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Balancing Innovation, '*Ordre Public*' and Morality in Human Germline Editing: A Call for More Nuanced Approaches in Patent Law

Duncan Matthews | ORCID: 0000-0002-8585-0711
Queen Mary Intellectual Property Research Institute (QMIPRI), Queen Mary University of London, 67–69 Lincoln's Inn Fields, London WC2A 3JB, UK
Corresponding author, e-mail: d.n.matthews@qmul.ac.uk

Timo Minssen | ORCID: 0000-0002-3286-4888
Centre for Advanced Studies in Biomedical Innovation Law (CeBIL), University of Copenhagen, Karen Blixens Plads 16, DK-2300 Copenhagen S, Denmark
timo.minssen@jur.ku.dk

Ana Nordberg | ORCID: 0000-0002-3009-1033
Faculty of Law, Lund University, Lilla Gråbrödersgatan 4–6, Lund, Sweden
ana.nordberg@jur.lu.se

Abstract

This article analyses the role that '*ordre public*' and morality exceptions can play in the granting of patents on inventions in the field of human germline editing and the consequences of this policy option. In order to provide the context for such an analysis, the article will, first, provide an overview of the current patent landscape for relevant genome editing technologies, drawing attention to recent patent disputes and, second, examine '*ordre public*' and morality exceptions under patent law in international, national and regional law, and the implications for innovation and access to novel treatments. The article argues that patent exceptions should not be used as a blunt policy instrument, nor interpreted in a way that is contrary to the patent system's overall objectives. The '*ordre public*' and morality based exceptions in the context of human germline editing should not be interpreted and applied in a way which results in outcomes counterproductive to the goal of balancing innovation with the protection of societal higher normative values. Instead, the application of the exception should be based on a sound understanding of both the underlying science as well as the broader

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ethical, social, and legal implications, thus enabling case-by-case decisions that provide the basis for patent claim amendments and nuanced purpose-bound protection. Further analysis and debate as to the role that such flexibilities can play in the context of genome editing technologies is therefore both necessary and desirable, and can be facilitated in the ways set out in this article.

Keywords

patent law – morality exception – genome editing – genome editing governance – law and ethics – CRISPR

1 Introduction

Genome editing technologies hold great potential for scientific research and society. Compared with previous technologies, they provide fast, efficient, precise, and relatively inexpensive tools to modify the cells of any living organism. Using genome editing techniques, cells of the body (somatic cells) can be modified, treating or potentially curing patients of chronic, lifelong illnesses. Editing the genome of human embryos can also repair the germline of human beings, eradicating hereditary diseases in new-born babies such as Duchenne muscular dystrophy, Huntington's Disease, beta thalassaemia and cystic fibrosis and creating resistance to life-threatening conditions for future generations.[1]

Genome editing offers bio-scientists a relatively simple tool to change any organism's deoxyribonucleic acid (DNA). This allows genetic material to be added, removed, or altered in particular locations in the genome. Several clinical trials have or are being conducted around the globe offering great hope for patients so far having very limited treatment options.[2]

1 For Duchenne muscular dystrophy see E.N. Olson, 'Toward the correction of muscular dystrophy by gene editing', *Proceedings of the National Academy of Sciences of the United States of America* 118 (22) (2021) e2004840117, https://doi.org/10.1073/pnas.2004840117; for cystic fybrosis, see G. Maule, D. Arosio and A. Cereseto, 'Gene Therapy for Cystic Fibrosis: Progress and Challenges of Genome Editing', *International Journal of Molecular Science* 21 (11) (2020) 3903, https://doi:10.3390/ijms21113903; for Huntington's Disease see T. Biswas, 'CRISPR in Huntington's Disease: Progress and Possibilities for Future Cure', *Synthego* (13 May 2021), available online at https://www.synthego.com/blog/crispr-in-huntingtons-disease.

2 For some examples of clinical trials see: H. Henderson, *CRISPR Clinical Trials: A 2021 Update* (3 March 2021), available online at https://innovativegenomics.org/news/crispr-clinical-trials-2021/.

The most commonly used genome editing techniques are zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs) and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). Each represents a type of engineered nuclease that can be used to recognise, bind, and cleave a specific sequence in the genome. In order to do so, ZFNs and TALENs require the creation of a custom protein for each targeted DNA sequence. Whereas ZFNs and TALENs are entirely protein based, CRISPR has both protein and ribonucleic acid (RNA) components, making it a simpler and less time-consuming process than ZFNs and TALENs CRISPR because the process requires only a short RNA sequence. More recently, new promising technologies, such as Rerotron Library Recombineering (RLR) have also emerged.[3]

Since 2012, CRISPR has been used in combination with Cas9 (CRISPR associated protein number 9, which plays a vital role in the natural immunological defence system of the body) to guide and cut DNA, and therefore editing a cell's genome. The CRISPR-Cas9 techniques, as well as follow-on technologies such as CRISPR-Cas 12a and CRIPR-Cas13, have provided a faster, cheaper, more accurate and more efficient method than other previously known genome editing techniques.[4] Yet, safety risks, ethical concerns and IP battles regarding the commercial control over the technology have also emerged due to the far-reaching implications and applications of the technology. Hence, genome editing also raises new challenges in terms of how governance systems regulate technologies.

This article argues that international organisations, policy makers and legislators need to pay greater consideration to the interface between patent policy, ethics, regulation and the governance of genome editing. Such consideration is crucial since the regulation of genome editing involves the critical public policy imperatives of avoiding unnecessary collective or individual risks, taking into account human rights, managing public expectations, ensuring fair and equitable access to the benefits of these new technologies' use, and acting in the public interest with regard to these potentially transformational healthcare technologies.

3 M.G. Schubert, D.B. Goodman, T.M. Wannier, D. Kaur, F. Farzadfard, T.K. Lu, S.L. Shipman and G.M. Church, 'High-throughput functional variant screens via in vivo production of single-stranded DNA', *Proceedings of the National Academy of Sciences of the United States of America* 118 (18) (2021) e2018181118, https://doi.org/10.1073/pnas.2018181118.

4 See also National Institutes of Health (NIH), *US. National Library of Medicine, 'Your Guide to Understanding Genetic Conditions: What Are Genome Editing and CRISPR-Cas9?'*, available online at https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting (accessed 30 March 2022).

On 12 July 2021 the World Health Organization (WHO) Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing published a set of reports entitled *Human Genome Editing: A Framework for Governance and Recommendations*.[5] The Expert Advisory Committee's *A Framework for Governance* highlights explicitly the role that patents and licences may play as an avenue for a form of governance of human genome editing. However, absent from the WHO Expert Advisory Committee's reports was either substantive discussion or recommendations on the role that morality exceptions can play in the granting of patents on certain inventions and the consequences of this policy option.

In collaboration with an international group of renowned patent law scholars, we published a response to the WHO Expert Advisory Committee's findings on 30 July 2021 and made explicit our recommendation, inter alia, that further consideration of the extent to which '*ordre public*' and morality exceptions in patent law impact on the sector.[6] In our research group's response, we have already highlighted the need for public debate and stated that it is a particularly important consideration for countries considering introducing or developing further guidance on the use of '*ordre public*' and morality exceptions to patentability in the area of genome editing. In this article we build on our previous response to the WHO Expert Advisory Committee's reports, undertaken with our colleagues, and propose a pragmatic way forward by way of our new and original contribution to the policy debate.

While it should be acknowledged that many of the issues considered in this article apply equally to somatic therapeutic uses (the cells of the body that are not involved in reproduction) and to agricultural or fisheries food production, human germline applications will remain the article's primary focus. We focus primarily on '*ordre public*' and morality issues concerning human germline editing, since in our view this specific application of genome editing technologies accords most closely and immediately with concerns about the patent policy implications in terms of the impacts on society outlined above.

