

CLONING OF HUMANS
Biological Foundations and Ethico-legal Assessment
Comment
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The successful generation, by Scottish animal breeders, of a mammal harboring the identical genetical material of another adult animal has created world-wide sensation and in some instances even scare. Many people ask about the meaning of this further step in a sequence of human interference in nature. Can this technique be applied to humans? If this were so, should it not be prevented and how could it be prevented? What are the limits imposed by our accepted ethical and legal principles? Are legal interdictions currently in force sufficient to secure observance of necessary limits on a national and international scale?

Answers to these questions require an explanation of the techniques of cloning and their possible application in humans (I), an assessment of its use in humans in the light of accepted ethical principles (II), an evaluation of its position within the legal system (III) before first conclusions can be arrived at for further actions (IV).

Biological fundamentals of cloning techniques and their possible use in humans

I.1 Definition of cloning

A clone is a group of genetically identical organisms. Clones are generated most simply by division, also called vegetative reproduction. It is a mechanism of reproduction in all bacteria but also in higher micro-organisms such as yeasts and fungi and even in many species of multicellular animals. Some higher plants reproduce by developing buds or shoots on stem or leaf surfaces that grow by cell division and eventually detach to become new individuals (clones). In this sense potatoes in our fields are also clones.

Most vertebrates exclusively reproduce bisexually, which does not involve generation of clones. On the contrary the genetic material of the progeny usually has a different genetic make-up because it constitutes a mixture of maternal and paternal genes. Genetically identical individuals (= clones) can be generated in a natural way only if embryos of early cleavage stages (see below) split spontaneously and if these cleavage products develop further and independently (see footnote). In the human species the rate of twins is on the order of 1 %. Approximately 20 % of these twins are identical (monozygotic) twins, i. e. clones. This means that at present many millions of people have genetically identical brothers and sisters. A similar low rate of monozygotic twins (0.2 - 0.4 %) is observed also in cattle and sheep. Identical triplets or even quadruplets have been reported but are extremely rare. There are some species of mammals, however, such as armadillos, who have litters with four to ten identical siblings, i. e. clones, generated by splitting of a single embryo. To be a clone essentially only means that the genetic material, the so-called genotype of the individuals, is identical. The phenotype, i. e. those external traits influenced by the genotype, do not necessarily have to be identical. This is so because not all traits of a living organism are determined solely by gene activities but are determined also by developmental conditions, in humans, e. g. in particular by the socio-cultural environment.

I.2 Application of cloning in experimental and domestic animal breeding

Clones of higher organisms are of great interest for medical basic research. Since the 1920ies attempts have been made to obtain strains of genetically almost identical mice by inbreeding, i. e. by continuous mating of brothers and sisters. Such strains played an important role in the analysis of the immune system and continue to do so. This is exemplified by such questions as how closely related two individuals must be in order to be able to accept each other's transplants. Lines of inbred animals are required also for studies of drug effects and side effects in experimental animals that should be as identical genetically as possible. Unfortunately, it has been impossible even by continuous inbreeding to obtain true homozygosity i. e. genetical identity. When addressing questions like these and also in clinical research aimed at elucidating mechanisms of genetically determined diseases or in nutrition biology use of these genetically identical clones would be helpful also in drastically reducing the numbers of experimental animals needed, due to the higher statistical validity.

The generation of clones would allow breeders of domestic animals a hitherto unobtainable exactness in evaluating the quality of meat, milk production, and other criteria. In combination with the new possibilities offered by genome analysis embryos could be selected before cloning on the basis of desired or undesirable traits. Embryos with an optimal set of genetic traits could then be grown as clones and used for classical reproduction. The problem of biodiversity would not be an issue as this strategy would be applied always only in special domestic animal breeding programs. As needs arise many different genetic lines would be required in these special domestic animal breeding programs. The same would apply to breeding of useful plants. Careful breeding practices would be a means, therefore, to prevent genetic depletion of useful domestic animal and plant races by currently employed techniques such as embryo splitting or newly developed cloning techniques.

