious physical and mental stress for the women concerned.

11. Experiments directed towards human reproductive cloning must be rejected without exception. Even if cloning techniques not involving unacceptable risks were one day to become available – a decidedly improbable assumption according to all currently available information – a research phase necessarily including human experiments of this kind would be unavoidable.

However, should a clone be born notwithstanding the prohibition of reproductive cloning, the nature of his genesis would not justify denying him human dignity.

3. Discussion

The above arguments have been thoroughly discussed in the National Ethics Council. The main points arising are set out below.

3.1. The clone (or “copy”)

3.1.1. Does the cloning process violate the clone's human dignity?

Violation by creation?
A categorical ban on cloning for reproductive purposes can be justified on the grounds that an act whose aim is the creation of a human being will always be impermissible if the nature and consequences of that creation violate his dignity. The violation of human dignity lies in the deliberate making of a
genetic copy and the intentional specification of the genetic endowment by third parties, as a rule for certain purposes (the form of the clone's creation), as well as in the fact that the clone will not later be able to decide against this specification (the consequences of his creation).

An objection to this argument is that, at the time of the act of production, there is not yet a being whose human dignity could be violated. Self-determination as an expression of human dignity cannot extend to the processes that determine an individual’s genetic constitution. Naturally begotten human beings have just as little influence over their own genetic constitution as clones. No one has the right to a given genetic endowment, and hence also the right not to have been born (or not to have been born as they were born).

**Violation of the prohibition of instrumentalization?**

Those who consider that cloning for reproductive purposes constitutes an instrumentalization that violates human dignity point out that the deliberate making of a genetic copy is as a rule done for a specific purpose; for example, couples who have lost a child or other relative might wish to clone the individual concerned with a view to replicating him at least genetically. Alternatively, they might want to obtain immunocompatible cells or tissues for a sick family member once the clone has been born. Similarly, an individual might wish to translate fantasies of immortality into reality.

Critics of this argument first of all fundamentally question the practical value of the notion of instrumentalization, on the grounds that it is ill-defined and used in different senses or merely as an empty formula. They then reject the charge of instrumentalization by pointing out that, in the course of their lives, people are repeatedly exposed to instances of and attempts at instrumentalization. These are prohibited only if, by the nature of the action, an individual is considered not primarily for his own sake but is instead used firstly, and essentially, as a means for the achievement of the aims of others. However, parents might love their cloned child for his own sake without necessarily having had a specific extraneous purpose in mind in creating him – for example, if they did not wish to resort to third-party egg or sperm donations and could have a child of their own only by cloning. Furthermore, some parents may perfectly well decide to have a child in the natural way for a specific purpose, such as to take over the family business or to overcome relational difficulties.

**Does specification of genetic endowment deny a clone the status of a subject?**

Human dignity is also considered to be violated if a clone is given a specific genetic endowment by the intentional action of a third party. In this respect the clone – unlike individuals whose genome is determined by a natural process at the time of conception – is subjected to an alien will in a substantial part of his personality, and hence with regard not only to the fact of his existence but also to the nature of his being; he is thereby turned into an object. Unlike the situation in, for example, the choice of a partner, with which, of course, a certain genetic selection is also made, the randomness of genetic recombination is precluded by cloning. Although genetic identity does not wholly condition future personality development, it nevertheless lays down the biological framework from which the individual will be unable to free himself.

For those who take the opposite view, this approach is based on a genetic determinism that must be rejected: the intentionality involved in the specification of the clone’s genetic endowment cannot be a deciding factor, because it is not necessarily immoral to pursue intentions in one’s choice of partner and in procreation. An unmanipulated genetic endowment is not an essential prerequisite for a child’s possession of the status of a subject. A subject’s individuality cannot be predicted or described even if his genetic endowment is known in detail.
Furthermore, this argument in favour of the prohibition of reproductive cloning is directed against an action that relegates the offspring’s subjecthood to the background, so that the offspring appears as a product and not a subject. The difference between a person and a thing, a human being and merchandise, is deliberately abolished. This is all the more serious because cloning is underlain by far-reaching social preconditions, which a large number of institutions and persons are purposefully seeking to bring about. Their intention is to specify the nature of the clone in such a way that his self-determination is threatened from the start.

Conversely, according to the opposite position, the categorical distinction between merchandise and a human being is not abolished simply by the coming into being of a genetic twin at a later date, and there is no inherent ethical merit in the chance workings of genetics.

3.1.2. Personal rights: safeguarding of future self-determination

The above remarks about the deliberate specification of genetic endowment can also be applied to the right to safeguarding of the conditions for free unfolding of the personality and self-determination – even at a time when the exercise of self-determination is not yet possible.

Those espousing the opposite position once again see this as an instance of latent genetic determinism and point out that the unfolding of an individual personality depends on a large number of – mainly social – circumstances.

3.2. The person who is cloned (the “original”)

3.2.1. Human dignity and personal rights

Cloning for reproductive purposes is sometimes also regarded as a violation of the human dignity of the cloned “original”.

This assumption would be justified in the case of involuntary cloning, which would constitute a failure to respect his personal rights. By the production of a clone, the “original” would be genetically replicated without his consent or even against his will, thus calling into question his genetic uniqueness. The cloning of deceased persons would infringe their post-mortal personal rights unless they have consented to it during their lifetime.

However, opinions differ on whether the voluntary replication of a living cell donor can also be seen as a violation of his individual human dignity.

It is argued that human dignity is an objective magnitude and does not therefore fall within its subject’s power of disposition. Involvement in such a serious infringement of human dignity as reproductive cloning would thus also violate the human dignity of the person who allows himself to be cloned.

The objection to this argument is that it necessarily involves a contradiction: human dignity is thereby turned against its personal subject, robbing him of his individual autonomy – which, however, the Basic Law precisely seeks to guarantee.

3.2.2. Freedom to reproduce

Whether a cell donor who is prepared to be cloned can invoke the freedom to reproduce is a matter of debate. Although the Basic Law does not contain any explicit provisions on this point, it is universally agreed that this freedom enjoys the protection accorded to fundamental rights. Again, no one denies that the freedom to reproduce is a high-level ethical good.

However, the freedom to reproduce is not an absolute right guaranteed without restriction. As with all other freedoms, restrictions on this right are permissible. These must serve a higher-order purpose and be consistent with the principle of proportionality. Examples of reasons for limiting the freedom to reproduce are damage to the clones themselves, on the one hand, and, on the other, risks to the fabric of society, the
potential for abuse, or the erosion of society’s fundamental convictions about rights. A further consideration is that cloning might entail a violation of human dignity.

3.3. Other persons involved in reproductive cloning

3.3.1. Harming and instrumentalization of oocyte donors

All successful cloning experiments hitherto carried out on animals have involved substantial consumption of oocytes. The harvesting of human oocytes is a stressful medical procedure that entails hormone treatment, surgical removal of oocytes by ovarian puncture, and a not insignificant health risk to donors. A possible alternative is considered to be the donation of ovarian tissue from an individual woman, provided that it was technically feasible to bring the large number of oocytes present in it to maturity.

Both cases give rise to the danger of development of a demand-driven market in oocytes or ovarian tissue, resulting in financial incentives and consequent possible risks to women’s self-determination.

Those espousing the opposite position consider that these problems of oocyte or ovarian tissue donation could be avoided by a requirement of informed consent.

Recent literature suggests that it may in future be possible to obtain oocyte-like human cells from stem cell cultures. The use of such a technique would invalidate the argument of instrumentalization or harming of women. However, it is doubtful whether such oocytes would be suitable for reproductive purposes.

3.3.2. Women who carry cloned embryos to term

Animal experiments have shown that cloning by nuclear transfer gives rise to reprogramming errors that impair the developmental potential of cloned embryos. Any such pregnancies would therefore be very likely to end in spontaneous abortions.

These are considered to constitute a source of considerable physical and mental stress for the women concerned.

Here again, according to the opposite view, women should have the right to give their autonomous informed consent to exposing themselves to these stresses.

3.3.3. Role of the medical profession

Some bring specifically medical arguments to bear against reproductive cloning. No one disputes that, from the medical point of view, the creation of a human being by cloning violates the professional principle of primum non nocere, as the procedure entails considerable health risks to the clone.

It is further argued that medical ethics require a woman wishing to become pregnant with a cloned embryo to be protected from expected or probable self-harm.

Others, while also favouring the prohibition of cloning, take the view that a pregnancy with a cloned embryo need not affect the woman so severely that the doctor ought, for this reason alone, not to conduct the procedure even if consent has been given.

Reproductive cloning is also opposed on the grounds that fundamental modification of the natural fertilization process of the union of an egg cell and a sperm cell and its replacement by something else, rather than its facilitation as in the usual techniques of assisted reproduction, cannot be reconciled with the medical treatment contract.

However, a counter-argument is that cloning for reproductive purposes could perfectly well be regarded as an extension of other forms of infertility treatment.

3.4. The society that would permit cloning

3.4.1. Freedom and equality

In a state with a liberal constitution, its citizens’ freedom and equality, which are also fundamental to the reciprocal protection of human dignity, are of paramount importance.
Some consider that if cloning for reproductive purposes were permitted, this would call into question a vital precondition for the members of society to treat each other as free and equal citizens. Since, in reproductive cloning, the genetic endowment is intentionally specified by third parties in such a way as to be identical to that of a living or deceased individual, the clone would as it were “owe” his genetic endowment to those who specified it, but could also blame them for it. This would undermine an essential prerequisite of equality in society.

Reproductive cloning represents the deliberate manufacture of human beings by the artificial replication of genetic individuality. This constitutes a threat to people’s certainty about universally shared and constitutionally based values and convictions, and hence also to the fundamental norms of the body politic. The collective self-conception of a society based on the equality of all human beings and the non-disposability of the individual would thereby be imperilled.