Based on the premise that the patent system is an integral part of how governance systems regulate technologies, we believe that patent policy needs to

5 WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing, *Human Genome Editing: A Framework for Governance* (2021), available online at www.who.int/publications/i/item/9789240030060, iii (accessed 23 July 2021).

6 D. Matthews, A. Brown, E. Gambini, T. Minssen, A. Nordberg, J.S. Sherkow, J. Wested, E. van Zimmeren and A. McMahon, 'The Role of Patents and Licensing in the Governance of Human Genome Editing: A White Paper', *Queen Mary Law Research Paper No. 364/2021* (30 July 2021), available online at SSRN: https://ssrn.com/abstract=3896308.

be considered carefully whenever regulation of genome editing is being scrutinised. In essence, governance through patents contains three major discussions: first, whether patents should be granted to certain inventions; second, how to guarantee ethical exploitation of patent rights; and, third, the interface between the enjoyment of patent rights to reward innovation and a fair and equitable access to technologies.

This article focuses on the first of these discussions, and in particular the role that morality exceptions can play in the granting of patents on certain inventions and the consequences of this policy option. In order to provide the context for such an analysis, the article will, first, provide a contextualising overview of the current patent landscape for relevant genome editing technologies, and highlight recent patent disputes. Then, we examine the extent of '*ordre public*' and morality exceptions under the TRIPS Agreement and national/regional patent law, and the implications for innovation and access to novel treatments. It is followed by a discussion of the actual and potential impact of such provisions on the governance of genome edition technologies. We will also carve out potential avenues of how to deal with these dynamics in the future. This will allow us to draw policy conclusions.

2 The Current Patent Landscape for CRISPR Gene Editing Technologies

Right holders may assert their patent rights, i.e. negative exclusionary rights, in different ways and in accordance with applicable regulations and standards. Their strategy will depend on a range of factors, such as the ambitions and goals of rights holders, the nature and applications of the patented technology, the competitive environment, as well as the scope, significance and validity of relevant exclusivities.[7] So far, hundreds of patents, directed to genome editing technologies, have been granted by patent offices across the world, with many more applications still under examination.[8]

Moreover, many pending patent litigations and disputes over different aspects of genome editing technologies are currently unresolved, which has resulted in considerable legal uncertainty. In addition, it is important to note

7 Note that exclusivities may be protected and enforced through other forms of IP which may affect patent strategies.

8 See D. Kwon, *A Brief Guide to the Current CRISPR Landscape*, available online at www.the-scientist.com/news-opinion/a-brief-guide-to-the-current-crispr-landscape-66128 (accessed 27 July 2021).

that patents are also sought for other genome editing technologies, including meganucleases, ZFNs, TALENs, and fundamental gene editing tools, such as genome editing vectors.[9] This complexity resulted in a rich diversity of patents and models of technology transfer, but it has also resulted in competitive struggles over the control of the technologies at both the pre-grant and post-grant level.[10]

Against this background, any discussion regarding the role of patents in genome editing governance must carefully consider the rapidly evolving patent landscape, including information of the prevalent forms of patents claims, licensing models, patentees and regional differences around the globe. It is therefore important to continuously monitor the outcome of patent litigations and regulatory developments.

Several landscaping studies have been conducted in the area, mostly focusing on patents and revealing substantial global differences across the genome editing technology landscape.[11] A common finding appears to be that the number of patents and patent applications, the procedures for patent prosecution, as well as the question of patent ownership and the licensing of gene editing technologies, such as CRISPR, varies considerably in various patent systems. Accordingly, what can be claimed as patentable and on which terms — if at all — human genome editing technologies are licensed can differ across regions.[12]

Concerning the situation in the US, studies of patent data highlight fierce competition not only in CRISPR-related science, but also in the race to the patent office between the main academic rivals, i.e., the Broad Institute (of Harvard University and the Massachusetts Institute of Technology — MIT), which is the home institution of Feng Zhang et al., and the University of

9 For more details and a good overview of these technologies, see G.D. Graff and J.S. Sherkow, 'Models of Technology Transfer for Genome-Editing Technologies', *Annual Review of Genomics and Human Genetics* 21 (1) (2020) 509–534.

10 *Ibid.*

11 See, e.g., '2020 CRISPR Patent Landscape — Where Do We Stand?', *IPStudies*, available online at www.ipstudies.ch/2020/10/2020-crispr-patent-landscape-where-do-we-stand/ (accessed 27 July 2021); P. Ghosh, 'Patent Landscape of CRISPR/Cas', in: A. Bhattacharya, V. Parkhi and B. Char (eds.), *CRISPR/Cas Genome Editing. Concepts and Strategies in Plant Sciences* (Berlin: Springer, 2020), pp. 213–220; J. Martin-Laffon, M. Kuntz and A.E. Ricroch, 'Worldwide CRISPR Patent Landscape Shows Strong Geographical Biases', *Nature Biotechnology* 37 (6) (2019) 613–620; J.S. Sherkow, 'The CRISPR Patent Landscape: Past, Present, and Future', *CRISPR Journal* 1 (1) (2018) 5–9; see WIPO, 'Patent Landscape Reports by Other Organizations', available online at www.wipo.int/patentscope/en/programs/patent_landscapes/plrdb_search.jsp?territory_code=CH (accessed 27 July 2021).

12 *Ibid.*, '2020 CRISPR Patent Landscape — Where Do We Stand?'.

California, which employs Jennifer Doudna.[13] Furthermore, the datasets confirm that "both license their core CRISPR technology IP to a number of large industrial players, such as DuPont in agricultural applications, as well as to a set of pioneering CRISPR spin-offs primarily heading for therapeutic applications, namely Editas Medicine out from the Broad Institute, CRISPR Therapeutics initially founded by Emmanuelle Charpentier, and Intellia Therapeutics out from the University of California."[14]

3 Patent Battles in the US and Europe

Genome editing technologies have been subject to considerable and ongoing patent litigation concerning the ownership of such technologies. As a result, a highly contested global patent landscape has emerged, characterized by a considerable lack of legal certainty. The main dispute in this context in the United States (US) and Europe, relates to patent claims over CRISPR Cas-9 technologies asserted by University of California (UC) Berkeley (where Prof Doudna's team worked, and in collaboration with Prof Charpentier, now at Max Planck), and Broad Institute MIT and Harvard (involving a research team led by Prof Feng Zhang). While the ongoing patent battles over claims directed to CRISPR-Cas9 technology within the European and US patent system have probably attracted most attention, disputes over these patents are also raging in other countries and regions such as Asia and South America.[15] Many of these disputes have evolved around the issues of priority[16] and the novelty requirements. These proceedings are often inter-related and they are monitored carefully around the globe, since decisions on priority claims in e.g. the US or European patent systems, often have a significant effect on the outcomes in pending litigations in other countries.[17] In our previous paper, written with colleagues in response to the WHO Expert Advisory Committee on Developing

13 *Ibid.*

14 *Ibid.* For a discussion of the problems related to this complex licensing landscape see V.M. de Grandpré and F. Lozon, 'Making Sense of the Battle for the CRISPR-Cas9 Patent Rights', *Osler* (15 March 2021), available online at www.osler.com/en/resources/critical-situations/2021/making-sense-of-the-battle-for-the-crispr-cas9-patent-rights (accessed 27 July 2021).

15 See, e.g., J.A. Tessensohn, 'Japanese CRISPR Patent and Biotech Developments in the Early Reiwa Era' *Biotechnology Law Report* 40 (3) (2021) 242–273.

16 For further explanation see V. Lin, 'What Is a Patent Priority Claim?', *Patent Trademark Blog/IP Q&A*, available online at www.patenttrademarkblog.com/patent-priority-claim/ (accessed 27 July 2021).