Utilization of clones would be considered in the field of xenotransplantation but also in gene farming, i. e. the production of proteins secreted into milk. In both cases genome interventions would be of decisive importance. It would be much easier, however, to carry out such manipulations at the level of cell lines in tissue culture rather than at the level of embryo cells. Altered cell lines could be used to generate, by cloning, different kinds of transgenic animals, pigs for example, provided that cloning would work in these cases as it has been reported for sheep.

I.3 Cell biology of cloning

In order to facilitate evaluation of cloning techniques some aspects of embryonic development in mammals will be outlined below: egg cells and sperms only contain a single set of chromosomes (haploid chromosomes) such that a fertilized egg cell with a normal (diploid) set of chromosomes can be generated upon fusion. Diploid cells contain two copies of each gene in most of their chromosomes, one derived from the father and one from the mother (the sex chromosomes in males are an exception). Mature egg cells are generated from precursor cells during oogenesis in a series of physiological processes in which the diploid set of chromosomes is reduced to a single set. Humans and cattle usually only develop a single egg cell that can be fertilized at a time. Sheep develop two to three of such egg cells and pigs have simultaneously 15 - 20 of such egg cells. Hormone treatment (superovulation) can be utilized to raise these numbers to 4 - 6 in humans, 6 - 10 in cattle and sheep, and up to 40 in pigs. Egg cells of cattle can be obtained by puncturing ovaries of live animals; they can be collected also from slaughtered animals. Mature egg cells are surrounded by a protein-rich coat, the so-called zona pellucida, and by several layers of follicle cells which must be penetrated

by the sperm. The first cleavages of the embryo are still carried out within the zona. At the so-called blastocyst stage (70 - 100 cells; after 7 days in cattle) the embryo emigrates from the zona pellucida. If this process is incomplete and if cells with developmental capacity still remain in the zona pellucida both portions develop independently of each other into identical twins. If these two portions are not completely separated from each other during emigration from the zona pellucida this will generate Siamese twins which, therefore, are always homozygous identical twins.

Cells that can develop into an intact adult organism are called totipotent. As a rule embryo cells of up to the 16 - 32 stage (also called morula stage) possess this capacity. A certain degree of differentiation is observed already at the next stage (70-100 cell stage).

The raspberry-like morula develops into a spherical body known as blastocyst. Its surface entirely consists of cells that are no longer totipotent while those cells on the inside of the hollow structure (inner cell mass) remain in a state of totipotency. The term totipotency will have to be defined in the light of knowledge gleaned from the Scottish sheep. Until now it had been assumed that differentiation in mammals leads to irreversible genetic modifications at very early developmental stages. At least in sheep it appears to be possible to reprogram such cells so that they will regain their totipotency although the molecular mechanisms of this reprogramming process are not known at present.

I.4 Cloning of experimental and domestic animals

In principle two techniques are available for generating clones of higher organisms.

- embryo splitting and
- nuclear transplantation into egg cells or embryo cells from which their own genetical material was removed.

Splitting of embryos at early cleavage stages by separation and partitioning of cellular aggregates of sufficient size is feasible but, for practical reasons, restricted to the generation of two or at most four individuals.

The concept of nuclear transplantation goes back to Hans Spemann (1930ies) and his question of whether genetic material remains unaltered during development of an organism or not. In the 1960ies J. B. Gurdon (Oxford) was first to show that transplantation of a nucleus from a skin cell of an adult frog into an enucleated egg cell does not lead to the development of an adult animal but at least to the generation of tadpoles. These experiments suggested that, at least in amphibians, a reprogramming of the genome was possible within certain limits. In mammals similar experiments have been carried out since the mid 1980ies. In these cases the donor nucleus was derived initially always from totipotent embryo cells of the earliest cleavage stages. These experiments were undertaken, and still are, by pursuing many different experimental designs.

