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PATENTABILITY OF HUMAN EMBRYONIC STEM CELLS – A COMPARATIVE ANALYSIS OF THE DEVELOPMENT IN THE EUROPEAN UNION AND IN THE UNITED STATES OF AMERICA

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ABSTRACT

The aim of this research is to present a comparative analysis of the development of patenting living matter in the European Union and in the United States of America, especially focusing on the case of human embryonic stem cells (hESCs). The development processes in the European Union and in the United States of America will be examined individually, as well as together, to point out similarities and differences and make discoveries by their comparison. This research will be conducted by using qualitative research methods, as they provide a possibility to attain detailed knowledge of the judgements of individual cases.

It is going to be examined what are the legal requirements for the patentability of hESCs in the European Union and in the United States, how have these requirements changed throughout times and what are the factors that have driven these changes. Also, the significance of the case law for these development processes will be examined in detail. In addition, some general knowledge on stem cell science will be reviewed in order to attain deeper knowledge on the case of patenting living matter and its development. Furthermore, the importance of protection of biotechnological inventions will be stressed as well as certain ethical aspects of human embryonic stem cell research. Finally, the research will focus on the current situation of the patentability of hESC research, and the challenges and issues emerging thereof.

Keywords: Intellectual Property Law, Stem Cell Patents, Human Embryonic Stem Cell Research, Protection of Biotechnological Inventions, Comparative Research

LIST OF ABBREVIATIONS

AIA	Leahy-Smith America Invents Act
EBA	The Enlarged Board of Appeal of the European Patent Office
ECJ	The European Court of Justice
EPC	European Patent Convention
EPO	European Patent Office
ESC	Embryonic Stem Cell
hESC	Human Embryonic Stem Cell
hpSC	Human Parthenogenetic Stem Cell
iPSC	Induced Pluripotent Stem Cell
NIH	National Institutes of Health
TBA	The Technical Board of Appeal of the European Patent Office
U.S.C.	The United States Code
USPTO	The U.S. Patent and Trademark office
WIPO	World Intellectual Property Organization

INTRODUCTION

During the past decades, stem cell research has become one of the most promising areas in biomedical research today, allowing increased scientific understanding of fatal diseases such as diabetes and cancer, and certain neurodegenerative diseases like Alzheimer's disease and Parkinson's disease. Moreover, stem cells might be the key to discovering treatments for fatal diseases and the possibilities to use them in medicine are extensive, especially those of embryonic origin; they can be used in scientific research to attain knowledge, or to be grown to become new tissue for use in transplant in regenerative medicine and for testing new drugs for safety and effectiveness, instead of animal testing.[1] In addition to the medical and scientific promise, stem cell research has a great commercial promise. Conducting the research requires significant time and financial investment which has rendered the patent protection for biotechnological inventions necessary.[2] To illustrate the commercial promise of this revolutionary technology, the global stem cell market size was estimated at USD 8,65 billion in 2018 and is expected to reach USD 15,63 billion by 2025.[3]

Exploiting embryonic stem cells (ESCs), especially those of human origin, raises multiple ethical and political concerns related to the onset of human personhood, human reproduction and the destruction and creation of embryos specifically for research purposes. On one hand, the hESC research should be conducted fulfilling the moral requirements and respecting the dignity of human life. On the other hand, supporting innovation by allowing patent rights for the inventions is necessary for the biotechnology industry to develop. This leads to the first question that is researched into: on what grounds can biotechnological inventions be patented in the European Union and in the United States? Later on, it can be discovered that the biotechnology industry develops fast and the legal starting point for the patentability has to be open to interpretation by

[1] Lehtonen, L. (2006). *Bio-oikeus lääketieteessä*, Helsinki: Edita Publishing Oy. p 177-178.
[2] *Ibid.*, p. 231-232.
[3] Grand View Research, Inc. Report on the global stem cells market size, February 2020. Available at: https://www.reportlinker.com/p05768015/Stem-Cell-Market-Size-Analysis-Report-By-Product-By-Application-By-Technology-By-Therapy-And-Segment-Forecasts.html?utm_source=PRN, 7.5.2020.

case law, which leads to the second research question that is: how has the case law in the European Union and in the United States modified the patentability requirements for biotechnological inventions? Finally, certain questions will arise relating to the legal state of patenting biotechnological inventions in the future and the challenges and issues emerging thereof. Also, the research questions will emphasize the mutual interaction of the development processes between the European Union and the United States.

This bachelor thesis is written by using qualitative research methods and completed by referring to the relevant case law and international legal instruments. The research questions will be studied from multiple perspectives to give a comprehensive overview of the development of patentability requirements of the hESC research in the European Union as well as in the United States. The development processes of both of these patent systems will be compared and contrasted individually, as well as together, in order to fulfill the aim of this research that is to provide a comparative analysis of the development of patentability of the hESC research in the European Union and in the United States. The hypothesis of this research is that the legal state concerning the patentability of hESCs has become clearer over time as a result of balancing both the ethical concerns related to it, as well as protecting the biotechnological innovation but there is still legal uncertainty related to this fast-developing area of scientific research.

The first chapter focuses on giving a short overview of stem cell science and classifying stem cells according to their properties, in order to demonstrate their possible use in medicine and scientific research in general. This is necessary in order to be able to understand the topic of this bachelor thesis thoroughly. Also, the ethical aspects related to the use of stem cells in medicine will be emphasized. The second chapter studies the concept of patents and the general patentability requirements for inventions both in the European Union and in the United States. On this chapter, the legal starting point for the patentability will be set and it will also be examined whether there are any exclusions or exceptions to the patentability according to the case law or other legislative changes. This leads to the third chapter that focuses on the patentability of biotechnological inventions, especially on the patentability of the hESC research. As the legal starting point for the patentability of inventions is already set, this chapter examines it from the point of view of biotechnological inventions explicitly. Also, it will be examined how have these legal instruments been interpreted in the practice of the Courts and what is their significance for the patentability of biotechnological inventions. Finally, the last chapter points out some observations following the comparative research of the development of patentability of biotechnological inventions in the

European Union and in the United States, and certain thoughts will be introduced concerning the current legal state and its further implications.

