

European Perspectives on Regulation of Heritable Genome-editing

Geetanjali Sharma*

Inhalt	
A. Introduction	342
B. Basics	344
I. The cell, the DNA and genes	344
II. From the germ cell to the embryo	345
III. Mutation, disease and inheritance	346
C. Gene editing techniques and CRISPR/Cas9	346
I. Gene-editing	346
II. What is Crispr?	347
III. Crispr/Cas9 applications in gene editing	347
IV. CRSIPR/Cas9 associated risks	348
1. Safety	348
2. Appropriateness	348
D. Regulation	349
I. Biomedicine Convention/Oviedo Convention	350
1. Editing human germ cells through CRISPR for research	350
2. Editing human germ cells through CRISPR to induce heritable changes	351
II. The European Convention on Human Rights	354
1. Editing human germ cells through CRISPR for research	354
2. Editing human germ cells through CRISPR to induce heritable changes	355
III. The Charter of Fundamental Rights of the European Union	356
E. Comment	360
F. Conclusion	363

* Geetanjali Sharma, LL.M. is a qualified Indian lawyer. She obtained her Master in Laws (European and International Law) in 2018 from the Europa-Institut on the DAAD – Angela Merkel Jawaharlal Nehru Scholarship. She is currently a research associate at the chair of European Public Law at the Free University Berlin (Germany). All opinions, errors and omissions are her own. Email: geetanjali.sharma@fu-berlin.de.

Abstract

New developments in genome editing techniques, such as CRISPR/Cas9, have raised significant questions before humankind. The promise of CRISPR /Cas9 lies in the ability to make precise edits in the human genome which may help prevent progeny from being born with severe genetic diseases. At the same time there are significant risks because we do not yet know about the safety of this technique or what its long-term effects are going to be. Also legitimate is the concern about potential for misuse for eugenic purposes. The scientific community is split on the question of whether research in this area should continue. This article explores answers for some of these questions in law applicable in Europe. I also attempt to answer the nagging question – if allowed to be performed, would such a technique be compliant with human dignity?

Keywords: Oviedo Convention, European Convention on Human Rights, Human Dignity, CRISPR, CRISPR/Cas9, Genome Editing, Informed Consent, Inheritance, Embryo, Eugenics

A. Introduction

Earlier last year as the world was on the cusp of a pandemic, CRISPR/Cas9, a genetic editing tool was used inside a person's body for the first time. The patient underwent a surgery to cure blindness, caused by a gene mutation. This mutation prevented a protein responsible for constituting light signals to the brain from being made, which rendered the patient unable to see.¹ The surgery conducted at the Casey Eye Institute in Portland, Oregon was designed to edit out this faulty gene from the retina of the patient in enough cells so as to restore vision. Once healed, the person will be able to see. So much so, the inventors of the tool, *Emmanuelle Charpentier* and *Jennifer Doudna* were awarded the Nobel Prize for chemistry later last year (2020).

Now let us consider another instance of use of the same genetic editing tool slightly prior to these events: In December 2018, a Chinese fertility scientist, *He Jiankui* claimed that he had created the world's first human genetically edited babies (called *Lulu* and *Nana*) resistant to HIV.² These children were reportedly born in the course of a project to help HIV positive fathers and HIV negative mothers conceive. Once the experiment was made public during a conference, *Dr. Jiankui* was convicted and sent to jail. Over a year on, concerns remain that the experiment may have led to incomplete edits in the body producing side effects.³

1 <https://www.theguardian.com/science/2020/mar/04/doctors-use-gene-editing-tool-crispr-inside-body-for-first-time> (27/4/2021).

2 *Raposo*, JBRA assisted reproduction 2019/3, p. 197.

3 <https://www.technologyreview.com/2019/12/03/65024/crispr-baby-twins-lulu-and-nana-what-happened/> (27/4/2021).

Why is the first instance cause for optimism while the second one resulted in alarm globally? The short answer is that there are two kinds of cells in the human body. Somatic cells are the kinds that die with an individual, while germ cells are those which are passed onto/result in children. This is why any genetic edits made to the latter will have consequence for humankind on the whole. In the first instance, surgery to restore vision was conducted in the somatic cells of the patient and, therefore, any unintended side effects are not going to be inherited by the progeny of the patient.⁴ In the second instance, edits were made to the germ cells of the parents, and any resultant changes will be inherited by the twins and the generations further.⁵ As such, it is not difficult to see that the second instance will have consequences for humankind on the whole.

In order to understand the implications of gene editing in humankind, the inquiry must start with the gene editing technique, CRISPR/Cas9 itself. What are the side effects of gene editing? Is editing in somatic (non-inheritable) cells acceptable? How does germ-line editing affect the human genome? Can the unwanted effects of germline editing techniques be sufficiently mitigated so as to allow research to continue? If so, will it have bearing as to human dignity? This article tracks whether and how far legal regulation in Europe and the EU has kept up.

