

<i>Charter</i>	Merck KGaA, Darmstadt, Germany
Human Stem Cell Principles	
Document Unit (Owner) : (CA) Corporate Affairs Applicability : Merck KGaA, Darmstadt, Germany, Group Approved by : Executive Board, GL	

Human stem cell principles

our position

Merck KGaA, Darmstadt, Germany, recognizes the potential benefits of conducting properly defined research with stem cells because of the therapeutic potential for the treatment of a variety of diseases, conditions, and injuries. Therefore, certain research with human stem cells is allowed with careful consideration of ethical and legal standards. We have established the SCROC to provide oversight and guidance on research we conduct involving human stem cells.



Human stem cell principles

our safeguards for research and applications



Merck KGaA, Darmstadt, Germany, will not pursue the reproductive cloning of human beings.



Consistent with current guidelines, we will not engage in the creation and use of human artificial gametes for reproductive purposes.



Wherever possible we use non-human animal stem cells, human iPSCs or human adult stem cells rather than hESCs.



For stem cell research involving genome editing, careful ethical and legal assessments are also made in accordance with our Genome Editing Principles.



We use hESC cell lines in ways that are compliant with the legal framework of the respective country regulations in which the research is conducted.



For human stem cell research with animals, careful ethical and legal assessments are also made in accordance with our Policy on Animal Welfare.



In accordance with the German Embryo Protection Act we will currently not engage in the production of human embryos for research purposes or in deriving hESCs.



Any use of hESCs and specified uses of iPSCs within the Merck group must undergo review by the SCROC. This includes collaborations or grants involving such research.



HUMAN stem cell principles our safeguards as a partner and supplier



Prior to finalizing any agreement with a partner, we will review and comply with ethical, regulatory, and legal requirements related to and contained within these Principles. We will make these Stem Cell Principles public and expect its customers and partners to comply with the provisions of this section.



We will not deliver any of its stem cell products and services, if we become aware of any projects by customers, partners or institutes directed at the creation of human embryos for research purposes or the cloning of human beings.



We will not hold shares or have board seats in companies who engage in activities outlined here. We will also not support or finance such activities of third parties and will not enter into collaborations with third parties to pursue such activities.



1. Objective

Research on human stem cells and their use for applications to regenerate tissues and organs can play an important role in developing novel therapies for various diseases, conditions, and injuries. Research, clinical and commercial activities in this field needs careful evaluation of ethical and legal concerns and require a clear framework within the Merck KGaA, Darmstadt, Germany, Group. Therefore, Merck KGaA, Darmstadt, Germany, has developed the following company Principles.

2. Scope

These company Principles provide Merck KGaA, Darmstadt, Germany, employees with background information on stem cells and with the current position of the company on the use of human stem cells.

All Merck KGaA, Darmstadt, Germany, scientists and researchers using, or otherwise working with, human stem cells are responsible for understanding and abiding by this Stem Cell Principle. In addition, Merck KGaA, Darmstadt, Germany, expects that Third Parties are up to date with respect to the on-going deliberations regarding the ethical aspects of stem cells and are responsible for making informed decisions regarding their own stem cell usage.

Merck KGaA, Darmstadt, Germany, has established the SCROC to not only provide oversight of specific types of stem cell research, clinical and commercial activities, but also to advise on important topics with ethical and legal impact in the area of stem cell research. Mandate, responsibilities, and procedures of the SCROC are further outlined in the "Merck KGaA, Darmstadt, Germany, Stem Cell Research Oversight Committee Charter". Merck KGaA, Darmstadt, Germany,'s SCROC works under the guidance of the Merck KGaA, Darmstadt, Germany, Ethics



Advisory Panel for Science and Technology (MEAP), formerly the Merck KGaA, Darmstadt, Germany, Bioethics Advisory Panel (MBAP), to help ensure alignment in regards with Merck KGaA, Darmstadt, Germany,'s overall ethics guidelines and principles.

