Report

of the

Central Ethics Committee for Stem Cell Research (ZES)

Ninth Report after the enactment of the Stem Cell Act (StZG) for the reporting period 1 January 2011 to 31 December 2011

1. The Central Ethics Committee for Stem Cell Research

The remit of the Central Ethics Committee for Stem Cell Research (ZES) is the review and assessment of applications to import and use human embryonic stem cell (hES cells) in accordance with the Stem Cell Act. This Act ("Act ensuring the protection of embryos in conjunction with the import and use of human embryonic stem cells (Stem Cell Act – StZG)" of 28 June 2002 (BGBl. I page 2277, http://www.gesetze-im-internet.de/stzg/index.html), amended by the Act amending the Stem Cell Act of 14. August 2008 (BGBl. I page 1708, http://www.bgbl.de/Xaver/start.xav?startbk=Bundesanzeiger_BGBl&bk=Bundesanzeiger_BGBl&start=//*[@attr_id=%27bgbl108s1708.pdf%27]), and the Regulation concerning the Central Ethics Committee for Stem Cell Research and the competent authority pursuant to the Stem Cell Act (ZES Regulation – ZESV) of 18 July 2002 (BGBl. I page 2663, http://bundesrecht.juris.de/zesv/index.html) govern the activities of the Committee. ZES issues recommendations on the applications vis a vis the Robert Koch Institute (RKI), the authority competent under StZG.

The Committee, which consists of 18 experts has an interdisciplinary composition (see Table 1). The members and deputy members of the Committee perform their duties on an honorary basis. In accordance with § 8 StZG five members represent the fields of biology and medicine and four members the fields of philosophical, medical and theological ethics; a deputy member is appointed for each member. The Committee was appointed for the first time after the enactment of the Stem Cell Act in 2002 by the Federal Government. The appointment term amounts to three years. For the now fourth appointment term 14 members and deputy members were reappointed in July 2011 and four members or deputy members were appointed to the ZES for the first time. In accordance with the ZES Regulation, the deputy members of the Committee, too, participate regularly in the deliberations on the applications.

In accordance with § 9 StZG, ZES determines on the basis of the documents submitted by the applicant, whether a research project for which an application is submitted which is to use hES cells meets the criteria of § 5 StZG and is ethically acceptable within this meaning. Within the framework of the application it has to be proven in a scientifically substantiated manner that the project pursues high-ranking research objectives in view of new scientific findings (§ 5 No. 1 StZG), that the scientific issues have already been subject to a preliminary clearing in other systems, including animal models (§ 5 No. 2a StZG) and that the targeted new findings require the use of hES cells (§ 5 No. 2b StZG). The results of the review of the applications are summed-up by ZES in a written opinion which is transmitted to the Robert Koch Institute (RKI).

The annual activity reports of ZES are published by the Federal Ministry of Health (BMG) (§ 14 ZESV) and can be accessed on the websites of BMG (http://www.bmg.bund.de) and RKI (http://www.rki.de/DE/Content/Kommissionen/ZES/Taetigkeitsberichte/taetigkeitsbericht_node.html).