Often scientific developments are too quick for regulation to keep up. Given that there are many open questions as to the long term impact of CRISPR/Cas9, several countries have completely banned it. Experts (barring exceptions) agree that human embryos genetically manipulated *in vitro* should not be used to initiate a pregnancy.⁶ Indeed CRISPR/Cas9, with its potential to be used in human germline, has proven so controversial that the scientific community had to call for a moratorium on its use in heritable cells.⁷ At the same time, this moratorium has been challenged by some.⁸ The rationale behind challenging the moratorium is that, instead of deciding whether the technique is used depending on which type of cells it is performed on, the law must prohibit willingness or gross negligence capable of provoking a change in the genome of descendants.⁹ The technology is so contentious that one of the inventors of this technique, *Jennifer Doudna*, has changed her stance on the issue of whether a moratorium is the right position.¹⁰ She initially argued for a moratorium but has recently

4 The use of gene editing in somatic cells has made considerable progress over the last decades towards clinical applications of gene therapy to treat diseases. See *National Academies of Sciences, Engineering, and Medicine*, Somatic Genome Editing, p. 83.

5 As will be discussed during the course of this paper, editing in human germline has not advanced to make the same amount of progress and is not yet considered safe.

6 *Baylis*, *Issues in Science and Technology* 2019/3, p. 43.

7 *Lander et al.*, *Nature* 2019, p. 165; *De Lecuona et al.*, *The Yale Journal of Biology and Medicine* 2017/4, p. 675.

8 *Chneiweiss et al.*, *Transgenic Research* 2017/5, pp. 709–713.

9 *De Miguel Beriain*, *Bioethics* 2019/6, p. 110.

10 <https://www.ft.com/content/6d063e48-4359-11ea-abea-0c7a29cd66fe> (27/4/2021).

advocated proceeding with research in this area albeit with caution.¹¹ In any event, CRISPR/Cas9 is increasingly being hailed as the tool to successfully and accurately edit genes affordably.¹² This means that the majority believes that research (without affecting human germline) should continue so as to ensure that it becomes safe enough for delivery in human beings.

Even if CRISPR/Cas 9 should become safe enough to be used, other issues arise concerning what purposes it ought to be used for. It is very likely that the technology would first be used to address severe genetic diseases such as sickle cell anaemia, Huntington's disease, haemophilia etc. But the question arises of whether this technology should allow parents to opt for enhancing certain traits, such as memory and intelligence? Does the law allow for changing the code of humankind? How are these questions to be approached?

In this article, the basics on cells and DNA are explained first. The process through which reproductive cells become an embryo has been laid out. The concepts of inheritance, mutation and disease are discussed briefly. Next, the CRISPR/Cas9 tool is explained. Then regulatory measures applicable to use of this technology in the EU and Europe are explained briefly. Lastly, issues concerning the ethics of heritable gene editing are discussed.

B. Basics

It is impossible to understand why gene editing might be permissible in somatic cells and not heritable cells without a basic introduction to the fundamental concepts of life and inheritance. While the readers more comfortable with legal discussions might wish to skip directly to later sections where challenges to regulation are discussed, a slight detour to understand basic scientific concepts is strongly encouraged.

I. The cell, the DNA and genes

Cells are simple units which make up an organism.¹³ Every living being is made of cells. Simpler organisms such as bacteria can be made of only a single cell. Complex organisms such as humans are made from numerous different kinds of cells.

11 <https://www.nytimes.com/2020/10/22/opinion/sway-kara-swisher-jennifer-doudna.html>? (26.1.2021). *Duodna* admits, "(...) But I have to say that when I first started thinking about that use of Crispr, I felt really opposed to it. I just thought I just can't – I can't see anyone justifying that. But in the intervening years, I guess I have come to appreciate a couple of things. One is that there's a lot of fundamental biology that is not known about early human development that might only be possible to discover using Crispr in embryos that are being utilized for research under appropriate guidelines, and not being allowed to develop beyond a few days, essentially, in the laboratory. And so I've come to feel that there is value in those kinds of experiments, if they're conducted under appropriate ethical guidelines. But I certainly don't think that the timing is right or that there's really any justification right now for using Crispr to edit embryos that are then implanted to create a pregnancy (...)"

12 *Sandor*, in: Sills/Palermo (eds.), p. 194.

13 <https://www.britannica.com/science/cell-biology#ref169655> (27/4/2021).

Inside a cell, various compartments called organelles are found. These organelles have different jobs. Most prominent is the nucleus which contains the genetic information necessary for the cell to grow and reproduce. This genetic information is found condensed in thread like structures called chromosomes. This genetic information is the code through which an organism is made.

At a molecular level, chromosomes are made of a chemical substance called the DNA or deoxyribonucleic acid. This chemical substance looks like a train twisted into a spiral. This track is composed of different base pairs (A, T, C, G).¹⁴ The information stored in the DNA is due to the specific sequences of these base pairs, each unit of which may be called a gene. The genes express themselves to form proteins called RNA which perform various functions inside a body.¹⁵

A gene is thus a unit of hereditary information. It is located on a fixed position on the chromosome. It contains sequences, which decide our skin and eye colour. The entire genetic information contained in an organism is referred to as the genome. The human genome has about 20,000 to 25,000 genes.¹⁶

II. From the germ cell to the embryo

Reproduction is the process through which life continues to exist. At the lowest level, reproduction is achieved at cellular level. Single celled organisms such as bacterium reproduce only at a cellular level i.e. one bacterium can reproduce to make two. Multicellular organisms both grow and reproduce. For instance, firstly, existing cells constantly divide to make new cells. On the other hand, individual organisms also give birth to babies.