3. Executive Summary

Merck KGaA, Darmstadt, Germany, acknowledges the ethical controversies surrounding the derivation and use of hESCs and has instituted safeguards for stem cell research and applications. These safeguards stipulate that wherever possible Merck KGaA, Darmstadt, Germany, uses non-human animal stem cells, induced Pluripotent Stem Cell (iPSCs) or human adult stem cells rather than human Embryonic Stem Cell (hESCs). Any research, clinical and commercial activities involving hESCs and specified research uses of human Pluripotent Stem Cell (hPSCs) within the Merck KGaA, Darmstadt, Germany, group must undergo review and advice by the Stem Cell Research Oversight Committee (SCROC). This includes collaborations or grants involving such research. Prior to finalizing any agreement with a partner, Merck KGaA, Darmstadt, Germany, will review and comply with ethical, regulatory, and legal requirements related to and contained within these Principles. Merck KGaA, Darmstadt, Germany, will not deliver any of its stem cell products and related services, if Merck KGaA, Darmstadt, Germany, becomes aware of any projects by customers, partners or institutes directed at research, clinical and commercial activities that are prohibited by Merck KGaA, Darmstadt, Germany, as specified here (see. 5.2 below).

4. Background

Stem cells have the ability to self-renew indefinitely through mitotic cell division and to give rise to various specialized cell types that form tissues and organs. There are several different types of stem cells:

- Human embryonic stem cells (hESCs) are derived from the inner cell mass of a blastocyst, an early-stage human embryo. hESCs produced by the first few divisions of the fertilized egg are totipotent; they can differentiate into any cell type of an embryo and its supporting tissues (e.g., placenta).
- Stem cells derived from nuclear transfer: somatic cell nuclear transplantation leads to a cloned embryo from which pluripotent stem cells can be derived which match the donor organism from which the cell nucleus came.
- Induced pluripotent stem cells (iPSCs) can be generated from adult cells by re-programming and can turn into any cell of the body.
- Adult stem cells, also called somatic stem cells, are stem cells which maintain and repair the tissue in which they are found. Most adult stem cells are lineage-restricted (multipotent) and are generally referred to by their tissue origin (hematopoietic stem cells, mesenchymal stem cell, adipose derived stem cell, endothelial stem cell, dental pulp stem cell, etc.).
- Cancer stem cells are a sub-population of cancer cells, which possess characteristics associated with normal tissue stem cells (i.e., self-renewal and the ability to differentiate into multiple cell types).

Some type of stem cell research raises ethical concerns. Many countries and local jurisdictions have legal frameworks regulating the production and use of certain types of stem cells, particularly hESCs. These ethical and legal issues must be considered when pursuing research and applications involving stem cells.



5. Merck KGaA, Darmstadt, Germany, Position

Merck KGaA, Darmstadt, Germany, recognizes the potential benefits of conducting properly defined research with stem cells because of the therapeutic potential for the treatment of a variety of diseases, conditions, and injuries. Therefore, certain research with human stem cells is allowed with careful consideration of ethical and legal standards. Merck KGaA, Darmstadt, Germany, has established the SCROC to provide oversight and guidance on research Merck KGaA, Darmstadt, Germany, conducts involving human stem cells.

5.1. Current Engagement

Merck KGaA, Darmstadt, Germany,, through internal research as well as in collaboration with external partners, develops new stem cell research tools, products, and therapeutic production processes.

5.1.1. Healthcare research programs

Merck KGaA, Darmstadt, Germany, is regularly investigating the use of human stem cells as tools in its research programs directed towards the fields of disease target identification and drug screening as well as drug safety, predictive toxicology, and metabolism. Merck KGaA, Darmstadt, Germany, Healthcare observes ongoing research utilizing stem cells for therapeutic purposes and collaborates with external partners (i.e., academic institutions and companies) on research programs with stem cells. These collaborations follow these Principles as well. Merck KGaA, Darmstadt, Germany, is actively engaged in research of the biology of CSCs with the aim of targeting their selective inhibition or elimination *in vivo* to generate new treatment modalities for cancer patients.