1. STEM CELL SCIENCE

Stem cell research is a fast-growing and promising area of scientific research, which focuses on stem cells in general, their properties and possible use in medicine. It has become one of the most promising areas in biomedical research today, allowing increased scientific understanding of fatal diseases such as diabetes and cancer, and certain neurodegenerative diseases like Alzheimer's disease and Parkinson's disease. In addition, the possibilities to use stem cells in medicine are extensive as they might be the key to discovering treatments for fatal diseases. Stem cells can also be used for testing new drugs for safety, effectiveness and quality, for example, nerve cells could be generated to test a new drug for a nerve disease and the test would show if the new drug had any positive or negative effect on the cells.[4] Despite the ethical concerns related especially to the use of stem cells of human origin, they have been the focus of interest in scientific research during the past decades.[5] In addition, because conducting the research requires significant time and financial investment, the patent protection for life science inventions is necessary for the biotechnology industry to keep developing.[6]

1.1. Stem cell classification

Stem cells are unspecialized cells that are able to differentiate into other types of cells and have the ability to divide in self-renewal in order to produce more of the same type of stem cells. Stem cells can be classified into embryonic stem cells, which are derived from the inner cell mass of blastocyst-stage embryos, and adult stem cells, which exists in several tissues of fully developed mammals and are able to multiply by cell division and regenerate damaged tissues. Stem cells can further be classified into totipotent, pluripotent and multipotent stem cells according to their cell potency, which refers to their ability to differentiate into specialized cell types. Totipotent stem

[4] Lehtonen, L. (2006). *Supra nota* 1, p. 177-178.
[5] *Ibid.*
[6] *Ibid.*, p. 231-232.

cells have the greatest potency to generate cell types as they are able to form all the cell types that exist in a body, including the extra-embryonic cells. Pluripotent stem cells have the second greatest ability to generate cell types as also they are able to form all the cell types in a body, however, excluding the extra-embryonic cells. Multipotent stem cells, on the other hand, are able to differentiate into a limited number of cell types in specific cell lineages. Embryonic stem cells fall under the category of pluripotent stem cells, whereas adult stem cells are multipotent.[7] Both adult and embryonic stem cells can be exploited in scientific research, however, the adult stem cells are not as versatile and durable as the embryonic stem cells, which has led to the fact that the possibilities to use adult stem cells are much more limited.[8]

1.2. Ethical issues related to the embryonic stem cell research

Because the human embryonic stem cells used in the research are extracted from human embryos, the hESC research raises multiple ethical and political concerns, which have framed the development of regenerative medicine and drug discovery. Further, the hESC inventions are considered controversial as they have the ability to introduce inheritable changes into the human genome.[9] Protecting the dignity of human life as well as protecting of biotechnological inventions, is one of the most significant controversies concerning the field of hESC research.[10] On one hand, the research should be conducted with dignity and respect towards human life, which is related to the views surrounding the moral status of the human embryo.[11] However, there are dissenting opinions relating to the onset of human personhood and whether an embryo is a person with a moral status similar to an adult, or whether an embryo becomes a person in a moral sense at a later stage of development.[12] On the other hand, the patent protection for biotechnological inventions is necessary for the biotechnology industry to keep developing, because conducting the research requires significant time and financial investment, which has also been justified as resulting in benefit for the society.[13] Patentability of biotechnological inventions can be restricted on moral

[7] *Ibid.*, p. 2-4.
[8] *Ibid.*
[9] Prifti, V. (2019). The limits of "ordre public" and "morality" for the patentability of human embryonic stem cell inventions, *The Journal of World Intellectual Property*, 22(1-2), 2-15.
[10] *Ibid.*
[11] Plomer, A., Torremans, P. (2009). *Embryonic Stem Cell Patents – European Law and Ethics,* New York: Oxford University Press Inc., p. 32.
[12] *Ibid*., p. 33.
[13] Chapman, A. (2009). The Ethics of Patenting Human Embryonic Stem Cells, *Kennedy Institute of Ethics journal*, 19(3), 261-288.

grounds, such as respecting human life and protecting the dignity of a human embryo,[14] but it has been also argued that these restrictions are unethical as they may limit the development of medical research.[15] Supportive arguments have been presented as some people believe that restrictions would guide the research into more appropriate subjects than human embryos.[16]

1.2.1. The moral and legal status of an embryo

Defining the term of human embryo and the moral as well as the legal status conferred to it is proven to be difficult, even though it would be critically important from the point of view of permissibility of certain types of research. Even those countries that have provided a definition for the term of human embryo, have left certain aspects outside of the scope of the legal definition, or lack a consistent and precise use of the term.[17] National Institutes of Health (NIH) defines the term human embryo as including "any organism…derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploids",[18] however, it does not define embryo by a reference to any particular point in time. Because the national legislations have left the term open to interpretation, the case law as well as the International conventions have a significant importance in interpreting the moral and legal status of a human embryo.

[14] Plomer, A., Torremans, P. (2009). *Supra nota* 11, p. 34–35.
[15] Lehtonen, L. (2006). *Supra nota* 1, p. 232.
[16] *Ibid.*
[17] Plomer, A., Torremans, P. (2009). *Supra nota* 11, p. 33–35.
[18] National Institutes of Health, Public Policy requirements: 4.2.5 Human Embryo Research and Cloning Ban, 2009. Available at: https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.2.5_human_embryo_research_and_cloning_ban.htm, 24.3.2020.

2. CONCEPT OF PATENTS

The World Intellectual Property Organization (WIPO) was created in 1967 as one of the specialized agencies of the United Nations (UN), in order to encourage creative activity and to promote the protection of intellectual property worldwide. According to the definition provided by WIPO, a patent is "an exclusive right granted for an invention, which is a product or a process that provides, in general, a new way of doing something, or offers a new technical solution to a problem."[19] In other words, a patent is a form of intellectual property that provides the inventor exclusive rights to the patented invention, which practically means that the patent owner has the right to prevent anyone else from making, using or selling the patented invention.

According to the European Patent Convention (EPC) Article 52, "European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application",[20] whereas according to the United States Code (U.S.C.), "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title" (35 U.S.C. § 101).[21] In other words, both these patent systems require patentable inventions to be new, non-obvious or to involve an inventive step and to be useful, or susceptible of industrial application. In addition to these, the US patent system has certain requirements related to the written description, enablement and best mode of the invention that are not codified in the European patent law.

According to the European patent law, the following is not to be considered patentable: 1) discoveries, scientific theories and mathematical methods, 2) aesthetic creations, 3) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for

[19] Word Intellectual Property Organization, Patents: what is a patent? Available at: https://www.wipo.int/patents/en/, 24.3.2020.
[20] European Patent Convention of 5 October 1973, Article 52.
[21] Title 35 of the United States Code § 101.

computers, and, 4) presentations of information.[22] Also, European patents are not granted in respect of: 1) inventions whose commercial exploitation would be contrary to public order or morality, for example, process of cloning human beings or the use of human embryos for commercial or industrial purposes, 2) plant or animal varieties or essentially biological processes for the production of plants or animals, or 3) methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body.[23] According to the US patent system, the invention must fall within one of the statutory categories of invention; process, machine, manufacture or composition of matter, and not to be a judicial exception, that is to say, the subject matter that the Courts have found to be excluded from the four statutory categories of invention. Abstract ideas, laws of nature and natural phenomena, including products of nature, are judicial exceptions. It can be concluded that the European patent system defines what is not to be regarded as patentable invention, whereas the US patent system defines the patent-eligible subject matter. Further, the European approach is seen as imposing ethical restrictions to patentability, which is not the situation in the Unites States.[24]

2.1. Novelty

In the European Union, "an invention shall be considered to be new if it does not form part of the state of the art.", moreover, "the state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application".[25] Therefore, an invention is considered to be new if it does not form a part of the state of the art, referring to the level of development reached at any particular time. The European approach to the state of the art constitutes a so-called "first-to-file" system, according to which the state of the art includes patent applications as of the dates of their filing.[26]

After the patent reform along the Leahy-Smith America Invents Act (AIA), the US Patent law defines the novelty requirement for patentable inventions as follows; "a person shall be entitled to a patent unless the claimed invention was patented, described in a printed publication, or in public

[22] European Patent Convention of 5 October 1973, Article 52.
[23] European Patent Convention of 5 October 1973, Article 53.
[24] Chapman, A. (2009). *Supra nota* 13, 265.
[25] European Patent Convention of 5 October 1973, Article 54.
[26] Storz, U. (2014). *Biopatent Law: European vs. US Patent Law*, Berlin: Springer Publishing, p. 44.

use, on sale, or otherwise available to the public before the effective filing date of the claimed invention" (35 U.S.C. § 102).[27] Pre-AIA, the US Patent law favored the "first-to-invent" system, which awarded the patent to the inventor who first thought of the idea and put it into practice. As the AIA went into effect, it switched the first-to-invent system to "first-inventor-to-file" system, which changed the point of view from the date of invention to the effective filing date. Even though, it is still required that it is the inventor who applies for the patent, this change along the AIA harmonized the US Patent system with the patent systems of the majority of the world, for example, the European Patent system that follows the first-to-file approach.