For growth, cell division must occur. Before a cell divides, it must accurately and completely duplicate the genetic information encoded in its DNA so as to allow the daughter cell to function. This process must be performed accurately to ensure that the daughter cells get the same instruction manual that the parent cells have. To ensure that this process is done correctly, cells have mechanisms to repair errors.¹⁷

Alongside this, human beings also give birth to babies, which is a more complicated process. Reproductive cells from the mother and father (ova and sperm) each containing half of the genetic information combined to create a fertilised egg which then undergoes a series of divisions.¹⁸ The cells continue to divide and specialize making what ends up becoming a human baby.

14 <https://www.britannica.com/science/cell-biology/DNA-the-genetic-material> (27/4/2021).

15 DNA strands serve as a template and allow for Ribonucleic acid (chemically similar to DNA with bases A, U, G, C) to be formed inside the nucleus. The RNA can then be “read” and “translated” to make proteins. Each region of the DNA which specifies a protein is hence called a gene.

16 <https://www.britannica.com/science/gene> (27/4/2021).

17 <https://www.britannica.com/science/cell-biology/Cell-division-and-growth#ref313848> (27/4/2021).

18 <https://www.britannica.com/science/embryo-human-and-animal> (27/4/2021).

III. Mutation, disease and inheritance

Heredity refers to processes through which characteristics are transmitted from parents to their offspring.¹⁹ This allows for a species to remain constant while no two individuals of a species are exactly alike. Both of these aspects are explained by genes. All individuals of a species have a set of genes which correspond to height, skin colour, eye colour, hair colour and so on. As to each individual, these traits will depend on which version of the gene it has inherited from its parents.

A mutation means that an alteration in the genetic material has occurred.²⁰ This could be due to a mistake in copying or environmental factors. Mutations can cause diseases. Let's consider the example of Huntington's disease, which is genetically inherited. It causes progressive breakdown of nerve cells in the brain. The gene responsible for this disease is the huntingtin gene (HTT). It comprises repeats of certain base pairs.²¹ The normal gene has between 10-35 repeats of the same sequence; 36-39 repeats means a person *may* develop the disease, 40 or more repeats means a person *will* develop the disease.

This is an example wherein a disease may be clearly traced to a single gene. Other genetic conditions are far more complex and arise from interaction of multiple genes as well as environmental factors.

C. Gene editing techniques and CRISPR/Cas9

I. Gene-editing

Genome editing enables precise changes to be made in the genome of a living cell.²² The earliest forms of this technology have been in discovery and development since the 1980s. It is, however, only recently that scientists have been able to make these changes precisely enough.

Gene-editing techniques hold promise. Ever since it became known that DNA held the key to inheritance, scientists have been trying to figure out how to generate and modify it. Targeting specific sites on the DNA and being successfully able to make changes, however, still remains tricky.²³ This became possible with the era of precision genome editing as it was discovered that certain enzymes such as restriction enzymes

19 <https://www.britannica.com/science/heredity-genetics> (27/4/2021).

20 <https://www.britannica.com/science/mutation-genetics> (27/4/2021).

21 As we noted above, DNA comprises of four base pairs, ATGC (Adenosine, Guanine, Cytosine, Thymine).

22 *Harrison/Hart*, *Experimental Physiology* 2018/4, p. 439.

23 *Gross/Charpentier*, "The Development and Impact of Genome Editing Technologies" in: Discussion paper focusing on the scientific relevance of genome editing and on the ethical legal and societal issues potentially involved, issued by the Ethics Council of the Max Planck Society, available at: <https://www.mpg.de/13811476/DP-Genome-Editing-EN-Web.pdf> (27/4/2021).

were able to target and modify DNA with increased efficiency.²⁴ Restriction enzymes are naturally occurring in bacteria as part of their defence mechanism against viruses. These enzymes are able to fragment DNA at a specific recognition site.²⁵ These, however, remained too cumbersome to design and weren't convenient to use.

II. What is Crispr?

A breakthrough came when the Crispr/Cas9 complex was discovered. These specifically were found to be much more effective than the prevailing restriction enzymes (e.g. TALENs) used for making the edits.²⁶ The Crispr/Cas9 complex was found in certain bacteria, which, like human beings, are susceptible to viral infections.²⁷ When a virus attacks a bacterium, it binds to the bacterium and injects its genetic material inside. This viral DNA is replicated, which ultimately burst out, killing the bacterium.²⁸

To prevent this, bacteria have developed certain strategies. One of these is the use of the Crispr/Cas9²⁹ complex.³⁰ In this scenario, when attacked by a virus, this Crispr system plucks out certain parts of the viral DNA and incorporates it into its own. This is a way for the bacterium to remember the virus which has attacked it. The bacterium then uses this new DNA to create a sentinel which then searches for matching viral DNA and destroys it, thus protecting the bacterium.

Put simply, bacterium learns from the viral DNA it is under attack from by incorporating it into its own DNA, which in turn enables it to destroy its attacker. In this way, it keeps a record of all the viruses which it has been attacked by, granting it future immunity from the virus. Such changes in bacterial DNA are passed on.