5.1.2. Life Science products for stem cell research and manufacturing

As a global supplier for the life science market, Merck KGaA, Darmstadt, Germany, develops and markets research tools, reagents, cell lines, and technologies in the field of stem cell biology. Life Science products are developed within Merck KGaA, Darmstadt, Germany, or in collaboration with academic and industrial partners. The product portfolio ranges from reprogramming and cultivation to characterization and separation of stem cells.

5.2. Safeguards for stem cell research and applications

Merck KGaA, Darmstadt, Germany, acknowledges the ethical controversies surrounding the derivation and use of hESCs. In doing so, Merck KGaA, Darmstadt, Germany, complies with the following:

- Merck KGaA, Darmstadt, Germany, will not pursue the reproductive cloning of human beings.
- Wherever possible Merck KGaA, Darmstadt, Germany, uses non-human animal stem cells, human iPSCs or human adult stem cells rather than hESCs.
- Merck KGaA, Darmstadt, Germany, uses hESC cell lines in ways that are compliant with the legal framework of the respective country regulations in which the research is conducted.
- In accordance with the German Embryo Protection Act Merck KGaA, Darmstadt, Germany, will currently not engage in the production of human embryos for research purposes or in deriving hESCs.
- Consistent with current guidelines, Merck KGaA, Darmstadt, Germany, will not engage in the creation and use of human artificial gametes for reproductive purposes.



- For stem cell research involving genome editing, careful ethical and legal assessments are also made in accordance with Merck KGaA, Darmstadt, Germany,'s Genome Editing Principles.
- For human stem cell research with animals, careful ethical and legal assessments are also made in accordance with Merck KGaA, Darmstadt, Germany,'s Policy on Animal Welfare.
- Any use of hESCs and specified uses of hPSCs within the Merck KGaA, Darmstadt, Germany, group must undergo review by the SCROC. This includes collaborations or grants involving such research.
- Prior to finalizing any agreement with a partner, Merck KGaA, Darmstadt, Germany, will review and comply with ethical, regulatory, and legal requirements related to and contained within these Principles. Merck KGaA, Darmstadt, Germany, will make these Stem Cell Principles public and expect its customers and partners to comply with the provisions of this section.
- Merck KGaA, Darmstadt, Germany, will not deliver any of its stem cell products and services, if Merck KGaA, Darmstadt, Germany, becomes aware of any projects by customers, partners or institutes directed at the creation of human embryos for research purposes or the cloning of human beings.
- Merck KGaA, Darmstadt, Germany, will not hold shares or have board seats in companies who engage in activities outlined here. Merck KGaA, Darmstadt, Germany, will also not support or finance such activities of third parties and will not enter into collaborations with third parties to pursue such activities.

6. Outlook

Merck KGaA, Darmstadt, Germany, will periodically review this position according to latest scientific, ethical, and legal insights. The SCROC regularly advises on important topics with ethical and legal impact, focusing on stem cell research or applications.

7. Glossary

Abbreviations	Definition
CSC	Cancer Stem Cell
hESC	human Embryonic Stem Cell
hPSC	human Pluripotent Stem Cell
iPSC	induced Pluripotent Stem Cell
MBAP	Merck KGaA, Darmstadt, Germany, Bioethics Advisory Panel
MEAP	Merck KGaA, Darmstadt, Germany, Ethics Advisory Panel for Science and Technology
SCROC	Stem Cell Research Oversight Committee

8. References

Group Standard "iMS-Document Management" (*ManGo Doc ID 20043334*)



9. Revision History

Version Number	Change short description	Replacement of Document
1.0	First Version	N/A
2.0	Updated according to new ISSCR guidelines; Merck KGaA, Darmstadt, Germany, position unchanged.	First Version