As a rule acceptor cells are mature fertilizable egg cells from which their own genetic material was removed either by ligation of those parts of the cell containing the genetic material or by aspiration of the nucleus by means of a glass capillary. Such cells devoid of genetic material are called cytoplasts. Donors of cell nuclei (so-called karyoplasts) are embryo cells up to the blastocyst stage. Donor and acceptor cells can be fused by electric

shocks. Alternatively the karyoplasts can be micro-injected directly into the cytoplasm. Until now the yields of these techniques were low. Approximately 1000 to 2000 calves were born world-wide by using these strategies.

The number of clones obtained in this way has been reported not to exceed 11 animals. Until now this design has not been of any practical importance. Clones obtained by nuclear transplantation are not absolutely genetically identical since, as a rule, they have two genetic ancestors, one representing the donor cell nucleus and the other providing the cytoplasm. Although the nucleus was removed from the cytoplasm it still contains several copies of a cellular organelle known as mitochondrion. Mitochondria are responsible for cellular energy generation and themselves contain a small genome. In humans this genome encodes 13 genes only and thus its contribution to the total number of genes (> 80.000) is of no quantitative importance. Identity can be assumed, therefore, for the vast majority of genetic traits of individuals generated by nuclear transplantation.

In order to increase yields the Scottish team at the Roslin Institute developed a working hypothesis according to which successful fusion of the cytoplasm of a fertilizable egg cell and the nucleus of an embryo cell would yield biologically active totipotent cells only if their growth stages had been adjusted to each other. If this were not be the case it was envisaged that the cytoplasm, under certain circumstances, would interfere with nuclear development. This hypothesis is based on the observation that living cells pass through certain stages and phases during growth in which they prepare for the reduplication of the genetic material and eventually carry out this step. This gave rise to the idea of synchronizing physiologically the recipient cytoplasm and the donor nucleus. Even the first pilot experiments utilizing embryo cells in a certain stage of growth revealed double the rates with which animals were obtained. It is also possible to arrest cells at certain stages of development by treatment with several agents. Such observations are the basis of many treatment regimens in cancer chemotherapy. Since it is difficult to synchronize embryo cells in this way the Roslin team resorted to using embryonic cell lines. Such cell lines are obtained if embryo cells are cultivated at places other than those in which they usually occur, e. g. by growth in vitro or growth in other organs such as kidney capsules. Under these conditions the cells usually cannot differentiate and thus retain their totipotency. Following their arrest in a certain stage of the cell cycle by growth factor withdrawal the use of such cells led to a further increase in the yield of cloned animals.

In the meantime this experiment surprisingly could be extended to cells derived from the mammary gland of sheep, albeit with low yields (one pregnancy out of 277 fused embryos). This work benefited from the fact that the embryonic genome in sheep cells begins to activate its own program only at the 8 - 16 cell stage. In earlier stages this is taken over by so-called maternal proteins still persisting inside the acceptor egg cell. In human and murine cells the activation of the genome already begins at the 2-cell stage. As a consequence of the late activation of the genome in sheep cells the newly introduced nucleus gains time for reorganization and can prepare its genome for a state which eventually restores totipotency.

The unsatisfactory yields of the procedure demonstrate that the working hypothesis of acceptor cytoplasm and donor nucleus synchronization was successful to a certain extent but that fundamental improvements are required to make this a practicable approach for domestic animal breeding.

If seen only as an exercise in reproduction biology the experimental designs described here can be applied in principle also to other mammals including humans. Whether this

is justifiable and permissible, however, is an ethical and legal problem rather than a question of biology.