17 See de Grandpré and Lozon, *supra* note 14.

Global Standards for Governance and Oversight of Human Genome Editing, we describe these recent developments in patent litigation in some detail. This trend for litigation continues, most recently in the dispute at the United States Patent and Trademark Office (USPTO) Patent Trial and Appeal Board (PTAB) over who invented the guide RNA molecule.[18]

4 Patent Governance through '*Ordre Public*' and Morality Exceptions

Patent rights create an exclusivity over the commercial exploitation of a given invention, but they also directly and indirectly dictate the direction of research efforts and activities. Patent laws of all countries include both some form of pre-grant limitations on what may be protected by a patent and post-grant limits to the free exercise of the rights conferred by a patent. Legal terminology may vary depending on local legal traditions, but most commonly these are enunciated in statutes, case-law and legal literature as either exclusions, exceptions or limitations.[19] Collectively these are known in legal circles as TRIPS flexibilities and allow national patent laws to contain mechanisms of public governance over technological innovation.

Pre-grant limitations can be an effective instrument for public governance, e.g., by delimiting the object, also known as subject-matter, of a patent. Pre-grant limitations also can intervene by excluding certain subject-matter from the concept of patentable invention (exclusions from patent subject-matter) or by determining that certain types of inventions cannot obtain patent protection (exceptions to the general rule of availability of patents to inventions in all fields of technology).

Post-grant measures may limit the rights conferred by a patent, by exempting certain activities (e.g., research exemptions) or persons from the scope of patent protection (e.g. liability exemptions for medical practitioners) or restricting the patent owner's contractual freedom concerning the patent as an object of property (e.g. compulsory licenses).

Post-grant limitations may exist in patent laws, but also in laws that regulate the introduction and use of a given technology in the market. Since the grant of a patent does not guarantee the possibility of commercialization, some substances may not succeed in meeting the necessary efficiency and

18 J. Cohen, New CRISPR Patent Hearing continues high-stakes legal battle, *Science* (4 February 2022), available online at https://www.science.org/content/article/new-crispr-patent-hearing-continues-high-stakes-legal-battle#.YgMGWwkTd2M.twitter.

19 When providing national or regional examples, the original terminology will be employed.

safety standards in clinical trials. Products originally approved as medicines may later in clinical practice be found to have long term side effects or provoke rare severe adverse reactions, and in such cases the market authorizations are withdrawn. Historically, some substances initially developed as medicines were later classified as illegal drugs, its sale completely prohibited or severely restricted.

Regulations in the medical and pharmaceutical sector offer several other examples of post-grant limitations to the rights conferred by a patent in order to protect public health. Most medicines can only be sold by licensed operators — pharmacies or dispensaries, and in many jurisdictions retailers are not always free to set the prices, since these are pre-negotiated between pharmaceutical companies that produced them and health authorities or insurance providers; most medicines also cannot be freely sold to customers, as a medical prescription is required. Professional standards, treatment protocols and medical deontological norms may further determine how and when drugs are prescribed (e.g. conservation rules for antibiotics).

In this paper we focus on a specific type of pre-grant patent limitation mechanism known as the '*ordre public*' and morality exception to patentability, which may include directly or indirectly a specific prohibition of patentability of methods for human germline modification. Such pre-grant patent limitation can be found in Europe and some jurisdictions around the globe and is most relevant in the context of governance through patent law of genome editing technologies.

4.1 *Patentability Exceptions and the TRIPS Agreement*

The World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (the TRIPS Agreement) explicitly allows WTO Members, in Article 27(2) and 27(3), to exclude certain inventions from patentability if justified by, in essence, overriding societal interest.[20] These overriding societal interests include 'to protect human, animal or plant life or health or to avoid serious prejudice to the environment'.[21] Specifically, Article 27(2) permits WTO members to "exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to

20 See also UNCTAD-ICTSD Project on IPRs and Sustainable Development, *Resource Book on TRIPS and Development* (Cambridge: Cambridge University Press, 2005) 378.

21 Article 27.2 TRIPS Agreement, World Trade Organization, Agreement on Trade-Related Aspects of Intellectual Property Rights (as amended on 23 January 2017), Annex 1C of the Marrakesh Agreement Establishing the World Trade Organization, signed in Marrakesh, Morocco on 15 April 1994, available online at www.wto.org/english/docs_e/legal_e/31bis_trips_01_e.htm (accessed 27 July 2021).

protect '*ordre public*' and morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law."

Although TRIPS does not provide for a definition of '*ordre public*' and morality, it expressly includes within this the concept the protection of life and health. In WTO Dispute Settlement Panel Report in *Canada — Patent Protection of Pharmaceutical Products*, the Panel confirmed that Article 8.1 of the TRIPS Agreement in the context of the prohibition on discrimination as to the field of technology contained in Article 27.1 of TRIPS "does not limit the ability to target certain products in dealing with certain of the important national policies referred to (in Article 8.1). It would appear therefore, that there exists considerable scope for WTO Members to include in national legislation exclusions based on the measures necessary to protect public health … and to promote the public interest …" under Article 27(2) of TRIPS.[22]

However, whether such tools are the most effective remedy to specific challenges to promote good governance of a given type of technology depends on a complex array of economic and social factors. For this reason, it can be observed that some countries have a very narrow approach to some of these flexibilities, and even abstain from enacting general '*ordre public*' and morality clauses. It is a question for each member state to decide if and how to legislate in this matter, and whether to enact or develop via case-law '*ordre public*' and morality exceptions to patentability. Article 8(1) and 27(2) of the TRIPS Agreement do not impose patentability exceptions. It merely provides member states with options or flexibilities concerning patentability to be used as legislative tools to promote public policy goals and ethical regulation of technology.

Exceptions from patentability on the ground of commercial exploitation being contrary to '*ordre public*' and morality are included in some regional patent treaties. Such clauses are either directly applicable or constitute grounds for national harmonization of national patent laws of the member states of the respective regional Patent Organizations,[23] these include the protocol on Patents and Industrial Designs within the framework of the African Regional

22 WTO, *Canada — Patent Protection of Pharmaceutical Products, Report of the Panel, WT/DS114/R* (17 March 2000), available online at www.wto.org/english/tratop_e/dispu_e/7428d.pdf, para. 7.92 (accessed 27 July 2021).

23 These implement and, in some cases, supplement the TRIPS Agreement including for example making use of the flexibilities allowed by Article 8 and further developed in Articles 27, 30 and 31 concerning patent exclusions, exceptions and limitations. World Trade Organization, TRIPS Agreement (as amended on 23 January 2017), Annex 1C of the Marrakesh Agreement Establishing the World Trade Organization, signed in Marrakesh,

Intellectual Property Organization (ARIPO),[24] Patent Regulations under the Eurasian Patent Convention adopted by the Administrative Council of the Eurasian Patent Organization (EAPO)[25] and the European Patent Convention administered by the European Patent Organization and European Patent Office.[26]

In parallel with these harmonization efforts, the national law of a large number of WTO members (see Table 1) also contains specific '*ordre public*' and morality provisions, conceptualized in the context of local legal traditions. However, it should be emphasized that not all WTO members have implemented in their respective national patent laws' '*ordre public*' and morality exceptions, and among those that have, application and enforcement practises may vary considerably.[27] Namely, some member states specifically preclude the patentability of human germline modification (Table 2), while others do not even contain general '*ordre public*' and morality clauses.[28] Furthermore, among the large number of countries that have '*ordre public*' and morality based patentability exceptions or exclusions, many do not necessarily enforce

Morocco on 15 April 1994, available online at www.wto.org/english/docs_e/legal_e/31bis_trips_01_e.htm (accessed 27 July 2021).