Field	Member	Deputy member
Biology	Prof. Dr. rer. nat. Hans R. Schöler Max-Planck-Institut für Molekulare Biomedizin Münster	Prof. Dr. rer. nat. Martin Zenke Institut für Biomedizinische Technologien Abt. Zellbiologie RWTH Aachen
	Prof. Dr. rer. nat. Anna M. Wobus **(Deputy Chairperson)** Leibniz-Institut für Pflanzengenetik und Kulturpflanzenforschung (IPK) Abteilung Zytogenetik Gatersleben	Prof. Dr. med. Ursula Just Biochemisches Institut Christian-Albrechts-Universität Kiel
Medicine	Prof. Dr. med. Gustav Steinhoff Klinik und Poliklinik für Herzchirurgie Universität Rostock	Prof. Dr. med. Mathias Bähr Neurologische Klinik Georg-August-Universität Göttingen
	Prof. Dr. med. Marion B. Kiechle **(Deputy Chairperson)** Frauenklinik und Poliklinik Klinikum rechts der Isar Technische Universität München	Prof. Dr. med. Ricardo E. Felberbaum Frauenklinik Klinikum Kempten Oberallgäu
	Prof. Dr. med. Anthony D. Ho Med. Universitätsklinik und Poliklinik Abt. Innere Medizin V Ruprecht-Karls-Universität Heidelberg	Prof. Dr. rer. nat. Maria Wartenberg Molekulare Kardiologie und Stammzellforschung Universitätsklinikum Jena
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Theology	Prof. Dr. theol. Klaus Tanner **(Chairman)** Wissenschaftlich-Theologisches Seminar Lehrstuhl Systematische Theologie/Ethik Ruprecht-Karls-Universität Heidelberg	Prof. Dr. theol. Hartmut Kreß Evangelisch-Theologische Fakultät Abteilung für Sozialethik und Systematische Theologie Rheinische Friedrich-Wilhelms-Universität Bonn
	Prof. Dr. theol. Dr. phil. Antonio Autiero Seminar für Moraltheologie Katholisch-Theologische Fakultät Westfälische Wilhelms-Universität Münster	Prof. Dr. theol. Konrad Hilpert Lehrstuhl für Moraltheologie Katholisch-theologische Fakultät Ludwig-Maximilians-Universität München

Table 1: Members and deputy members of the Central Ethics Committee for Stem Cell Research (ZES), Status: December 2011

2. Deliberation on and review of applications pursuant to § 5 StZG during the reporting period

In 2011 seven meetings of ZES were held and a total of 10 applications for the import and/or use of human ES cells and two applications for extensions of already approved research projects were discussed. ZES issued positive opinions on nine applications and the applications for extension. These projects meet the prerequisites of § 5 StZG and are ethically acceptable within its intendment (§ 9 StZG). For an application in respect of which there were further enquiries, the applicant requested the suspension of the application procedure. Two applications, in respect of which ZES had already issued positive opinions during the last reporting period, were approved by the Robert Koch Institute during the current reporting period. These two applications are likewise covered by this report. A summary overview of the applications under StZG approved by RKI during the reporting period, in respect of which ZES issued a positive opinion in each case, is given in Table 2.

	Applicant	**Research topic**	**Date of positive ZES opinion**
1 (59)	Dr. Jan Pruszak Albert-Ludwigs-Universität Freiburg	Studies on neural development processes in humans using human pluripotent stem cells	15.11.2010
2 (60)	Max-Planck-Gesellschaft Institut für Infektionsbiologie, Berlin	Generation of neutrophilic granulocytes from human embryonic stem cells	08.12.2010
3 (61)	Dr. Alexander Kleger Universitätsklinikum Ulm	Molecular characterisation of the function of calcium-activation of potassium channels during the cardiogenesis from murine and human embryonic and induced pluripotent stem cells	17.01.2011
4 (62)	Evotec AG Hamburg	Development of a cell model for the clarification of cellular and molecular processes involved in the pathogenesis of Huntington's disease using human embryonic stem cells	17.01.2011
5 (63)	PD Dr. Beate Winner Friedrich-Alexander-Universität Erlangen-Nürnberg	Development and characterisation of human model systems for neurodegenerative diseases including human embryonic stem cells	14.03.2011
6 (64)	Max-Planck-Gesellschaft Institut für molekulare Biomedizin, Münster	Molecular biological studies on the germ cell differentiation capacity of human induced pluripotent and embryonic stem cells	13.04.2011
7 (65)	GSI Helmholtzzentrum für Schwerionenforschung GmbH Darmstadt	Studies on the effect of different types of ionising radiation on human embryonic stem cells and their *in vitro* differentiation	16.05.2011
8 (66)	Prof. Dr. Ezio Bonifacio Technische Universität Dresden	Differentiation of human embryonic stem cells and induced pluripotent stem cells in insulin-producing beta cells	16.05.2011
9 (67)	Lonza Cologne GmbH	Development of test systems for the	15.06.2011

