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Von Frau Susanne Braun

Legal aspects of biomedical research: an overview[1]

Dr. Susanne Braun

Introduction

Biomedical research relates processes, techniques and material of molecular and cell biology with the content and aims of medicine. In its knowledge base a "revolution" is globally taking place opening new applications with profound impacts throughout our societies and economies. Biomedical research is developing towards a personalised and preventive medicine based on genetic predisposition, targeted screening, diagnosis, and the innovative drug treatments. For example pharmacogenomics applying information about the human genome to drug design, discovery and development, will support this radical change. Stem cell re-

[1] Fassung eines Vortrags im Rahmen der „European summer academy of bioethics" im Heinrich Pesch Haus, Bildungszentrum Ludwigshafen im August 2002. Die Fußnoten wurden aktualisiert.

search and xenotransplantation offer the prospect of replacement tissues and organs to treat degenerative diseases.
The expansion of knowledge base is accompanied by a unprecedented speed in transformation of frontier scientific inventions into practical use and products even producing new scientific disciplines such as genomics and bioinformatics and novel applications as already mentioned.
There are different issues of biomedical research as legal, ethical, social and economical one's, giving rise to an intensive –sometimes very emotional- broad public debate. This debate has contributed to awareness and concrete improvements on important issues. The scientific and technological progress raised difficult policy issues and complex regulatory challenges because a responsible policy to govern these fastmoving technology and respecting all stakeholders interest is necessary. This corresponds to the "precautionary principle", which should help to control the dilemma of balancing the freedom and rights of individuals, industry and organisations with the need to reduce the risk of adverse effects to the environment, human, animal and plant health ... and help to find the correct balance for a proportionate, non-discriminatory decision-making process with detailed scientific and other objective information"[2].
This overview will be divided into two parts. Starting with general remarks about relevant regulation for biomedical research, in the second part problems of specific biomedical applications will be presented.

Part 1 General remarks: regulation in biomedical research

There are various national and international rules that can be qualified as legal, ethical or professional ones with the purpose to protect the interests of the persons participating in research or medical treatment and to ensure the quality of the research's and treatments results and meeting with general public approval.

1 International and European regulations

1.1 The European Council'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[3]

The Convention is the first legally-binding international text designed to preserve human dignity, rights and freedoms, through a series of principles and prohibitions against the misuse of biological and medical advances. There was a need to make a greater effort to harmonise existing standards. It is a framework convention setting out a common general standard for the protection of human rights and human dignity excluding animal and plant biology insofar as they do not concern human medicine or biology. According to Article 33 the Convention has to be signed by the Member states of the Council of Europe, by the non-member states which have participated in its elaboration (Australia, Canada, the Holy See, Japan and the

[2] Statement of the European Commission about the precautionary principle, 02.02.2000.
[3] European Treaty Series No 164; http://www.legal.coe.int/bioethics/gb/html/conv.htm

United States of America) and by the European Community. Then the Convention is subject to ratification, acceptance or approval and enters into force when five states, including at least four Member states of the European Union have expressed their consent to the bound by the Convention (entry into force only in theses states). Till now 31 Member states have signed, ratification and entry into force took place in 13 Member states; the non-member states haven't signed the Convention till now. Germany has not acceded to this Convention because most of the regulations already exist and it is feared that the national protection standard in Germany would suffer, although Art. 27 states that none of the provisions of this Convention shall be interpreted as limiting or otherwise affecting the possibility for a party to grant a wider measure of protection with regard to the application of biology and medicine than is stipulated in the Convention.

Its starting point is that the interests of human beings must come before the interests of science or society. The concept of human dignity constitutes the essential value to be upheld. It is at the basis of most of the values emphasised in the Convention laying down a series of principles and prohibitions concerning bioethics, medical research, consent, rights to private life and information, organ transplantation, public debate etc. It bans all forms of discrimination based on the grounds of a person's genetic make-up and allows the carrying out of predictive genetic tests only for medical purposes. The treaty allows genetic engineering only for preventive, diagnostic or therapeutic reasons and only where it does not aim to change the genetic make-up of a person's descendants. It prohibits the use of techniques of medically assisted procreation to help choose the sex of a child, except where it would avoid a serious hereditary condition.

The Convention sets out rules related to medical research by including detailed and precise conditions, especially for people who cannot give their consent. It prohibits the creation of human embryos for research purposes and requires an adequate protection of embryos where countries allow in-vitro research. Furthermore it states the principle according to which a person has to give the necessary consent for treatment expressly in advance, except in emergencies, and that such consent may be freely withdrawn at any time. The treatment of persons unable to give their consent, such as children and people with mental illness, may be carried out only if it could produce real and direct benefit to his or her health.

The Convention stipulates that all patients have a right to be informed about their health, including the results of predictive genetic tests. The Convention recognises also the patient's right not to know about his/her health constitution.

It prohibits the removal of organs and other tissues which cannot be regenerated from people not able to give consent. The only exception is, under certain conditions, for regenerative tissue (especially bone marrow) between siblings.

Furthermore the Convention recognises the importance of promoting a public debate and consultation on these questions. The only restrictions are those prescribed by law and which are necessary in a democratic society in the interest of public safety, for the prevention of crime, for the protection of public health or for the protection of the rights and freedoms of others.

The Convention foresees additional protocols[4] to clarify, strengthen and supplement the overall Convention. The Steering Committee on Bioethics (CDBI), or any other committee designated by the Committee of Ministers or the Parties may request the European Court of Human Rights to give advisory opinions on legal questions concerning the interpretation of the Convention.