Ethical assessment

The disapproval shown towards the applicability of the newly discovered cloning technique to a large extent expresses the moral conviction that cloning of humans would transcend a border that man should not go beyond. Fright of the novelty of such a technique certainly plays a role. After all never has there been reproduction without the necessity of genetic material derived from two sexually different people having to come together. With the exception of multiple births as the result of simultaneous conception there has never been a human being possessing the same genetic material as another human being. It is beyond doubt that, should these limitations imposed upon mankind by nature itself cease to exist, there is no reason for not subjecting ourselves to these constraints on moral and legal grounds.

Moral convictions are valuable guidelines but not sufficient reasons for deciding where to draw lines in view of expanded options. We are forced, therefore, to obtain ethical and legal judgments based upon reasoning. A proven method to arrive at reasoned decisions suggests to question the legitimacy of goals for which the newly acquired room for maneuver can be claimed and to check the justifiability of utilized resources with respect to intended and unintended consequences. Criteria that can be drawn upon are broad-based ethical principles such as those expressed legally in human rights codices, international law conventions, and, above all, in our constitution.

II.1 Aims

The following possible aims of the application of cloning of humans have been forwarded for both cloning strategies, i. e. for embryo splitting and nuclear transplantation: improvements in the treatment of infertility, avoidance of genetically inherited diseases, replication of deceased individuals or of those deemed particularly valuable, possibilities of organ and tissue donations by cloned humans, duplication in the form of a twin, improvements of research on embryos aimed at avoiding genetic diseases or aimed at their treatment.

What, however, are the ethical and legal principles to evaluate the legitimacy of such aims? One will have to begin with the fundamental principle of the inviolability of human dignity which, as a fundamental right, entails the right to live, the right to physical integrity, and the right to self-determination. In turn, these fundamental rights themselves unequivocally and invariably tie all third party interventions in the psycho-physical integrity of human beings to informed consent. In addition, there are the principle of equality as well as the legitimate claim for protection. The latter is innate to human individuality and its realization and also to human social existence as exemplified in the form of families and its associated structure of human reproduction. As far as cloning of human embryos is concerned the application of these principles depends upon the nature and the status that we bestow upon human embryos.

a.

To begin with, a review of the possible actions discussed above in the light of these principles reveals that it cannot be the fact per se of the resulting human having the same genome as another human being that prohibits cloning of humans. It is beyond doubt that

the individual genome as the unmistakable natural developmental framework for the physical nature of this individual enjoys the particular kind of protection that is due to the individual person and that person's physical integrity. Yet, individuality and personal identity of a human being are not incorporated in the genetic make-up but are the result of developments that are realized in interactions with the environment. If one wants to comply with the person's dignity and to avoid genetic determinism the same dignity innate to all other humans must be bestowed upon humans originating from natural multiple births. Even if a cloned human being were to exist in defiance of all prohibitions this being would have the same dignity as all other beings.

Problematic with cloning of humans, therefore, is not the correspondence of a genome with that of another human being but the fact that a human being is created as a means to an end, which is not him/herself. It is the fact that, for this purpose, the genetic identity with another human being is inflicted upon the creation. This is obviously the case if a human being is cloned for the express purpose of taking the place of another human with an identical genome, of serving as a donor of organs or tissues for others, or of being, as a child, the genetic recapitulation of the person who donated the transplanted nucleus - not to mention cloning for eugenic or commercial purposes. In each case the genetic identity is manipulated as a means that the created human is to minister to. The created is to be the one having the same genome; the created is to exist to serve another by its genetic identity. With this, however, several of the principles mentioned above are violated: to manipulate a human being in its genetic identity for subjection to third party claims is an instrumentalization touching at the very core of the person. This instrumentalization violates that which is due to humans as persons and which is protected by the predicate of dignity, i. e. to be an end in itself. A child produced as a twin would be subject to expectations of having to recapitulate the human being whose genome it carries. It would have to live a life already lived and would be accepted only because of its own genetic identity matching that of another rather than for its own 'foreign' identity. Hence it is the connection with third party purposes which makes duplication of the genome an offense against the dignity of an individual person and the rights resulting from it. Duplication of the genome deprives humans created by directed cloning of their elementary possibility to be respected in their genetically unexpected identity such as everyone else also.