Furthermore, the broad consensus underlying the call for the prohibition of cloning for reproductive purposes is quite probably also rooted in feelings of shame and indignation, or of horror, at an act felt to be monstrous.

However, it is argued, too, that there is no reason to assume that a clone would not be accepted by his fellows as free and equal. In modern societies, acknowledgement of a person as an equal does not depend on his biology. Moreover, the nature of his creation would either remain concealed from his fellow-citizens or, in certain circumstances, become known only after many years – as in the case of disclosure of an adoption. Just as the clone would not thereby be deprived of social respect and esteem, the knowledge that he is a clone would not destroy the identity he has built up by socialization processes extending over many years.

Finally, a society accustomed to dealing appropriately with genetic inequality could be relied upon to cope with genetic equality in the same way.

### 3.4.2. Generational and family structures

Another objection to reproductive cloning is that it would disrupt generational and family structures that have hitherto been seen as self-evident. For example, a child cloned from his “father” would be at one and the same time his father’s genetic twin and a half-brother and uncle to previous children. A woman who bore the clone of her own mother would, in physiological terms, be the mother of her mother’s twin – that is, her aunt. The child would have only one genetic parent, who need not even be related to the biological mother and the social parents. Relationships of vital importance for social identification would thereby be blurred.

However, an objection to this argument is that it overestimates the importance of genetic factors in the sense of family. There are also other cases in which relationships are defined independently of biological descent (e.g. adoption or sperm donation).

### 3.4.3. Cloning in the service of eugenics and the breeding of human beings

To a much greater extent than natural procreation or assisted reproduction techniques such as preimplantation genetic diagnosis or the choice of sperm donors, cloning would permit the selection, or at least the attempted selection, of future human beings in accordance with criteria based on their genetic characteristics. Cloning could be used to “produce” human beings with desired genetic characteristics by copying an existing genome with these characteristics.

This is regarded as a form of positive eugenics – because it would not only exclude unwanted genetic characteristics but also entail the deliberate selection of desired ones. Over and above individual donors’ decisions concerning the replication of their own genetic information, cloning techniques could conceivably be accompanied, at some point in the future, by deliberate optimization of individual genetic endowment by
genetic engineering. The feasibility of multiplying desired characteristics by genetic modification in conjunction with cloning by nuclear transfer has been demonstrated in animal experiments.

An objection to this argument is that cloning and germ line manipulation would have to become a standardizable method of reproduction in order for it to be misused for the purposes of positive eugenics. However, such misuse could be ruled out precisely in the situation where cloning is the exception.

The consideration that such acts would remain exceptional does not, in the view of the National Ethics Council, in any way invalidate the fundamental arguments against reproductive cloning.

E  CLONING FOR THE PURPOSES OF BIOMEDICAL RESEARCH: ETHICAL AND CONSTITUTIONAL ASSESSMENTS

Position A
Retention of the prohibition of research cloning

1. Position statement

As in the case of reproductive cloning, the aim should be to secure a worldwide ban on research cloning and, at national level, to prohibit it by specific criminal-law sanctions. The prohibition should be clarified, in particular, by incorporation of a definition of embryos created by nuclear transfer and by an explicit statement that it also applies to cases in which the embryo’s capacity for development is limited or eliminated by interventions before and/or after nuclear transfer. Should a worldwide ban not be achieved, provision should additionally be made, as in the Stem Cell Law, for penal sanctions against German offenders for acts committed abroad.

2. Preliminary note

Cloned embryos are used and consumed not only for reproductive purposes, but also, as stated in Section B 4.2, for research and, in particular, for the development of stem cells and stem cell lines. Although the main elements of the two cloning processes coincide in the phase leading up to the genesis of an embryo (see Section B 1.2), they exhibit substantial differences thereafter; for this reason, the ethical and constitutional aspects of research cloning must be considered separately. These are discussed in the following pages.
The process of assessment has led to different conclusions within the National Ethics Council, which are presented separately in this Opinion as Positions A, B and C respectively. The considerations set out below are regarded as decisive by the members who hold that a cloned embryo is entitled to full protection of dignity and life from the beginning (Position A). These on the whole coincide with corresponding considerations in Position C, which also opposes the sanctioning of research cloning. The only difference is that, in Position C, the prohibition would be based on the current state of science and research, whereas Position A advocates retention of the current ban without a reservation of this kind.

3. Assessment of the creation of cloned embryos in terms of the protection of dignity and life

3.1. Status of the cloned embryo and the resulting basis for its protection

According to ethical principles and the fundamental decisions on which our Constitution rests, human life is not a good among other goods, but the underlying good to which all fundamental rights relate. It therefore enjoys particular protection by way of the inviolability of human dignity provided for at the very beginning of the Basic Law (sentence 1 of Article 1) and the right to life enshrined therein (sentence 1 of Article 2(2)). (This is explained in more detail in the National Ethics Council’s Opinions The Import of Human Embryonic Stem Cells of December 2001 [“Opinion I”] [pp. 27–29] and Genetic Diagnosis Before and During Pregnancy of January 2003 [“Opinion II”] [p. 74ff.].) Divergent views are held on the interrelationship between the two provisions. The most convincing of these would appear to be that human dignity is a primary basic value from which fundamental rights are derived and on the basis of which encroachments on fundamental rights are examined from the point of view of their constitutional permissibility. The two protective principles therefore interlock.

Conceptions differ, too, on the point in time when protection commences. Some consider that it begins only at nidation or even at birth. Others argue in favour of a graduated development of protection, reaching its full extent only at birth. In the opinion of the advocates of the present position, these notions are irreconcilable with the fundamental value of life, which requires that the earliest biologically tenable moment be chosen for the commencement of full protection. As stated in earlier Opinions of the National Ethics Council (see Opinion I, p. 27ff., and Opinion II, p. 74f.), that is the moment of karyogamy. The corresponding point in cloning is that of nuclear transfer, because from then on the criteria of potentiality, identity and continuity are satisfied, and, with them, all essential prerequisites for human existence – that of potentiality because the embryo already possesses the real capacity to develop into a born human being; of identity, because one and the same living organism is involved from the beginning; and of continuity because, from this moment on and throughout all phases of human existence up to death, a process is in hand whereby any discontinuity other than death cannot but appear arbitrary. The fact that the embryonic disc can still divide for a short time after karyogamy, giving rise to monozygotic twins, does not contradict the assumption of identity, as this division merely has the effect that the criterion of identity is met by two organisms (for a more detailed consideration, see Opinion I, p. 29).

The above remarks apply equally to the commencement of the protection of dignity and to that of the protection of life. The two cannot be separated from each other. For there is no reason to assume that the word “Mensch” [human being] in the first sentence of Article 1(1) of the Basic Law means anything different from the word “jeder” [everyone] in the first sentence of Article 2(2) and that at the beginning there might be such a thing as a life without dignity.
The concept of a gradually increasing protection of dignity and life – which would be tantamount to dividing human dignity into a “strong” variant to which born human beings are entitled and which is unquestioned, and a “weak” variant intended, for instance, only to protect embryos from being consumed “in a grave manner” for extraneous purposes – falls substantially short of the notion of full protection from the beginning that is advocated here. After all, it subjects embryos, prior to each of the stages of protection deemed applicable, not only to limitations but also to the termination of their existence, requiring only that this should take place “respectfully” or in a manner that is not “grave”. This already raises the question of how the destruction of an embryo can possibly be described as “not grave” or how an embryo can be destroyed “respectfully”. Recent proposals to ban specific methods and actions do not suffice in this respect any more than the regulation and monitoring arrangements recommended in Position B – for the ultimate implication of the concept here rejected is that one and the same organism, within its lifetime, is treated for a certain period as a human entity of inferior status and only thereafter as a human being. Nor is this view in any way altered by the circumstance that Position B ultimately refers to human blastocysts rather than cloned human embryos. The blastocyst, after all, is not categorically different from an embryo, but an intermediate stage in embryonic development, which began with fertilization (see Opinion II, p. 13f).

The concept of graduation proves to be inappropriate in other respects too, because in practice it imposes the obligation of explanation and justification on those who reject the relevant actions. To maximize the effectiveness of protection, however, this obligation should lie with those wishing to permit the conduct of such actions on life. It therefore also concerns the burden of proof that totipotency is not, or is no longer, present in a specific case – e.g. a stem cell consumed for the purpose of developing stem cell lines. Nor is it possible to agree with the view that the concept of graduation is more in line with the legislation currently in force because the sanctions provided for therein take account of the particular circumstances of the individual developmental phases. Although this is true in certain cases, such as crisis pregnancies, it does not alter the fact that our legal code also fundamentally deprecates the ending of the life of an unborn human being.

The subject of human dignity and of the right to life is every human entity from the beginning of its existence as described above. It is not permissible to lay down additional requirements for qualification as a subject of human dignity, as is sometimes advocated, because other criteria, such as self-awareness, sentience or, indeed, the capacity for action, are not demanded for born human beings either. The position adopted here is also consistent with the requirements relating to the dignity of the human species, which is placed alongside individual human dignity both in the literature and in the decisions of the courts, and which is based not on individual entitlement to protection but on the general limits imposed on mankind with regard to the treatment of members of the human species. The prohibition of instrumentalization, whereby an individual cannot be denied intrinsic value and be abused or even destroyed as a mere means to the achievement of extraneous ends, is thus relevant in this connection too.