1.2 The Directive on the Legal Protection of Biotechnological Inventions of the European Community[5]

According to recital 13, the Directive is providing the legal framework for biotechnological inventions in order to ensure the EU-wide protection of intellectual property in this field and, at the same time, to obliterate existing differences capable of hampering free trade and of jeopardizing the functioning of the internal market. The legal protection of biotechnological inventions does not necessitate the creation of a separate body of law in place of the rules of national patent law. The rules of the national patent laws remain the essential basis for the legal protection of biotechnological inventions. Although the Directive had to be implemented into national patent law in all Members states of the European Union until July 30th, 2000, the German Government still accepted with its decision from July 25th 2003 a draft law implementing the directive into German law, with only some changes.

The principal objective of the Directive is to clarify the distinction between what is patentable and what is not and in particular to confirm that discoveries, the human body at the various stages of its formation and development and processes for cloning human beings and for modifying the germ-line genetic identity of human beings may not be regarded as patentable inventions. Member states must ensure that their national patent laws conform with the provisions of the Directive, which establishes clearly the patentability of biological material, sets out the scope of protection of patented biotechnological inventions, provides for dependency licences for plant varieties and regulates deposit, access and re-deposit of biological material which cannot be described in a patent application.

Inventions which are new, involve an inventive step and are susceptible of industrial application are patentable even if they concern a product consisting of or containing biological material. Biological material means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system. Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention.

Plant and animal varieties and essentially biological processes for the production of plants or animals, including crossing or selection, are not patentable.

The human body and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions. However, an element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention.

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4 First Additional Protocol prohibiting human cloning; European Treaty Series No 168. http://www.legal.coe.int/bioethics/gb/html/conv.htm. Before signing this Protocol, the Convention has to be signed. Another draft protocol about biomedical research exists and has to be discussed by the Member states. The draft Protocol see Taupitz J., Biomedizinische Forschung zwischen Freiheit und Verantwortung, 2002, p. 197.

5 Directive 98/44/EC, 06.07.1998, OJ No L 123, 0013.

According to Art. 6 (1) of the Directive, inventions are unpatentable where their exploitation would be contrary to ordre public or morality. Examples are determined in Art. 6 (2): processes for cloning human beings; processes for modifying the germ-line genetic identity of human beings; uses of human embryos for industrial or commercial purposes; processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such pro- cesses. The Commission's European Group on Ethics in Science and New Technologies is to evaluate all ethical aspects of biotechnology[6].
The protection conferred by a patent on a biological material possessing specific characteristics as a result of the invention extends to any biological material derived from that biological material through propagation or multiplication and possessing those same characteristics. The protection conferred by a patent on a product containing or consisting of genetic information extends to all material in which the product is incorporated and in which the genetic information is contained and performs its function.

1.3 Universal Declaration on the Human Genome and Human Rights by the United Nations[7]

This Declaration of the United Nations Organisation seeks to advance the objectives of international peace and of the common welfare of mankind. The states should make every effort to promote the principles about human dignity and the human genome, the rights of the persons concerned by research, treatment or diagnosis, the research on the human genome, the conditions for the exercise of scientific activity and to promote their implementation. The Declaration has no legal-binding character.

1.4 Charter on Fundamental Rights[8]

This Charter was proclamated on December 7th 2000 to enforce the protection of fundamental rights without creating legally-binding rules. It is only a declaration.

2 German situation

In Germany only a few special regulations for biomedical research exist: the Embryo Protection Act, Stem Cell Act and the DNA-fingerprint in the Criminal Procedure Law. All biomedical processes, especially discoveries of present-day medical science in the field of human embryonic development have to be interpreted in the light of fundamental values as laid down in the German Fundamental Law.

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6 In this aspect, the EU approach of patenting in biotechnology differs from the US legal framework in that field which does not explicitly refers to ethics.

7 Declaration from December 11th 1998, http://www.unesco.org/ibc/en/genome/index.htm

8 OJ No C 364, 18.12.2000.

2.1 Fundamental values

2.1.1 Human dignity and personality right

The principal and highest value of the German Fundamental Law is the human dignity regulated in Art. 1: “The dignity of man is inviolable. To respect and protect it is the duty of all state authority.” Similar formulations can be found in the preamble of the Convention for the Protection of Human Rights and Dignity with regard to the application of Biology and Medicine and in Art. 1 of the Charter on Fundamental Rights of the European Union.

It is the duty of all state authority to respect and protect human dignity but although for each citizen because of a kind of “private” dimension of the fundamental rights. The obligation of active protection of human dignity is naturally addressed towards the State[9] but everyone is obliged to respect and protect it. It is a basic value with effects for all dimensions of social life and so as well in medical science and research[10]. But what is meant by human dignity and when this dignity will be violated?

The Fundamental Law contains no further concreteness of the notion of human dignity. Human dignity is mentioned in the "perpetuity guarantee" of Article 79(3) of the Fundamental Law providing that the specified articles of the Fundamental Law, as Art. 1, cannot be amended, but Art. 79 does not determine its content. So it seems that the concept of human dignity is full of ambiguities, without any fixed content. But this corresponds exactly to the concept of human dignity. It is not an absolute notion independent of the individual situation and interpretation. The German Federal Constitutional Court decided that the legal notion of human dignity is not a static but a dynamic one[11] influenced in its development in a reciprocal action with social value ideas. This is the essential reason why all national and international regulations referring to human dignity do not fix a concrete content. The Federal Constitutional Court gave no positive determination nor a concrete definition of human dignity. It is known that dignity always involves an element of autonomy and if this autonomy is disregarded, human dignity is infringed[12]. The individual should not be degraded to the status of a “mere object”. But this can at best be an indicator of a violation of human dignity[13].