Evidently the effect of chance which governed fusion of haploid germ line cells to a novel individual genome during the process of reproduction is to protect the individual from becoming an object of biological predetermination by third parties. Thus it guards the freedom of human beings from being the subject of genetic determination by third parties. However, if it is the heteronomy of the natural genesis of an individual genome which safeguards, against despotism and license, the freedom of development that corresponds with the dignity of a person it seems that there exists some right of a person to be born of two biological parents and not to have been manipulated in one's genetic identity. Unlike an identical twin a human being resulting from purposeful cloning would be subject to heteronomous purposes which would deprive the development of individuality of that openness and freedom which is protected under the title of the freedom of development of personality.

b.

One cannot argue against this with reasons that take into consideration certain interests of individuals such or constellations which do not necessarily precipitate the apprehended instrumentalization - such as infertility of both partners or danger of transmitting a severe genetic disease. Obviously free development of an individual is linked in a holistic sense so closely to the respect of the structure of natural reproduction

that, for the sake of dignity and freedom of the individual, one must respect also the dignity of natural reproduction innate to the human species. It is the possible disappearance of limits imposed by nature upon human affairs that lets us discover more deeply the humane reason of such limits. If subjugation to the same conditions of nature were abolished in this point not only would claims of the afflicted individual be violated but biological manipulation would also alter elementary attitudes in the sequence of generations and would lead to new inequality among human being and thus violate the protection of the family and the principles of equality as well as laws against discrimination derived thereof.

c.

Against these reasons one could raise the objection that they would apply only to cloning aimed to bring to life a human being possessing the same genome as another human being; that this would not be the case if cloning had the aim to produce human embryos for purposes of diagnosis or research in order to improve treatment of infertility or, by means of pre-implantation diagnosis, to provide parents with children who are not afflicted by genetic diseases transmitted by their parents. Indeed, an assessment of these goals requires to resort to reasons other than those discussed above. Admittedly these reasons depend upon the moral and legal status attributed to the different developmental stages of the human embryo. If one starts out with the notion that, beginning with the moment of fusion of the two nuclei, human beings are subject to the protection of human dignity - as is the case with the German embryo protection law and the decision of the Federal Constitutional Court - cloning for the purpose of diagnosis as well as cloning for research are equally prohibited since the embryo in its entirety is used here as a means to an end. This assessment would be different if this status were not given to all stages of the embryo. Many legal systems for which this is applicable still bestow a 'special' status upon the embryo which, although not of equal rank, grants worthiness of protection. Moreover, the human rights convention for biomedicine of the Council of Europe demands 'adequate protection' of the embryo and bans the generation for research purposes such that embryo splitting also does not meet with a lawless gray zone. This issue, however, has to be clarified on an international basis and this should be pursued with vigor.

In summary one arrives at the conclusion that the aim of human cloning cannot be reconciled ethically with principles of human dignity and the protection of embryos and thus has to be considered illegitimate.

II.2 Means

Apart from an assessment of the legitimacy of aims of human cloning one must also evaluate its justification as a means. If one starts with the fact that cloning of humans is impossible without carrying out respective research on humans and that this research entails embryo research or experimentation on humans that are ethically unjustifiable and also prohibited according to German law, cloning of humans thus also for these reason is out of the question. In addition this would precipitate all ethico-legal problems connected with artificial fertilization such as the question of superfluous embryos, surrogate motherhood and others. If special risks other than those mentioned above still remained for the cloned human after completion of research in view of the unobtainable informed consent by the person concerned this would be another reason to be added to those mentioned already, which would preclude applications. Since means have to be assessed always also with respect to social tolerance all consequences à propos relationships between generations and within families must be considered also.