	Köln	identification and analysis of active substances using genetically modified human embryonic stem cells	
10 (68)	Medizinische Hochschule Hannover	Studies on the genomic integrity of human embryonic and induced pluripotent stem cells during long-term cultivation	14.09.2011
11 (69)	CellGenix GmbH Freiburg	Development of media and cytokines for the cultivation and hepatic differentiation of human embryonic stem cells under GMP conditions	14.09.2011
Extensions of already approved applications			
12 Extension of the approval (39)	Zentrum für Integrative Psychiatrie gGmbH Kiel	Studies on the pluripotency of human induced pluripotent stem cells and embryonic stem cells using total genomic and proteomic approaches. Development of algorithms to assess the presence of cellular pluripotency	16.05.2011
13 Extension of the approval (02)	Prof. Dr. Jürgen Hescheler Institut für Neurophysiologie Universität Köln	Studies on the expression and function of olfactory receptors during the cardiomyogenesis from human ES cells	16.11.2011

Table 2: Overview of research projects that were approved during the reporting period 2011 by RKI following a final positive assessment by ZES. The numbers in brackets in the left column correspond to the approval numbers in the RKI register (http://www.rki.de/DE/Content/Gesund/Stammzellen/Register/register_node.html)

The first research project (59th approval) is to make a contribution towards the understanding of neurogenesis in humans. The objective is to better understand those processes which are relevant for the development of neural (precursor) cells from hES cells and which control the interplay of the cells during neuronal development. Through the identification of specific combinations of surface markers on neural precursor cells the characterisation of certain neural precursor cells is to be made possible, possibly new types of neural precursor cell types are to be identified and the interaction between different neural precursor cell populations is to be analysed during neural differentiation. Furthermore, soluble factors are to be identified which influence the cells differentiating to the neural line, for instance on the levels of signal transduction and transcription. Finally the findings made in the project are to serve for the harvesting of different types of human neuronal cells by means of improved differentiation protocols and to study their maturation and integration into the nerve tissue after transplantation in animal models. In addition, comparative studies between hES cells and human-induced pluripotent stem cells (hiPS cells) are to clarify whether and in how far the two cell types are similar or different in terms of their development potential for certain neural cell types.

The second project (60th approval) focuses on the study of cellular and molecular processes of a cellular immune response mechanism identified recently, the so-called extra-cellular traps, which are formed by neutrophile granulocytes (neutrophile extra-cellular traps, NETs). Since primary neutrophiles are not available *in vitro* because of their short life span and instability, human neutrophile granulocytes are to be obtained from hES cells and extensively characterised. The objective of the project is to gain insights into the molecular bases of the

development of neutrophile granulocytes and to identify and characterise potential sub-populations of these cells. In order to better understand the molecular mechanisms of the NETs formation, the screening of an siRNA library based on lentiviral vectors is to identify those genes whose expression is relevant at the formation of functioning NETs.
The development of a novel approach to the cardiac differentiation of hES cells as well as their optimisation and validation is the focus of the third project (61st approval). The approach which is based on the modulation of calcium-activated potassium channels (SK channels) resulted in the mouse model in the stimulation of the cardiac differentiation whereby in particular cardiac pacemaker cells were enriched. With this new approach cardiac pacemaker cells of a high purity and constant quality are to be obtained. Furthermore, the studies are to provide information on (i) whether and in how far SK channels are involved in human heart cell differentiation, (ii) which isoforms of the SK channel proteins are relevant in this connection and (iii) which intracellular signal pathways are involved in the differentiation process. Moreover, hiPS cells obtained from keratinocytes are to be studied in terms of the presence of SK channels and their role in triggering differentiation processes in comparison with hES cells.

The fourth project (62nd approval) deals with studies concerning the clarification of cellular and molecular processes which are involved in the pathogenesis of Huntington's disease (Chorea Huntington). For this purpose neural cells are to be obtained from hES cells which express the cellular phenotype associated with Huntington's disease in the strongest manner (so-called medium spiny neurons, MSN). As a result of the transfer of the mutant Huntington gene (mHtt) in neural precursor cells differentiated from hES cells and subsequent differentiation to MSN, a cellular model is to be established for Chorea Huntington. Initially it is to be used for the study of known substances showing an effect on the Chorea Huntington phenotype. Later potential active substances are to be identified which have an impact on the expression of the typical cellular properties connected with Huntington's disease.