The Court decides in every individual case, if a certain action is an intrusion of human dignity. Every action and omission have to be valued and assessed. To decide if a biomedical process would violate the human dignity, an assessment and a search for a justification of this specific measure has to take place including as well the respect of the aims of that measure and of comparable situations. To avoid arbitrary disregard of the individuals’ dignity, different relevant situations have to be compared by the jurisdiction with “signal effects” of the Federal Constitutional Court. Consequently each step of the technological or medical development has to refer to the preceeding ones. The argumentation way is turned back as in the case law because hitherto existing arguments or rules, already used in the past for solving arising questions and conflicts, have to be used in the context of the new questions and, if necessary, modifying or refining them step by step.

However it is obvious that human dignity is an absolute limit for science and research being not at legislators disposal. But if the argument, human dignity is violated, is applied for all

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9 BVerfGE 39, 1 (42) – “to protect and promote this life and to guard it against illegal interference from others”.

10 Taupitz J., Der rechtliche Rahmen des Klonens zu therapeutischen Zwecken, in: NJW 2001, p. 3433 (3435).

11 BVerfGE 45, 187 (228 f.); BVerfGE 96, 375 (399f.).

12 Donner H./Simon J., Genomanalyse und Verfassung, in: Die öffentliche Verwaltung 1990, p. 907 (913).

13 BVerfGE 30, 1 (25).

biomedical operations or procedures, it would be used as a "knock-down"-argument[14], stopping all further discourse in this area, because any further argumentation becomes obsolete. To avoid this effect, it will be necessary that the notion human dignity is understood as a "summary-term" referring to a group of values[15] and that further detailed arguments and declarations will be given in the individual cases. Human dignity has a key function, serving as a checking device in the process of actual juridical decision making and "becoming operative when issues of human dignity are at stake"[16].
This means human dignity itself cannot be object of assessment, but the verdict of a human dignity violation is based on an assessment, a global assessment of the Federal Constitutional Court.

Art. 1 is completed by Art. 2 (the protection of human life). Art. 2 (1) guarantees expressively the general freedom of action, an active element, and the general personality right, a more passive element, including the respect for the inner personality sphere, the intimate and private sphere as the preservation of their basic prerequisites[17]. Art. 2 (1) can be restricted. Concerning the general personality right the Federal Constitutional Court developed the sphere theory as a marking point for these restrictions: The basic sphere, an inviolable domain of private life style, is absolutely protected and every action of executive organs will be prohibited[18]. Beyond this sphere, the domain of private life style being in a social relation could be restricted if there is a predominant interest of the public and a strict respect of the principle of proportionality[19]. A part of this general personality right is the right of informational self determination guaranteeing the individual person a free decision which personal data shall be given to whom, at which time and for which purposes these data can be used[20]. The person has to know about the probable consequences for herself when using these information[21]. This right is not limited to the automatic data processing[22]. Another part of the right of informational self determination is the right not to know[23], especially of the family members of the examined person who do not want to know about their genetic constitution. It is not necessary to argue directly with the basic fundamental right of human dignity, because the general personality right is based on Art. 1 (1) and so directly related to the principle of human dignity[24]. For the individual it is important to have the freedom to develop his own personal identity without being burden with a foreknowledge[25]. Consequently the governmental instruction concerning data storage would principally be forbidden[26] as well as any sanction in

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14 Simon J., Human Dignity as a Regulative Instrument for Human Geniome Research, in: Mazzoni (ed.), Ethics and Law in Biological Research, 2002, p. 35 (42); Simon J., Die Menschenwürde als regulierendes Prinzip in der Bioethik, in. Knoepffler/Haniel (eds.), Menschenwürde und medizin-ethische Konfliktfälle, 2000, p. 227ff.

15 Hailer M./Ritschel D., The general notion of human dignity and the specific arguments in medical ethics, in: Sanctity of Life and Human Dignity, 1996, p. 91 (92).

16 Hailer M./Ritschl D. (1996), p. 101.

17 BVerfGE 54, 148 (151); Gretter B., Gesetzlich geregelte Informationspflicht gegenüber Risikoträgern von genetisch bedingten heilbaren Krankheiten?, in ZRP 1994, p. 24 (26).

18 BVerfGE 27, 1 (6); 27, 344 (350).

19 BVerfGE 6, 389 (433); 27, 344.

20 BVerfGE 65, 1 (63).

21 Sokol B., Gesundheitsdatenbanken und Betroffenenrechte. Das isländische Beispiel, in: NJW 2002, p. 1767 (1768).

22 BVerfGE 78, 77 (64).

23 Wiese G., Gibt es ein Recht auf Nichtwissen?, in: Jayme E. (ed.), Festschrift für Hubert Niederländer, 1991, p. 475; Donner/Simon, DöV 1990, 907 (912).

24 BVerfGE 27, 344 (351). Its respect in legal relations with private third persons will be guaranteed by § 823 I Civil Law, foreseeing damages in case of violation of the general personality right.