III. Crispr/Cas9 applications in gene editing

It became clear that Crispr/Cas9 can be used as an efficient tool to edit genomes of a wide range of organisms including humans. Applications have been shown through ongoing research in cancers including lung cancer, Ewing's sarcoma and acute myeloid

24 These enzymes are Zinc finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs) were the first of these enzymes. See *Kim et al.*, Proceedings of the National Academy of Sciences 1996/3, pp. 1156–1160; *Miller et al.*, Nature biotechnology 2011/2, p. 143.

25 Zinc-Finger Nuclease (ZFN) and Transcription Activator Like Effector Nucleases (TALENs) are examples of artificial restriction enzymes used to edit target DNA with greater efficiency. Each of these however had their own difficulties that they were either too difficult to design and had to be reengineered for every target. See, in plants, *Bonawitz et al.*, Plant Biotechnology Journal 2019/4, p. 750; *Novak*, in: Kumar/Barone/Smith (eds.), p. 295.

26 *Pennisi*, Science 2013, p. 835.

27 *Le Rhun et al.*, RNA Biology 2019/4, p. 380.

28 *Duckworth/Gulig*, BioDrugs 2002/1, p. 57.

29 Stands for Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) array along with CRISPR-associated (cas) genes.

30 *Doudna/Charpentier*, Science 2014, p. 1077.

leukemia.³¹ A dominant mutation in the gene responsible for cataracts has also been successfully corrected in mice.³²

IV. CRSIPR/Cas9 associated risks

1. Safety

The scientists calling for a moratorium on clinical germ-line editing raise several concerns. Firstly, long-term effects of editing on human beings require further study.³³ Which side effects will result from tinkering with germ cells or embryos in the resultant human beings is not fully understood.³⁴ Key concerns within the domain have been off-target changes, mosaicism and potential alterations affecting offspring later in life (epigenetic effects).³⁵ Off target edit occurs when the edit takes place at an unintended site which can permanently alter sequences or disrupt normal gene function.³⁶ Mosaicism simply means that all cells did not take the intended edits, leaving the individual with a mix of edited and unedited cells.³⁷ This may completely defeat the purpose of undertaken edits in order to achieve resistance; all cells in the body would need to have taken the edits.

2. Appropriateness

Once the concerns about safety are allayed, the next question to ponder over would be the appropriateness of its use. There is no societal consensus as to whether gene editing in human beings is appropriate. There is larger support for use of gene editing to treat rare genetic diseases such as sickle cell anemia and Huntington's disease, but would it be appropriate to use it for enhancement in otherwise healthy individuals? So, tomorrow, should it become possible to allow a gene-edit to make someone a faster runner or a better concentrator?

The proponents of allowing enhancement advance a three pronged argument. *Foster* analyses these from a legal perspective.³⁸ The first argument is that human beings constantly attempt to enhance and improve themselves anyway. We drink coffee to

31 See respectively, *Choi/Meyerson*, Nature communications 2014, pp. 1–6; *Torres et al.*, Nature Communication 2014/1, p. 1 ff.

32 *Li et al.*, Journal of Molecular Cell Biology 2015/4, pp. 284–298.

33 *Fogleman et al.*, American journal of stem cells 2016/2, p. 39.

34 *Vogel*, Bioethics 2015, p. 1301.

35 For concerns in the area of genome editing see, *Rath*, in: Schroeder et al. (eds.), p. 109; On epigenetic effects, see Next-generation genome editing, Nat Biotechnol 2015, p. 429.

36 *Wang et al.*, Scientific reports 2020/1, p. 1.

37 Drawing from the earlier example of CRISPR babies *Lulu* and *Nana* who were edited by *He Jiankui*, it is posited that the twins could have mosaicism. See *Musunuru*, Opinion: We need to know what happened to CRISPR twins *Lulu* and *Nana*, MIT Technology Review, 3.12.2019, available at: <https://www.technologyreview.com/2019/12/03/65024/crispr-baby-twins-lulu-and-nana-what-happened/> (27/4/2021).

38 For an analysis of gene-editing and human dignity, see *Foster*.

concentrate better or get education to sharpen our minds. Secondly, some enhancements are dignity enhancing and can improve quality of life for many. This does not discount that this technology could not be abused, but legislative safeguards may be put in place to prevent abuse.³⁹

These arguments, however, must be carefully considered. As to the first, if we are only to consider the alteration to oneself, the question is what alteration to an individual would be considered dignity enhancing and indeed permissible? Some might consider deafness a condition which warrants alteration, and some might not.⁴⁰ When it comes to those alterations which might be passed on, while it is true that human beings constantly attempt enhancement, some distinction has to be drawn between coffee or drugs which do not leave long lasting impact, and even if they do, it is limited to the individual versus something which alters one's genetic composition. These will have consequences not just upon oneself but the progenies to come. It is true that permanent changes to oneself can be dignity enhancing, if one considers examples of transformative surgery. The only question that remains is whether it is dignity compliant to take away the option from ones' progeny to obtain an unaltered genetic composition. A careful analysis would be needed: How is it to be decided which qualities may be allowed and which human beings are eligible to obtain these enhancements for an appropriate legislation to then be enforced?