2.1.1. Grace periods

The novelty grace period allows the invention to be publicly disclosed before the application filing date, in order to grant protection against unintended or necessary prefiling disclosures, or disclosures by unknowing applicants. The European patent system does not rely on the grace periods as extensively as the US patent system, even though the European Patent Office (EPO) allows two grace periods that are quite limited in scope.[28] First, there is a six-month grace period related to the illegal disclosure of an invention and it can be granted for an inventor in a situation where there has been an evident abuse in a disclosure against a hopeful applicant.[29] In this case, the applicant should apply for the patent within six months from the illegal disclosure. Second, there is another six-month grace period that is not so often used and is related to the disclosure of inventions at official exhibitions.[30] The US patent system applies a grace period of one year, according to which the applicant has one year from the date of publication to apply for the patent, before being barred from patenting.[31] Again, it must be emphasized that the grace periods recognized by the European patent system are quite limited in scope and not comparable to those offered by the US patent system.

Despite the grace periods allowed by the EPO, the European patent system practically requires absolute novelty,[32] in which case the novelty of an invention can be destroyed by any disclosure which makes the invention publicly known before the application filing date. However, the

[27] Title 35 of the United States Code § 102.
[28] European Patent Office, Guidelines for Examination, 12.2 Time limit for payment of extension and validation fees, Available at: https://www.epo.org/law-practice/legal-texts/html/guidelines/e/a_iii_12_2.htm, 24.3.2020.
[29] Storz, U. (2014). *Supra nota* 26, p. 49.
[30] *Ibid.*
[31] Struve, F. (2013). Ending Unnecessary Novelty Destruction: Why Europe Should Adopt the Safety-net Grace Period as an International Best Practice, *William Mitchell Law Review*, 39(4), 1403-1440.
[32] *Ibid.*

concept of absolute novelty is seen as not fitting into the reality of modern research, capital, and inventors' knowledge of the patent system, which is why there is a need to balance the strict nature.[33] On the other hand, is argued that grace periods are in controversy with the fundamental belief according to which patents should be granted to inventions that are new and not disclosed previously to the public,[34] and because they provide an extended period of uncertainty.[35] As a solution, a so-called safety-net grace period has been suggested, which would protect against the inventor's own novelty-destroying disclosures to prevent the disproportionate results of complete destruction of novelty.[36]

The EU and the US patent systems' approach to novelty is considered quite similar in general, though with certain differences. The European approach is considered simpler because the European patent system does not rely on the grace periods as extensively as the US patent system.[37] On the other hand, the novelty of an invention in the EU can be destroyed if the information concerning it is disclosed to a single individual who can legally further disclose that information, whereas the United States' grace periods grant some leeway on examining the novelty of an invention, which is why the European approach is seen as stricter.[38]

2.2. Inventive step and non-obviousness

According to the Article 56 EPC, patentable inventions must involve an inventive step: "An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art",[39] moreover, the person skilled in the art is a skilled practitioner with average knowledge and ability in the field of technology in question, and who is aware of the common general knowledge in the art at the relevant date.[40] The US patent system approaches this similarly, as according to the 35 U.S.C. § 103: "A patent for a claimed invention may not be obtained, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of

[33] *Ibid.*
[34] *Ibid.*
[35] Metzler, R., (2009). Not all grace periods are created equal: building a grace period from the ground up, *Marquette Intellectual Property Law Review*, 13(2), 371.
[36] Struve, F. (2013). *Supra nota* 31.
[37] Storz, U. (2014). *Supra nota* 26, p. 47.
[38] *Ibid.*
[39] European Patent Convention of 5 October 1973, Article 56.
[40] *Ibid.*

the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains."[41] In other words, the patentable invention should have an 'inventive step', meaning, it should not be obvious to a person of ordinary skill in the relevant field of technology – the invented technology is obvious if a person of ordinary skill in the relevant field of technology would have considered it obvious, considering the state of art known at the time.

The principles of novelty and inventive step or non-obviousness are designed to work together to ensure the patentability of genuinely new inventions, because patents should be granted only for inventions that are exceptional.[42] Because the novelty principle examines whether the invention is within the existing state of the art, the principle of non-obviousness or inventive step determines the distance beyond the state of the art.[43] In regard of assessing the patentability of biotechnology inventions explicitly, it has been suggested that the rapid technological progress in the biotechnology industry is problematic from the point of view of inventiveness principle;[44] the arguments supporting the inventiveness that were accepted in the past, might now be rejected as being obvious to a person skilled in the art. This means that, in a sense, biotechnology industry is a victim of its own success.[45]

2.3. Industrial application and utility

For an invention to be patentable in the European Union, it must be susceptible of industrial application. According to Article 57 EPC, "an invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.",[46] which EPO has later clarified by stating that the application's description should indicate explicitly how the invention can be exploited in industry.[47] Also, the utility requirement in the United States is stated in the 35 U.S.C. § 101, according to which "whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor ".[48]

[41] Title 35 of the United States Code § 103.
[42] Barton, J. (2003). Non-obviousness, *The Journal of Law and Technology,* 43(3), 475-695.
[43] *Ibid.*
[44] Storz, U. (2014). *Supra nota* 26, p. 11-12.
[45] *Ibid.*
[46] European Patent Convention of 5 October 1973, Article 57.
[47] European Patent Office, Guidelines for Examination, 4.9. Industrial application, Available at: https://www.epo.org/law-practice/legal-texts/html/guidelines/e/f_ii_4_9.htm, 25.3.2020.
[48] Title 35 of the United States Code § 101.

Furthermore, the US patent system sets forth the requirements of written description, enablement and best mode in the 35 U.S.C. § 112 pre-AIA: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention".[49] These three requirements are separate and distinct from each other. According to the case law, a patent specification must sufficiently precisely describe the invention in order to a person skilled in the art to understand that the inventor possessed the subject matter claimed, referring to the written description requirement.[50] The enablement requirement, on the other hand, includes teaching person skilled in the art how to produce and use the invention.[51] The case law indicates that the best mode requirement was codified in order to prevent some people to obtain patent protection without making a full disclosure and retaining the best for themselves.[52] Even though the best mode requirement was removed from the list of possible invalidity defenses under AIA, it is still important to meet the best mode requirement because if it is not disclosed, it will not be a part of the patent application. Furthermore, it might result in violation of the written description requirement.