### 3.2. Acts constituting violation

According to this position, the acts constituting violation are the consumption of the cloned embryo and its creation with the prior intention of thus consuming it. Owing to this connection, the resulting instrumentalization of the cloned embryo is a particularly serious matter; indeed, it is even more serious than in the case of research in which “excess” embryos are consumed, because these were, after all, initially created with a view to bringing about a pregnancy. A subsequent change of purpose following the creation of the cloned embryo, so that
the aim is now to bring about a pregnancy, would make no difference to this assessment, because reproductive cloning constitutes an even worse violation of the protection of dignity (see Section D3 above). There is no evidence of the existence of objectives other than those of research – which, for the purposes of this Opinion, includes therapeutic and pharmaceutical objectives – and of reproduction, but these would in any case not justify a different ethical and constitutional evaluation.

It has recently been argued that the protection of dignity and life would be unaffected if the embryo’s potentiality and continuity, and hence also its capacity for development, were limited in time by manipulative acts after, before or during transfer of the cell nucleus into the enucleated oocyte, and were therefore in practice prevented.

The following considerations are adduced against this argument.

If the act takes place after transfer, it constitutes an instrumentalization preparatory to consumption. This is just as impermissible as consumption itself. Acts before or during transfer, including the deliberate creation of a defective embryo, also violate the protection of dignity and life. This is because they affect an entity that, in the absence of this manipulation, would at least for a time possess the capacity for development and life, which it would lose prematurely precisely by virtue of the manipulation. What comes into being is therefore not a non-embryo, but an embryo with an extremely short lifetime. After all, the argument that the lifetime was limited prior to the fusion of the sperm and egg cells also fails to convince if the effect of such an act is the death of a fetus in the fourth month or of a child in the fourth year of life. Both cases involve not facts of nature, but deliberate decisions by the person performing the relevant act.

These considerations show that the differences of opinion once again turn on the moment at which the full protection of dignity and life is deemed to commence. Again, the instrumentalization in question appears to be particularly serious and not readily reconcilable with the respect owed, in the view of the advocates of the concept of graduation, to an embryo of this kind on the same basis as to any other embryo, because the treatment it receives would be no different from that normally accorded to embryos in animal experiments.

### 3.3. Alleged contradictions in values

An objection sometimes voiced to the position adopted here is that the third sentence of Article 2(2) of the Basic Law permits derogations from the right to life and even, in certain circumstances, the killing of human beings. Furthermore, it is alleged, a ban on research cloning would be inconsistent with the view taken of other, comparable situations. Both objections are unconvincing.

Our legal code allows the killing of a human being only for the purpose of saving another acutely threatened life from an attacker – for instance, in cases of self-defence or defence of another person in emergency. In this connection, self-defence is also lawful, subject to considerations of proportionality, for the defence of other legal goods to which high value is assigned. However, this is always the case only if the person who is killed presents a danger. As a rule, no danger is presented by embryos – particularly if specifically created for consumption. Instead, they are themselves exposed to the greatest danger from the beginning.

Human life is also extinguished in the case of a termination of pregnancy carried out by virtue of specific medical indications or after counselling within a specified period (in the latter case, the termination, although unlawful, is not subject to penal sanctions). The law currently in force thus takes account of the fact that a unique connection exists between the mother and the life growing inside her and that a pregnancy impinges in a very particular way on a woman’s physical and mental
integrity and right of self-determination. However, this situation cannot be equated with the creation and consumption of embryos in the laboratory, as all the specific circumstances mentioned above are then lacking and the decision is in the hands of a third party—namely, the research worker.

3.4. Justification on the grounds of freedom of research

It has been argued for some time that embryo-consuming research is permissible for priority research objectives at least in the case of so-called excess embryos. On the basis of the fundamental right of the freedom of research enshrined in the first sentence of Article 5(3) of the Basic Law, the sanctioning of this research is now being demanded also for embryos created specifically for research purposes and, more particularly, ones produced by cloning. Because this might potentially lead to therapies for hitherto incurable diseases, it is claimed that this demand can also be justified by the right to life and bodily integrity mentioned in the first sentence of Article 2(2) of the Basic Law.

This view must be rejected.

First of all, it is highly debatable whether the prospects of curing such diseases might indeed be improved by the results of research on cloned embryos; there might after all be promising alternative research approaches. Serious misgivings in this connection have recently been voiced by the Deutsche Forschungsgemeinschaft [German Research Foundation] and the Bundesärztekammer [German Medical Association]. These are reproduced in detail in Position C. Apart from these considerations, an individual’s right to life and bodily integrity is first and foremost a right of defence against external agencies, and cannot be adduced to justify acts affecting the life of others. For this reason, the consumption of embryos for this purpose cannot be justified even by the understandable hope of sick persons that their lives or health might one day be preserved, or at least their suffering relieved, by new therapeutic methods possibly accruing from such research. Again, limits are set to the freedom of research when its exercise would encroach on other values protected by the Constitution and, in particular, would infringe the fundamental rights of third parties. However, as already stated in Section 2.1., that is precisely the case with embryo-consuming research (on this point, see also Opinion I, p. 36f.). As it happens, the Constitution already limits the freedom of research on grounds of animal protection.

3.5. Assessment of embryo splitting

The considerations set out in Sections 2.1. to 2.4. above also apply mutatis mutandis to research on embryos produced by splitting.

4. Assessment of the possible consequences of sanctioning research cloning

4.1. General considerations

For an ethical and legal consideration of whether an act is permitted, can be permitted, can be prohibited or is prohibited, the consequences of that act are also relevant. The reasons for this assertion are set out in detail in Opinion II (p. 81 ff.), to which reference should be made. Since the protection of dignity and life are at issue in the present case too, a preventive ethic of responsibility should take priority over a pragmatic evaluation in assessing the probability of the occurrence of these consequences.
4.2. Estimation of individual practical consequences

4.2.1. Effect on the current prohibition of research involving the consumption of embryos created for research purposes

The consumption of embryos produced sexually – for instance, by in vitro fertilization – for research purposes is prohibited in Germany. This ban corresponds to a similar prohibition in the Council of Europe’s bioethics convention, which has not yet been signed by the Federal Republic. Demands have recently been voiced for this prohibition to be lifted not only for so-called excess embryos but also for embryos created from the outset solely for this purpose by in vitro fertilization. If the creation of embryos for research purposes by cloning were permitted, this ban could no longer be upheld. Since, as stated, the relevant embryos in both cases are equally deserving of protection, the difference in genomic composition would no longer justify retention of the ban. In the artificiality of their creation, there is in any case no significant difference between the in vitro and cloning methods.

4.2.2. Risk of utilization of advances in research cloning for reproductive cloning

That the techniques of reproductive cloning and research cloning are identical is undisputed. It would therefore be quite impossible to prevent advances in the technique of research cloning – e.g. in reprogramming – from being utilized for reproductive cloning too.

4.2.3. Risk of instrumentalization of women

As stated in Section D3 of this Opinion, reproductive cloning would most likely entail an appreciable demand for oocytes, with a consequent need for radical medical manipulation, hormonal stimulation and ovarian puncture. This could give rise to the development of a demand-driven market whose incentives might threaten female self-determination and turn women into suppliers of merchandise. All this applies equally to research cloning. The oocyte requirement might even be much higher in the event of vigorous (fundamental) research activity, especially if this were subsequently to lead to pharmaceutical research. For instance, the South Korean research project of January 2004, which has already been mentioned several times, alone consumed 242 oocytes from 16 women in order to obtain just one stem cell line. This situation is considered in more detail in Position C.

4.2.4. Effects on our image of man and our conception of ourselves

On this point too, Opinion II (p. 91 ff.) includes specific considerations, some of which are reflected in Section D3. The sanctioning of research cloning would be particularly conducive to further blurring of the boundary between human organisms on the one hand and, on the other, objects and instruments produced, used and consumed for purposes not inherent in those objects and instruments themselves.

Hermann Barth, Gebhard Fürst, Peter Radtke, Eberhard Schockenhoff, Hans-Jochen Vogel
Position B
Limited sanctioning of research cloning

1. Position statement

The use of human blastocysts produced by cloning for the purposes of fundamental research with a therapeutic objective is in principle acceptable. However, both the content of the research and the procedures employed call for regulation.

There are no moral grounds for attributing the status of a person to a blastocyst created in this way, nor does the Basic Law require it to be regarded as a subject of human dignity and possessor of the right to life.

With the advent of research cloning, another sphere previously beyond the scope of human intervention would come under man’s control. Yet there is no reason to believe that this would jeopardize the humanity of people’s relations with each other or the self-conception of a society based on freedom and equality.

In this context, the general principle of freedom (the “presumption of freedom”) enshrined in the Basic Law and, in particular, the high status assigned to the freedom of research are relevant. Of course, legal restrictions may be imposed on this freedom too; however, what calls for justification is the specific restriction and not the individual use made of the freedom.

It is hoped that research cloning will in the future lead to potential cures for serious illnesses (e.g. Parkinson’s disease or diabetes mellitus) and physical pathologies (such as paraplegia). The reduction or avoidance of suffering and pain is a generally recognized moral precept. Its counterpart is the state’s constitutional obligation to protect life and bodily integrity and consequently to permit the development of methods of medical therapy.

It is impossible to say in advance whether the hopes placed in research cloning will be fulfilled; the question can be answered only by the research itself. The same applies to other research approaches to the derivation of stem cells. Uncertainty is the starting point of research and not a valid argument against its sanctioning.

Research cloning calls for state regulation, and each such project must also be subject to approval and monitoring.

Research cloning should be permissible only where the scientific problems concerned cannot be solved with animal models. In particular, where human oocytes are to be used in cloning experiments, adequate evidence of scientific justification must be given and all relevant circumstances must first be determined by work on animals.

When, and for as long as, human oocytes are needed for research cloning, effective precautions to protect donors must be taken.

The implanting of cloned blastocysts into a woman’s uterus must be prohibited without exception.