II.3 Résumé

The possibility of cloning humans opens up entirely novel lines of action that confront us with ethical questions hitherto unknown. Answering these questions will require an intensive discussion of all matters concerned. The more so as these activities touch on our basic attitudes towards life and personal dignity. Even a preliminary evaluation clearly demonstrates that it is necessary on ethical and legal grounds to draw lines where this had not been necessary before, because nature herself draws these lines. This evaluation shows clearly that this necessary drawing of the line will succeed only if we will take our bearings from accepted ethico-legal principles and focus our attention on physical, psychical, and social conditions without which, according to his nature, man cannot succeed. From this double perspective a first analysis reveals that cloning of humans is ethically unjustifiable as far as aims as well as means are concerned.

Legal assessment

III.1 Cloning involving the use of human genetic material according to the embryo protection law currently in force

In principal agreement with the ethical assessment from a legal point of view the unlawfulness of cloning of humans in Germany is practically undisputed. The Benda commission (Final report pages 59 pp.) already voted for a ban under criminal law. § 6 of the German embryo protection law (referred to subsequently as 'ESchG' = Embryonenschutzgesetz) in force since Dec. 15th 1990 forbids cloning by law:

'(1) Those who, by artificial means, effect that a human embryo with the same genetic information than another embryo, a fetus, an adult, or a deceased person, is generated, is liable to sentence of imprisonment of up to five years or liable to penalty.

(2) Likewise under liability are those who transfer into a woman an embryo as delineated in Section 1.

(3) The attempt is liable to prosecution.'

The discourse following below of whether § 6 ESchG - and possibly other relevant regulations contained thereon - will require amendments in view of the novel developments and conceivable further technologies will be restricted to legal questions of cloning involving the human genome; the problem of whether cloning of animals should or should not be regulated legally will not be addressed.

A.

The splitting of totipotent cells is already subject to prosecution according to §2 Section 1 ESchG in that the term 'utilized' is used. § 6 Section 1 ESchG, however, takes precedence as a *lex specialis*. According to both constituent facts even the attempted act is liable to prosecution. Inappropriate deficiencies of jurisdiction thus are not apparent.

B.

Several points will have to be addressed with respect to the liability of punishment of cloning by exchange of cellular nuclei as applied to humans:

It has been questioned whether cloning by transfer of nuclei will really result in human embryos having the same genetic material as another (§6 ESchG Section 1). It is said that, due to the methods employed, approximately 1 % of the genetic material will not be transferred by means of the transferred cellular nucleus. The genetic information of the cloned being, therefore, would then be identical only with 99 % of that of the 'original'. If interpreted teleologically, and by taking into account the official title of §6 ESchG, hardly any legal professional, however, would negate the 'sameness'. This is because the legal rather than the mathematical concept of 'sameness' applies in this case. In the legal sense there is no reason not to regard as 'same' - in accordance also with colloquial use of the language - what a mathematician would classify as 'approximately same'. In order to clarify this point with an innocuous example: the refrigerator may contain the same cups (seen legally as belonging to the same set) although some of these cups may show more discernible signs of use than others.

The view represented here also prevails in the legal specialized literature (see in particular the commentary on the embryo protection law by Keller, Günther, and Kaiser, Stuttgart 1992, §6 note #6 of the commentary)

b) Furthermore the constituent fact attribute 'Embryo' (also §6 Section 1 ESchG) appears to be problematic: in accordance with the legal definition in §8 Section 1 ESchG the embryo in the legal sense of this law is 'already the fertilized developable human egg cell beginning with the time of fusion of the nuclei...'. Since cloning by fusion of nuclei does not involve fertilization it appears that this definition would not apply in this case as also in the case of parthenogenesis. This, however, would lead to the absurd consequence of a cloned human not undergoing embryonic development. However, since §6 ESchG aims at providing a comprehensive 'all round' protection and to all intents and purposes to prevent generation of copies of human individuals (see Keller, Günther, and Kaiser, *loc. citato*, §6 end of note #7 of the commentary) the legal definition of § 8 cannot be applied simply to the term 'embryo' in §6. It is apparent that §8 does not intend to provide a concluding and final definition of the term 'embryo' - as implied also by the use of 'already'. Quite contrarily the aim is to guarantee inclusion of earliest developmental stages.