[49] Title 35 of the United States Code § 112.
[50] The US Court of Appeals for the Federal Circuit, 598 F.3d 1336, 1341 (2010), *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*
[51] *Ibid.*
[52] The US Court of Appeals for the Federal Circuit, 52 F.3d 1043, 1050 (1995), *Glaxo Inc. v. Novopharm Ltd.*

3. BIOTECHNOLOGY PATENTS

Biotechnological inventions have a significant role in saving, improving and extending human life. Regardless of this, patenting these scientific inventions can be a very complicated and time-consuming process as there are usually highly controversial ethical issues related. In addition to the moral concerns, the patentability issues around biological materials can be related to the conflict on whether the invention is merely a creation of nature that occurs naturally and, therefore, ineligible for a patent.[53] On one hand, it can be argued that biological materials are discoveries and, therefore, excluded from patentability. On the other hand, certain biological materials can be regarded as patent-eligible human-made inventions. Another issue is related to the uncertainty about whether the patent covers also the possible changes in the biological material that is capable of changing and reproducing itself. From the point of view of patentability of the hESC research exclusively, the most important question has been whether genes and gene editing are patentable.[54]

3.1. Patenting biotechnological inventions in the European Union

Like other types of inventions, also biotechnological inventions must be new, involve an inventive step and be susceptible of industrial application, in order to be patentable in the EU. The law governing the patentability of stem cell technologies in the EU is structured around the EPC and the Directive 98/44/EC on the legal protection of biotechnological inventions (Biotech Directive), as well as the case law from the European Court of Justice (ECJ) and the EPO, and the legislation of the Member States. The significance of the Biotech Directive is indicated by the fact that the patentability requirements under the Biotech Directive are also transposed into the EPC for harmonization purposes.

[53] Davey, S. et al. (2015). Interfacing of Science, Medicine and Law: The Stem Cell Patent Controversy in the United States and the European Union, *Frontiers in Cell and Developmental Biology*, 3(71), 1-5.
[54] *Ibid.*

3.1.1. Morality clause

The European patent system takes a morality-based approach to the patentability of life science inventions and biotechnological research should be conducted with respect towards the dignity of human life, which is codified in the Biotech Directive Article 6(1): "Inventions shall be considered unpatentable where their commercial exploitation would be contrary to *ordre public* or morality". Also, the exclusion from patentability on grounds of public order or morality was codified in Article 53(a) EPC already in its original form in 1973, which now stands as follows; "European patents shall not be granted in respect of inventions the commercial exploitation of which would be contrary to *ordre public* or morality", (hereinafter 'morality clause'). Nevertheless, the morality clause does not provide any definition for the concepts of public order or morality, which has led to the fact that these concepts have been clarified by case law over time. According to the practice of the EPO, the concept of public order covers also the protection of public security, the physical integrity of individuals as part of society, as well as the protection of the environment. Furthermore, the moral aspects should be examined based on the accepted norms in a particular culture, and if the exploitation of invention is not in conformity with these norms, it should be excluded from patentability on moral grounds.[55]

It is affirmed in the case law of the ECJ as well as the EPO that any invention requiring the prior destruction of human embryo or their use as a base material, whatever the stage at which it takes place, is excluded from patentability on grounds of morality. The Enlarged Board of Appeal of the European Patent Office (EBA) has outlined in its decision in *WARF*, issued in 2008 that a patent under the EPC cannot be granted for an invention which necessarily involves the use and destruction of human embryos, however, leaving open the possibility of patenting inventions that use publicly available hESCs that are derived from cell lines.[56] The non-patentability of inventions requiring the prior destruction of human embryo was later confirmed in the decision of the Technical Board of Appeal of the European Patent Office (TBA), *Culturing Stem Cells/TECHNION*, issued in 2014, even though the patent was first refused because the cell lines were not publicly available at the filing date of the application. Later, the patent was refused on grounds of morality by making use of publicly available hESC lines which were derived by a process resulting in the destruction of human embryos.[57] This conformed the earlier practice of the

[55] The Technical Board of Appeal of the European Patent Office, T 356/93, 21.2.1995.
[56] Mahalatchimy, A. et al. (2015). The impact of European embryonic stem cell patent decisions on research strategies, *Nature Biotechnology*, 33(1), 41-43.
[57] The Technical Board of Appeal of the European Patent Office, T 2221/10, 4.2.2014.

ECJ in its landmark decision *Oliver Brüstle v Greenpeace,* where it was also held that inventions that require the prior destruction of human embryo are non-patentable, however, *TECHNION* is seen as closing the door which was left open in *WARF*.[58] After being confirmed in two distinct legal frameworks, it is argued that the exclusion posing an ethical barrier to patentability is a certainty in the EU.[59]

3.1.2. Embryo exclusion

Besides the morality clause, "uses of human embryos for industrial or commercial purposes" are considered unpatentable, as stated in the Biotech Directive Article 6(2)(c) and the EPC Rule 28(c), (hereinafter 'embryo exclusion'). The patenting of ESCs that are totipotent, is prohibited based on the embryo exclusion and the subject matter exclusion, as they belong to a stage in the formation of the human body, but the patenting of pluripotent ESCs has been a more complex issue.[60] The terms of human embryo and the use for industrial or commercial purposes have later been clarified by case law. In the *Brüstle* decision, which concerned a patent application on isolated and purified neural precursor cells processed from ESC and removed at the blastocyst stage, the embryo exclusion was also set to cover the use for purposes of scientific research, allowing only the use for therapeutic and diagnostic purposes to be patentable on certain conditions.[61] The later practice of EPO has indicated that also a process for recovering pluripotent ESCs from blastocyst without destroying the embryo, for industrial or commercial purposes, is in contravene with the embryo exclusion.[62]

Both the ECJ as well as the EPO have interpreted the term of human embryo broadly in their case law. In *Brüstle,* it was held that "any human ovum must, as soon as fertilized, be regarded as a 'human embryo' if that fertilization is such as to commence the process of development of a human being".[63] Therefore, the capacity to develop into a human being was highlighted. Also, the view rejected earlier in *WARF*, according to which an embryo comes into being 14 days after fertilization,[64] was rejected also in *Brüstle*,[65] allowing a broader interpretation for the term.

[58] Mahalatchimy, A. et al. (2015). *Supra nota* 56.
[59] *Ibid.*
[60] Minssen, T., Nordberg, A. (2015). The evolution of the CJEU's case law on stem cell patents: Context, outcome and implications of Case C-364/13 International Stem Cell Corporation. *Nordic Intellectual Property Law Review,* 5, 493-503.
[61] The European Court of Justice, C-34/10, 18.10.2011, *Oliver Brüstle vs Greenpeace*, point 53(2).
[62] The Technical Board of Appeal of the European Patent Office, T 1836/10, 9.4.2013.
[63] The European Court of Justice, C-34/10, 18.10.2011, *Oliver Brüstle vs Greenpeace.*
[64] The Enlarged Board of Appeal of the European Patent Office, G 2/06, 25.11.2008, point 20.
[65] The European Court of Justice, C-34/10, 18.10.2011, *Oliver Brüstle vs Greenpeace*, point 53(1).

