GERMAN LEGISLATIVE RESPONSE TO SCIENTIFIC DEVELOPMENTS IN HUMAN GENETICS

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I. INTRODUCTION

Human genome research has both influenced and involved in an interdisciplinary way the entire fields of biology and medicine as well as large sectors of science and biotechnology. Even before the entire decoding of the human genome, research in human genetics raises hopes of new preventive, diagnostic and therapeutic possibilities. Apart from potential benefit, the increasing knowledge of the biological fundamentals of human life and the heredity of man is nevertheless connected with the fear of abuse and possible risks. Already in the mid 1980's the conflict between risks and benefits resulting from genetic research led to wide ranging debates on how different fields of human genetics should be regulated in Germany. This report gives an overview of statute law and drafts as well as political recommendations and guidelines relating to certain issues of human genetics.

II. BASIC CONSTITUTIONAL RIGHTS

Freedom of science and research is guaranteed by the constitutional law of the Federal Republic of Germany (art. 5o., sec. 3). This freedom

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can only be limited by other constitutional rights. In this respect, the constitutional rights of human dignity as well as human life and human health have to be considered in particular. In the first place, it is with the legislator to put such constitutional restrictions into concrete legal terms and thereby to balance competing constitutional rights.

III. LEGAL REGULATIONS

Despite the significant depth of the debate and the diversity of its topics only few formal laws have been enacted by the German legislator.

1. *Genetic Engineering Act*

On 1o. july 1990, the Genetic Engineering Act (Gentechnikgesetz) entered into force. This Law comprehensively regulates the production and use of genetically modified organisms. It regulates the handling of genetic engineering in research and production facilities in enclosed systems, the deliberate release of genetically modified organisms to environment as well as putting products into circulation, which consist of genetically modified organisms or contain such. The purpose of the law is inter alia to protect humans, animals, plants and the environment against possible dangers of genetic methods and products. The enforcement of the most important prohibitions and requirements is guaranteed by compulsory registrations and licence requirements as well as penal provisions. However the genetic engineering act does not contain specific regulations for the field of human genetics. It does not apply in particular to the application of genetically modified organisms at humans (2 sec. 2). Thus it does not apply for example to a patient's treatment with genetically modified cells. However, genetic preparatory work in the laboratory, for example the genetic manipulation of human cells in vitro, is subject to the compulsory registration or licence requirement. It is disputed, whether the actual application at human beings is already beginning when the patient enters the treatment room or only with the application itself. In the latter case the treatment room would have to be classified as genetic engineering facilitiy and consequently would be subject to the compulsory registration or licence requirement, which would not correspond to the real needs. In fact

the legislative grounds show that the legislator intended to exclude medical facilities from the range of application of the Genetic Engineering Act.

2. *Embryo Protection Act*

Some parts of human genetics have been regulated in German Law since 1o. january 1991, when the embryo protection act (Embryonenschutzgesetz, subsequently referred to as ESchG) entered into force. However, the regulation object of the law does not mainly concern genetic applications but regulations to reproductive medicine and research with human embryos. Embryo research interest is not only in sterility therapies but increasingly also in the development of new preventive, diagnostic or therapeutical methods which are multiplied by the means of human genetics. The protection of the embryo is conflicting with high ranking research goals.

By passing the embryo protection act the legislator has fulfilled his constitutional duty to take precautionary and preventive measures in view of the risks and dangers connected with reproductive technologies and human genetics. He thereby imposed considerable restrictions to embryo research. The embryo protection act is a penal law. It is providing prohibitions that were regarded to be indispensable with the legal protection of high-ranking objects. The prohibitions of the embryo protection act aim at safeguarding human dignity and protection of human life from its conception. In Germany the commencement of individual human life is considered to be the completed act of fertilization, i. e. the union of the germ cells‘ chromosomes leading to the formation of a new individual genome. Thus already the fertilized human ovum is defined as an embryo within the meaning of the act. The same goes for each totipotent cell taken from an embryo and capable of division and development into an individual being.

A. *Cloning human embryos*

According to the embryo protection act, any artificial intervention seeking to create a human embryo genetically identical to another human embryo or foetus or to another human being, whether living or deceased, is prohibited (6 sec. 1 ESchG). Within the legislative process and the public debate in the 1980s all parties unreservedly and unanimously supported the

prohibition of cloning, irrespective of the methods employed, as it would contravene human dignity in a particularly blatant way to assign hereditary factors to a human being. The interdiction comprises both reproductive and therapeutic cloning, which means that already the creation of a totipotent cell sharing with another the same nuclear gene set is prohibited. Therapeutic cloning is carried out by nuclear transplantation. It is especially aimed at providing embryonic stem cells and developing organs or tissue that is genetically identical to the donor and thus not causing repulsion. Despite of this high-ranking medical goals of human stem cell research, the German government is still presenting itself being clearly against therapeutic cloning and does not intend to repeal the legal prohibition. Thus for the present Germany will retain the current ban.