The interpretation of 'embryo' in §6 as an entity which includes every developable egg cell (i. e. developable into somatic cells, see also Section D) having undergone a process of initialization comparable to the process of fertilization is not excluded by §8. It would require more precise clarification, however, to decide when the act involving replacement of cellular nuclei in the sense of §6 ESchG has been completed. One would already have to view the process of enucleation as an attempt entailing criminal prosecution if this process were carried out with the explicit aim of obtaining cells into which another nucleus could be transferred in a subsequent step. It does not matter in this case that both partial acts are carried out by one and the same person. Those who provided others with enucleated human egg cells and knew or anticipated that these would be utilized in cloning would be liable at least as someone aiding and abetting the act.

c) On the other hand legal liability to prosecution also according to §5 ESchG would have to be rejected routinely. Those who would enucleate an egg cell would artificially alter the genetic information of a human germ line cell in the sense of §5 Section 1 ESchG; if this were carried out in preparation of the transfer of another human cell nucleus into this cell this would be against the excluding provisions of §5 Section 4 no 1 since the goal of usage for nuclear transfer excludes the possibility of using this cell for fertilization.

C.

Given that a freshly fertilized egg cell before the first cell division were used as an acceptor cell during the cloning procedure the problem of interpretation discussed under B. b) would not emerge. Apart from this even the process of enucleation, if carried out on an early embryo, is usage that is liable to prosecution according to §3 Section 1 ESchG. This process of enucleation does not serve the purpose of conservation (of the embryo) in the sense of §2 Section 1, due to the status of the nuclear information as the trait characteristic of the identity: those who exchange the nucleus of a developable fertilized egg cell do not conserve this embryo but create another.

D.

If cloning were possible one day by stimulating any somatic cell of the being to be cloned such that it would behave 'like a fertilized egg cell' one would have found a procedure dispensing with the use of any germ line cells. For this reason such a procedure would not be subject to legal prosecution according to §§2 and 5 ESchG. Nevertheless after what has been said in B. b) there are no major objections to view this in accordance with the ban of cloning in §6 Section 1 ESchG; the provision in §6 Section 1 does not require explicitly that the generated embryo must be derived from germ line cells. Crucial for the trait 'embryo' must be the ability to develop into a complete human being rather than the derivation from certain cell types.

E.

A possible regulatory loophole might be envisaged in view of a further modification of cloning by the 'nuclear exchange method'. This has been pointed out by D. v. Bülow (Dolly und das Embryonenschutzgesetz, Deutsches Ärzteblatt. 1997, pp. C-536, 539): if, before its introduction into the enucleated cell, the genetic information of a 'replacement nucleus' were altered by genetic engineering methods in such a way that also in the legal sense the term 'identical genetic information' could not be applied any longer the provision of §6 Section 1 ESchG banning cloning would no longer be applicable. If a nucleus thus modified were introduced into an enucleated egg cell one would also not have to see a violation of §5 Section 1 ESchG (artificial alteration of a human germ line cell) because of the provisions in §5 Section 4 No 1. The definition of §5 Section 1 ESchG 'used for fertilization' would not apply simply because of its absence. There are at least three different ways in which this loophole, which, of course, currently exists only in theory - could be closed by an amendment to the embryo protection law (see also the propositions made by D. v. Bülow Deutsches Ärzteblatt. 1997, page C-539) as follows:

by generally prohibiting, in §6 ESchG, the transfer of a nucleus into an enucleated human cell, by supplementing the embryo protection law with another statute prohibiting generation of a human embryo without fertilization of a human egg cell by a human sperm; to what extent such a comprehensively formulated statute for protecting the natural core of human reproduction would actually require a special prohibition of cloning shall not be discussed further at this point -,

or

by restricting the exclusion of elements of the offense in §5 Section 4 ESchG more than has done before: one might think, for example, of supplementing §5 Section 4 No 1 last half of the sentence 'that these are utilized for fertilization of generation of an embryo in other ways').