2. Opinion

2.1. Introduction

Research cloning, in much the same way as preimplantation genetic diagnosis or stem cell research, poses the question of whether the ending of early embryonic life is compatible with the Constitution and our fundamental ethical convictions. If the blastocyst (i.e. the cluster of about 200 cells four or five days after fertilization or, where applicable, cell nuclear transfer) were entitled to the same thoroughgoing protection of dignity and life as born individuals, the answer would necessarily be negative. After all, however valuable the research, there can be no justification for sacrificing human beings for it. Yet the assumption that the early embryonic cellular cluster benefits from the protection of dignity and life to the same extent and with the same force as a born person is ultimately unconvincing. It is not consistent with the prevailing legal situation of the Federal Republic
of Germany and of many other states with liberal constitutions, nor can it be justified by compelling ethical arguments. In particular, however, the thesis proves to be untenable owing to serious contradictions of values when compared with other phenomena relating to the treatment of unborn life. Nor can the thesis of “full protection of human dignity and life from the beginning” be derived from the Basic Law, let alone from the decisions of the Federal Constitutional Court.

2.2. Human dignity and research cloning

1. The guarantees of human beings’ right to life and dignity are individual and personal. It is beyond doubt that they apply primarily to born persons. The long history of ideas on human dignity, which is by no means confined to the Christian tradition, has always been directed first and foremost to born human beings and not to prenatal life. The historical trend of concrete guarantees of human dignity after the Second World War, too, as embodied in the United Nations Charter, the Universal Declaration of Human Rights and the German Basic Law, has been towards protection from torture, humiliation, stigmatization and comparable forms of degradation. Having regard to the recent past, the aim at the time was to ensure that the people in our midst were not treated as animals or “subhumans”. Although the post-war Parliamentary Council that drafted the Basic Law discussed such issues as the right to life of the unborn organism in utero, albeit without reaching a conclusion, it did not consider the possibility that human dignity might be extended to unborn life, let alone to such life in the pre-nidation phase.

2. An utterly fundamental question is whether there is any moral and constitutional justification for equating a cloned blastocyst created by artificial manipulation with an embryo resulting from fertilization. Two different answers are given to this question, both in the general debate and by the advocates of the present position.

Those who claim a special status for cloned blastocysts justify their view on the grounds of the fundamentally different circumstances and of the fact that, in the production of this entity, there is from the outset no reproductive intention. Furthermore, the experimental method of cell nuclear transfer differs from natural or artificial fertilization. In addition, the result differs from that of fertilization in that, instead of two different parental sets of chromosomes coming together to form a new individual genome, only the existing chromosome set of the provider of the cell nucleus has been copied – and, moreover, with the intention of obtaining tissue bearing his nuclear genome. The formation of the resulting entity, which does not occur in nature as such, is inconceivable without this artificial manipulation.

The other view (which is also shared by many who ultimately reject research cloning) in principle assigns the same status to all blastocyst-stage entities with the capacity for development, regardless of whether they originated from cloning techniques or from (natural or artificial) sexual procreation. This means that the general arguments concerning the status of early embryonic human life must be reviewed in the case of entities formed by nuclear transfer too. The National Ethics Council has already considered these issues in earlier Opinions. According to the position maintained here, early embryonic life – i.e. at the stage prior to nidation and individuation – cannot be deemed a subject of individual human dignity. Hence research cloning cannot simply be prohibited on the grounds of alleged “instrumentalization” contrary to human dignity, inherent in creation for the purpose of subsequent destruction.

3. As analysis of the theories of human dignity commonly advanced in the ethical and constitutional debate shows, these
theories afford no justification for regarding a blastocyst as a subject of the guarantee of human dignity; nor do the much discussed arguments from continuity, potentiality and identity convincingly support such a conclusion. Again, even if that principle were accepted, it would not follow that the protection of an embryo’s dignity would be the same in every respect as that accorded to a born human being. It is therefore by no means the case that research cloning would necessarily constitute a violation of the guarantee of dignity enjoyed by early embryonic life. The grounds for the two theses – that a blastocyst is not a subject of the guarantee of human dignity and that there is no violation – are set out below.

The question of the possible violation of human dignity is generally answered by invoking the prohibition of instrumentalization or the so-called object formula (according to which it is inconsistent with human dignity for a human being to be treated as a mere object or means to an end). Both of these notions are thus based on the concept of a violation of human dignity, but fail to give an independent answer to the objectively and logically prior question of who the actual subject of human dignity is. In the case of a born human being, it is obvious that the relevant individual is the subject. However, as with the right to life, it is impossible to avoid the question of whether embryonic life in its early, pre-nidation stage can already be conceived as a subject of human dignity. For this purpose it is insufficient to note the existence of a violation in negative terms; instead, what is needed is a positive specification of the extent of the personal guarantee of human dignity. This calls for a consideration of the nature and constitution of human dignity.

Examination of the various relevant theories shows that most of them cannot accommodate an extension to early embryonic life at the pre-nidation stage. This is true in particular of approaches (e.g. that of Niklas Luhmann) which regard dignity as the capacity for successful self-representation and hence as a function to be performed by individuals in relation to each other, because only born human beings have this capacity. However, it is also the case if the notion of human dignity is seen as enshrined in solidarity with one’s fellows within a concrete community based on mutual recognition (Hasso Hofmann); this would mean that all persons who are (already and still) among us, regardless of their individual capacities at any given time, must be deemed to belong to the group of subjects of human dignity, but this would not be so for early embryonic life. Similarly, Jürgen Habermas considers human dignity to be not an intrinsic possession but something that is constituted only with the onset of interpersonal relationships based on mutual recognition; it is only at birth that the socially individuating act of incorporation into the intersubjective living world is consummated.

Finally, those authors who invoke Immanuel Kant to argue in favour of the extension of human dignity to life at the pre-nidation stage are confronted with the problem that, for Kant, the dignity of man is rooted in free self-determination and moral autonomy. His postulated prohibition of treating others as a mere means to an end is directed towards man as a rational being who gives himself his own laws in relation to his fellows; it presupposes communication and fundamental autonomy, which can certainly not be attributed to a blastocyst.

However, the dignity of even the earliest forms of human life on the basis of the Christian notion of the imago Dei is unanimously upheld by the Catholic Church (although admittedly in the context of a turbulent history of dogma), whereas Protestantism shows a greater pluralism of views. In so far as religious positions are derived from doctrine, it is surely inappropriate for these to underlie the interpretation given to such a vitally important and universally binding provision as Article 1(1) of the Basic Law.
The argument from identity invokes the personal identity existing between a subsequently born human being and the embryo in vitro or in vivo that he previously was. In effect, the gap between the person and an earlier stage in his development is bridged by the notion of identity. The burden of the argument is that it is from the beginning the same living organism whose legal status is at issue. However, the idea of a guarantee of human dignity extending back to the prenatal stage is limited by an important chronological boundary – that of the formation of the primitive streak, about 14 days after fertilization; until then, a multiple birth is still possible. But the possibility of backward projection of a subsequently achieved personal identity, in the sense of “That is what I was, and it could only give rise to me”, ends at the point when individuation commenced. The above principle could not logically be applied to the stage before that – i.e. the first 14 days – because it was then not yet certain whether one organism or several organisms would develop from the blastocyst. Yet it is precisely this earlier stage that is relevant in research cloning, which deals with cellular clusters at the blastocyst stage four or five days after nuclear transfer. Life at this stage, while species-specific, is not yet individuated: it is human life, which, however, does not yet constitute a human being.

The argument from potentiality, it is sufficient, for the ascription of full legal status to early embryonic life, for it to possess the possibility of further development to the stage of a born human being, who would (later) indisputably be a subject of human dignity and the right to life. However, this backward projection of a subsequent legal state to an earlier stage of development meets with the fundamental objection that it is neither logical nor conclusive, and is moreover wholly foreign to our legal code. Just as an acorn has yet to become an oak and an eight-year-old schoolboy, as a minor, is not yet a 22-year-old student who is of age, the early embryonic cellular cluster cannot be
regarded as a subject of the guarantee of human dignity simply because the born person (possibly) developing from this cluster would one day indisputably possess this status. Again, as a British author has pointed out, we are all potentially dead, but this does not mean that, having regard to this future status, we would wish to be treated like corpses while we are still alive.

5. Furthermore, the inadequacy of the argument from potentiality has emerged with particular clarity in the specific context of the debate on research cloning. Firstly, the previously presumed certainty as to precisely which developmental potential justifies the specific status disappears (see a)). Secondly, it is now possible to envisage the production of cloned blastocysts whose developmental potential is deliberately blocked from the outset so as to make them non-totipotent, and therefore by definition not embryos (see b)).

The biological property whose presence is linked by the argument from potentiality to human dignity and the right to life is the embryo’s totipotency, understood as its capacity to develop in suitable circumstances into a child (attention was drawn in Section B to the vagueness and ambiguity of the concept of totipotency). It is accepted that this developmental potential can be realized only if a large number of external conditions are satisfied at the same time. In the case of natural procreation, these are the in any case complex conditions of an intact pregnancy. With artificial fertilization, there is the additional condition of artificial transfer to a receptive uterus. In research cloning, finally, totipotency is achieved asexually – by nuclear transfer or, in the future, perhaps even by reprogramming of a somatic cell. Again, these new “external conditions” are wholly artificial, but ultimately also help to promote a biologically predetermined potential. Since the advocates of the argument from potentiality would surely not wish to extend its scope to all somatic cells, they must make a decisive normative distinction between the totipotency of a traditional embryo (seen as the foundation of its human dignity) and the (ethically meaningless) “potential for totipotency”, manifestly enjoyed by every cell. Such a normative distinction of embryonic potential is not self-evident, nor, in view of the complex nexus of conditions, can it be achieved simply by classifying it as an “active potential”. Such a distinction in fact points to prior metaphysical assumptions, which are not universally shared, to the effect that the ends of nature, the preordained purposes of humanity or the divine will are manifested in embryos.