The ethics of allowing other non-clinical/enhancement interventions to be made are not as clear. Concerns about this technique being motivated by eugenics are rightly raised but still need more assessment. As such, the talk of "designing a baby" packs more than it reveals. *Fukuyama* investigates these arguments adroitly and clarifies that gene editing for superficial purposes is not as easy as it is sometimes made to sound, for there are no clear-cut demarcated genes for intelligence or memory.⁴¹ As such, one cannot simply pick attributes as one chooses items on a menu to order. Human beings are complicated, resulting from a mix of genetic and environmental factors. Nonetheless, as we have seen above, it is undeniable that genetics plays a crucial role in who we end up becoming. As science progresses, there may come a time when it becomes possible to clearly demarcate edits leading to better memory, attention span etc. in the offspring. The question then arises: Should individuals be allowed to choose for their progeny to have an edited intelligent gene? The answer would require an assessment of compatibility of such procedures with laws and regulations, in particular human dignity.

D. Regulation

We now examine the laws applicable in Europe which regulate the issues of heritable genome editing. First, the Oviedo Convention, which deals with the issue of heritable

39 *Foster*, p. 147.

40 See *Baylis*, in chapter 2 she undertakes an excellent analysis of how certain conditions might be perceived as candidates of gene editing by some and others might prefer to stay with those conditions and view the latter as dignity consistent.

41 *Fukuyama*, pp. 24 f.

genome editing head on is examined. In addition, the European Convention on Human Rights as well as the EU Charter on Fundamental Rights are also considered. This is done so as to investigate whether these allow use of Crispr-cas9 for genome editing and if so, for what purpose.

I. Biomedicine Convention/Oviedo Convention

In April 1997, the Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to Application of Biology and Biomedicine (Convention on Human Rights and Biomedicine) was opened for signature. At the time of writing, 29 states belonging to the Council of Europe are parties to the Oviedo Convention and six further have signed it; only 17 of the EU Member States are among the parties.

The Oviedo Convention is the first legally binding international text designed to preserve human dignity, rights and freedoms through a series of principles and prohibitions against the misuse of biological and medical advances.⁴² Differences in attitudes of Member States can be gleaned across Europe as some perceive the Convention to be too liberal (Germany, Austria) and others too restrictive (UK, Belgium).⁴³

The Oviedo Convention regulates two instances on use of gene editing technologies. First are interventions on embryos for research *in vitro* not leading to pregnancies. The second are interventions leading to heritable changes in human beings.

1. Editing human germ cells through CRISPR for research

The first scenario (gene editing is performed for research and the resulting embryos are not used to initiate a pregnancy) is regulated by Art. 18 of the Convention which provides that “1. Where law allows research on embryos *in vitro*, it shall ensure adequate protection of the embryo. 2. The creation of human embryos for research purposes is prohibited.”⁴⁴

At the outset, Art. 18(2) forbids the creation of embryos for research. The surplus eggs left over from fertility treatments may thus be used.⁴⁵ Moreover, research on embryos may only take place when the protection of embryos is ensured. In Art. 18(2), embryos are not to be created for research purposes.

Therefore, research involving gene editing may thus be conducted upon these surplus eggs only if the embryos are destroyed afterwards and not used to initiate pregnancies. The question is what is meant by adequate protection that Member States are sup-

42 *Frischbut/Werner-Felmayer*, *Medicine* 2020/10, p. 635.

43 *Ibid.*

44 Notably, the provision leaves the definition of an embryo up to the Member States which differ. In the UK, an embryo is a live fetus resulting from fertilisation, when two cells have emerged. Spain categorises the set of cells until 14 days as pre-embryo, 14 days to 2.5 months as embryo and afterwards as fetus. Germany considers an embryo to be a fertilised human egg that can develop from the instant of cell nuclei fuse. See *Hyun et al.*, *Stem Cell Reports* 2020/2, pp. 169–174; *Komarova*, *Wiadomosci Lekarskie* 2020/8, p. 1748.

45 *Araki/Isbii*, *Reproductive biology and endocrinology* 2014, p. 8.

posed to afford to embryos.⁴⁶ As such, genetic interventions on embryos for research are likely to cause significant impact; it is thus not clear what adequate protection means.⁴⁷ If the embryo is to be experimented upon to conduct gene editing, it is understood that it will ultimately be destroyed and not implanted to initiate a pregnancy.

However, in order to understand the drafting of the provision, it might make sense to view it in terms of the intention of the drafters at the time.⁴⁸ It could be that they wanted to allow only those interventions which might improve the chances of implantation or assist human reproduction. As an example the French decree no. 97-613 released in May 1997 specified conditions under which research on embryos may be performed: “the outcome of the study must be one of the following: (i) it must represent a direct benefit for the embryo under study, especially in terms of improving its chances to implant; (ii) it must participate in the improvement of assisted reproductive technology-in-vitro fertilization (ART-IVF) technology by improving the knowledge of the physiology and pathology of human reproduction.”