24 Section 3, Article 10 (j), Protocol on Patents and Industrial Designs within the framework of the African Regional Intellectual Property Organization (ARIPO), adopted on 10 December 1982, at Harare (Zimbabwe), and amended by the Administrative Council of ARIPO on 11 December 1987, 27 April 1994, 28 November 1997, 26 May 1998, 26 November 1999, 30 November 2001, 21 November 2003, 24 November 2006, 25 November 2013, 17 November 2015, 5 December 2016, 22 November 2017, 23 November 2018 and 20 November 2019, available online at www.aripo.org/wp-content/uploads/2020/01/Harare-Protocol-2020-Edition-1.pdf (accessed 27 July 2021).

25 Rule 3 (4), Patent Regulations under the Eurasian Patent Convention Adopted by the Administrative Council of the Eurasian Patent Organization (EAPO AC) at its second (1st ordinary) session on 1 December 1995, with the amendments and addenda adopted by EAPO AC up to its thirty-sixth (27th ordinary) session on 10–11 September 2020 (non-official English translation), available online at www.eapo.org/en/documents/norm/instr2020_eng.pdf (accessed 27 July 2021).

26 Article 53 (a) EPC, available online at www.epo.org/law-practice/legal-texts/html/epc/2016/e/ar53.html (accessed 27 July 2021).

27 T. Minssen, 'Patenting Human Genes in Europe — and How It Compares to the US and Australia', in: D. Matthews and H. Zech (eds.), *Research Handbook on Intellectual Property and the Life Sciences* (Cheltenham: Edward Elgar, 2017), Chapter 3, p. 26. See A. Nordberg and T. Minssen, 'A 'Ray of Hope' for European Stem Cell Patents or 'Out of the Smog into the Fog'?: An Analysis of Recent European Case Law and How It Compares to the US', *International Review of Intellectual Property and Competition Law* 47 (2) (2016), 138–177, DOI: 10.1007/s40319-016-0449-x.

28 WTO Standing Committee on the Law of Patents, Twelfth Session, Geneva, June 23 to 27, 2008, *Annex II of Report on the International Patent System* (*document SCP/12/3 Rev.2*) (status as of October 2021), available online at https://www.wipo.int/export/sites/www/scp/en/national_laws/exclusions.pdf.

them, since local patent offices do not conduct *ex oficio* substantive examinations, and thus such rules are only enforced through judicial activity.[29]

TABLE 1 Countries with national laws providing exceptions from patentability on the ground of commercial exploitation being contrary to *ordre public* or morality include:

Albania, Algeria, Andorra, Argentina, Armenia, Austria, Azerbaijan, Bahrain, Barbados, Belarus, Belgium, Belize, Bhutan, Bolivia, Bosnia and Herzegovina, Brazil, Bulgaria, Chile, the People's Republic of China, Hong Kong China, Colombia, Costa Rica, Côte d'Ivoire, Croatia, Cyprus, Czech Republic, Denmark, Dominica, Dominican Republic, Ecuador, Egypt, El Salvador, Estonia, Ethiopia, Finland, France, Georgia, Germany, Ghana, Greece, Guatemala, Hungary, Iceland, India, Indonesia, Ireland, Italy, Japan, Jordan, Kazakhstan, Kenya, Kyrgyz Republic, Latvia, Liechtenstein, Lithuania, Luxembourg, Madagascar, Malaysia, Malta, Mauritius, Mexico, Moldova, Morocco, Mozambique, Netherlands, New Zealand, Nicaragua, Nigeria, Norway, Republic of North Macedonia, Oman, Pakistan, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Poland, Portugal, Republic of Korea, Romania, Russian Federation, Serbia, Singapore, Slovak Republic, Slovenia, South Africa, Spain, Sri Lanka, Sweden, Switzerland, Syrian Arab Republic, Tajikistan, Thailand, Trinidad and Tobago, Tunisia, Turkey, United Kingdom, Uruguay, Uzbekistan, Zambia.

SOURCE: WIPO STANDING COMMITTEE OF THE LAW OF PATENTS (SCP), APRIL 2020 AND DIRECT LEGAL SOURCES

TABLE 2 Countries with national laws providing specific exceptions from patentability on processes for modifying germ line identity of human beings include:

Albania, Armenia, Bosnia and Herzegovina, Croatia, Czech Republic, Denmark, Ecuador, Estonia, Finland, France, Germany, Hungary, Italy, Mexico, Moldova, Norway, New Zealand, Portugal, Russian Federation, Serbia, Slovak Republic, Spain, Sweden, Switzerland, Turkey, United Kingdom.

SOURCE: WIPO STANDING COMMITTEE OF THE LAW OF PATENTS (SCP), APRIL 2020 AND DIRECT LEGAL SOURCES

29 In general, patent offices' search and examination practices can be categorized into three types of policy options: (i) formality examination only; (ii) formality examination and prior art search; and (iii) formality examination, prior art search and substantive examination.

In the following sections we analyze patent laws in the USA and Europe as examples of two divergent patent policy options that directly affect genome editing.

4.2 *Jurisdictions without Statutory Exceptions from Patentability: Developments in the US*

As mentioned, there are several jurisdictions without explicit '*ordre public*' and morality exceptions from patentability in their laws and statutes, including the notable example of the US. Such an approach does not always mean that corresponding issues are not addressed by these patent systems. Although morality issues have been considered in the context of the US utility doctrine and claims directed to, or encompassing, human organisms are categorically excluded from patentability,[30] there are no enforceable statutory provisions in US Law directly corresponding to '*ordre public*' and morality exceptions to patentability.[31] Conversely, most jurisprudential activity concerns the determination of the boundaries of subject-matter eligibility and corresponds, in EPC terminology, to an exclusion from patentability concerning natural laws, products, phenomena or abstract ideas.[32] The US Supreme Court decision in *Diamond v. Chakrabarty* (1980)[33] clarified that whether an invention embraces living matter is irrelevant to the issue of patent eligibility, with the seminal conclusion that statutory subject matter under section 101 includes "anything under the sun that is made by man."

More recent decisions have introduced a stricter approach to patent eligibility. In *Bilski v. Kappos* (2010)[34] the Supreme Court ruled on the contested topic of the general patent eligibility of method patents. Section 101 of the US Patent Act lists the types of claims allowed in patent applications: "process, machine, manufacture, or composition of matter."[35] The Court rejected a categorical exclusion from patent eligibility of business methods (such as the

30 See: Minssen and Nordberg, *supra* note 27.

31 The HR 1249 (the so-called "America Invents Act") introduced an immediately effective ban on patents covering tax strategies and/or claims "directed to or encompassing" human organisms (see section 33). These will apply to all pending applications.

32 Historical authors refer to this approach as the "moral utility" doctrine. See M.A. Bagley, 'Patent First, Ask Questions Later: Morality and Biotechnology in Patent Law', *William and Mary Law Review* 45 (2) (2003) 469–547.

33 *Diamond v. Chakrabarty* 447 US 303 (1980); 206 USPQ 193 (The Supreme Court of the United States).

34 *Bilski v Kappos* 130 s. Ct. 3218; 177 L.Ed.2d 792 (2010).

35 35 U.S.C. para. 101, available online at https://uscode.house.gov/view.xhtml?path=/prelim@title35/part2/chapter10&edition=prelim (accessed 27 July 2021).

ones existing in Article 52 of the EPC), while also rejecting the machine-or-transformation test.

In *Mayo v. Prometheus* (2012), the US Supreme Court focused again on Section 101 and its implicit exception that excludes patents on laws of nature, natural phenomena, and abstract ideas, here concerning the question of patent eligibility of a '*medical method*'.[36] The matter was again raised in *Association for Molecular Pathology v. Myriad Genetics* (2013), concerning the controversial patents on the BRCA1 and BRCA2 genes.[37] Here the US Supreme Court decided on the patent eligibility of isolated genes concluding that a naturally occurring DNA segment was a product of nature and not patent eligible under 35 U.S.C. para. 101 merely because it was isolated, but cDNA was patent eligible because it was not naturally occurring. In *Alice Corp. v. CLS Bank International* (2014),[38] although in this case concerned a software patent,[39] the deliberations of the Supreme Court are also instructive to the patent eligibility of the pharma sector because the court discussed the boundaries between non-patentable abstract ideas and patent eligibility of implementations of ideas.