The fifth research project (63rd approval) initially aims at the establishment of protocols for the differentiation of hES cells to corticospinal motor neurons. Precursor cells of these motor neurons are to be identified and characterised. The goal is to make available human *in vitro* model systems for the analysis of different neurodegenerative diseases which are associated with this cell type. These are, for instance, amyotrophic lateral sclerosis (ALS), hereditary spastic paraplegia (HSP) and primary lateral sclerosis (PLS). Based on these cell models new therapeutic strategies for the treatment of these diseases are to be developed. In the further course of the research work also hiPS cells are to be analysed, in parallel to hES cells, in view of their differentiation capacity in different types of neural cells in order to receive information about the specific differentiation potential of hiPS cells. This is considered to be a prerequisite to the utilisation of patient-specific hiPS cells as starting material for the generation of disease-specific neuronal cells.

The clarification of the molecular processes playing a role during the differentiation to female germ cells in humans is the object of the sixth project (64th approval). Protocols for the differentiation of hES cells to primordial germ cells (PGCs) are to be developed and optimised. The further differentiation into female human germ cells is to be achieved through the co-cultivation of the PGCs with somatic cells, isolated from follicular or ovarian stroma tissue, and by transplantation of aggregates, consisting of human PGCs and, for instance, murine ovarian stroma cells, under the renal capsule of female immunodeficient mice. These experiments could result, amongst other things, in findings about the possible influence of the niche in which germ cells develop *in vivo,* on the process of follicle formation and on processes concerning initiation and progression through meiosis. In addition, hES cells are to be used for comparative studies on the differentiation capacity of hiPS cells to germ cells. Results from these studies are the basis for further analysis, with which molecular and cell biological causes for defects during the germ cell development are to be clarified using hiPS cells of female patients, e.g. with primary ovarian insufficiency.

In the wake of the assessment of the work planned here, during which also genetic modifications of hES cells differentiating to germ cells are to be carried out, it was, more particularly, necessary to discuss whether and in how far the Act for the protection of embryos (EschG) is opposed to the eligibility of the work with hES cells planned here for approval. After extensive deliberations, including the calling in of external experts, this was negated.

Studies on the effect of different types of ionising radiation on hES cells and their differentiation, planned in the seventh project (65th approval), aim at improving the understanding about the influence of this radiation on the early embryonic development of humans. Goal is to clarify which DNA damages are caused in hES cells by ionising radiation, which DNA repair systems are used to remedy the respective DNA damages in hES cells and what consequences has radiation exposure on the cell cycle of hES cells. The influence of ionising radiation on early cellular differentiation processes is to be determined in embryoid bodies (EBs) which have been differentiated from irradiated and non-irradiated hES cells or which were only irradiated after induction of differentiation. In this connection the influence of ionising radiation on the processes of differentiation in cardiac cells and neural precursor cells is likewise to be studied.

The eighth research project (66th approval) concerns the development of efficient methods for the differentiation of hES cells to functional and vital insulin-producing pancreatic beta cells. In further development of established differentiation protocols hES cells are to be differentiated within a three-dimensional culture system to insulin producing islet-like cell clusters and pancreatic precursor cell types formed during the process are to be analysed. The islet-like cells produced *in vitro* are then to be transplanted into diabetic mice to verify their further maturation and functionality *in vivo*. Particularly the influence of co-transplantation of human bone derived marrow mesenchymal stem cells on the survival capacity and functionality of the transplanted pancreatic tissue will be analysed. Apart from hES cells hiPS cells are to be used in the studies in order to clarify whether the two cell types have a comparable pancreatic differentiation potential. In its further perspective the project aims at creating the basis for tissue engineering in respect of diabetes mellitus.

The establishment of human-specific and convincing test systems based on pluripotent cells, which contribute towards the development of improved medicines and are to increase patient safety is the goal of the ninth project (67th approval). The focus of the project is on the transfer of cell-based assays to hES cells. Establishing accordingly modified hES cell lines and differentiating them in a directed way, populations of human cells are to be obtained with which the effect of active substances on specific intracellular processes can be determined simply, efficiently and in high-throughput procedures. Furthermore, the development of a bioreactor large-scale culture system is planned, as far as possible with synthetic culture media. This is a prerequisite to the isolation of hES cells in large amounts and high quality. The planned differentiation of hES cells in cardiomyoytes, neural cells, hepatocytes and immunocytes is likewise to be established in bioreactors. These cells, which are provided with the corresponding marker gene systems and cell-based assays, are to replace existing test systems which are mainly based on human primary cells and *in vivo* test systems of animal origin and whose validity is often not sufficient. All studies are to be carried out based on a comparison between hES and hiPS cells.