At the time, the broad interpretation of human embryo accepted by the ECJ in the case of *Brüstle* raised certain concerns about the patentability of those human stem cells that do not have the potential to develop into a human being.[66] In 2014, the ECJ issued its decision on the case of *International Stem Cell Corporation v Comptroller General (ISCC)*, which concerned patentability of those human stem cells that do not require the prior destruction of an embryo and do not have the inherent capacity to develop into a human being, such as human parthenogenetic stem cells (hpSCs), or induced pluripotent stem cells (iPSCs). In *ISCC*, it was stated that the moral restrictions apply only to such cells derived from embryos that have the "inherent capacity to develop into a human being",[67] providing an ethically justifiable leeway for patenting of those human stem cells that do not require the prior destruction of an embryo nor have the inherent capacity to develop into a human being, such as hpSCs and iPSCs.[68] Even though the *ISCC* is generally seen as a clarification for the broad interpretation of human embryo established in *Brüstle*, another interesting perspective has been introduced, which considers whether *ISCC* should be seen as an exception to *Brüstle* or as creating a wider reversal of jurisprudence,[69] as those inventions that were regarded unpatentable under *Brüstle* as giving rise to human embryos, might be considered patentable under *ISCC.* On the other hand, it has been suggested that the extensive interpretation of human embryo would imply that any invention based on hESCs could not be patented,[70] even though the legal state on this part is still unclear. It is suggested that the *ISCC* should be seen as a clarification that narrows the extent of the embryo exclusion.[71]

3.2. Patenting biotechnological inventions in the United States

The patentability requirements under the 35 USC §101 apply to biotechnological inventions as well, therefore, patent-eligible biotechnological invention is "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof".[72] In general, the utility requirement is not problematic from the point of view of stem cell patents in the United States, however, it is important to acknowledge that it differs from the requirement of industrial

[66] Minssen, T., Nordberg, A. (2015). *Supra nota* 60, 495.
[67] The European Court of Justice, C-364/13, 18.12.2014, *International Stem Cell Corporation v Comptroller General*, point 39.
[68] Minssen, T., Nordberg, A. (2015). *Supra nota* 60, 494–495.
[69] Mahalatchimy, A., Wong, A. (2018). Human stem cells patents-Emerging issues and challenges in Europe, United States, China, and Japan, *The Journal of World Intellectual Property*, 21(5-6), 326-355.
[70] *Ibid.*
[71] *Ibid.*
[72] Title 35 of the United States Code § 101.

applicability, which renders unpatentable certain types of methods that are not industrially applicable. Compared to the morality-based approach adopted by the EU, the United States' approach to the patentability of hESCs is different, as the US patent system does not provide a similar morality clause as a restriction.[73] Furthermore, the US patent system provides no statutory exemption for the patentability of stem cells, even though according to the AIA, "notwithstanding any other provision of law, no patent may issue on a claim directed to or encompassing a human organism".[74]

3.2.1. Judicial exception of natural phenomena

The patentability requirements under §101 have been clarified by the judicial exceptions following the case law of the US Supreme Court.[75] In order a biotechnological invention to be patentable in the US, it must not fall under any of the categories of judicial exceptions, the most relevant of which is the exception of natural phenomena. The meaning of this judicial exception was clarified in the landmark case of the US Supreme Court from 1980, *Diamond v. Chakrabarty*, which concerned the patentability of genetically engineered bacterium capable of breaking down multiple components of crude oil. In this case, the Court decided that a patent may be obtained on "anything under the sun that is made by man". It concluded that an invention cannot be excluded from patent-eligible subject matter under the §101 merely based on the fact that it is living subject matter, therefore, an invention consisting of living subject matter is not automatically cast into the judicial exception of natural phenomena.[76] In another case providing guidance for patent-eligibility of natural products, *In re Bergy*, it was similarly held that the biologically pure culture does not fall under the category of products of nature and the patentability is not affected by the fact that the micro-organism is alive.[77] Also, it is argued that the Court's decision in *In re Bergy* was an important factor in opening doors for patent protection for stem cell inventions, including ESCs derived from animals and, later on, hESCs.[78] Further, a principle established in the Federal Circuit's judgment in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, increased the patent scope to include anything that produces "a useful, concrete and tangible result",[79] which

[73] Mahalatchimy, A., Wong, A. (2018). *Supra nota* 69.
[74] Leahy–Smith America Invents Act (AIA), Pub. L. 112-29, sec. 33(a), 125 Stat. 284.
[75] The U.S. Supreme Court, 450 U.S. 175, 3.3.1981, *Diamond v. Diehr.*
[76] The U.S. Supreme Court, 447 U.S. 303, 16.6.1980, *Diamond v. Chakrabarty.*
[77] The U.S. Court of Customs and Patent Appeals, 596 F.2d 952, 29.3.1979, *In re Bergy*.
[78] Fendrick, S., Zuhn, D. (2015). Patentability of Stem Cells in the United States, *Cold Spring Harbor Perspectives in Medicine*, 5(12), 1-7.
[79] The U.S. Court of Appeals for the Federal Circuit, 149 F.3d 1368, 23.7.1998, *State Street Bank and Trust Company v. Signature Financial Group, Inc.*

gave a great advantage to many patent applicants in the field of biotechnology at that time.[80] Even before *Chakrabarty*, it has been established in the practice of the Court that biotechnological inventions that do not possess different characteristics than those found in nature, fall under the category of natural phenomena.[81] *Chakrabarty* is seen as removing barriers to patenting of biotechnological inventions and allowing the wide-scale development of biotech industry,[82] and it is argued that the broad view of patent-eligibility adopted in this decision allowed the United States to be at the cutting edge of the development of the biotechnology industry at least for the following three decades.[83]

3.2.2. Mayo-Myriad Guidance

In order to examine the patent-eligibility under the §101, the Court created a two-part analytical framework in the landmark case of *Mayo Collaborative Services v. Prometheus Labs*, which included examining whether the patent claim is directed to any of the judicial exceptions – if not, then the invention is patent-eligible under the §101. However, if it is directed to any of the judicial exceptions, it must be examined whether the claim is 'significantly more' than the judicial exception, in order to alter the claim patent-eligible.[84] The Court decided in *Mayo* that a process of determining the effects of a particular dosage of drug in the subject's blood, even though it takes a human action to trigger, was "well-understood, routine and conventional", falling into the judicial exception of laws of nature. The Court's decision in *Mayo* was the first to restrict the extensive view of patent-eligibility under the §101, while providing a significant change to the broad view of patent-eligibility adopted in *Chakrabarty*, where it was held that a patent may be obtained on anything under the sun that is made by man. It is still suggested that the application of the *Mayo* framework is not settling the unclarity of patent-eligible subject matter and has resulted in unpredictable outcomes.[85] Moreover, *Mayo* raised concerns especially about patentability of biotechnological inventions that involve methods of detection, diagnosis and treatment,[86] even though it was argued to have significance for patent-eligibility of inventions in