As of today, patent rules in the US do not specifically prevent the patentability of genome editing technology nor restrict patentability of modification of germ line identity of human beings. However, the abovementioned case-law illustrates how a patent system may choose to address many of the public policy concerns in a general and systematic manner through the application of patent eligibility standards. In contrast, jurisdictions such as most European

36 *Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 132 S. Ct. 1289 (2012). See Timo Minssen and David Nilsson, 'The US Supreme Court in Mayo v. Prometheus — Taking the Fire from or to Biotechnology and Personalized Medicine?', *Queen Mary Journal of Intellectual Property* 2 (4) (2012) 376–388.

37 *Association for Molecular Pathology, et al. v. Myriad Genetics, Inc.* 569 US 576, 133 S. Ct. 2107 (2013). An account of the developments leading to the Myriad decision is provided by R.M. Schwartz and T. Minssen, 'Life after Myriad: The Uncertain Future of Patenting Biomedical Innovation & Personalized Medicine in an International Context', *Intellectual Property Quarterly* 3 (2015) 189–241; E. van Zimmeren, D. Nicol and R. Gold, 'The BRCA Patent Controversies: An International Review of Patent Disputes' in S. Gibbon, G. Joseph, J. Mozersky, A. zur Nieden and S. Palfner (eds.) *Breast Cancer Gene Research and Medical Practices: Transnational Perspectives in the Time of BRCA* (London: Routledge, 2014), 151. For a discussion of the ethical issues and gene patentability in this context see A. McMahon, "Gene Patents and the Marginalisation of Ethical Issues', *European Intellectual Property Review* 41(10) (2019) 608–620.

38 *Alice Corp. v. CLS Bank International*, 573 US 208 (2014).

39 Regarding the impact of the *Alice* decision on biotechnology patents, see M. Aboy, K. Liddell, C. Crespo, I.G. Cohen, J. Liddicoat, S. Gerke and T. Minssen, 'How Does Emerging Patent Case Law in the US and Europe Affect Precision Medicine?', *Nature Biotechnology* 37 (10) (2019) 1118–1125.

countries address such concerns through rules based on the exceptions from patentability allowed under Article 27(2) of the TRIPS Agreement.

4.3 *Jurisdictions with Statutory 'Ordre Public' and Morality Exceptions: Developments in Europe*

Patentability prohibitions based on '*ordre public*' and morality have a long tradition in European national laws and already existed in several jurisdictions in the nineteenth century.[40] Thus, historically these provisions' origin pre-dates both the TRIPS Agreement, and regional treaties such as the EPC. Currently, the general '*ordre public*' and morality clause is prescribed in Article 53 (a) of the EPC in terms very close to those of Article 27 (2) the TRIPS Agreement.[41] Similar clauses are also observed in the respective national patent codes or laws of at least each of the 38 countries that are full members of the European Patent Organisation.

The EPC does not provide a direct statutory definition of '*ordre public*' and morality, however the implementing regulations to the EPC[42] exemplify categories of inventions that will fall under the scope of the provision. These regulations incorporate both the jurisprudence of the EPO Boards of Appeal and European Union (EU) rules contained in the Biotechnology Directive.[43] The inclusion of the Biotechnology Directive patent substantive provisions and related Court of Justice of the European Union (CJEU) jurisprudence in the implementing regulations indirectly extends their scope of territorial application to those member states of the EPO which are not part of the EU. Although the EPO, is an international organization based on an international treaty — the European Patent Convention (EPC) — and is independent from and not subject to the treaties and legislation of the EU, the EPO Administrative

40 See L. Bently, B. Sherman, D. Borges Barbosa, S. Basheer, C. Visser and R. Gold, 'Exclusions from Patentability and Exceptions and Limitations to Patentees' Rights', *WIPO Standing Committee on the Law of Patents SCP/15/3 Annex I* (2010), available online at https://www.wipo.int/edocs/mdocs/scp/en/scp_15/scp_15_3-annex1.pdf.

41 Article 53(a) EPC 2000 reads as follows: 'European patent shall not be granted in respect of: (a) inventions the commercial exploitation of which would be contrary to '*ordre public*' or morality; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States.'

42 Implementing Regulations to the Convention on the Grant of European Patents of 5 October 1973 as adopted by decision of the Administrative Council of the European Patent Organisation of 7 December 2006 and as last amended by decision of the Administrative Council of the European Patent Organisation of 15 December 2020.

43 Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions [1998] OJ L213/13 (Biotechnology Directive).

Council policy has been to incorporate EU patent law and policy into its own legal order via the implementing rules to the EPC.[44]

The Biotechnology Directive, enacted by the EU in 1998 after a decade-long legislative process, was an attempt to improve legal certainty regarding both patent eligibility and patentability exclusions and exceptions applicable to the, then emerging, biotechnology field. It contains rules that distinguish patentable inventions from non-patentable discoveries, as well as examples of what inventions might not fall under the scope of the '*ordre public*' and morality exception.

Article 5 of the Biotechnology Directive focusing on patent subject-matter, clarifies that the human body which, at various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions since these are considered a mere discovery of a naturally occurring element. Nevertheless, Article 5 of the Biotechnology Directive also declares that an element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to a natural element, provided that the industrial application of a sequence or a partial sequence of a gene is disclosed in the patent application.

Regarding exceptions from patentability, Article 6(2) of the Biotechnology Directive sets out a non-exhaustive list of examples of biotechnological inventions that are excluded from patentability on '*ordre public*' and morality grounds, including: (a) "processes for cloning human beings"; (b) "processes for modifying the germ line genetic identity of human beings"; and (c) "uses of human embryos for industrial or commercial purposes."

It is important to again emphasize that the EPO is not an institution of the European Union and not all of its members are EU member states. Therefore, EU directives and CJEU decisions are not legally binding for the EPO. Even if such rules and jurisprudence can be invoked during proceedings and the BoA may decide to find the arguments substantively persuasive. It has also been part of the EPO institutional practice to incorporate CJEU patent jurisprudence in the guidelines for examination. These are two parallel systems that although interlinked, are not always completely equivalent. Regarding '*ordre*

44 The key articles 5 and 6 of the Biotechnology Directive are included in Rules 28 and 29 of the Implementing Regulations to the Convention on the Grant of European Patents. Administrative Council Decision, OJ EPO 7/1999, 437.

public' and morality exception both the EPO BoA and the CJEU have established interpretative guidance through a number of high-profile cases.

The EPO BoA, through the *OncoMouse* case[45] developed a balancing test weighing animal suffering against the therapeutic value of the invention under consideration.[46] In *Relaxin*,[47] it was instead suggested that the main criterion for morality assessment rested on whether the invention is so abhorrent to the public that it would seem inconceivable.[48] While in *Plant cells*,[49] it was stated that 'the concept of "*ordre public*" covers the protection of public security and the physical integrity of individuals as part of society',[50] and that the concept of morality is related to the accepted norms which are deeply rooted in the culture inherent in European society and civilisation.[51]

The specific criteria and acceptable sources of evidence that can be taken into consideration for determining the actual substantive content of what constitutes an accepted norm that is deeply rooted in European society remains mostly undetermined. In *Transgenic Animal* (a decision issued after the adoption of the EU Biotechnology Directive) it was stated that no single definition of morality based on, for instance, economic or religious principles, represents the content of an accepted standard in European culture.[52] In *WARF*, the EPO found that the legislature had made morality part of the EPC[53] in the context of innovation linked ultimately with embryos and declined to grant patents.[54]

Currently, any genome editing invention that implies at some point in time the destruction of an embryo, even if such destruction, is absent from the patent application (namely in either the claims or description), is not patentable. An invention that uses human embryonic stem cells (hESCs) is only patentable

45 T 19/90 Harvard/*Onco-mouse* [3 October 1990] OJ EPO 1990, 476.

46 *Ibid.*, reasons 5.