III.2 Legal-political necessity of international agreements

A mere national prohibition of cloning would have a weak footing in view of international research. Scientists would then select more permissive countries. Broadening the scope of offenses liable to prosecution to include those committed in foreign countries by supplementing appropriately the (German) International Criminal Law might gain political ground only if a not insubstantial number of other countries were to ban cloning in their respective national laws. Although the legal situation in other countries cannot be dealt with in detail here one can conclude in summary, however, that on an international scale a rejection of cloning of humans prevails widely.

The human rights agreement for biomedicine does not mention cloning in explicit terms; however, it is reasonable to assume that a ban is implicit in article 13. Any moves aimed at formulating an explicit ban of cloning of humans in this protocol deserve emphatic support. one should also remember the decision of the European parliament of March 16th, 1989, demanding a ban of cloning reinforced by penal provisions, and the recommendation No 1046 (1986) of the Council of Europe, which also declares itself in favor of a comprehensive ban of cloning in humans.

III.3 Résumé

As a whole the embryo protection law needs some interpretation but, without stretching the legal text too far, it renders itself sufficiently to interpretation such that legal-political unjustified loopholes with respect to the incorporation of current methodologies can be prevented. In this respect there is no necessity, therefore, to expand it by adding further elements of offenses. At most one might consider a clarifying broadening of the legal definition of 'embryo' and 'germ line cell' (§8 ESchG) with respect to those cases mentioned in Section II.2.D above concerning the creation, by cloning or non-cloning, of human life without the biological act of fertilization (on this note see also: D. v. Bülow, loco citato, p C-538). An amendment of the embryo protection law would be required, though, to provide for future conceivable methodologies which might combine an exchange of nuclei with a (considerable) alteration of the replacement nucleus (such as in those cases discussed in Section II.2.E).

Conclusions

from a scientific point of view it remains to be seen whether the possibility of cloning of mammals developed in Scotland will be confirmed. Should this be the case an application in humans cannot be considered impossible. from an ethical point of view a first examination in the light of accepted ethical principles shows that cloning of humans is permissible neither in view of the legitimacy of the goals nor with respect to the justifiability of the means. from a legal point of view cloning of humans - by embryo splitting as well as by nuclear transplantation - is prohibited according to German laws. At all events adjustments in the wording of the legal text are required for clarification. The German legal position only has a limited applicability as long as international binding regulations have not been agreed upon. The human rights convention for biomedicine of the European Council appears to be a suitable foundation for such an urgently required international regulation going beyond EU regulations. This convention will allow embodiment of a suitable ban in the projected protocol of embryo protection. Since this convention has been signed by member states of the Council of Europe only and by the USA and Canada, further international agreements will be required. An

international ethico-legal discourse will be required to develop the framework for such agreements. an effective German contribution to this discourse will require an in-depths clarification of the matter and an intensive analysis of international positions and their recitals. This would entail a treatment not only of ethical principles and problems associated with their application but also treatment of aspects of philosophy of science and anthropology, as well as of social aspects of questions raised by cloning. This will be impossible without the participation of sciences involved in forming ethical propositions. To meet these requirements the professional interdisciplinary ethical discourse in Germany should be developed and supported further.

Footnote

1) Also cell cultures, e. g. human blood cells, which are generated by asexual propagation of single cells, are clones by definition. In the following text only the generation of entire identical individuals or embryos capable of developing into such individuals will be treated since cell culture clones - including human cells - do not require further ethico-legal evaluation as long as they do not serve for cloning of individuals.