The tenth research project (68th approval) focuses on extensive studies on the genetic stability of human pluripotent cells under different culture conditions, in particular during long-term cultivation in suspension culture. In this connection the question is to be clarified whether the long-term cultivation has a different impact on the genetic stability of hES cells and hiPS cells. It has been known for some time that long-term cultivation leads to modifications in the genome of pluripotent stem cells. It is, therefore, intended to optimise the conditions for the cultivation of pluripotent cells in such a way that the cells remain as stable

as possible during long-term culture. Furthermore, strategies are to be developed with which possible genetic modifications can be suppressed, e.g. by using substances which lead to cell death of aneuploid cells or affect cellular DNA repair mechanisms. In addition, the mutation process is to be followed on a chromosomal, sub-chromosomal and DNA level and the mutation rate is to be determined quantitatively. The findings obtained in the project are then to be used to establish protocols for culturing hES cells in larger amounts than those usual on a laboratory scale, in particular in bioreactors.

The eleventh project (69th approval) which is promoted by the European Union within the framework of the project "InnovaLiv" ("*Innovative strategies to generate hepatocytes for treatment of metabolic liver diseases: Tools for personalized cell therapy*") aims at the development of media, media additives and growth factors under GMP conditions for the cultivation of hES cells as well as for their differentiation in liver cells (hepatocytes). The media components used for the cultivation of hES cells are to be gradually replaced by components produced under GMP conditions. Then the hES cells are to be differentiated to human hepatocytes, whereby the growth factors required are likewise to be gradually replaced by the corresponding GMP-compliant substances. The availability of sufficient amounts of transplantable hepatocytes in GMP quality is a prerequisite to future clinical use of these cells. Furthermore, it is planned to utilise the media and media additives, developed during the research project, for the establishment and cultivation of hiPs cells and their hepatic differentiation under GMP procedures.

Within the framework of the 39th project approved in accordance with StZG further research activities were applied for during the reporting period using hES cells (12th project), which required an extension of the approval by RKI and a further discussion on the level of ZES. Based on the existing studies of the applicant on the molecular causes underlying the pluripotency of hES and hiPS cells it has to be assumed that pluripotency is a relatively stable phenotype of a cell which seems, however, to exist in different conditions blending into one other. For that reason it is planned to characterise in more detail the different conditions of pluripotency in selected hES and hiPS cell lines initially on the levels of the transcriptome, epigenome and proteome. Then a model is to be established to forecast those cellular conditions in which an irreversible determination of the cell for the differentiation has naturally occurred. The research goal of developing an algorithm with which it can be estimated whether a given cell type is pluripotent or not, formulated in the original application, continues to be studied and is to be confirmed by further research work using hES cells.

For the second project approved in accordance with StZG, too, further research activities using hES cells were applied for during the reporting period (13th project). The research project aims at a better understanding of processes occurring in the cardiac differentiation process on the cellular level. It is to be extended by studies which deal with receptors in the human heart being part of the family of olfactory receptors and whose genes are expressed during the development of cardiac cells derived from hES cells. Ligands binding to these receptors are to be identified and characterised in terms of their effect on developing heart cells. Furthermore, cellular signal transduction pathways, which are modulated as a result of the ligand binding in these cells, are to be identified and characterised in more detail. The studies on the properties of hES cell derived cardiac cells are to be carried out by a comparison with cardiac cells derived from hiPS cells.

Further information on the content of the approved projects which have received a positive assessment by ZES prior to their approval, can be taken from the register of RKI (http://www.rki.de/DE/Content/Gesund/Stammzellen/Register/register_node.html).
The central arguments of ZES concerning the high ranking status of the research projects, their sufficient preliminary clearing and the necessity to use human ES cells have been taken into account at the assessment of the research projects by RKI.