47 Decision of the EPO Opposition Division, Howard Florey Institute/*Relaxin* [8 December 1994] OJ EPO 1995, 388 and T 272/95 Howard Florey Institute/*Relaxin* [23 October 2002] unpublished.

48 Howard Florey Institute/*Relaxin*, *supra* note 47, reasons 6.2.1.

49 T 356/93 Plant Genetic Systems/*Plant cells* [21 February 1995] OJ EPO 1995, 545.

50 *Ibid.*, reasons 5.

51 *Ibid.*

52 T 315/03 HARVARD/*Transgenic Animal* [6 July 2004] OJ EPO 2005, 246.

53 See A. Warren-Jones, 'Finding a "Common Morality Codex" for Biotech — a Question of Substance', *International Review of Intellectual Property and Competition Law* 39 (6) (2008) 638–661.

54 WARF/*Embryonic Stem Cells* [2009] EPOR 15, 143 para 41, and A. Plomer, K.S. Taymor and C.T. Scott, 'Challenges to Human Embryonic Stem Cell Patents', *Cell Stem Cell* 2 (1) (2008) 13–17.

if stem cell lines were obtained from parthenotes.[55] According to the CJEU in *Brüstle*, this limitation even applies if the destruction occurred at an undetermined historical moment and does not form part of the core of the invention, as described in the claims.[56] The CJEU[57] focused on establishing the meaning of embryo within the Directive and did not engage with wider questions of human dignity and morality, despite the opinion of the Advocate General in this case.[58] The *Brüstle* jurisprudence, later also adopted by the EPO, contrasts with the restrictive approach to patenting regarding genetic innovation in earlier EPO BoA decisions, including the balancing test adopted concerning animals in *Harvard/Onco-mouse*[59] where the BoA balanced the negative impact (on the animals) with the longer term expected benefit for humans.

Modifying the germline genetic identity of human beings is currently specifically covered by the morality patentability exception under the EU Biotechnology Directive and adopted by the EPO under the corresponding Rule 28(1)(b) in the EPC Implementing Regulations. This specific exception to patentability follows prohibitions of germline modifications outside patent laws, such as those contained in the in UN UNESCO Declarations,[60] The Council of Europe Bioethics Convention (Oviedo Convention).[61] Germline interventions are prohibited also in several national jurisdiction and heavily

55 C-364/13, *International Stem Cells Corporation v Comptroller General of Patents, Designs and Trade Marks* ECLI:EU:C:2014:2451.

56 Minssen and Nordberg, *supra* note 27.

57 Case C-34/10 *Oliver Brüstle v Greenpeace e.V* [2011] OJ C 362/5 Judgment of the Court (Grand Chamber) of 18th of October 2011.

58 Opinion of Advocate General Bot of 10 March 2011, Case C-34/10 *Oliver Brüstle v Greenpeace e.V*.

59 *Supra* note 45, 476; D. Beyleveld and R. Brownsword, *Mice, Morality and Patents: the Oncomouse Application and Article 53a of the European Patent Convention* (Intellectual Property Institute 1993), also considered in Warren-Jones, *supra* note 53; A. Bonfanti, 'Environmental Risk in Biotech Patent Disputes', *European Journal of Risk Regulation* 3 (1) (2012) 47, 49–56.

60 Universal Declaration on the Human Genome and Human Rights, adopted by the UNESCO General Conference on Nov. 11, 1997 and endorsed by the United Nations General Assembly, 53rd session, resolution AIRES/53/152, 9 December; International Declaration on Human Genetic Data, adopted by the UNESCO General Conference on 16 October 2003; Universal Declaration on Bioethics and Human Rights, adopted by the UNESCO General Conference, 19 October 2005.

61 Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, signed in Oviedo, 4 April 1997, European Treaty Series No. 164.

regulated in others.[62] Rule 28(1) (b) explicitly includes in the morality exception 'processes for modifying the germ line genetic identity of human beings'. Because the wording of the exception expressly refers to *'processes'*, product claims have to be considered on a case-by-case basis under the general '*ordre public*' and morality exception, making EPO decisions on the morality of the invention to some extent depend on the type of claim.[63]

The text of the Biotechnology directive contains several relatively vague and undetermined autonomous concepts of EU law, these have been a source of legal discussion and require clarification. Under a literal interpretation, all genome editing interventions resulting in modifications of the germline will be excluded from patentability, including also therapeutic interventions with well-defined curative purposes and not in any way connected with eugenic purposes or elective interventions. EU law and thus the biotechnology directive, is traditionally not intended to be interpreted merely following its literal meaning, but rather using a teleological interpretation method.[64] Therefore, it has been argued that concerning therapeutic interventions a less strict

62 Concerning Europe, see, for example, the restriction imposed by Article 13, Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (CETS no. 164). Only 28 countries have ratified, those who did not ratify include the EU as an institution and the following EPO member states: Ireland, Italy, The Netherlands, Poland, Sweden and the UK. For an account of both European and non-European jurisdictions, see F. Baylis, M. Darnovsky, K. Hasson and T.M. Krahn, 'Human Germline and Heritable Genome Editing: The Global Policy Landscape', *The CRISPR Journal* 3 (2020) 365–377, http://doi.org/10.1089/crispr.2020.0082. For comparative discussion, see also C. Romano, J. Almqvist (Eds.), *Human Germline Genome Modification and the Right to Science: A Comparative Study of National Laws and Policies* (Cambridge: Cambridge University Press, 2020); S. Slokenberga, K. Siemaszko, Z. Warso and H.C. Howard, 'SIENNA D2.2 Analysis of the legal and human rights requirements for genomics in and outside the EU (V2.0)', *Zenodo* (2019), available online at https://zenodo.org/record/4066659#.YjBN3Y_MI2w; A. Nordberg, 'Report: Genome Editing in Humans: A Survey of Law, Regulation and Governance Principles', Panel for the Future of Science and Technology (STOA), *European Parliament* (forthcoming, 2022).

63 A. Nordberg, 'Patents, Morality and Biomedical Innovation in Europe: Historical Overview, Current Debates on Stem Cells, Gene Editing and AI, and de Lege Ferenda Reflections' in D.J. Gervais (ed.), *Fairness, Morality and Ordre Public in Intellectual Property* (Cheltenham: Edward Elgar, 2020), pp. 243–267.

64 Concerning legal interpretation and construction of international patent law, see also with further references, A. Nordberg, 'Legal Method and Legal Interpretation in International Intellectual Property Law: Pluralism or Systemic Coherence' in S. Frankel (ed.), *Is Intellectual Property Pluralism Functional?* (Cheltenham: Edgar Elgar, 2019), Chapter 4, p. 96.

interpretation would be reasonable as a contextual interpretation would allow patents on in vitro methods.[65]

This line of argumentation is supported by recital 42 of the EU Biotechnology Directive, which has interpretative value. This recital states that the germline exception from patentability is not intended to be applicable to claims for 'inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it'. The EU patent law concept of embryo is broad extending to any fertilized ova capable of developing into a human being, as defined under the doctrine of the CJEU in *Brüstle* and *ISCC*. This broad interpretation of the legal concept of embryo entails that a therapeutic intervention at the blastocyst stage is considered a therapeutic intervention in an embryo. Therefore, it can be argued that germline editing for a therapeutic purpose is patentable.[66] Likewise, following such reasoning but now *a contrario*, methods for germline editing would be patentable as long as not able to result in modifications to a human being, meaning for example processes to be applied for research purposes in parthenotes which are not considered by the jurisprudence of the CJEU as capable of developing into a human being, since the prohibition in Article 6.2 Biotechnology Directive/Rule 28(1)(b) EPC only applies to modifying human beings.