B. *Preimplantation genetic diagnosis*

The preimplantation genetic diagnosis (PGD) is among the most controversial topics in public discussion. Due to the present conditions of the embryo protection act, PGD is not carried out in Germany up to now.

In the initial stage of research preimplantation diagnosis was only feasible by using a totipotent cell which is regarded as an embryo in the meaning of the embryo protection act. Thus already the separation of this cell is an act subject to penalty as it is legally defined as cloning: Any artificial intervention seeking to create a human embryo genetically identical to another human embryo is prohibited (6 sec. 1 ESchG).

Since PGD is carried out by using trophectoderm cells (*i. e.* cells that are definitely not totipotent) it is controversial whether this method is compatible with the embryo protection act. The discussion concentrates on the following topic: According to 2 sec. 1 of the embryo protection act, interference with the development of an embryo in vitro is permitted solely if it serves the welfare of the embryo. In view of this prohibition it is disputed whether the preimplantation diagnosis is carried out for reasons others than those serving to preserve the embryo. Surely the PGD is not carried out with the direct intention to harm the embryo. However, in case of a pathological result, for example in form of a genetic disease or malformation, the transfer of the embryo will be canceled as a rule. Therefore critics object most strongly to PGD making possible the selection and manipulation of human life and persecuting eugenic tendencies. The main conflict is between this moral criticism on the one hand and

individual freedom with regard to family planning on the other. In particular, the interest and fear of couples with the risk of transmitting a serious genetic disorder have to be taken into consideration. Supporters point out that PGD is less straining to mother and child than an abortion that might be indicated and legally carried out later on. In this context it is criticised, that the embryo in vitro is even more protected than the unborn child in the womb.

The discussion is still going on. The German Society for Human Genetics holds the opinion that preimplantation diagnosis within the framework of (professional) laws basically should be available to all women who carry a special genetic risk for a severe childhood disease, disorder or malformation. The German Medical Association put up for discussion a draft of guidelines for preimplantation genetic diagnosis that follows the same line. The German government too does not come out against PGD in general. The replacement of the Federal Minister of Health in January 2001 has resulted in a course adjustment. While the former minister was working on a Reproductive Medicine Draft that inter alia should explicitly prohibit PGD, this draft has been chilled by the present Minister quite now. According to recent statements PGD is considered conceivable in case of certain genetic diseases.

C. *Research with human stem cells*

The embryo protection act provides the relevant legal foundations for the distinction between different regimens for the preparation of human stem cells. Embryonic stem cells (ES-cells) are derived from cells of the early mammalian embryo (*i. e.* the human blastocyst). In contrast, embryonic germ cell lines (EG-cells) have been established from primitive reproductive cells of a fetus. In Germany, the generation of human stem cells is permitted from fetal tissues only.

The preparation of ES-cells isolated from the inner cell mass of an early embryo is carried out for reasons others than those serving to preserve the embryo. Thus it is not compatible with the provisions of the embryo protection act (2 sec. 2 ESchG). This is true also if the development of the embryo might not be impaired by the removal of some cells.

However, the embryo protection act does not contain provisions for the generation of EG-cells taken from a dead fetus. It solely regulates the protection of an embryo from its conception to the nidation. As there are no

other legal prohibitions, the removal of primordial germ cells from dead fetuses is a legal act. Explicit reference is made to the Guidelines for the use of fetal cells and fetal tissue provided by the German Medical Association. According to these professional standards, cells and tissue taken of dead, aborted fetuses may be used for scientific or therapeutic purposes. Under no circumstances, the decision to have an abortion must depend on the scientific use. For example, it is not allowed to promise any privilege that might influence the pregnant woman. Besides she has to give informed consent to the intended use of the fetus.

While it has been shown that due to German law embryonic stem cells must be established from fetal tissue only, research with any kind of embryonic stem cells once established is permitted. Embryonic stem cells are pluripotent and not able to give rise to a human being. These cells cannot be regarded as an embryo in the meaning of the law and thus are not subject to penalty.

a. Gene therapy

The aim of gene therapy is to correct changes to the human genetic heritage which may result in hereditary diseases. There are two distinct forms of gene therapy. Somatic gene therapy aims to correct the genetic defects in the somatic cells and to produce an effect restricted to the person treated. Gene therapy on germ cells aims at correction that would be carried out on the cells whose function is to transmit genetic information to future generations. Only the latter is subject to the embryo protection act.

b. Germline therapy

The embryo protection act prohibits the artificial modification of the hereditary information of the germ cell line (5 ESchG). Consequently, genetic modifications of spermatozoa or ova for fertilisation are not allowed. Interventions aimed at modifying genetic characteristics of the human germline have been regarded unjustifiable because of irreversible consequences that likely would arise due to misses within the experimental phase. These failures may not only endanger the individual but also the descendants.