25 Cramer S., Genom- und Genanalyse – rechtliche Implikationen einer „Prädiktiven Medizin", 1991, p. 255.

26 Rademacher C., Zulässigkeit einer Genanalyse?, in: NJW 1989, p. 736; other meaning Deutsch E., Die Genomanalyse. Neue Rechtsprobleme, in: ZRP 1986, p. 1.

case of refused consent. An exception could be the protection of the right of life of third persons and the preservation of serious health damages[27].
These contents of the general personality right will be essential especially with regard to the modern biotechnology developments and the associated dangers for the personality and individuality[28].

2.1.2 Freedom of research

In Germany biotechnological processes in health sector, especially embryo research, are situated in an area of tension between the protection of human dignity according to Art. 1 Fundamental Law and the freedom of science and research according to Art. 5 (3) German Fundamental Law. Similar regulation exists in Art. 13 of the Charter on fundamental Rights of the European Union. Principally the fundamental rights of the German Fundamental Law can be limited by provisions of general laws. The freedom of research may only be restricted in favour of high-level objects of constitutional protection (so called "verfassungsimmanente Schranke"). Constitutional limitations pertaining to the freedom of research with respect to work on and with embryos have been incorporated in concrete term into the Embryo Protection Act. Prohibitions of the Embryo Protection Act are intended to guarantee human dignity and the protection of life from initial stages.
The ethical and legal assessment of scientific research has to respect above all the methods employed in research and the aims pursued by scientific research.

According to § 6 it is an offence to create an embryo that is genetically identical to another embryo, fetus or any living or dead person.

2.2 Special Law: The Embryo Protection Act

This Act is a special penal law for the protection of the embryo in vitro. § 8 (1) defines that an embryo is "an already fertilised human oocyte from the time of fusion of the nuclei capable of further development, and any totipotent cell removed from an embryo that is able to divide and to develop into an individual under the required conditions". According to § 1, stating the criteria for an abuse of medically assisted reproduction, it is an offence to

- fertilise a human egg for any other purpose than to start a pregnancy in the woman who produced the egg;
- use an embryo for any other purpose other than its maintenance and healthy development; and
- separate and use totipotent cells of an embryo for research and diagnosis.

§ 2 regulates the abuse of human embryos and not the remainder of cryoconserved embryos that are no longer utilised for reproduction. It must be assumed, that such fertilised frozen oocytes exist, which, at the request of the genetic mother, could and can no longer be utilised to induce pregnancy.

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[27] Wiese G., Genetische Analysen bei Arbeitnehmern, in: DÄBl. 1992, p. 656 (658).
[28] BVerfG, NJW 1980, p. 2070ff.

With this Act a high standard of embryo protection exists in Germany, but basing on the scientific knowledge prevailing at the time of its enactment, in 1990, a lot of discussions about the actuality of the Embryo Protection Act and the necessity of modifications began. Meanwhile the more than ten years old knowledge has become outdated, leading to the fact that some provisions seems to be no longer adequate. So for example the definition of an embryo is no longer tenable following the demonstration in animal experiments that an entire organism can develop not only from totipotent embryonic cells but that cell nuclei of adult body cells can be converted back into a totipotent stage from which an organism can develop following their fusion with the nucleus of oocytes.

Part 2 Special remarks: problems of biomedical applications

1 Embryo research[29]

The determination of the constitutional and moral status of human embryos is of fundamental importance to the permissibility of biomedical research with embryos. Should an ovum artificially stimulated to begin the earliest stages of cell division be considered as human embryo having human dignity?

Neither a right to protection of dignity nor a right to "absolute" protection of life for this early embryonic life can be derived from Article 1(1) and the first sentence of Article 2 (2) of the German Fundamental Law. From birth on, moral respect becomes unconditional, and the right to life is no longer subject to any balancing of considerations or differentiation.

Since the decision of the Federal Constitutional Court against the liberal abortion law, human dignity is applied in an extended way to the early and residual stage of human life, stating that human dignity is a property of human life wherever it exists[30], where human life is meant to include the life of the human zygote from conception on, even in case of in-vitro-fertilisation. The Federal Constitutional Court decided that an embryo has human dignity and a right on life protection without declaring that volume and comprehension of the embryo protection are the same as in case of an already born human being. The formulation of the Court was very cautious: human dignity and life protection for an embryo exist “at any rate” **since the nidation** in the womb. According to another decision[31] of the Court only since the nidation life can no more being divided. In fact before the nidation, multiple human individuals could be created from one single egg cell (twins from one egg). That is the reason why, before nidation, the genetic individuality and in this sense the genetic particularity of a human being is not finally determined. The nidation would be an essential criteria for the legislator having the possibility but not the obligation to begin with a legal differentiation[32]. The early human embryo has the capacity of being conscious only in the sense of a potentiality without already owning the dispositions. This will come in a later stage of development. The distinction between disposition and potentiality could justify an assessment in conflict situations between the human dignity of the born human being and the human dignity of an embryo. Moral or legal assessment are surely justified where abortion is medically indicated, because here the life of the pregnant woman must be weighed against that of the embryo or foetus. But in case of embryo research human dignity cannot be an object of assessment. Insofar every scientific embryo research will be qualified as an instrumentalisation of the embryo. Prenatal examinations of the genetic predispositions of the embryo are **forbidden if** they degrade the unborn child to the status of a mere object being then a violation of Art. 1 German Fundamental Law. According to this, the German Embryo Protection Act from 1990, as a secondary law, strictly prohibits any kind of intervention in a human mebryo that is not conducive to the embryo’s own survival. When this Act came into force, most of the people were satisfied that the embryo protection has been realised in a very stringent way. Meanwhile this

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29 See report of the Steering Committee on Bioethics (CDBI), the protection of the human embryo in vitro, 19.06.03, CDBI-CO-GT3 (2003) 13.