During the reporting period nine applications of research groups, which had so far not worked with hES cells, and three applications by groups which had already received a corresponding approval in the past were approved by RKI after review by ZES. Summing up, ZES has deliberated on a total of *72 applications* for import and/or use of hES cells during its nine years of activities. In addition, *five applications for extensions* of already approved projects were assessed. This means that a total of 77 opinions were submitted to RKI of which 70 applications and five applications for extension included a recommendation for approval of the research activities using hES cells applied for. Two applications were postponed. RKI followed in all cases the recommendation of the Committee.

At present 53 groups at 39 research institutions have approvals for studies involving hES cells. According to knowledge available to ZES, results originating from the approved research projects of 16 research groups have been the subject matter of 55 scientific original publications in which holders of approvals under StZG are mentioned as authors in charge. Further original publications have resulted from co-operation projects on the European and international level in which holders of approvals under StZG were involved.

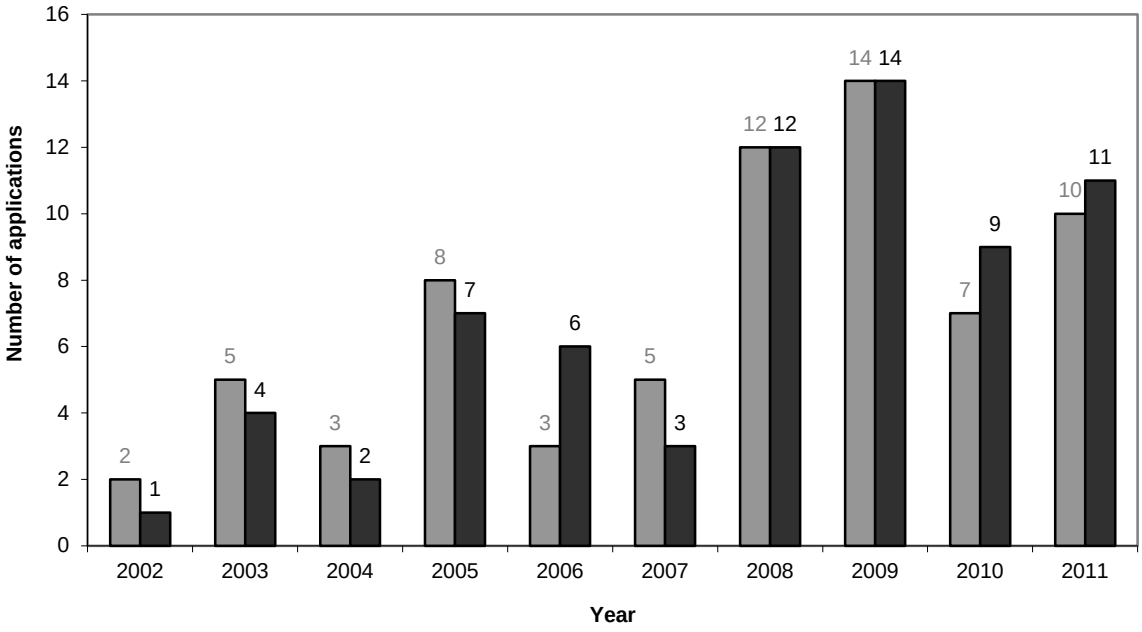

Figure 1: Number of applications reviewed by ZES (light grey bars) and applications approved by RKI (black bars) under StZG in the respective calendar year. Extensions of applications, on which ZES has likewise submitted opinions, are not taken into account.

3. Developments and tendencies in stem cell research

1. Figure 1 shows the progress of the number of applications under StZG since 2002. It can be clearly seen that the number of applications reviewed by ZES and approved by RKI during the reporting period remains on the level of the average of the past years. It should be stressed that in eight of a total of 11 research projects approved during the reporting period cell lines are used, whose import and use only became possible after the amendment of StZG in 2008. Furthermore, during the reporting period for 10 of the projects the import and use of hES cell lines was approved, whose import and use had already been possible prior to the amendment of the cutoff date defined by StZG. This could also be attributable to the reference character of certain “old” cell lines which is discussed in literature.