The law does not rule out interventions for therapeutic purpose which might have unwanted side-effects on the germ cell line (5, sec. 4, num.

3, ESchG). Such may be the case, for example, for certain treatments of cancer by radiotherapy or chemotherapy, which may affect the reproductive system of the person undergoing the treatment.

c. Somatic gene therapy

Somatic gene therapy is not especially laid down by law. Moreover legislative measures are not considered necessary. A review of the current situation shows that clear rules exist which apply to somatic gene therapy. In this connection, the law governing the manufacture and circulation of drugs (Arzneimittelgesetz, AMG) as well as the canons of medical professional ethics are of central importance.

Genetic preparations for somatic gene therapy are defined as drugs in the meaning of the AMG. The regulations are valid for the production, the admission and the monitoring of genetic drugs. Basically, somatic gene therapies have to be classified as medical research that is subject to the provisions of the AMG ensuring the protection of the patient (40 42 AMG). Accordingly somatic gene therapy may only be undertaken by medical professions and when quality control as well as effectiveness and harmlessness of the genetic preparations are met. Each research project has to be evaluated by the responsible ethics committee. The admissibility of clinical trials with somatic gene transfer is moreover subject to the guidelines on the gene transfer into somatic cells established by the German Medical Association in 1995. After this, somatic gene therapy should only be applied on serious diseases which cannot be cured by other means and which often take a lethal course.

3. *Discussion on a reproductive medicine draft*

In 1994 the legislative competence of the Federal Parliament (Bundestag) was extended to the fields of artificial fertilization and investigation and artificial modification of hereditary information. Accordingly, the former Federal Minister of Health was working on a Reproductive Medicine Draft that covers global regulations on reproductive medicine as well as embryo or genetic research. The embryo protection act was supposed to be abrogated and integrated in the draft in order to reconsider the ethical tenability of the present regulations and to assess whether they are still flexible enough in the light of the proliferating research findings.

As mentioned the draft has been put on ice for the moment. To the present Minister's opinion, the latest developments in embryonic research do not hurry up legislation. Rather new legal regulations should only be enacted after further public debate. About this the Chancellor points out the danger that debate could be emotionally influenced by an alliance of those hostile to progress and conservative fundamentalists. Instead, he called for a sensible balance between the economic advantages of genetic research and ethical reservations. All legal regulations should tread this line and be reasonably compatible with legislation in other European countries. In an interview on 21 December 2000 he defined the limit which no government should exceed when addressing genetic engineering: The ultimate boundary is still to be Article 1 of the Basic Constitutional Law which says: "...The dignity of man is inviolable". The Chancellor emphasised, however, that within these limits the government's role is no longer to restrict debate but to extend it.

To his opinion, Germany should retain the current restriction on embryonic stem cell research and instead focus its efforts on the relatively advanced research in the field of adult stem cells. The Chancellor rejected steps to relax the ban on embryo research before medical alternatives to this promising approach have been examined more thoroughly. Apart from this, the ethically justifiable potential of genetics should be exploited to medical treatment.

4. *Draft of the biopatent act*

With the advent of the EU Directive 98/44 on the legal protection of biotechnological inventions, the EU member states are obliged to adjust their national patent law. For the purpose of the Directive, new inventions, which involve an inventive step and are susceptible of industrial application, shall be patentable even if they concern biological material.

The basic principle is laid down in art. 5o. of the EU Directive. According to this provision, ...the human body, at the various stages of its formation and development, and the simple discovery of one of its elements including the sequence or partial sequence of a gene, cannot constitute patentable inventions. 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, even if the structure of that element is identical to that of a natural ele-

ment. The industrial application of a sequence or a partial sequence of a human gene must be disclosed in the patent application. Thus the simple discovery of an element of the human body is not patentable. But if that element from the human body has been isolated, purified or otherwise produced by a technical process, it becomes a patentable invention, because it is not merely confined to the discovery of the element as such, but gives a teaching to methodical action and it has a technical effect as its major goal and consequences.

The limit of patentability is regulated in Article 6 EU Directive: Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality. Thus processes for cloning human beings and modifying the germ line genetic identity of human beings as well as uses of human embryos for industrial or commercial purposes in particular are considered unpatentable.

Two years after the approval of the EU Directive in 1998 the German government presented the draft of a Biopatent Act which puts the Directive in concrete terms and lays down corresponding regulations on the patentability of biotechnological inventions. Moreover it is clarified in explicit terms, that research processes which are prohibited by the embryo protection act are considered unpatentable.