Although there are currently no BoA decisions concerning the application of exceptions in the field of genome editing, patent applications procedural history shows that the EPO actively makes use of the '*ordre public*' and morality exceptions as governance tools to assess and manage what types of inventions should be excluded from patentability on grounds that they are, broadly speaking, socially undesirable and/or violate human dignity. Rather than relying only on adversarial procedures (refusals and appeals) EPO administrative procedural rules and praxis on patent processing and examination allow the EPO examining division to regularly invite applicants to voluntarily introduce amendments to claims — known as disclaimers — explicitly excluding from the claims the use of a process for modifying the germline genetic identity of human beings.[67]

65 A. Nordberg, T. Minssen, S. Holm, M. Horst, K. Mortensen and B. Lindberg Møller, 'Cutting Edges and Weaving Threads in the Gene Editing (Я)evolution: Reconciling Scientific Progress with Legal, Ethical, and Social Concerns', *Journal of Law and the Biosciences* 5 (1) (2018) 35–83; A. Nordberg, T. Minssen, O. Feeney, I. de Miguel Beriain, L. Galvagni and K. Wartiovaara, 'Regulating Germline Editing in Assisted Reproductive Technology: An EU Cross-Disciplinary Perspective', *Bioethics* 34 (1) (2020) 16–32, with further references.

66 Nordberg, *supra* note 63, p. 243.

67 I. Schneider, 'Patent Governance, Ethics and Democracy: How Transparency and Accountability Norms Are Challenged by Patents on Stem Cells, Gametes and Genome

Disclaimers have routinely been added to genome editing-related patent applications introducing claim limiting expressions such as "non-human," "human germline not modified" or "wherein the cells are not germ cells."[68] European patent claims have also been allowed to the "composition" or "vector system."[69] These procedural aspects of the patent examination process are particularly important and attest to the relevance of the governance role assumed by the '*ordre public*' and morality exceptions. Moreover, they were relevant for the European Academies Statement on Patent-Related Aspects of CRISPR-Cas Technology[70] issued in 2016, which concluded that the patent granting practice of the EPO is fit for purpose and flexible enough to take account of future regulatory developments related to genome editing technology.

5 The Impact of '*Ordre Public*' and Morality Patent Exceptions on Human Germline Editing

Applying '*ordre public*' and morality exceptions provisions has for long been a source of controversy and academic debate.[71] Enforcing such clauses during patent examination procedures, involves determining what is contrary to '*ordre public*' and morality and thus involves ethical normative decisions being made by administrative institutions (the EPO or national patent offices).

Editing', in: T.C. Berg, R. Cholij and S. Ravenscroft (eds.), *Patents on Life: Religious, Moral and Social Justice Aspects of Biotechnology and Intellectual Property* (Cambridge: Cambridge University Press, 2019), 263–288.

68 *Ibid.*

69 Examples include the European Patents EP 2800811 (UC Berkeley) and EP 2771468 (Broad Institute) with similar amended claim language, i.e. "provided that said method is not a method of modifying the germline genetic identity of a human being" (in the case of the Broad '468 EP, this wording being upheld during Oral Proceedings at the EPO, 5–7 February 2020, even if the patent was ultimately revoked on other grounds, as explained in Section 2 above).

70 ALLEA, *Statement on Patent Related Aspects of CRISPR-Cas Technology* (18 July 2016), available online at https://allea.org/allea-releases-statement-patent-related-aspects-crispr-cas-technology/ (accessed 27 July 2021).

71 For some background see: Nordberg, *supra* note 63, p. 243; EU Commission Expert Group on the development and implications of patent law in the field of biotechnology and genetic engineering, 'Report on patents in the field of human stem cells of the Expert Group on the development implications of patent law in the field of biotechnology and genetic engineering' (2016), available online at https://ec.europa.eu/growth/industry/policy/intellectual-property/patents/biotechnological-inventions_en (accessed 27 July 202)1; S. Sterckx and J. Cockbain, *Exclusions from Patentability: How Far Has the European Patent Office Eroded Boundaries* (Cambridge: Cambridge University Press, 2012), p. 75.

Commentators argue that patent offices lack the structure, technical expertise, institutional culture of transparency and accountability, or indeed the democratic mandate to make such determinations.[72] Likewise, even the role of the CJEU and national courts in determining standards of morality for patent law purposes has been questioned.[73]

Arguments linked to the nature of patents, as negative exclusionary rights, and its function as guarantee to economic incentive to innovation speak against the efficiency of such provisions as a governance tool. After all, granting a patent does not mean that the patent proprietor would be allowed to use the invention in any possible way. The use of the patented technology would still have to comply with the applicable regulations. On the contrary, denying patentability puts an invention in the public domain, and does not mean its commercialization and use will be restricted. It could further be argued that logic would dictate that such use would increase and become less controllable in the absence of patents. A patent right holder could be theoretically obliged to (a) exclude certain unwanted uses from the claim language thereby restricting the scope of protection to morality-accepted purposes or (b) follow regulatory obligations to deny licenses on unwanted uses of the patented invention. This would help to monitor, control and govern the uses of such technologies.

In that way, patentability exceptions can also have an indirect governance and symbolic effect precisely from the economic incentive mechanism. The enforcement of exceptions from patentability effectively diminishes the availability of the economic incentive provided by patent rights to the target inventions or technologies and thus commercial actors in the pharmaceutical sector are comparatively more reluctant to invest large sums in research and product development, adapting manufacturing capabilities, distribution channels, professional training and marketing of products that are not covered by a market exclusivity. Furthermore, because the exception generally signals society, economic actors and consumers that such technology is unethical, commercial entities will think carefully before associating their 'brand' with such technologies.

The '*ordre public*' and morality exception applicable to a given type of inventions also functions as a chilling effect on academic research, not only due to the stigma of working with technology that is classified by an administrative authority as 'immoral' but also because patents are to some extent included in

72 See, e.g., J. Pila, 'Adapting the *Ordre Public* and Morality Exclusion of European Patent Law to Accommodate Emerging Technologies', *Nature Biotechnology* 38 (2020) 555–557; Nordberg, *supra* note 63, p. 243.

73 See with further references, Nordberg *supra* note 64, p. 96.

academic portfolios used for assessment of career progression. Research funding agencies and private foundations also tend to be cautious about providing grants to technologies falling under the '*ordre public*' and morality exception. Ultimately, however, it should be acknowledged that perhaps this cannot be attributed solely to an indirect pedagogic effect of patentability norms, but is instead more likely to be the cumulative result of a variety of regulatory and governance considerations. Still the result is that alternative incentives such as grants, prizes and academic awards will typically also be severely reduced and that lack of incentive will extend beyond a specific unethical application of the technology and affect the entire field. A cautionary example is stem cell research in Europe after the Brüstle decision, discussed above.[74]

Moving forward, and as the technology further develops and specific therapeutic applications are developed, it is essential that interpretation issues are clarified. In particular two essential concepts in the text of the exception should be carefully considered: (a) 'modifying the germ line'; and (b) 'genetic identity of human beings'.