30 BVerfGE 39, 1 (41).

31 BVerfGE 88, 203 (251).

32 Taupitz J., Der rechtliche Rahmen des Klonens zu therapeutischen Zwecken, in: NJW 2001, p: 3433 (3438).

extensive protection of the embryo outside mothers womb initiated a lot of discussions in Germany and questions arose if regulations of the Embryo Protection Act have to be modified. In Great Britain for example embryo research is legal under the conditions that the research is clinically relevant, that the donor of the tissue consents and that the zygote is cultivated in vitro only up to the stage of development of fourteen days.
In case of abortion, most of the legal systems accept that unborn life, being the subject of the embryo research, can be sacrificed not only in favour of concretely threaten life of other persons but although for other values[33]. Of course, embryo research and abortion are not comparable because in case of abortion a concrete conflict situation of the concerned woman and her autonomy right exists. But the absolute protection of the embryo is not only abolished in the particular situation of pregnancy but by the acceptance of a loop or other contraceptives too. All these measures cause regularly the death of fertilised egg cells, embryos. If this is accepted as an all-day practice, then there is no convincible argument why essential cure aims are not an important factor of assessments leading to a relative life protection of fertilised eggs, embryos. But the German National Ethic Council stated that these processes - contrarily to the use of embryos for research - belong to the intimate sphere of sexuality and unlike processes in a laboratory, are therefore not subject to external control[34].

2 Human Cloning

Cloning means the identical reproduction of organisms without any genetic modification. Two cloning procedures exist: the embryo-splitting and the somatic cell nucleus transfer. Additionally there is a difference between the therapeutic cloning and the reproductive cloning.
Reproductive cloning means the identical reproduction of entire organisms. Therapeutic cloning is the transfer of somatic cell nucleus into enucleated oocytes producing embryos that can be raised in culture to the blastocyst stage in the same way as oocytes obtained by normal fertilisation. The cells obtained from such blastocysts would not only be identical with the genome of the patient. By treatment with suitable growth and differentiation factors it would be possible, in principle, to obtain donor cells from these individual-specific stem cells. Following their transfer into the patient immunological transplant rejection reactions presumably would not be elicited. Opposed to the reproductive cloning, creating whole organisms, this concept is called therapeutic cloning.
There are several rules prohibiting human cloning, as e.g. the first additional protocol to the Council of Europe's Convention on Human Rights and Biomedicine and Art. 11 of the Universal Declaration of the United Nations recommends to prohibit reproductive cloning of human beings. § 6 German Embryo Protection Act forbids the separation of totipotent cells by embryo splitting whether for research, diagnosis or reproductive cloning. The method of nuclear transfer is not explicitely mentioned[35]
So actually it is discussed, if therapeutic cloning will be forbidden too.

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[33] Taupitz J., NJW 2001, p. 3433 (3437).

[34] German National Ethics Council, Opinion on the import of human embryonic stem cells, December 2001, http://www.nationalerethikrat.de/stellungnahme/stellungnahme.html.

[35] Engels E.M., Human embryonic stem cell – the German debate, in: Nature 2002, p. 636ff (638): ..:... but according to the most usual interpretation the meaning of the law would be violated. … all nontherapeutic interventions … are forbidden by German law.

3 Stem cells

Stem cells are cells found in all vertebrate animals, including human beings. There are various potential therapeutic applications of research on stem cells because of their property of dividing to give cells either identical to themselves or differentiated into particular types of cells. Damaged or diseased cells or tissues could be replaced. It is thought probable that stem cells will find use in therapy of degenerative diseases or injuries as neurodegenerative disorders, muscular dystrophies, cardiac disfuntion and juvenile-onset diabetes. Other potential applications for human stem cell cultures include uses for studying fundamental processes of human development or for toxicological testing and drug design. Non-human animal stem cell lines may also be used to produce genetically modified animals. It is also possible that genetically modified non-human animal stem cell lines may be developed for human therapeutic purposes.

Different types of stem cells can be distinguished according to the sources from which they are retrieved. Thus, there are: **adult stem cells** (multipotent stem cells present in adults), **stem cells of foetal origin** (haematopoietic stem cells can be derived from the umbilical cord blood; foetal tissue obtained after pregnancy termination can be used to derive multipotent stem cells like neutral stem cells which can be isolated from foetal neural tissue and multiplied in culture, though they have a limited life span. Foetal tissue can also give rise to pluripotent EG cells isolated from the primordial germ cells of the foetus), **stem cells of embryonic origin** (pluripotent ES cells are those which are derived from an embryo at the blastocyst stage. Embryos could be produced either by in vitro fertilisation or by transfer of an adult nucleus to an enucleated egg cell or oocyte.)

Because of the differing positions about the moral status of the human embryo, the protection of life of the early embryonic phases of development in general and of the “surplus” or “excess” embryos in particular, the research on ES cells and their use initiated an intensive ethical and legal debate[36]. The Embryo Protection Act does not explicitely mention Es cell research. By the enactment of the German Stem Cell Act[37] a strict prohibition of any research on embryos leading to their destruction was uphold. The import of ES cells was prohibited too, establishing at the same time criteria for the exceptional import and use of ES cells. So

- the cells must have been derived before 1 January 2002 and in accordance with the law from whree they originate;
- the research on ES cells is only allowed for high-ranking reasearch aimsin the context of basic research or for or for the extension of medical knowledge for the development of diagnostic, preventive and therapeutic proceduresthat can be applied to human treatment;

[36] Taupitz J., Import embryonaler Stammzellen, in: ZRP 2002, p. 111; Raasch J., Das Stamzellgesetz, in: Kritische Justiz 2002, p. 285ff; Engels E.M., Nature 2002, p. 636ff.; Recommendations of the Deutsche Forschungsgemeinschaft concerning research with human embryonic stem cells, 3 May 2000; German National Ethics Council, Opinion on the import of human embryonic stem cells, December 2001, http://www.nationalerethikrat.de/stellungnahme/stellungnahme.html

[37] Law from 28.06.2002; BGBl. I, p. 2277.