[80] Nicol, D. et al. (2019). International Divergence in Gene Patenting, *Annual Review of Genomics and Human Genetics*, 20, 519-541.
[81] The U.S. Supreme Court, 333 U.S. 127, 16.2.1948, *Funk Bros. Seed Co. v. Kalo Inoculant Co.*
[82] Medlock, N., Robinson, D. (2005). Diamond v. Chakrabarty: A Retrospective on 25 Years of Biotech Patents, *Intellectual Property & Technology Law Journal*, 17(10), 12-15.
[83] *Ibid.*
[84] The U.S. Supreme Court, 566 U.S. 66, 20.3.2012, *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*
[85] Aboy, M. (2020). One year after Vanda, are diagnostics patents transforming into methods of treatment to overcome Mayo-based rejections?, Nature Biotechnology, 38(3), 279-283.
[86] *Ibid.*

many fields.[87] In another landmark case of the US Supreme Court, *Association for Molecular Pathology v. Myriad Genetics*, the Court expanded this legal framework to concern also the judicial exception of natural phenomena. In the *Myriad* case, the Court held that naturally occurring DNA segments that are isolated from their natural environment, are excluded from patent-eligible subject matter on the grounds of being products of nature and, therefore, falling under the category of natural phenomena.[88] The Court's decision still indicated that complementary DNA, which does not occur in nature, could be regarded as patent-eligible subject matter.[89]

Following the Supreme Court's decisions in *Mayo* and *Myriad*, the U.S. Patent and Trademark office (USPTO) issued a memorandum "Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products", (hereinafter 'the Mayo-Myriad Guidance'), implementing a new procedure for assessing the patent-eligibility under the §101. The procedure included analyzing; 1) whether the invention is directed to any of the statutory patent-eligible subject matter categories, 2) whether the patent claim falls under any of the judicial exceptions, and – if yes, 3) whether the claim as a whole recites something 'significantly different' than the judicial exception.[90] Even though the decisions in *Mayo* and *Myriad* cases are directed to diagnostic methods, their significance has been emphasized applying to a wider range of subject matter. Further, the Mayo-Myriad Guidance does not explicitly identify stem cells, but it is argued that the breadth of the Guidance would indicate that also stem cells are included.[91] Compared to the *Chakrabarty*, where the patentability of genetically engineered micro-organisms was confirmed, in *Myriad* it was held that "separating the gene from its surrounding genetic material is not an act of invention",[92] significantly changing the patent-eligibility landscape by narrowing the scope of patent protection of many biotechnological inventions, including stem cell patents. Moreover, it is argued that both *Mayo* and *Myriad* have rendered molecular tests unpatentable and this way undermining the possibilities to improve methods of detection, diagnosis and treatment in medicine.[93] As a result, complementary DNA

[87] Morrison, A. (2012). Mayo v. Prometheus: Patent Eligibility of Claims Covering Natural Laws, *The Colorado Lawyer*, 41(7), 77-84.
[88] The U.S. Supreme Court, 569 U.S. 576, 13.6.2013, *Association for Molecular Pathology v. Myriad Genetics, Inc.*
[89] Morrison, A. (2012). *Supra nota* 87.
[90] Fendrick, S., Zuhn, D. (2015). *Supra nota* 78.
[91] *Ibid.*
[92] The U.S. Supreme Court, 569 U.S. 576, 13.6.2013, *Association for Molecular Pathology v. Myriad Genetics, Inc.*
[93] Liddicoat, J., Liddell, K., Aboy, M. (2019). The Effects of Myriad and Mayo on Molecular Test Development in the US and Europe: Interviews from the Frontline. *The University of Cambridge Faculty of Law Legal Studies Research Paper Series*, 33, 1-34.

could be patentable whereas isolated DNA could not,[94] but the extent of human-made alteration that is needed for a stem cell not to be considered an isolated form, is not defined.[95]

This was later confirmed in *Ariosa Diagnostics Inc. v. Sequenom Inc.*, where it was held that a method of detecting cell-free fetal DNA, which is a naturally occurring DNA that circulates in the blood stream of an expecting mother, is excluded from patentability as representing a natural phenomenon and not fulfilling the criteria of non-obviousness set in the 35 U.S.C. § 103.[96] The significance of *Ariosa* has been highlighted, especially from the point of view of biotechnology inventions, as it confirms the non-patentability of naturally occurring DNA segments that are isolated from their natural environment, previously established in the *Myriad* case.[97] On the other hand, in *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals*, it was held that a method of treatment where the drug dosage is adjusted based on the patient's genotype for lowering the risk of possible side effects, is not directed to a judicial exception.[98] The key difference compared to *Mayo* was the fact that *Vanda* applied the relationship of the patient's genotype and the risk of possible side effects, and claimed the additional step of adjusting the drug dosage as a part of directing the treatment method, whereas *Mayo* focused on diagnostic test which involved the adjustment of the drug dosage as a part of the diagnosis.[99] The further influence of *Vanda* decision remains to be seen, although it is argued to have the potential to develop the patent-eligible subject matter and extend the patentability of those biotechnological inventions affected by *Mayo.*[100]

[94] The U.S. Supreme Court, 569 U.S. 576, 13.6.2013, *Association for Molecular Pathology v. Myriad Genetics, Inc.*
[95] Davey, S. et al. (2015). *Supra nota* 53.
[96] The U.S. Court of Appeals for the Federal Circuit, 788 F.3d 1371, 12.6.2015, *Ariosa Diagnostics Inc. v. Sequenom Inc.*
[97] Mahalatchimy, A., Wong, A. (2018). *Supra nota* 69.
[98] The U.S. Court of Appeals for the Federal Circuit, 887 F.3d 1117, 13.4.2018, *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Ltd.*
[99] Memorandum of The United States Patent and Trademark Office, Recent Subject Matter Eligibility Decision: Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals, available at: https://www.uspto.gov/sites/default/files/documents/memo-vanda-20180607.PDF, 29.3.2020.
[100] Aboy, M. (2020). *Supra nota* 85.