According to the above, research may thus be permitted if it increases chances of implantation through improvement of culture media, or freezing conditions i.e. provides benefit to the embryo. Such intervention would not alter the genome of the baby. Similar questions arose as to whether this text would allow research on arrested embryos. An educated guess would be that the legislator wanted to prohibit all research on embryos barring the practice of PGD (pre-implantation genetic diagnosis).⁴⁹

2. Editing human germ cells through CRISPR to induce heritable changes

The second scenario is that of gene editing on embryos which are then used to initiate a pregnancy. Article 13 of the Oviedo Convention provides that any intervention to modify the genome may only be undertaken for “*preventive, diagnostic or therapeutic* purposes and only if its aim is not to introduce any modification in the genome of any descendants.”⁵⁰

Art. 13 imposes two conditions for an intervention to be allowed. First, its purpose must be preventive, diagnostic or therapeutic. Second, it must not aim to introduce any changes to the genome of the descendants. Therefore, the first example of gene editing in a patient’s eye to cure blindness would have been compliant with this provision since it

46 Gunning, Eur. J. Health L. 1999/6, p. 168.

47 Ibid.

48 Viville/Nisand, Human Reproduction 1997/11, p. 2341.

49 Ibid.

50 In December 2015, the Council of Europe issued a press release restating the role of Art. 13 of the Convention, available at: https://www.coe.int/en/web/human-rights-rule-of-law/events/-/asset_publisher/E5WWthsy4Jfg/content/statement-by-the-council-of-europe-committee-on-bioethics-ethics-and-human-rights-must-guide-any-use-of-genome-editing-technologies-in-human-beings-?inheritRedirect=false (27/4/2021). In October 2015, it released the Report of the IBC on Updating Its Reflections on the Human Genome and Human Rights, which called on the states and governments to “agree on a moratorium on genome engineering of the human germline, at least as long as the safety and efficacy of the procedures are not adequately proven as treatment”.

was done with a therapeutic purpose i.e. to cure blindness. Moreover, since it was performed in the somatic cells i.e. retina, it would not introduce any heritable genetic edits. On the other hand, while the aim of gene-edits in *Lulu* and *Nana* may be viewed as therapeutic or preventive,⁵¹ they fail the second threshold of Art. 13, i.e. aiming to introduce a change in the genome of the two twins. Therefore, instead of saying that modifying the genome for therapeutic, diagnostic or preventive purposes is not allowed, it has the same legal effect, albeit in a roundabout manner.⁵² The success of gene editing in embryos is in any event fraught with uncertainty. A recent study showed that attempts at making edits in DNA in embryos either affects large swathes of surrounding DNA or lost large segments of the chromosome itself.⁵³ One opinion is that Art. 13 permits clinical applications and not clinical research as such.⁵⁴

But could it be argued that this provision be sidestepped, for instance by undertaking preventive, therapeutic and diagnostic changes, undertaken without their aim being to introduce modifications in the genome? Such reading of the provision would, however, contradict the meaning and purpose of the provision, which does not rule out radiation and chemotherapy which may still have effects on the genome of the embryo but *do not aim* to do so. This is precisely the reason why this provision allows editing in somatic cells since it satisfies the first condition and is not hit by the second condition.

There have been speculations as to the reason why the heritable genome editing is banned altogether. It is not clear whether germ-line editing is categorically prohibited, or it was because the effects of such technology are not well understood. There were certainly concerns about misusing germline engineering for eugenic ends.⁵⁵ Moreover, another reason for prohibiting this research was that it is feared that therapeutic genome editing would prove risky and premature.⁵⁶ Others have argued that the reason for the ban is rooted in the principle of human rights and dignity and cannot be reduced to concerns about safety and efficacy alone.⁵⁷

The provision should not be given expansive meaning because terms such as “healthy”, “disease”, and “disability” understood in the traditional sense will give room for circumvention. Attempts have been made to rebut these concerns by calling human dignity a vague concept.⁵⁸

The Oviedo Convention opened for signature in 1997, prior to the latest discoveries in the area of Crispr/Cas9. This perhaps explains why the Convention does not appear

51 *National Academies of Sciences, Engineering, and Medicine*, Enhancement, Enhancement, p. 137 ff.

52 See also Explanatory Report to the 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, Oviedo, 4.IV.1997 (ETS 164), para 91.

53 *Ledford*, *Nature* 2020, pp. 17 f.

54 *Poli*, in: Boggio/Romano/Almqvist (eds.), p. 355.

55 *Sykora/Caplan*, *The Council of Europe*, EMBO Reports 2017/11, p. 1871.

56 Committee on Social Affairs, Health and Sustainable Development, “Genetically engineered human beings”, Motion for a recommendation, Doc. 13927, 30 November 2015.

57 *Baylis/ Ikemoto*, EMBO Reports 2017/12, p. 2084.

58 *Sykora/Caplan*, EMBO Reports 2017/18, p. 2086.

to address it head on. As such, the 1998 protocol prohibiting human cloning by way of embryo splitting and nuclear transfer in wake of successful mammal cloning does not encompass making genome edits.⁵⁹ Also, the 2002 Protocol on Transplantation of Organs and Tissues of Human Origin for Therapeutic Purposes does not apply to reproductive organs or tissues as well as embryonic or foetal organs or tissues.⁶⁰ Another Protocol (2005) concerning biomedical research⁶¹ protects rights of persons involved in research by addressing risks versus benefits of research, consent, protection of persons not able to consent, scientific quality, and so on. This protocol does not apply to research on embryos *in vitro*. Accordingly, the question of whether research involving gene editing on supernumerary embryos may be carried out, and if so, under what rules, is not answered by this protocol. Similarly, the Protocol Concerning Genetic Testing for Health Purposes ensures rules applicable to human beings concerned by genetic tests such as non-discrimination, quality, utility, information and consent to genetic tests.⁶² According to Art. 2, the protocol does not apply to genetic tests carried out on the human embryos or foetus.