- the cells must be derived from embryos that were produced for the purpose of satisfying a wish for a child by artificial fertilisation but are no longer used for this purpose for reasons unrelated to the constitution of the embryo itself;
- the research purposes could not be realised with stem cells of other origin e.g. using stem cells of animals.

To avoid any penal sanctions, it is necessary that no connection between ordering ES cells abroad and their derivation from embryos exists. Otherwise the importers would count as instigators or accomplices in the destruction of embryos.

Under legal and ethical aspects, the research on adult stem cells is not really debated. If the mechanisms of reprogramming adult stem cells could be detected, patients could be treated with their own adult stem cells and this could be an alternative to ES cell research[38].

4 Prenatal diagnosis (PNG) and preimplantation genetic diagnosis (PGD)

PND covers a variety of different techniques before the birth of a baby with the aim to identify high-risk pregnancies and births at an early stage and to ward off dangers to the life and health of mother and child. Abortion is permitted for medical indications including hereditary diseases. In Germany, PND is allowed and controlled by professional self-regulation.

By PGD, an embryo a few days old after in-vitro fertilisation is examined for chromosomal or specific genetic defects. Embryos that lack the relevant chromosomal or genetic defects are selected for implantation into the woman's uterus. In some European countries PGD is practiced as in Belgium. In Germany, PGD is not undertaken but intensively discussed if consistent with the Embryo Protection Act. According to § 1 being an offence to fertilise a human egg for any purpose other than to start a pregnancy in the woman who produced the egg, the removal of a totipotent cell is prohibited. Thus, PGD is implicitly prohibited. The ethical and legal issues arising in connection with PGD concern not only the moral and constitutional status of the embryo but also the rights of couples, of the woman or the physician interested in having the possible contradiction in values between the attitude to the termination of pregnancy after PND and the ban on PGD. On the one hand a ban of PGD could violate the fundamental rights of the concerned persons:

- **rights of the couple**: Art. 6 Fundamental Law protection of marriage and family including also the wish having a baby (and even the further medical possibilities to realise this wish by artificial insamination e.g.), and Art. 1 and 2 Fundamental Law (right of self determination);
- **rights of the woman**: Art. 2 (2) physical and mental integrity, and Art. 1 human dignity;
- **rights of the physician**: Art. 12 freedom of profession which can only restricted if it is necessary for the realisation of a very important aim of the common welfare[39].

On the other hand the human dignity of the embryo could justify such a restriction, if the human dignity of the embryo is accepted and PGD would be an offence against this human dignity, when the embryo becomes mere object. So PGD only for sex selection will not al-

[38] Jiang, Y. et al., Pluripotency of mesenchymal stem cells derived from adult marrow, in: Nature 2002, p. 41ff; Engels E.M., Nature 2002, p. 636 (641).

[39] BVerfGE 7, 377 (401) – Dreistufentheorie.

lowed. But if severe risks of chromosomal or genetic defect exist, it is medically indicated and should be allowed[40].

5 Xenotransplantation

Xenotransplantation is the use of live animal cells, tissues and organs in the treatment or migration of human diseases. The world-wide critical shortage of human organs available for transplantation and advances in genetic engineering, in the immunology and biology of organ/tissue rejection, have renewed scientist's interest in investigating xenotransplantation as a potentially promising means to treat a wide range of human disorders (e.g. epilepsy, insulin dependend diabetes mellitus, Parkinson disease etc.). But beside the potential benefits many problems actually exist as the potential risk of transmission of infectious agents from source animals to patients, their close contacts and the general public[41]. Furthermore the complexities of informed consent and the animal welfare issues have to be respected[42]. In Germany, there is no special law upon Xenotransplantation. The **Transplantation Law** from 1997 cannot be applied because a xenotransplant is a non-human organ and therefore not concerned by the rules of this law. As far as the transplantation is made by a physician, what is not cogent in Germany, the **Physician Professional Law** could be respected concerning the transplantation of organs. Furthermore the existing laws and rules - as the Drug Law, the Genetic Engineering Law, the Infection Protection Law, the Animal Protection Law– could be applicable. But with view to the potential risks of Xenotransplantation, there could be an obligation of the State to regulate Xenotransplantation by a prohibition or an special authorisation criteria if constitutional rights are violated. The Federal Constitutional Court recognised such an obligation because of the fundamental rights being not only defending rights of the citizens against the state but also it is constitutes values and rights in the sense of an objective system[43]. Actually no obligation of the State exists justifying a regulation of Xenotransplantation because human dignity, protected by Art. 1 German Fundamental Law , is not violated if human gene segments are introduced into an animal organism to reduce an immunological rejection of the xenotransplant. The mixture of human and animal genes preparing a Xenotransplantation is only made for human's sake, to transplant an animal organ. § 7 Embryo Protection Act consequently forbids to fertilize a human egg cell with the animal sperm or to fertilize an animal egg cell with the sperm a human being creating a differentiating embryo. Following the opinions in literature, the connection of human and animal genes should only be forbidden in case of fertilisation of a human egg cell but the implantation of human DNA-segments into animal organs with the aim to transplant these organs into human beings later on should be allowed[44].