4. THE FUTURE OF STEM CELL PATENTS

4.1. Implications of the recent case law in the European Union

In light of the European case law on patentability of life science inventions, the European patent law excludes the patentability of inventions that are obtained by destruction of human embryos, including the use of publicly available cell lines derived by a process destroying human embryos.[101] Those human stem cells that have the inherent capacity to develop into a human being, are excluded from patentability,[102] whereas the ones that do not have the inherent capacity to develop into a human being, such as hpSCs and iPSCs, might be patent-eligible.[103] Also, processes for human cloning such as techniques of embryo splitting, designed to create a human being with the same genetic information as another human being, are considered non-patentable.[104] Furthermore, inventions that include hESCs for modifying the human germline genetic identity, or to create chimeras, i.e. combination of cells or tissues for two or more different species, are excluded from patentability under the European patent legislation.[105] The uses of human embryos for commercial or industrial purposes,[106] including scientific research,[107] are excluded on grounds of the embryo exclusion, but the use of hESCs for therapeutic or diagnostic purposes which is applied to the human embryo and is useful to it, could be patentable.[108] Considering the inventions that do not involve the destruction of an embryo, there is no consensus on whether the inventor should prove that the invention does not involve the prior destruction, or whether a general claim

[101] The Technical Board of Appeal of the European Patent Office, T 2221/10, 4.2.2014.
[102] The European Court of Justice, C-34/10, 18.10.2011, *Oliver Brüstle v Greenpeace*.
[103] The European Court of Justice, C-364/13, 18.12.2014, *International Stem Cell Corporation v Comptroller General*.
[104] European Patent Convention of 5 October 1973, Rule 28.
[105] *Ibid.*
[106] European Patent Convention of 5 October 1973, Rule 28(c).
[107] The European Court of Justice, C-34/10, 18.10.2011, *Oliver Brüstle v Greenpeace*.
[108] *Ibid.*

of non-destruction of embryos is sufficient, resulting in the fact that it may be easier to obtain a patent in certain European countries than the others.[109]

4.1.1. The 'inherent capacity to develop into a human being' as an indicator of subject matter eligibility

As a result, the legal state of the patentability of certain human stem cells that do not have the inherent capacity to develop into a human being, such as hpSCs and iPSCs, is still unclear. The non-patentability of human embryos that require prior destruction, whatever stage it takes place, can be justified by the following assumption: human embryos have human dignity, which would be violated by their destruction for commercial purposes.[110] Following the ruling in *ISCC*, hpSCs do not fall under the patentability exclusion because human parthenotes do not have the inherent capacity, i.e. 'totipotency', to develop into a human being,[111] and therefore, are not human embryos. Following this reasoning, if human parthenotes are not regarded as human embryos, they do not have human dignity, and the same reasoning would apply to iPSCs as well.[112] However, the expression 'inherent capacity to develop into a human being' is open to interpretation, for example, the stage of development that is required for an entity to have the capacity to develop into a human being, is not defined. This issue could be approached by classifying human embryos according to their ability to develop into a specific stage of development, for example birth. However, if this was the case, most of the entities that are currently regarded as human embryos, could not be described as such anymore.[113] Therefore, it would be better to classify them according to their typical than actual development, for example, human parthenotes are not typically able to develop into a human being, which is why they are not regarded as human embryos.[114] In any case, classification based on the stage of development is problematic as there is no scientific proof how far human parthenotes can in fact develop because this kind of research is prohibited on grounds of reproductive cloning.[115] According to the current scientific knowledge, parthenotes can develop to the blastocyst stage. On the other hand, it has been shown that animal parthenotes can develop into adulthood, though, with a shorter life expectancy, which would indicate that also human

[109] Mahalatchimy, A., Wong, A. (2018). *Supra nota* 69.
[110] Schickl, H., Braun, M., Dabrock, P. (2017). Ways Out of the Patenting Prohibition? Human Parthenogenetic and Induced Pluripotent Stem Cells, *Bioethics*, 31(5), 409-417.
[111] The European Court of Justice, C-364/13, 18.12.2014, *International Stem Cell Corporation v Comptroller General*.
[112] Schickl, H., Braun, M., Dabrock, P. (2017). *Supra nota* 110.
[113] *Ibid.*
[114] *Ibid.*
[115] Moradi, S. et al. (2019). Research and therapy with induced pluripotent stem cells (iPSCs): social, legal, and ethical considerations, *Stem Cell Research & Therapy*, 10(1), 1-13.

parthenotes might be able to develop until birth.[116] Further, it is not defined what capacity to develop into a human being can be regarded as inherent. In *Brüstle*, the ECJ distinguished a human parthenote and a parthenote objected to additional manipulation, meaning that a human parthenote is not a human embryo as it requires additional manipulation to reach the required stage of development. On the other hand, even human embryos created in vitro require additional manipulation to be able to develop into a human being, which leads to the question regarding the amount of external manipulation that is allowed for the capacity to develop into a human being to be still regarded as inherent.[117]

4.2. Implications of the Mayo-Myriad Guidance in light of the stem cell patents

In general, the US patent system is seen as having a more liberal approach to patenting life science inventions, compared to the European patent system. The decisions of the Supreme Court, such as *Chakrabarty*, have indicated a broad view of patent-eligible subject matter and the lack of ethical barrier to patenting has allowed granting a wide scale of biotechnology patents, including hESC patents, in the United States.[118] The patent-eligibility landscape was changed significantly along the *Mayo* and *Myriad* decisions, which narrowed the scope of patent-eligible subject matter.[119] To demonstrate the significance of these cases, they were already at the time recognized as imposing a threat to the patentability of stem cells,[120] and even argued to impose an ethical barrier to patenting, similar to the European patent system's morality clause.[121] In any case, it is not misleading to conclude that the decisions in *Mayo* and *Myriad* resulted in far-reaching impacts for the biotechnology industry and established a certain turning point for the patentability of life science inventions, including stem cell inventions, in the United States.[122] Nevertheless, different observations have been pointed out on the further implications of these decisions. On one hand, these decisions have been found to render the US patent system's liberal hESC policies to approach the strict patent policies of the European patent system.[123] On the other hand, it has been suggested

[116] Schickl, H., Braun, M., Dabrock, P. (2017). *Supra nota* 110.
[117] *Ibid.*
[118] Woessner, WD., Chadwick RA. (2019). Section 101: What's Left To Patent In The Life Sciences After Myriad, Mayo, And Alice?, *Journal of the Patent and Trademark Office Society*, 101(1), 121-176.
[119] *Ibid.*
[120] Fendrick, S., Zuhn, D. (2015). *Supra nota* 78.
[121] Mahalatchimy, A. et al. (2015). *Supra nota* 56.
[122] Aboy, M. et al. (2019). Mayo's impact on patent applications related to biotechnology, diagnostics and personalized medicine, *Nature Biotechnology*, 37(5), 513–518.
[123] Mahalatchimy, A., Wong, A. (2018). *Supra nota* 69.

that these decisions have rendered the US patent law on patent-eligible subject matter to diverge from the European patent law, [124] which allows a broader range of patentable subject matter, including elements isolated from the human body or produced by means of a technical process, including the sequence or partial sequence of a gene, even if the structure of that element is identical to that of a natural element.[125] In any case, the US patent laws governing the subject matter eligibility are still unsettled, though, the applications directed to natural stem cells and their applications have been rejected. In light of the current legal state, the major issues related to stem cell patents concern the expanded scope of ineligible subject matter, as well as overcoming the obviousness rejections. After *Myriad* it can be said that stem cells, either embryonic or adult cells, are not patentable if there are no distinctive structural, functional or other properties from the natural cells in human body.[126] Concerning other human stem cells, such as iPSCs, also they face the risk of falling under patent-ineligible subject matter if the cells are indistinguishable from naturally-occurring stem cells. Regenerated tissues, on the other hand, are likely to be patentable as they differ from the original tissue. Furthermore, the methods for stem cell production, maintenance and differentiation remain patent-eligible, assuming they fulfill the 'significantly more' requirement set forth in the Mayo-Myriad Guidance.[127] Even though the isolated DNA is in principle classified as unpatentable subject matter following the *Myriad* decision, a patent has been granted for an invention claiming isolated stem cells, because the applicant was able to disclose a constituent that does not exist in the natural counterpart of the invention.[128]