Specific consideration must be given to the situation in which, in research cloning, the entity created lacks totipotency from the beginning – for instance, if it does not possess the capacity to nidate or to commence embryogenesis. It is perfectly conceivable that this state might not only one day be identifiable by diagnostic means, but that it might in addition be possible to bring it about by deliberate manipulation in the production of the relevant entity, perhaps as one property among others. This could also not be regarded as a manipulation of an existing embryo whereby human dignity is violated. After all, notwithstanding the debate about the argument from potentiality, no one can deny that a blastocyst lacking totipotency, which could not develop into a child under any circumstances, is, if only by definition, not an embryo.

The objection that it is immoral to bring into the world an embryo deliberately affected by a severe defect is invalid: if the criterion of the existence of an embryo is the property of totipotency, but this, either spontaneously or intentionally, does not arise, then, clearly, no embryo comes into being.

6. Given that the blastocyst, four or five days after cell nuclear transfer, is not entitled to protection of human dignity as a born human being would be, the prohibition of instru-
mentalization repeatedly adduced against research cloning is also untenable. Günter Dürig’s “object formula”, which has been espoused by the Federal Constitutional Court and is nothing other than the constitutional formulation of the prohibition of instrumentalization, tellingly refers to the “specific human being” whose human dignity is violated if he “is abased to the status of an object, a mere means to an end, a fungible magnitude”. However, a cellular cluster at the blastocyst stage can surely not be regarded as a “specific human being”. This means that, in determining whether the use of a blastocyst for research resulting in its consumption constitutes an instrumentalization irreconcilable with human dignity, the intention of the action is decisive. In so far as the aim is to obtain fundamental scientific knowledge about the processes of cell biology with the long-term objective of curing serious diseases, this cannot be seen as involving humiliation or degradation comparable to the “abasement” inherent in recognized cases of violation of the dignity of born human beings (such as torture, stigmatization or ostracism).

7. Nor, ultimately, can the decisions of the Federal Constitutional Court be adduced as a counter-argument to the position here upheld. The often-quoted phrase “Where human life exists, it is entitled to dignity” (BVerfGE [Decisions of the Federal Constitutional Court] 39, 1 [41]; 88, 203 [252]) occurs in two judgements whose scope was explicitly limited by the Court from the outset to the post-nidation and post-individuation phase (BVerfGE 39, 1 [37]; 88, 203 [251 f.]). The phrase is therefore irrelevant to the pre-nidation phase, which is the only one relevant to research cloning. The Court’s judgements in any case lay themselves open to the justified charge of inconsistency, because the legal provisions concerned, which are in force and have been declared constitutional (abortion within the first 12 weeks on the basis of urgent medical indications, or subject to counselling; or the admission of embryopathic and criminological indications), manifestly conflict with the alleged guiding principle of the dignity of prenatal life. In other words, the content of the actual decisions conflicts with the initial premises. In particular, the specific time limits stipulated for abortion to be permissible, after each of which it is rendered more difficult (from the phase up to nidation, to which the criminal law does not apply, via the 12- and 22-week limits, to the exceptional case of a medical indication on the grounds of danger to the life of the pregnant woman) cannot be reconciled with the unconditional nature and absoluteness of human dignity attributed by the Court to the unborn child. In practice, the Federal Constitutional Court therefore espouses the notion, advocated here, of graduated protection of prenatal life. It would be inconsistent to dispense with this graduation in the assessment of research cloning.

2.3. Protection of life and research cloning

The situation with regard to the right to life proves to be very similar to that of the guarantee of human dignity. Here too, the general consensus is that all born human beings benefit from the strict protection of life. The state demands the sacrifice of individual lives or, as the case may be, accepts it as justified, only in exceptional situations (self-defence, shooting to kill with the aim of saving life, or military action). However, precisely with regard to prenatal life, there is more to the matter than these few exceptions. This is already clear from the “medical indication” newly introduced in 1995. Under the current legislation, which is universally regarded as fair, if the fetus (which may already be seven or eight months old) endangers the life of the pregnant woman, it is considered permissible and “justifiable” for it to be killed – something that would be out of the question in the case of a conflict between two born individuals.
The “medical indication” is logical only if it is assumed that born and unborn life are not equivalent. This approach conforms to widely accepted moral intuitions and to the legal situation both in the Federal Republic and in other states with democratic constitutions. The specific legal position is that prenatal life benefits from protection under the law which in effect increases step by step in accordance with its growth – i.e. “graduated” protection. The closer the moment of birth, the more weight is attached to protection of the unborn child; the more remote this moment, the less the extent of the protection. In the Federal Republic, this is also evident from the fact that, in natural procreation, early embryonic life up to the phase of nidation wholly lacks legal protection: the use of nidation-inhibiting contraceptives or of the “morning-after pill” is lawful although it may result in the killing of early embryonic life within just under two weeks of its coming into being. Those who advocate full protection of the dignity and life of unborn entities from the beginning ought logically to regard this legal situation as an unacceptable violation of fundamental constitutional values and minimum ethical standards.

The same applies to the ban on the implantation of a cloned embryo provided for in Section 6(2) of the Embryo Protection Law: such an embryo must not be transferred and must therefore die, although it is unanimously held that a subsequently born clone would benefit from the same dignity and right to life as anyone else (see Section D above). Such provisions in fact not only reflect a widespread legal consensus, but are also in line with the moral feelings and ethical valuations on the basis of which we make an important distinction between a blastocyst a few days after fertilization, which has neither implanted nor individuated, and is at the same time wholly insensitive to pain, on the one hand, and a fetus capable of extrauterine life at an advanced stage of development a few weeks before birth, on the other. The fact that both our legal code and our moral sense provide for a graduated protection of life is also evident in the circumstance that significantly less stringent requirements are laid down with respect to the absence of criminal-law sanctions for abortion up to the twelfth week of pregnancy than at a later stage. If full protection of life were indeed to apply “from the beginning”, prenatal life ought not to enjoy less protection in the twentieth week than in the first few days of its existence. Again, the fact that a woman in the tenth week of pregnancy can have an abortion without penal sanctions if she has undergone counselling, whereas the same action in the fifteenth week of pregnancy would be punishable without a specific medical indication, shows that the often voiced argument that the law should take account of the particular situation of conflict is invalid. The decisive factor in the distinction is not a newly arisen situation of conflict, but solely the circumstance that the prenatal life has grown and the moment of birth has drawn closer.

It follows from the foregoing that, even if the blastocyst stage is seen as possessing the right to life enshrined in Article 2(2) of the Basic Law, the legal code could provide for appropriate restrictions in favour of research cloning, given the not yet individualized, let alone personalized, stage of development of human blastocysts prior to nidation, on the basis of a comparative assessment of the legal situation applicable to the termination of pregnancy.

2.4. Freedom of research, the state’s duty of protection and therapeutic possibilities

Since there is no categorical barrier to research cloning either in the guarantee of human dignity or in the protection of life, the presumption of freedom inherent in the Basic Law must initially be seen as applicable to the relevant activities. According to this presumption, the freedom of the individual is in principle unlimited and does not call for justification, whereas restrictions placed on it by the state are limited and do require justification.
An additional factor that specifically concerns the freedom of research is the high priority which that freedom is acknowledged to possess, which is reflected not least in the lack of any provision in Article 5(3) of the Basic Law for simple statutory derogation. For this reason, any restrictions must necessarily possess a higher level of justification: they require special justification under the Constitution itself, based in particular on third parties’ fundamental rights or on other constitutionally enshrined rights.

A further important aspect relevant to the question of fundamental rights may also be adduced, and is applicable to research cloning in so far as the research concerned is intended to facilitate the long-term development of medical therapies and treatment methods for the most severe diseases and disabilities. It is that fundamental rights are not only defensive rights of the individual against the state. The state in fact also has a duty to adopt a “protective and supporting” stance towards fundamental rights, as the relevant formulation of the Federal Constitutional Court puts it. The Basic Law thus imposes a responsibility on the state in this respect. With regard to the protection of life and health, this means that the duties of the state to protect fundamental rights certainly include promoting the development of new treatment methods and therapies, or at least not frustrating, let alone prohibiting, them. The state admittedly has a very broad and flexible field of action at its disposal in this respect. However, it is absolutely clear that Article 2(1) of the Basic Law does not merely constitute an obstacle to biomedical research but, on the contrary, supports it. This may be an important consideration in decisions in which the various factors are weighed against each other.

The “ethic of healing” implicitly addressed in this notion is in turn sometimes justified, in the constitutional literature, on the grounds of human dignity. At any rate, it is an undisputed element of the duty of moral solidarity.

All the same, there can of course be no certainty that research with cloned cellular clusters will actually lead to effective therapies for diseases such as Parkinson’s or diabetes mellitus or physical pathologies such as paraplegia. This question can be answered only by relevant fundamental research – that is, only by the limited and duly monitored sanctioning of research projects in this field. Consequently, although a moratorium on research may be acceptable for the Federal Republic of Germany in the present state of science, a swift review may be necessitated by progressive advances. If not, the burden of gathering information would in the long term be imposed on other states, while Germany would profit from the results – which would surely constitute an ethical and moral double standard. After all, should therapies for hitherto untreatable diseases be developed abroad on the basis of research cloning, they could not possibly be withheld from patients in Germany.

2.5. Regulation of research cloning

In order reliably to preclude any misuse of cloned blastocysts for human reproduction in the event of the sanctioning of research cloning in Germany, regulation and monitoring would be essential. Appropriate means might be registration of the production of such blastocysts and limitation of research to licensed centres. At any rate, there would need to be documentation that records full details, for subsequent reference if required, of the creation, transfer and use of these blastocysts.