The further step to transplant an animal organ into the human body would neither violate human dignity. By this step human beings will not loose their identity. Their feeling and think-

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40 Statement of the German National Ethics Council, December 2001, http://www.nationalerethikrat.de/ stellungnahme/stellungnahme.html

41 Beckmann J.P./Brem G./Eigler F.W:/Günzburg W./Hammer C./Müller-Ruchholtz W./ Neumann-Held E.M./Schreiber H.-L., Xenotransplantaqtion von Zellen, Geweben oder Organen, 2000.

42 Jungebloth S., Rechtliche Aspekte der Xenotransplantation, in: Quante M./Vieth A. (eds), Xenotransplantation, 2001, p. 67 (76); Simon J./Braun S., Xenotransplantation: The role of infection protection for risk assessment, in: Transplantationsmedizin 2002, p. 184ff.

43 BVerfGE 39,1 (41); 46, 160 (164);49, 24 (53); 49, 89 (142).

44 Keller R./Günther H-L/Kaiser R., Embryonenschutzgesetz, 1992, § 7 Rz. 24.

ing will be touched without being totally influenced or manipulated. Human beings will not give up their own identity.
Human beings right on life and physical integrity, protected by Art. 2 sect. 2 German Fundamental Law is neither violated. Principally individuals could have different claims in the medical area against the State resulting of the social State principle without having a direct claim of introduction of a specific therapy or free access to certain therapies. But otherwise the State can restrict the therapy offer to minimize the risks for patients, other persons and the society for example by infections. Even mere danger or potential risks could already activate the protection obligation of the State. Respecting the state of the art of Xenotransplantation actually neither a regulation prohibiting Xenotransplantation could be justified as a result of the protection obligation of the State. Finally the protection of animals mentioned in Art. 20a German Fundamental Law as a determined aim of the State cannot avoid the harm of the physical integrity of animals in favour of human beings sake[45].

6 Genetic data banking

In the last few years there was an important expansion of human DNA sampling and data collecting in order to exploit and study the genetic information collected. In the next years the storage and use of such genetic information will be of an increasing importance. Actually the German government discusses the use of genetic data in Labour Law, research and for insurance purposes[46].
As in other countries a lot of databanks already exist in Germany and the genetic testing commerce has become an important market with a global total turnover of 1,3 Mrd US-Dollar[47]. The potential benefits seems to justify the establishment of genetic databanks but the possibility of misuse imposes a responsibility of proper management and protection of the subjects' interests. The availability of personal genetic information poses many problems concerning privacy, confidentiality of the data and informed consent, because genetic data are highly specific information, revealing facts not only about the examined person but about the members of his or her family and having therefore a great impact on a person's life or lifestyle. Therefore genetic research has to be conducted with sufficient safeguards to protect individual interests, without obstructing legitimate medical research activities of benefit to society. The European Parliament declared: "The use of and access to personal genetic information should be debated with a view to legislation, which should particularly focus on protecting the individual's personal integrity on the requirement to obtain his consent… Member states should protect individuals' right to genetic confidentiality to ensure that genetic profiling is used for purposes beneficial to individual patients and society as a whole; there should be an exception to this general principle of confidentiality where genetic fingerprints held in DNA databases are used to identify and convict criminals"[48] .

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45 Concerning the meaning of Art. 20a German Fundamental Law see Braun S., Tierschutz in die Verfassung – und was nun? Die Bedeutung des neuen Art. 20a GG, in: DÖV 2003, p. 488ff.

46 Simon J., Gentests und Versicherungen, 2002; Buyten R./Simon J., Gendiagnostik beim Abschluss privater Kranken- und Lebensversicherungsverträge, in: VersR 2003, p. 801.

47 Goerdeler J./Laubach B., Im Datendschungel, in: ZRP 2002, p. 115 (116).

48 European Parliament resolution A4-0080/2001 on the future of the biotechnology industry.

There is a wide range of application fields of genetic data banking. Above all, the medical sector is the most important area. The origin of diseases could be detected and new diagnosis and therapy methods could be more efficiently developed by constructing genetic profiles. The genetic data registration of entire populations or groups makes the construction of genetic profiles possible. Furthermore the use of genetic fingerprinting in criminal cases, on the legal basis of § 81 a, c and completed by § 81 e, f, g Criminal Procedure Code, has been operationalised and developed through court rulings. Finally genetic data could be used for certification of parentage. A clear distinction exists between legislation and policy that relates to criminal databanks and that which relates to medical databanks. The further remarks will focus on the medical sector.

In Germany no special law of genetic data banking exists. Information can only be used according to the constitutional principles especially the fundamental rights and the data protection regulations.