4.2.1. *Vanda* as a solution in overcoming *Mayo*-based rejections

The Federal Circuit's recent decision in *Vanda* has been argued to open a new door for biotechnological inventions affected by the earlier case law, especially *Mayo*. Even though the claims in both cases are very similar, patent applications that were rejected as directed to a method of diagnosis under the *Mayo* framework, could seek to amend into a claim for a method of treatment, presuming the view of the Federal Circuit in *Vanda* is upheld by the Supreme Court.[129] To illustrate, a recent study indicates the effectiveness of claim amendments based on *Vanda* in overcoming the *Mayo*-based rejections, by a patent application allowance rate of 84,2%. Moreover,

[124] Liddicoat, J., Liddell, K., Aboy, M. (2019). *Supra nota* 93.
[125] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, Article 5.
[126] Mahalatchimy, A., Wong, A. (2018). *Supra nota* 69.
[127] *Ibid.*
[128] US Patent for Postnatal stem cells and uses thereof Patent 9,175,264, available at: https://patents.justia.com/patent/9175264, 24.4.2020.
[129] Aboy, M. et al. (2019). *Supra nota* 122.

the results indicate that in order to overcome the *Mayo*-based rejections, a large scale of methods of diagnostic claims are being amended to method of treatment claims.[130]

However, *Vanda* has also raised certain concerns about its legal ramifications as its further significance remains to be seen.[131] Further, it is argued that for diagnostic companies, *Vanda* solution is inadequate for overcoming *Mayo*-based rejections, facing the risk of divided infringement as the method of treatment claim or administration step cannot be attributed to the defendant diagnostic company.[132] As a result, the continuity of the Mayo-Myriad Guidance, as well as the *Vanda* solution have been questioned, even the possibility of changing or abandoning the *Mayo* framework has been pointed out. However, there is no consensus on whether the issue is emerging from the legal state adopted after *Mayo* and *Myriad*, or whether it is the legal refinements following the *Vanda* case, as there are highly dissenting opinions. To illustrate the controversy, a draft bill announced in 2019 suggesting the bypassing of judicial exceptions to subject matter eligibility, including the Supreme Court decisions in *Mayo* and *Myriad*, received a whole spectrum of reactions.[133]

4.3. 'Directed to' and 'as such' as indicators of patent claim eligibility

In respect of the legal state following the *Vanda* solution, it is important to notice that it is concentrated on the significance of the words 'directed to'. If a patent claim applies natural law in the treatment method, it is examined, whether the claim is directed to a judicial exception of laws of nature. Further, it will be examined, at which point a patent claim integrating the laws of nature into patentable invention, is directed to a patent-eligible invention instead. The European approach, on the other hand, is not stressed with a similar evaluation, which is why it has been considered more appealing by some parties.[134] Furthermore, the European patent law gives priority for the words 'as such', for example, claims shall not be granted to "discoveries or scientific theories…as such",[135] which similarly as 'directed to', is open to interpretation. In any case, the case law of the EPO indicates that such a claim including any technical element is sufficient to render the claim

[130] Aboy, M. (2020). *Supra nota* 85.
[131] *Ibid.*
[132] Holman, C. (2018). Vanda v. West-Ward Pharmaceuticals: Good News for the Patent Eligibility of Diagnostics and Personalized Medicine, with Some Important Caveats, *Biotechnology Law Report*, 37(3), 117-125.
[133] Aboy, M. (2020). *Supra nota* 85.
[134] *Ibid.*
[135] European Patent Convention of 5 October 1973, Article 52.

patent-eligible. The European approach therefore highlights the technical element of the patent claim, which is argued to be less demanding to achieve compared to the US approach that is to prove the claim as a whole recites something significantly different than the judicial exception.[136] To demonstrate, the non-patentability of naturally occurring DNA segments that are isolated from their natural environment, has been conformed in the case law of the US Supreme Court a few times.[137] In comparison, the UK Court has decided in a similar case that the claims were patentable as they did not exist naturally and were technical in nature.[138]

[136] Aboy, M. (2020). *Supra nota* 85.
[137] The U.S. Court of Appeals for the Federal Circuit, 788 F.3d 1371, 12.6.2015, *Ariosa Diagnostics Inc. v. Sequenom Inc.*
[138] The UK Patents Court, EWHC 1726 (Pat), 16.12.2016.

CONCLUSION

The aim of this research was to present a comparative analysis of the development of patenting living matter, especially focusing on human embryonic stem cells, in the European Union and in the United States of America, by examining their development processes both individually, as well as together, to point out similarities and differences, and to make discoveries by their comparison.

The first question that was researched into, dealt with the legal requirements for the patentability of biotechnological inventions. As this research has provided, the controversy between respecting human dignity, and on the other hand, protecting biotechnological research, has described the development of patenting life science inventions. Using embryonic stem cells, especially those of human origin, raises multiple ethical and political concerns related to the onset of human personhood, human reproduction and the destruction and creation of embryos specifically for research purposes, resulting in the fact that the hESC research should be conducted fulfilling the moral requirements and respecting the dignity of human life. On other other hand, supporting innovation by allowing patent rights for the inventions is necessary for the biotechnology industry to develop. The legal starting point for the patentability has been open to interpretation by the case law and, in addition, as the development process on the biotechnology industry is ongoing, the case law has had a significant importance on patenting inventions on this area of research. Also, the general moral, as well as political, opinions and standpoints will change and develop throughout times, or adapt due to certain events. Finding the balance between protecting the biotechnological innovation and, while doing so, fulfilling the moral requirements in order to establish the legal requirements for the patentability of life science inventions, is a complex and time-consuming process, which, in a sense, might never be completely finished. In any case, it can be concluded that the case law both in the European Union, as well as in the United States, has had a significant importance in the development of the patentability of hESC research.

The conclusion, as stated above, led to the second research question which focused on the more detailed importance and consequences of the case law on the area of patentability of biotechnological inventions in the European Union and in the United States and their possible interaction. In general, the legislation concerning the patentability of biotechnological inventions has been open to interpretation and, even though certain ground rules for the patentability are established by the legislation, the most remarkable legal turning points have been established by the case law. In addition, the case law has had a significant importance in clarifying certain terms and concepts. Moreover, it can be said that the general moral and political opinions emerge from the case law, which have had a great importance in modifying the patentability requirements of life science inventions as they are today. Also, this research described the current legal state of the patentability of the hESC research and pointed out certain issues and challenges emerging from the current situation. It remains to be seen, how the most recent judicial decision will be applied in the future and what is their greater impact for the patentability of biotechnological inventions. Finally, it can be stated that this bachelor thesis proved right the hypothesis of this research; the controversy on balancing the ethical aspects concerning the patentability of hESC research and, on the other hand, protecting the biotechnological innovation, have modified the patentability of innovations on this area of scientific research. However, further questions arise concerning the legal state of the patentability of biotechnological inventions as new discoveries are made, and new techniques are invented in this fast-developing area of research, which requires constantly developing regulation and case law.

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