However, restrictions on the handling of cloned blastocysts are demanded not only by considerations of possible misuse, but also by society’s intuitive aversion to manipulation of the early stages of human life. Acknowledging this does not on any account mean that the status of persons must be ascribed to these blastocysts, for in other cases we are perfectly prepared to accept the existence of a middle path between the maximum possible level of protection enjoyed by a person and the arbitrary
treatment of an object. For instance, considerations of reverence forbid the arbitrary treatment of human corpses, but we have for centuries been prepared, for important medical or criminological reasons, to accept acts that would be inconceivable with a living human being. This does not invalidate the respect we accord to dead bodies.

Nor is there any reason to fear that research cloning would contribute to a brutalization of society. Since the human ethos is directed towards experiences and situations in the living world, it has no difficulty in distinguishing between a microscopic structure in the laboratory, the fruit of the womb in an expectant mother’s body and a human being who “has come into the world” by being born. Any attempt to abolish these distinctions by subtle conceptual definitions will meet with emotional resistance. The fear of brutalization underestimates this capacity to discriminate, which is substantially independent of the state of scientific knowledge. For example, in the medical practice of artificial fertilization (IVF) that has been recognized in many countries for decades, significant numbers of excess blastocysts are necessarily destroyed after every successful treatment. There is no evidence that this has resulted in an increase in the number of terminations of pregnancy or unlawful killings in these countries.

Analogous circumspection is appropriate in the handling of cloned blastocysts for scientific purposes. For this reason, no research should be carried out on cloned human blastocysts if the hoped-for results can also be obtained with animal model systems or other human cells. Research on cloned human blastocysts should be allowed only after adequate preliminary clarification of the relevant issues in animal experiments. Conversely, it would be impracticable to insist on a direct therapeutic objective for such research in each case, because, since it is fundamental research, the results that might accrue from it are by their nature unpredictable, so that concrete results cannot be demanded.

2.6. Possible misuse of research cloning

One of the objections to research cloning is that a sharp line of distinction cannot be drawn between it and reproductive cloning. It is pointed out that, if the course of events were different from that planned (i.e. limitation to research on blastocysts) – that is, if the blastocyst were implanted into a woman’s uterus and the pregnancy proceeded to term – a cloned human being might be born, the result being a universally condemned situation. This argument draws our attention to a risk whose existence can certainly not be denied; equally, however, it cannot be effectively averted by a ban on research cloning.

As a general principle, specifically directed efforts to avoid misuse are essential for techniques with the potential for harmful as well as beneficial consequences, but their legitimate use must not be prohibited as a precaution. The production and use of knives are rightly not prohibited, although a knife may be a lethal weapon in a criminal’s hand. The proven means, which has been applied in all spheres of society since time immemorial, of precluding undesirable (criminal, excessively risky or for other reasons deprecated) acts is the sanction. Accordingly, the prohibition of reproductive cloning constitutes a suitable and adequate measure for countering the misuse of research cloning.

The stability of a ban on reproductive cloning would rest on the foundation that the creation of a human being by cloning is universally rejected in society. There is no evidence that this assessment might later be called into question if the creation of cloned blastocysts for research – that is, for a purpose quite different from reproduction – were permitted.

The fact that research cloning may in the long term be a significant factor in the development of medical therapies is another argument against a blanket ban. Such a ban would not significantly reduce the risk of misuse; but might well prevent advances in scientific knowledge that hold out the promise of a cure for the seriously ill. The loss of this prospect would not be offset by any discernible gain in the form of a reduction in the risk of misuse.
2.7. Problem of oocyte donation

A final point is that, in the present state of the art of producing cloned blastocysts, human oocytes are required in numbers dependent on the nature and objective of the relevant research. Since the harvesting of oocytes involves appreciable stress for the donor, it is hoped that new techniques in the field of cell biology will make it possible to dispense with the donation of oocytes by women. However, as long as there is no alternative to such donation, it, like other acts undertaken for research purposes, is justifiable subject to the donor’s informed consent. The information to be imparted must include, in particular, details of the possible risks of the extraction and the intended application. Both commercialization and the exploitation of material hardship must be precluded. If the above conditions are satisfied, there is no question of an instrumentalization of donors contrary to human dignity.

The instrumentalization of donors who have given their informed consent can be ruled out in particular where oocytes do not have to be taken from their bodies specifically for research purposes, but remain over from assisted reproduction or can be obtained from ovaries removed on medical grounds.

2.8. Embryo splitting

All the above considerations apply equally to embryo splitting, in which a cellular cluster arises from a zygote formed by cell nuclear transfer or fertilization and is split. The ethical and constitutional permissibility of embryo splitting will always depend on the context and on the intended subsequent use. Where the resulting entities are used for the purposes of fundamental research with the aim of developing cell therapies, there is no question of a violation of an individual’s dignity or right to life either in this use or in the prior splitting. However, should such an entity, obtained by splitting, be implanted in a woman’s uterus, the prohibition of reproductive cloning unanimously advocated by the National Ethics Council in Section D of this Opinion would apply.

2.9. Need for legislation

Whether the Embryo Protection Law as currently worded prohibits research cloning is disputed (see Section C). The Law thus needs to be made more specific, whether or not research cloning is deemed acceptable in principle. According to the view put forward here, the conditions under which research cloning is permissible need to be specified in detail (“prohibition with provision for exceptions”).

Wolfgang van den Daele, Horst Dreier, Detlev Ganten, Volker Gerhardt, Christiane Nüsslein-Volhard, Peter Propping, Heinz Putzhammer, Jens Reich, Bettina Schöne-Seifert, Richard Schröder, Jochen Taupitz, Kristiane Weber-Hassemer
Position C
Prohibition of research cloning at present

1. Position statement

The production of human embryos by cloning for scientific or therapeutic purposes is at present ethically unacceptable. It must be prohibited by appropriate legal instruments.

Should research yield ethically acceptable ways of obtaining stem cells without the use of embryos, such an approach should be encouraged.

2. Reasons

1. Therapeutic prospects: The expectation that so-called therapeutic cloning and associated derivation of stem cells might lead to the possibility of treating serious illnesses and reducing suffering arouses hopes that are understandable both in themselves and in terms of their origin. In the debate on the permissibility of fundamental research, however, it is illegitimate to argue on the basis of possible therapies with totally uncertain prospects. Again, the present state of research has given rise to appreciable medical misgivings concerning the therapeutic use of stem cells derived from cloned human embryos. These include in particular the inefficiency of the experiments, possible genetic and epigenetic damage to the cells produced in this way, and their debatable immunocompatibility.

2. Instrumentalization: The aim of both therapeutic and scientific cloning does not involve giving the created embryos any prospect of development. Instead, they are destroyed shortly after formation for the purposes of developing new methods of treatment or of gaining new scientific knowledge. These two objectives of cloning thus unequivocally fall within the definition of the banned instrumentalization of human life. However, instrumentalization calls into question the recognition and respect to which human embryos are entitled as entities belonging to the human species, or at least as subjects of fundamental rights. It is therefore impermissible. Should cloning yield concrete treatments for human diseases, this would not eliminate the problems associated with the instrumentalization of embryos and the donation of oocytes. In this case, the conflicts arising between fundamental rights would call for re-evaluation.

3. Consumption of oocytes: Female oocytes are for the time being indispensable to cloning by nuclear transfer. Their harvesting entails physical risks to the women concerned. From the ethical point of view, therefore, oocytes are a highly problematical raw material for research and therapy. Oocytes donated in the context of infertility treatment are no alternative, as they are already a scarce resource throughout the world. Hence the existence of risks such as that of commercialization of the female body, which is incompatible with women's dignity. At the same time, the exploitation of women's financial hardship cannot be precluded. Again, many countries lack the capacity for appropriate monitoring of oocyte harvesting. In this context, it will be virtually impossible to prove that donations were made voluntarily and to verify the granting of informed consent. For this reason, invoking women's right of self-determination does not suffice to legitimize the extraction and use of oocytes for cloning purposes.

4. Responsibility for research: It is precisely the finite nature of man, his vulnerability and susceptibility, that have induced him since time immemorial to attempt to overcome illness, ageing and death. The human urge for knowledge, the
interest in understanding the fundamental processes underlying human life and in moulding, planning and safeguarding the future constitute an important motive for research in human medicine. But, however important the quest for ever new knowledge, it is equally vital, whenever research is at issue, to give due consideration to the legitimacy of its resources and to its consequences.

It is a fundamental principle that research on the developmental status of cells and its modification must be possible. Yet, in order to justify such research projects, it is insufficient to invoke the freedom of research. Instead, the permissibility of a given research project must be determined on the basis of its proportionality, the lack of alternatives to it and its priority. None of these three criteria is currently met by either scientific or therapeutic cloning:

- A generalized hope that therapies might possibly be developed can legitimate neither the production and consumption of human embryos for research purposes nor the instrumentalization and endangerment of women through oocyte donation.

- Not all ethically acceptable research alternatives in man, for example using stem cells, have yet been exhausted.

- Finally, as long as a plausible case has not been made for the existence of direct therapeutic applicability to concrete groups of patients, the priority of this research remains unproven.

5. Research prospects: Besides cloning by nuclear transfer, other methods and techniques whereby the state of cells or cell nuclei can be modified so as to resemble an embryonic cell are now being developed. These include, for example, parthenogenesis, the aggregation of embryonic stem cells into blastocysts, nuclear transfer into oocytes obtained in vitro from cultured embryonic stem cells, and the reprogramming of somatic cells so as to return them to an earlier stage of development.