2. In the context of the deliberations on applications under StZG it became clear that there is a high interest in the investigation of pathogenesis mechanisms of genetically caused diseases in Germany, too. Outside Germany hES cells can be used for such studies which originate from embryos, in which a genetic defect causing a disease was diagnosed within the framework of a PGD. According to the knowledge available to ZES there are currently around 200 hES cell lines with genetic defects which are specific for at least 50 hereditary diseases internationally renowned. In reviewing the applications during the reporting period it became clear that in Germany, too, there is a need to use hES cell lines, which were established after the conduct of a PGD, for research purposes in parallel to the possibility to use hiPS cells for pathogenesis research. Since these hES cell lines may not, however, be imported into Germany and used here in accordance with § 4.2 StZG, disease-specific hES cells must be made available through the detour of genetic modification of genetically normal hES cells instead of being able to use internationally already available cells. Particularly with regard to the most recent decisions about the legitimacy of PGD in Germany, the Committee sees further need for discussion on the issue, whether the currently existing ban on importing and using hES cells from embryos no longer used for reproductive purposes in the result of a PGD and donated for research purposes remains consistent.

3. The preliminary clearing of issues envisaged in the research project in terms of *in vitro* models with animal cells or in animal models must be submitted by the applicant in accordance with § 5 StZG and constitutes the prerequisite to the eligibility for approval of an application. ZES must check in each application procedure again whether this prerequisite is met. Due to the meanwhile more than 10 year international research activities with pluripotent stem cells of humans, knowledge about the properties of these cells, in particular about hES cells, has been considerably extended. Issues relating for instance to the differentiation capacity in a certain cell type have meanwhile been clarified repeatedly and fundamentally in respect of hES cells so that a proof of concept in cells of other species for the preliminary clearing of the fundamental issue of interest is frequently no longer necessary. At the same time it has been shown repeatedly that a preliminary clearing of certain in-depth aspects concerning humans, due to species-specific differences in mice or other model systems, is in all probability not resulting in any relevant gain in knowledge for the research project and would, therefore, not contribute towards the further plausibilisation of the project. For this reason ZES considered at the review of various projects that a preliminary clearing of certain research aspects is not expedient and consequently not necessary.

4. In view of the need for the use of hES cells the question becomes increasingly relevant whether and in how far hiPS cells can replace hES cells in research projects. On the one hand, many research aspects in respect of hiPS cells have not yet been studied. On the other hand, there are partly inconsistent findings published in literature on the equivalence of hES and hiPS cells, for instance in terms of epigenetic properties or concerning their differentiation capacity. The mere abstract assumption that research questions which are to be answered by using hES cells could also, under certain circumstances, be answered by studies in hiPS cells is not sufficient for ZES to refer a researcher to the use of hiPS cells. So far the Committee always considered the use of hES cells to be necessary if, according to the current state of scientific knowledge, the comparable qualification of other cells than hES cells is not positively proven in view of achieving the research goals.

5. In the research projects assessed during the reporting period, references to the future application of research with hES cells become more visible than in the past. This concerns both, objectives in the therapeutic field as well as future possibilities to use hES cells for the development and testing of medicinal products. Research activities for the development of new processes based on hES cells for the identification, validation and testing of new active substances can be justified ethically according to ZES under StZG if high-ranking research goals are pursued within the meaning of § 5.1 StZG and the other prerequisites of § 5 StZG

are met. There is a high interest in developing medicines with as few risks as possible. The use of human-specific test systems derived from hES cells can possibly contribute to this. In this connection potential side effects could, for instance, be identified at a very early stage in the development of medicines. In international research there are indications that such test systems are not only useful in pharmaceutical research but also for the determination of toxicity, for instance embryotoxicity, of environmental chemicals. This could support environmental health protection and possibly have medical benefits.

6. At one of its meetings ZES dealt with the judgement of the European Court of Justice (ECJ) of 18 October 2011 in respect of Case C-34/10. As a result of this judgement, inventions are excluded from patenting, "… if they require the prior destruction of human embryos or their use as base material". To the extent that the German Federal Supreme Court endorses this decision, a patent registered by Professor Brüstle, which describes the differentiation of neuronal (precursor) cells from hES cells, could be declared as null and void. The decision by the ECJ, which refers exclusively to aspects under patent law, may have an impact on the selection of research projects in Germany, but does not directly affect the activities of ZES within the framework of the approval of research projects.

The ninth report was unanimously approved at the 63rd ordinary meeting of ZES on 18 January 2012.