Regarding interpreting what standard should be used to determine when a claim for a process should be excluded on grounds of 'modifying the germ line', it should first be considered that there is considerable diversity and variation in any given species' genetic pool — including humans. Interventions that erase such diversity in order to select, introduce or remove certain traits might modify the genetic identity of the individual subject to the intervention. However, treatments that merely remove mutations known to be responsible for severe diseases are no different to surgically removing a tumour, and by analogy it is as such that these genome editing therapies should be considered, even if such intervention also passes on and is also curing descendants. Meaning that in such cases, there is not in a strict sense a modification of the germline (in the sense of introducing something ad novum) but rather a therapeutic genetic surgery repairing a damaged germline. The concept of modification of the germ line should be narrowly constructed in cases where patent claims are directed to genetic treatments to improve health, prevent diseases, and promote wellbeing. Such claims should be allowed[75] in light of the abovementioned Recital 42 of the Biotechnology Directive which clarifies for interpretative purposes that the germline 'exclusion does not affect inventions for

74 See also A. Odell-West, 'Invention and the Human Embryo', *Intellectual Property Quarterly* 1 (2020) 1–19, p. 19, who argues that the dignitarian perspective adopted in the case fails to adequately consider the balance between investor and society interests.

75 Provided that these are in vitro treatments that do not fall under the exception for medical methods under Article 53 (c) EPC.

therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it'.

The patent exception preventing the patentability of 'processes for modifying the germ line genetic identity of human beings' is based on the understanding that eugenic practices are an offense to '*ordre public*' and morality. In fact, such practices are largely unanimously understood as offensive to human dignity.[76] Unlike the dystopic scenario of eugenics programs where a large number of individuals are created as a result of in vitro fertilization and genetic editing, therapeutic interventions to repair damaged DNA will only result in curing individuals and preventing disease from passing down a family line. This means that the exception should not be interpreted as applicable to individual therapeutic intervention to correct genetic mutations or irregularities affecting a given family. Under a narrow interpretation of the exception, only those modifications that affect the global identity of humanity would be considered an offense to human dignity and a danger to the human genome, as the collective heritage of humanity. Individual therapeutic interventions will not have a global impact on the collective human genome and as such also here a narrow construction would not interpret such therapeutic treatments as processes that modify the genetic identity of human beings, since these only restore or treat a DNA abnormality of specific individuals and not the collective human identity.

Although challenges remain and the search for balance runs throughout patent law, it has been argued that pursuing limitations and disclaimers, or refusal to grant, may start a chain reaction leading to an overall reduction of incentives to innovate and invest in controversial areas for R&D.[77] However, given that most technologies have dual or multiple types of uses — including some ethically objectionable and some highly desirable — the problem remains as to how to reduce incentives to the first and still incentivise the latter.

Finally, the implementation of the European model as a type of public technology governance tool is highly dependable on the existence of a

76 See, for example, J. Habermas, *The Future of Human Nature* (Cambridge: Polity Press, 2003), 27; F. Fukuyama, 'How to Regulate Science', *The Public Interest* (2002) 3–22; E. Fenton, 'Liberal Eugenics & Human Nature: Against Habermas', *The Hastings Center Report* 36(6) (2006) 35–42. Views to the contrary have also been expressed, e.g., J. Harris, 'Enhancements are an obligation', in: J. Savulescu and N. Bostrom (eds.), *Human Enhancement* (Oxford: Oxford University Press, 2013) pp. 131–154.

77 See S. Harmon, G. Laurie and A. Courtney, 'Dignity, Plurality and Patentability: The Unfinished Story of Brüstle v Greenpeace (Case Comment)', *European Law Review* 38 (1) (2012) 92–106; Nordberg et al., *supra* note 65, 35.

fully-functioning patent examination system and cannot be adopted in countries with a mere patent recognition system.

Patent exceptions should not be used as a blunt policy instrument, nor interpreted in a way that is contrary to the patent system's overall objective.[78] Namely, the morality-based exception concerning germline editing should not be applied in a way which results in outcomes counterproductive to this objective. The application of the morality exception should be based on a good understanding of the science and should enable case-by-case decisions that provide the basis for claim amendments and nuanced purpose bound protection.

Above all, we would caution against outcomes whereby patent law would regard certain germline editing inventions as falling within the scope of the '*ordre public*' and morality exceptions, whereas at the same time research regulation can enable scientists to conduct research on such inventions in many settings. Such a paradox would lead to a situation, as happened in the Brüstle decision,[79] whereby scientists operating on the basis that conducting legally compliant research by following all research guidelines might be constrained in the commercial exploitation of their inventions by a contrary position in patent law.

6 Conclusions

Our analysis has illustrated how legal systems can set limits on the patentability of human genome editing as an instrument of governance, including the exceptions from patentability on grounds that the commercialization of certain inventions is contrary to '*ordre public*' and morality. Some patent systems have already incorporated this exception and that there is variety in the

78 Trevor Cook expresses similar views in T. Cook, *Pharmaceuticals Biotechnology and the Law*, 3rd edn. (New York, NY: LexisNexis, 2016), p. 238, in which he emphasises that the function of patents has traditionally been to prevent others from the use of a particular technology, not to serve as a tool to regulate the creation and distribution of technology.

79 Considering the wide variety of regulations and national perceptions pertaining to research involving genome editing (https://www.frontiersin.org/articles/10.3389/fpos.2021.793134/full (on diverse genome editing landscape, published 27 January 2022)) or germline editing (https://www.liebertpub.com/doi/10.1089/crispr.2020.0082 (on diversity in germline editing landscape)), there is a plausible risk for such outcomes. See also Romano and Almqvist, *supra* note 62; Slokenberga et al., *supra* note 62; and A. Nordberg, 'Genome editing in Humans: a survey of Law, regulation and governance principles' (report, forthcoming, April 2022).

application of patent law by courts and patent offices in the way this provision has been interpreted.

Such '*ordre public*' and morality exceptions can have a considerable impact on the patentability and hence most likely on the developments and availability of novel therapies that would involve modification to the germ line. Balancing the great risk for potential misuses on the one hand, and the risk that novel and potentially life-saving therapies are not being developed on the other hand, as we state with colleagues in our response to the WHO Expert Advisory Committee's reports, there is consequently a need for greater understanding and more inclusive public debate on the role of patents and the broader legal system considerations in countries considering introducing or developing further guidance on the use of '*ordre public*' and morality exceptions to patentability in the area of genome editing .

In our view, we need to pursue more nuanced approaches to the application of '*ordre public*' and morality exceptions in patent law in order to allow for a case-by-case application. As we pointed out previously, the assessment of risks and benefits of patent exceptions need to be research-based, taking into account inputs from all relevant stakeholders as well as those engaged directly in patent and innovation law and policy.

While recent social science landscaping studies are welcome, we believe that a more comprehensive comparative legal analysis is required. Such an approach should take into account the complexities of patent law and procedure in order to better inform the policy debate. In addition to identifying which countries currently have '*ordre public*' and morality exceptions, there is also a need to examine in more detail how the law is applied in practice when it is subject to decisions by patent offices and by the courts.

An additional step would be defining clear guidelines for examination and application of the '*ordre public*' and morality exceptions, with special emphasis on the exception for 'processes for modifying the germ line identity of human beings'.

Such a debate on patent exceptions needs to acknowledge that imposing a complete ban on patentability of inventions concerning germ line modifications may in fact reduce incentives to the prevention and treatment of serious genetic diseases.

Above all, patent exceptions should not be used as a blunt policy instrument, nor interpreted in a way that is contrary to the patent system's overall objective to promote innovation for the benefit of mankind and society. In particular, the '*ordre public*' and morality based exceptions in the context of human germline editing should not be interpreted and applied in a way which results in outcomes counterproductive to the goal of balancing innovation

with the protection of societal higher normative values. Instead, the application of the exception should be based on a sound understanding of both the underlying science as well as the broader ethical, social, and legal implications, thus enabling case-by-case decisions that provide the basis for patent claim amendments and nuanced purpose-bound protection. Further analysis and debate as to the role that such flexibilities can play in the context of genome editing technologies is therefore both necessary and desirable, and can be facilitated in the ways set out in this article.

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