However, positive verification in man of whether the results of such experiments constitute human embryos – that is, entities with the capacity to develop into a complete organism – is impossible, for the transfer of such structures to a woman would be contrary to accepted ethical principles. In view of the experimental manipulability of the developmental stage of cells and of the ethical preclusion of directly demonstrating the existence of totipotency, additional criteria for evaluating the developmental potential of cells produced in this way are needed. It would be possible to distinguish ethically acceptable modifications or methods from others that ought for good reasons to be avoided. However, each individual method should be examined for ethical acceptability not only in the context of research but also in the event of possible subsequent therapeutic application. A possible criterion is the utilization of oocytes extracted from the female body. Where the ethical objections presented in item (3) above apply, such experiments are impermissible.

3. Opinion

3.1. Cloning without reproductive intent

Advances in modern research in the fields of cell biology, molecular biology, reproductive biology and reproductive medicine have made it possible to create human embryos not only by fertilization of an ovum with a spermatozoon but also by means of cloning based on the transfer of somatic cell nuclei into enucleated oocytes (nuclear transfer). The resulting embryos can undergo systematic experimentation or be used for the derivation of stem cells.
However, the fact that a technique is feasible does not mean that it is legitimate—especially where the rights or claims of others are affected. The more ethical, legal and social problems such a technique raises, the more closely the evidence and arguments adduced in its favour must be scrutinized.

Two main reasons are given for the cloning of human embryos other than for reproductive purposes:

» First, it holds out the prospect of obtaining embryonic stem cells for therapeutic purposes that would be immunocompatible and not subject to rejection by the potential recipient (therapeutic cloning).

» Second, it is hoped that the procedure will facilitate research not only on fundamental mechanisms of developmental biology but also on specific diseases (research cloning).

The arguments adduced in favour of cloning for these purposes are examined below. To arrive at a valid assessment of the procedure, the objectives of non-reproductive cloning are considered separately and weighed against the relevant uncertainties and medical and ethical risks.

### 3.2. Cloning for therapeutic purposes

Cloning by nuclear transfer permits the creation of blastocysts that are substantially, if not wholly, genetically identical to the individual from whom the cell nucleus was obtained. It is hoped that a stem cell line potentially derivable from such blastocysts would be immunocompatible with the donor and therefore not be rejected when transplanted. However, no one can say today whether this will be the case and whether such cells obtained from cloned blastocysts will ever be usable for therapeutic purposes. There are good reasons for doubting the therapeutic value of cloning.

### 3.2.1. Inefficiency of the method

The doubts are based, firstly, on the inefficiency of the method. Although cloning has now been tested for nearly eight years in animal experiments, it remains difficult and comparatively unproductive. Whereas, in animal experiments, blastocysts have arisen from some 25% of the enucleated oocytes into which somatic cell nuclei were transferred, far more oocytes are required in order to attain this proportion. This is because not all cells can be used, because isolation of the inner cell mass from the blastocysts is not always successful, and because an embryonic stem cell culture can seldom be established from these cells.

The experiments of a Korean group working on the cloning of human embryos show that these results can perfectly well be extrapolated to man. The initial complement of material comprised 242 oocytes taken from 16 donors. Some 176 enucleated oocytes into which a somatic cell nucleus had been transferred yielded 30 blastocysts, from the isolated inner cell masses of which it was possible to culture just one stem cell line. Referred to the initial number of oocytes, then, the success rate is less than 0.5%.

Even if the efficiency of cloning by nuclear transfer were to improve significantly in the next few years, it would be virtually impossible for sufficient individual embryonic stem cell lines to be obtained thereby for the treatment of individual patients. An aggravating factor, albeit without the same ethical implications as the fact that a number of women would still have to donate oocytes for a single patient, is that such a procedure, if recognized as a therapeutic option to be applied in principle given the relevant medical indications, would surely far outstrip the financial capacity of the public healthcare system if required by a relatively large number of patients. It is therefore highly probable that the common severe illnesses will not prove to be curable by this approach—yet this argument is repeatedly adduced in favour of cloning.

35 Hwang et al. (2004).
3.2.2. Defectiveness of the method
Further doubts as to the therapeutic applicability of cloned stem cells arise from the relative uncontrollability of the reprogramming of somatic cell nuclei and the difficulty of verifying its results. Although some scientists consider that stem cells derived from cloned embryos are functionally no different from those obtained from embryos created by in vitro fertilization, only human experiments could show whether this assumption is justified. In a culture, it is virtually impossible to ensure that the stem cells derived from cloned embryos are in fact free of defects liable to cause functional or growth disorders when transplanted into a patient’s body.

At present, it is not even known whether embryonic stem cells derived from embryos created in vitro can be used in human patients without risk – that is, whether their growth can be controlled and they do not form tumours. Since embryos created by IVF have arisen by the fusion of two gametes and not by the reprogramming of a somatic cell nucleus, the stem cells derived from them can as a rule be assumed to lack such reprogramming defects. It is therefore reasonable not to contemplate the derivation of stem cells from cloned embryos for therapeutic purposes – apart from all the fundamental ethical arguments – until the therapeutic value of embryonic stem cells has been demonstrated in principle. However, no such demonstration has been forthcoming.

3.2.3. Immunocompatibility not established
The principal justification advanced for deriving stem cells from cloned blastocysts is their presumed immunocompatibility with the organism of the individual from whom the cell nucleus used for cloning is derived. However, it must be remembered that not only the nuclear genome of the oocyte but also its mitochondria contain genes that are transmitted to all daughter cells arising from it. No one knows whether the products of these genes might be recognized as foreign by the recipient’s organism and trigger the rejection of these cells. Until this question has been answered by analogous animal experiments, it is unjustifiable, or at least premature, to adduce the argument of immunocompatibility in support of the need to obtain stem cells from cloned embryos. Again, immunocompatible stem cells could apparently also be derived from an adult human organism itself. If so, this method would be unequivocally preferable because its underlying conditions and consequences are less problematic.

To sum up, the notion that cloning might have a therapeutic objective is currently no more than a vague hope, unproven where human applications are concerned. Rather than concrete options for treatment, then, we have only good intentions and hopes – the avoidance of suffering and the prospect of therapies for future patients. By themselves, such hopes do not constitute a sufficient argument for giving priority to cloning over the rights and claims of specific other parties and entities – the oocyte donors and human embryos – and for invalidating the ethical objections.

3.3. Cloning for the purposes of research
It follows from the foregoing that the aim of non-reproductive cloning today is to obtain fundamental scientific and medical knowledge. Any restrictions on the acquisition of such knowledge are relaxed if it enjoys “priority” and/or if “there is no alternative” to it. The scientific and cultural significance of the gaining of fundamental knowledge is not in dispute. Nevertheless, such research, if it is not directly necessary for therapeutic reasons and does not serve specific groups of patients, can hardly be described as enjoying “priority”.

A method – in the present case, the cloning of human embryos – would be considered to have no alternative if specific fundamental knowledge could not be obtained except by its use. However, this is by no means the situation here. For
preclinical fundamental research, it is comparatively immaterial whether human, primate or other mammalian clones are used.

Consequently, it cannot be maintained that research on the production of human clones, and research conducted on human clones, enjoys priority or that there is no alternative to it. The main reasons then remaining are the human urge for knowledge and the will to create. The cultural importance of these aspirations must of course not be underestimated. Yet fundamental ethical arguments, both individual and social, based on considerations of human rights may be adduced in favour of restricting the exercise of this freedom. These concern the legitimacy of the resources needed for cloning and the status of the cloned human embryo.

3.3.1. Use and consumption of female oocytes

Female oocytes are at present an indispensable and irreplaceable prerequisite for cloning by nuclear transfer. Their cytoplasm contains all substances needed for the reprogramming of somatic cell nuclei. However, the harvesting of human oocytes raises far-reaching problems. Women wishing to donate oocytes must receive hormone treatment to stimulate the simultaneous maturation of a number of egg cells in their ovaries. Both hormone treatment and surgical follicular puncture under anaesthetic for harvesting the mature cells entail by no means negligible health risks for donors. These alone render this method of obtaining oocytes for scientific or therapeutic purposes highly problematical.

Moreover, oocytes are a scarce resource. This is already the case for infertility treatment. The oocytes donated in countries whose legislation so permits do not suffice even to satisfy the demand from couples wishing to use such cells to initiate a pregnancy. For this reason, an international grey market in oocytes has already come into being, whereby women can undergo treatment for a financial consideration and surrender their oocytes to clients. This trend towards commercialization would in all probability be accentuated if female oocytes were required in large quantities for cloning experiments. The female body would be turned into a resource.

However, even without commercialization, the recruitment of oocyte donors raises ethical issues and problems that extend beyond the direct and indirect risks to the individual women who undergo the medical procedures necessary for obtaining oocytes. These include proof of the voluntary nature of the donation and verifiability of informed consent, as well as the possible exploitation of hardship in poor countries, whose female citizens might be inclined to accept the health risks of oocyte donation in return for the prospect of relief of their economic plight.

All in all, the risks and ethical issues bound up with the extraction and use of oocytes for producing cloned embryos constitute a powerful argument in favour of harvesting and utilizing oocytes only for reproductive purposes. It is essential to avoid the creation of a climate of expectation in which women must defend their right to bodily integrity against the scientific and medical demand for oocytes.

3.3.2. Instrumentalization of cloned human embryos

The recent experiments conducted by the Korean-American group mentioned earlier have shown that the transfer of human cell nuclei into enucleated human oocytes also leads to the formation of embryos that can develop at least to the blastocyst stage. This raises the extremely challenging question of the biological and moral status of artificially created entities of this kind. Not only the processes of formation of such blastocysts but also their properties can now be influenced and to some extent controlled in the course of scientific experimentation. Hence the natural initial conditions for the existence of such entities can no longer constitute a guide to ethical evaluation.