The Constitutional situation depends on the kind of data banking system, if it is a governmental or a private one, because fundamental rights are only defensive rights against the State and cannot be directly applied between privates[49]. In case of a governmental data banking system, human dignity should not be violated. While a total storage of individual hereditary factors was supposed to be an intrusion of human dignity[50], the storage of single genetic characteristics seems not to be an offence against human dignity, although associated with intensive effects for the concerned person[51]. The use of personal data like the name of the patient or his symptoms related with a gene databank should not violate the general personality right. If the individual should know his hereditary factors or perhaps lethal or later appearing diseases against his will, there are convincing arguments to deny a global intrusion of human dignity but there will be an offence against the general personality right. So much the more if the disease could appear in the near future and then the perhaps curative ability of most human beings to suppress would be overstrained[52]. The typical uncertainty related with the storage of genetic data, if the stated disease risk will be realised, would be another burden[53]. Because the corresponding diagnosis could only be statistically-epidemiologically interpreted for a group of persons. The individual has to live with the uncertainty. This could be a threat especially in case of lethal disease risks whose intensity could vary from individual to individual and even lead to an existential conflict[54]. Only a right not to know could avoid the probable loss of impartiality, frankness and finally freedom towards the own future. Meanwhile this meaning is widely accepted, generally recognizing the necessity of an informed consent[55]. The individual must have the possibility to chose the right not to know his hereditary factors even if healthy disadvantages are related with his decision[56], even if the genetic data storage would only or mainly be made to discover endogenous health risks for

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49 BVerfGE 21,369; 50, 336f., 68, 205.

50 Benda E., Erprobung der Menschenwürde am Beispiel Humangenetik, in: Aus Politik und Zeitgeschichte, Beilage zur Wochenzeitung „Das Parlament“, B 3/85, p. 33 : Totalsequenzierung.

51 BVerfG, NJW 2001, 879: The Federal Constitutional Court decided that it is not possible to construct a personality profile when examining the non coded part of DNA.

52 See the second report of the „interministerielle Kommission des Landes Rheinland Pfalz“ 1989, p. 45.

53 Bundesärztekammer, Richtlinien zur Diagnostik der genetischen Disposition für Krebserkennung, in: Deutsches Ärzteblatt 95 (22) 1995, A-1396.

54 Vitzthum W. Graf, Rechtspolitik als Verfassungsvollzug? Zum Verhältnis von Verfassungsauslegung und Gesetzgebung am Beispiel der Humangenetik-Diskussion, in: Keller R./Günther H.-L./Kaiser P. (eds), Fortpflanzungsmedizin und Humangenetik, 1991, p. 69.

55 Schöffski O., Gendiagnostik: Versicherung und Gesundheitswesen, 2000, p. 121.

56 Donner/Simon (1990), p. 912 f.

preventive aims and to instruct later on preventive or therapeutically indicated participating obligations. The right not to know includes the free decision of the individual life style. It has to be at the individuals disposal, which concrete health diagnosis would threat the individual so to ignore further information. A restriction of the right not to know for instance in cases of severe diseases would not be compatible with the right of self determination. It would be different if the citizen defends his right not to know his hereditary factors against the interest of the State or other private persons or if he voluntary offers material or information about his genetic constitution. This would be an expression of his personality. A prohibition to inform about the own genetic data, would contradict the right of life, physical integrity or free personality development, if it aims at a defence of disease risks or supporting research.

In case of an increasing correlation between genetic characteristics of an individual and certain diseases, more and more negative stigmatizing social prejudices towards the concerned person or groups of persons will be expected. In principle everyone has the right to keep secret his genetic diagnosis instead of revealing the genetic diagnosis. Insofar a situation demanding for an intensive protection exists. But there will be problems, if in case of a genetic diagnosis the right to know of the examined person collides with the right not to know of the same persons or another person[57], for instance a family member. If a person is positively tested for Chorea Huntington and her grand father already had this disease, then it will be sure that one parent would be carrier of this disposition as a connecting link and would get this disease. This is a constellation of private family relations which cannot be solved with regular legal measures. The prohibition not to disseminate the test result or not to tell genetic data to any person cannot effectively be established inside a family community. It has be to asked if the right not to know can be guaranteed even in such a constellation. So among others a restrictive access to genetic examinations could be possible. But this would mean that genetic testing is not available for anyone. The contradictory legal positions and interests have to be assessed and criteria have to be developed, who and under which conditions could make genetic testing. The right to know would be more important if the concerned subject would be of a higher value, for instance if a testing result would be of great influence for life styling whether by a therapeutic treatment or a prophylactic life style of the concerned person. At the same time the other person has so much the more the right not to know. A result free of contradiction would not be possible. Anyhow, the necessary genetic testing must be accessible for those persons, whose serious disease could be efficiently treated. But the concrete criteria for this access in the individual cases don't exist and it seems very difficult to define them.

Finally, the right of the person whose genetic data are collected and stored could collide with the freedom of research protected in Art. 5 (3) Fundamental Law. Then the colliding values have to be assessed.

[57] Schneider: Wissen ist Ohnmacht. NZZ Folio, 09.2000 (Gene-Der Mensch und sein Erbe), http://www-x.nzz.ch/folio/archiv/2000/09/cover.html: Nancy Wexler, member of a Chorea Huntington family, said, that she wants to know that she has not this disease, but she doesn't want to know that she has the disease".

Summary

The specific biomedical applications contain several problems always focusing on the same fundamental principles. Collisions of these principles cannot be avoided. A permanent social consensus has to be established concerning the aims and restrictions of biomedical progresses. This procedure will be influenced by additional factors as competitiveness. With view to an economical pressure of a globalised world a pure national consensus will not be enough. It has to be ensured that the development and application of biomedical research take place respecting the fundamental values recognised by the national constitutions and by the EU in the Charter of Fundamental Rights and the existing national, supra- and international regulations. The further development should be handled in a responsible way in harmony with ethical values and social goals without disadvantages for the competitiveness. An informed choice should facilitate demand-driven applications and a science-based regulatory oversight should enhance public confidence. But neither national nor European policies should be developed in isolation.

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