In a statement in December 2015, the Council of Europe's Committee on Bioethics noted that, while there was growing interest in exploring applications of the new editing technique, several ethical, social and safety issues remained. It moreover emphasized the applicability of Art. 13 of the Oviedo Convention to Crispr/Cas9.⁶³ Work, however, is now being done to update and examine the fitness of the Convention to present. A new Strategic Action Plan on Human Rights and Technologies in Biomedicine (2020–2025) developed by the Committee on Bioethics of the Council of Europe aims to make further strides.⁶⁴ One of the tasks identified is to examine Art. 13 of the Oviedo Convention in light of developments in gene editing technologies.⁶⁵

The other issue to be reckoned with is whether genome editing vitiates consent of the progeny which is necessary according to Art. 5 of the Oviedo Convention. Indi-

59 Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings, ETS No.168.

60 See Art. 2, Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin, ETS No. 186.

61 Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, CETS No. 195.

62 Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes, CETS No. 203. This protocol does not apply to genetic tests carried out on a human embryo or foetus. The Protocol applies to genetic tests carried out for the purposes of health which aim to identify the genetic characteristics of a person that are inherited or acquired during early development. This would include chromosomal analysis, DNA or RNA analysis. In this regard, see *Lwoff*, Eur. J. Hum. Genet. 2009/11, p. 1374 f.

63 *Council of Europe*, Committee on Bioethics, 2 December 2015, DH-BIO/INF (2015) 13, available at: https://www.coe.int/en/web/bioethics/genetics/-/asset_publisher/fFC0raLbK7U6/content/gene-editing?inheritRedirect=false (14.3.2021).

64 *Lwoff*, *European Journal of Health Law* 2020/3, p. 343 f.

65 Strategic Action Plan on Human Rights and Technologies in Biomedicine (2020–2025), available at: <https://www.coe.int/en/web/bioethics/strategic-action-plan> (9.2.2021), p. 9.

viduals providing embryos may consent to the gene editing intervention, but what about the consequences for the progeny inheriting the said changes?⁶⁶ While parents are legal custodians of children and take many decisions concerning medical procedures until the children attain majority, none of them have the ability to alter the genetic makeup of those children. Consequently, this poses an additional hurdle as to the compatibility of genome editing techniques with the convention.

II. The European Convention on Human Rights

The European Convention on Human Rights (ECHR) was enacted by the Council of Europe in 1950. All EU Member States are parties to the Convention alongside other European States, making the total number of accessions 43 at the time of writing. Individuals may bring forth violations of rights enshrined under the Convention and Protocols before the European Court on Human Rights provided all domestic remedies have been exhausted.⁶⁷ Here we examine what the ECHR states in relation to gene editing in human beings.

1. Editing human germ cells through CRISPR for research

In order to ascertain whether the convention allows gene editing on embryos for research purposes, the protections an embryo enjoys under the Convention must be determined. Art. 2(1) of the ECHR provides that “Everyone’s right to life shall be protected by law. No-one shall be deprived of his life intentionally save in the execution of a sentence of a court following his conviction of a crime for which this penalty is provided by law”.

Moreover, Art. 3 provides that “No one shall be subjected to torture or to inhuman or degrading treatment or punishment.” It is clear that while the Convention leaves the question of determining at what stage life begins to States as being within their margin of appreciation,⁶⁸ it evidently determined that an embryo pre-implantation did not have a right to life.⁶⁹ The Convention does not accord a right to life to an embryo, but provides that protection must be accorded to it, given its potentiality and capacity to become a person.⁷⁰ In *Vo v. France*, a woman alleged a violation of Art. 2 of the Convention due to discontinuation of her pregnancy owing to a procedure performed by mistake by her doctor. Since this case did not concern a clash between the rights of mother and the foetus, the court focused on the positive obligations of the state to ensure the protection of patients’ lives.⁷¹ Any resultant dignity to be accorded to an

66 *Smolenski*, *The American Journal of Bioethics* 2015/12, p. 35 f.

67 See Art. 35(1) of the ECHR.

68 *Belova*, *Kutafin University Law Review* 2019/1, p 7.

69 See Grand Chamber Judgment, *Evans v. The United Kingdom*, 10.4.2007.

70 See Grand Chamber decision of 8.7.2004, *Vo. v. France*, Application No. 53924/00, paras 84 f.

71 *Ibid*, para 88.

embryo will thus begin at life. As such, the ECHR does speak on whether gene editing research not leading to pregnancies is prohibited because of lack of dignity.

2. Editing human germ cells through CRISPR to induce heritable changes

Just as the ECHR does not spell out a ban on research on gene editing for the purposes of research, it does not pronounce a ban on heritable genetic editing either. In 1982, the parliamentary assembly noted that the right to life and dignity which are protected under Art. 2 and 3 spell out a right to genetic heritage that is not to be meddled with.⁷²

This however does not prohibit therapeutic application of gene modification in order to eradicate certain genetically transmitted diseases.⁷³ As such, we know from the previous section that through mere research involving gene editing on embryos without initiating pregnancy, the right to life of the embryo is not affected. Given that the Convention is not hostile to interventions in order to provide therapy for rare genetic diseases it may be posited that it is consistent with human dignity to use gene editing to rid embryos of serious genetic diseases when no alternatives are present and there is a reasonable guarantee of success.