A human embryo normally originates from a fertilized ovum within the female body. With the introduction of in vitro fertilization and cloning, the conditions whereby an embryo
comes into being have radically changed. On the one hand, the location of the process has been moved outside the female body, while, on the other, its biological and material foundations have become in part obsolete. Instead of arising exclusively through the fertilization of female by male gametes, embryos can now also be created from enucleated oocytes in conjunction with somatic cells.

What has manifestly not changed is the fundamental capacity of the entities formed in this way to develop into a complete organism. Even if relevant human experiments are precluded on ethical grounds, animal experiments suggest that some at least of the embryos thus created have the potential to form a fully fledged organism. If so, and as soon as this is achieved, it is appropriate for such organisms to be deemed to belong to the human species.

If cloning is carried out for scientific or therapeutic purposes, the embryos are then inevitably destroyed in experiments directed towards obtaining scientific information or when stem cells are extracted from them. The aim in cloning for the purposes mentioned is thus not to give the embryos created a chance of development. Such cloning therefore unequivocally falls within the definition of instrumentalization. After all, unlike embryos that are created for the purposes of artificial fertilization and may no longer be needed for reproduction, these embryos are not produced for their own sake; their creation and destruction take place exclusively in the interests of others. While these interests are transparent and legitimate, they can nevertheless not justify the treatment of embryos as a mere material resource for cloning. Such a use constitutes a suspension of the recognition and respect to which human embryos are entitled as entities belonging to the human species or, at least, as subjects of fundamental rights.

The production of human embryos for scientific purposes, with the sole intention of discovery and creation and ultimately resulting in their destruction, is inherently illegitimate. Since it belongs to the human species, each human embryo must necessarily be assumed to have an interest in life. The weighing of this interest against the interests and rights of others could – if at all – be contemplated only if the rights of another individual were concretely and directly affected. This is not the case in the research situation.

### 3.3.3. New techniques – new issues

In addition to cloning by somatic nuclear transfer, other methods are currently being developed with the potential to create cells or to alter the state of cell nuclei in such a way as to resemble that of an embryonic cell. One such method is parthenogenesis, the artificial activation of an unfertilized egg cell. For a long time it was assumed that embryos produced in this way were not capable of development. Recently, however, it was shown in the mouse that they can not only develop into adult animals but also produce offspring.\(^{36}\) Other techniques whereby the creation of embryos appears possible or at least cannot be ruled out include the aggregation of embryonic stem cells into blastocysts; the fertilization of egg cells obtained in vitro from cultured embryonic stem cells; the reprogramming of somatic cells to return them to an earlier stage of development; and the creation of cloned chimeras from human somatic cells and enucleated oocytes of other mammalian species. In view of the rapid development of this field of research, this enumeration must be deemed provisional only; the future is likely to see the development of further techniques, each of which must be considered individually in terms of its ethical acceptability.

Some of the entities yielded by these methods exhibit characteristics and properties commonly ascribed to embryos. It is then necessary to decide whether these entities are in fact embryos, and, if so, to determine the reasons for this ascription. Given the relevance of the term “human embryo” to the ethical and legal debate, precise definition of both the term and the entity is essential.

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\(^{36}\) Kono et al. (2004).
3.3.4. Problems of verification of experimentally inducible totipotency

The basic criterion for distinguishing between embryos and other cellular clusters is the capacity of the former to develop into a complete organism (totipotency). Before the birth of the cloned sheep Dolly, totipotency was assumed to exist only in the cells of the early embryo resulting from the fertilization of an ovum by a spermatozoon; today, however, this property can be induced experimentally in other cells too, at least in non-human mammals. Although this is presumably also feasible in man, direct verification is impossible, as it would require the ethically unacceptable transfer of such entities into a woman’s uterus.

The information needed to arrive at a scientifically based ethical judgement is therefore not available. One possible way of dealing with this uncertainty is to draw conclusions from analogous experiments with animals. The drawing of conclusions by analogy is a recognized scientific method, which, in the history of science, has afforded many valuable indications concerning processes not amenable to direct investigation. Yet there are also many examples which show that animal experiments cannot be directly extrapolated to man.

Another possible approach to this uncertainty is to assume totipotency in cases of doubt (in dubio pro vita). This would ensure that human embryos with the potential to form a complete organism were not experimentally created and consumed. However, another consequence might be that a large number of experimentally produced human cells or cellular clusters were rendered subject to protection even though it could never be proved (nor ought it to be proved) that complete human organisms could develop from them. In the extreme case, protection would have to be granted to any human cell subjected to experimental manipulation if there is reason to suspect that its development potential has been altered in the direction of attaining the capacity to form a whole organism.

If these far-reaching conclusions are accepted, two problems arise. First, on the purely practical level, it would be virtually impossible to monitor such experiments. Second, the principle of embryo protection would thereby be taken to absurd lengths. After all, if every cell subjected to actions aimed at altering its state of differentiation were potentially regarded as an embryo, then – to exaggerate somewhat – ethical boundaries and legal provisions would lose their specific, unequivocally identifiable object.

In view of the experimental manipulability of the developmental stage of cells and the ethical impossibility of direct determination of the existence of totipotency, additional criteria must be established for assessing the developmental potential of cells produced in this way. This would make it possible to distinguish between ethically acceptable modifications or techniques and others which there are good reasons for avoiding. However, each such method should be examined for ethical acceptability not only in the context of research but also with a view to its possible future therapeutic application.

3.3.5. An additional criterion: the utilization of human oocytes

One of the criteria that could be applied to this end is whether human oocytes obtained as such from the human body are used in an experiment. The following three reasons can be adduced.

First, there are a number of indications that the process of reprogramming a somatic cell nucleus is influenced by the nature of the oocytes used. For instance, the Korean scientists directly attributed their successful cloning of human embryos to the fact that they used very fresh oocytes. Cryopreserved oocytes are manifestly less suitable for the purpose; a lower success rate is observed in reproductive medicine too when these are used for in vitro fertilization. Again, oocytes of animal origin seem incapable, or almost incapable, of supporting
embryonic development on the basis of a human genome. Nor is it clear to what extent embryos created with oocytes obtained from embryonic stem cell cultures would be capable of normal development. Although this possibility cannot be completely ruled out, the experience and knowledge gained so far strongly suggest that the developmental capacity of such entities, created unconventionally on the basis of human cells, is reduced in proportion to the heterology and artificiality of the oocytes used for the purpose.

The use of oocytes obtained direct from the human body necessarily ensures that the course of embryonic development will be smooth, and hence that all factors required by the oocyte or embryo are present. In the absence of an acceptable direct method of proof, then, there is reason to believe that entities produced in this way are more likely to be capable of development into a complete organism than ones created with the aid of other initial cells or materials. For this reason, in the assessment of experimental methods of modifying the differentiation status of cells, particular attention should be given to whether oocytes obtained from the human body were used.

A second argument against cloning experiments using human oocytes concerns the risks and stresses to which women are exposed, the danger of exploitation of hardship, and the problems of verifying informed consent. These issues have been addressed earlier in this document.

A third consideration is that oocytes (like spermatozoa), as reproductive bodily substances, have not only biological particularities but also a specific symbolic significance. Unlike other bodily cells, they are not only the material substrate of individual reproduction, but also underlie the preservation of the species. They represent fertility and the procreative capacity, while at the same time standing for the necessary complementarity of the male and female principles in sexual reproduction. They also constitute a genealogical bridge between past and future generations.

Even if oocytes do not possess a developmental potential of their own and therefore cannot be equated for regulatory purposes with totipotent cells, as reproductive bodily substances they have biological and symbolic properties that distinguish them from other bodily cells. Although the ethical and legal relevance of this special status has not yet been comprehensively established, there are good reasons for attributing particular significance to these cells in the evaluation of cloning experiments. In particular, however, the ethical problems associated with the harvesting of oocytes constitute a powerful argument in favour of prohibiting their use in cloning experiments.

Eve-Marie Engels, Regine Kollek, Christiane Lohkamp, Therese Neuer-Miebach, Spiros Simitis
Joint recommendation on research cloning

Notwithstanding the divergent positions set out above, the National Ethics Council unanimously recommends that research cloning should not be permitted in Germany at present.
Selected bibliography


Klonen beim Menschen: eine alte Debatte – aber immer noch in den Kinderschuhen


The members of the German National Ethics Council

Prof. Dr Drs h. c. Spiros Simitis (Chair)
Prof. Dr Regine Kollek (Deputy Chair)
Prof. Dr Dr Eckhard Nagel (Deputy Chair)
Dr Hermann Barth
Prof. Dr Wolfgang van den Daele
Prof. Dr Horst Dreier
Prof. Dr Eve-Marie Engels
Rt Rev. Dr Gebhard Fürst, Bishop of Rottenburg-Stuttgart
Prof. Dr Detlev Ganten
Prof. Dr Volker Gerhardt
Christiane Lohkamp
Prof. Dr Martin J. Lohse
Prof. Dr Therese Neuer-Miebach
Prof. Dr Christiane Nüsslein-Volhard
Prof. Dr Peter Propping
Heinz Putzhammer
Dr Peter Radtke
Prof. Dr Jens Reich
Prof. Dr Eberhard Schockenhoff
Prof. Dr Bettina Schöne-Seifert
Prof. Dr Dr h. c. Richard Schröder
Prof. Dr Jochen Taupitz
Dr Hans-Jochen Vogel, Former Federal Minister of Justice
Kristiane Weber-Hassemer, Former Permanent Secretary of Justice in the State of Hesse
Dr Christiane Woopen

Staff of the secretariat

Carola Böhm
Dr Katja Crone
Ulrike Florian
Dr Rudolf Teuwsen
Andrea Weichert
Dr Christina de Wit