However, the question whether human life shall be patentable is still playing a central role in the political and social debate, and many politicians as well as the German Medical Association have declared themselves against the patentability of the human genome as it is considered incompatible with human dignity. The government therefore came to a compromise solution. The draft was passed unanimously, but the government is meant to support a revision of the Directive by the European Union.

IV. Further aspects of human genetics without legal regulation

The investigation of the human genome reveals fields of knowledge and action of hitherto unknown dimension. This is particular true for predictive genetic testing that provides prognostic knowledge that may be beneficial but also harmful. For these reasons the scientific investigation of human genetics has been associated with an interdisciplinary research programme dealing with the ethical, legal and social implications. These

investigations focus on the determination of resulting risks and burdens, of required ethical and legal restrictions as well as social implementations. The starting point for all ethical and legal assessments of genetic test procedures has to be respect for the dignity and identity of all human beings.

1. *Genetic testing*

Practical application of scientific knowledge in the field of human genetics is exercised mainly by genetic diagnosis and counselling. So far there are no special legal provisions in Germany that regulate genetic testing. However it has been subject to various statements and guidelines provided by political or social institutions (for example the Ethics Advisory Body at the Ministry of Health, the German Medical Association or the German Society of Human Genetics) as well as to scientific discussion. The main principles and consequences required are briefly presented subsequently.

Respect for the dignity of individuals particularly requires the right of self-determination as well as the individual's right to know or even not to know genetic information. Genetic test procedures and predictive genetic diagnosis in particular may be carried out only for the individual's benefit and if the person concerned has given free and fully informed consent. Any form of discrimination on grounds of the genetic heritage is to be opposed.

Tests which are predictive of genetic diseases or which serve to detect a genetic predisposition or susceptibility to a disease may be performed only for health purposes and in case of medical indication. Predictive diagnosis should be carried out on persons of legal age only, except for disorders in which preventive or therapeutic treatment could be initiated in childhood.

Genetic diagnosis should be carried out by physicians only. The exclusive right of the medical profession to carry out genetic tests serves the patient's well-being. Moreover the individual's autonomy is to be protected by providing professional genetic counselling. Only in this case it can be assumed that the person concerned acts of his/her own free will in the knowledge of the full impact of the decision. As free availability of genetic test kits on the world market and via internet will not be pre-

vented in the long run, the importance of professional care and application will even increase.

2. *Genetic testing prior to an insurance contract*

Within German law there is a basic distinction between social insurance on the one hand and private insurance on the other, which has to be taken into consideration with respect to genetic testing. German social law provides compulsory health and social insurance to cover elementary risks of life. These social insurance programs are based on the principle of solidarity. They are financed by compulsory contributions from employers and employees, depending on the level of income. So the insurance contract as well as the premium is not based on individual risk calculation. Therefore, with social insurance predictive genetic testing is no object.

The situation is different with private insurance. Insurance coverage and premium are based on the principle of mutuality and risk calculation. Within a process of risk selection and classification (commonly referred to as "underwriting") an applicant is obliged to give information on his state of health and to have a medical examination at the request of the insurer. Thus it is the applicant's duty to disclose knowledge of already existing diseases or diseases that might break out subsequently in all probability. It is disputed, however, whether this also applies to genetic testing and genetic information. The key points in the debate are discrimination on grounds of the genetic heritage on the one hand and antiselection as a potential problem of insurance companies on the other. Moreover, predictive genetic tests in case of private insurance contracts are considered to entail a disproportionate interference in the right to privacy.

In Germany, there is no specific legislation with respect to genetic tests or genetic information to date. Nevertheless, the Association of German Insurance Companies stated a renunciation of genetic tests: German insurers do not demand a specific genetic test within the underwriting process at present nor do they have any reason to do so in future. In an interview on 1 march 2001, the Minister of Justice voiced support for this point of view. She considers it necessary to ban genetic testing and moreover the use of information resulting from these tests for insurance purposes.

3. *Genetic testing prior to an employment contract*

An employer is allowed to ask for the applicant's state of health only if as an exception he has a legitimate interest in the information required. As a rule, predictive genetic tests only state on the probability of a future disease. But this risk of future diseases or even an inability to work is to be taken by the employer. Moreover the applicant's right not to know genetic information has to be considered. This is especially true if one takes into account that the genetic diagnosis might influence not only the occupational but the entire life of the individual concerned. For these reasons it is accepted that in general genetic tests should neither be demanded nor accepted or otherwise exploited on completion of a contract of employment. However, genetic diagnosis is exceptionally permissible as a last resort to find out whether the occupation might be damaging to the employer's health or whether the applicant's predisposition might considerably endanger third parties.

V. FURTHER READING

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