Costa and Pavan v. Italy did not concern gene editing but access to PGD i.e. a technique which would allow genetic diagnosis prior to implantation of an embryo inside the uterus to achieve pregnancy artificially. The applicants in this case were healthy carriers of cystic fibrosis who wished to rely on this technology to select embryos free from this disease for implantation. The argument that PGD could be used for eugenic purposes was raised but did not impress the court since the Italian law did not rule out eugenic selection through abortion being carried out on medical grounds. The court noted that the Italian law as such lacked consistency given that it effectively forces the couple to achieve natural pregnancy and then abort the embryo if it carries disease but would not allow to select healthy embryos through PGD for implantation.⁷⁴

72 In Recommendation 934 of 26 January 1982 on Genetic Engineering, the assembly stressed that the “rights to life and human dignity, guaranteed under Art. 2 and 3 of the ECHR, imply the right to inherit a genetic pattern which has not been artificially changed, and called on the committee of ministers to draw up a European agreement on what constitutes legitimate application to human beings of the techniques of genetic engineering”. Also see Recommendation 1046 (1986) and Recommendation 2115 (2017).

73 See Recommendation 1046 (1986), which under the Appendix Rules governing the use of human embryos or foetuses and the removal of their tissues for diagnostic and therapeutic purposes, states that, “Therapy on embryos in vitro or in utero or on the foetus in utero shall not be permitted, unless it is for very clear and precisely diagnosed embryonic maladies, with grave or extremely bad prognosis, where no other solution is possible and therapy would offer reasonable guarantees of successful treatment of those illnesses”, available at: <http://assembly.coe.int/nw/xml/XRef/Xref-XML2HTML-en.asp?fileid=15080&lang=en> (27/4/2021). Moreover, Recommendation 2115 (2117) speaks only of a *de facto* moratorium on genome editing in human beings, available at: <https://assembly.coe.int/nw/xml/XRef/Xref-XML2HTML-en.asp?fileid=24228&lang=en> (27/4/2021).

74 *Costa and Pavan v Italy*, Application no. 5427/10, 28.8.2012, paras 58 f.

Similar arguments about eugenic selection were also raised in *R.R. v. Poland* wherein a woman was denied abortion of a foetus known to have genetic abnormality. The court held that the question of voluntary termination of pregnancy for eugenic reasons could not be derived from the State's positive obligations to provide adequate medical care.⁷⁵

In the same breath, the ECHR affords a large margin of appreciation when it comes to allowing research on supernumerary embryos. For instance, in the case of *Parillo v. Italy*, the Applicant wished to donate embryos for the purposes of research which she and her partner had frozen. Because her partner had passed away, she did not wish to use those embryos herself but that those are donated for the purpose of research towards advances in diseases difficult to cure. She was however not allowed to do this because of an Italian law which prohibits research on embryos. The Applicant invoked Art. 8 of the Convention which protects the right to private and family life, to say that she should be allowed to donate the embryos for the said purpose. The court disagreed stating that protection of embryos was provided for under the Convention which did not require states to authorize destructive research on embryos, since this choice fell within the margin of appreciation.⁷⁶

Most recently, there has been the case of *Nedescu v. Romania* wherein the Applicants asserted that by being prevented from accessing embryos, they had suffered a violation of Art. 8 of the Convention.⁷⁷ The court concurred stating that preventing the couple from retrieving their embryos amounts to a violation of Art. 8.⁷⁸

The only country signatory to the ECHR which may be likely to give a greenlight to heritable genome editing in humans is the UK.⁷⁹ The compatibility of this technique with the Convention, however, has not yet been tested before the European Court of Human Rights.

III. The Charter of Fundamental Rights of the European Union

According to Art. 51(1) of the Charter, the Union and the Member States must remain in conformity with the Charter when implementing Union law. It is important to keep in mind that the Union only has competences which have been conferred upon it by the Member States.⁸⁰ Moreover, in areas where this competence has been conferred upon the Union, it may only act if and in so far as the objectives of the proposed action cannot be sufficiently achieved by the Member States.⁸¹ The prerogative is to decide whether gene editing on human cells for research or for the purpose of inducing heritable changes has not been conferred upon the Union. The subject-matter is only

75 *R.R. v. Poland*, Application No. 27617/04, 26.5.2011, para 166.

76 *Parillo v. Italy*, Application No. 46470/11, 27.8.2015, para 126.

77 *Nedescu v. Romania*, Application No. 70035/10, 16.1.2018, para 65 f.

78 *Ibid.*, para 75.

79 *Dickenson/Darnovsky*, *Nature Biotechnology* 2019/4, pp. 355–357.

80 See Art. 5(1) TEU.

81 See Art. 5(3) TEU.

found incidentally in certain EU laws where it has competences. These are discussed below briefly.

The EU can take measures to enhance competitiveness of the EU industry. Regulation 1291/2013⁸² was enacted under Art. 173(3) and 182(1) TFEU with the aim of enhancing the competitiveness of the EU industry through better exploitation of the industrial potential of policies of innovation, research and technological development.⁸³ This regulation in particular regulates funding allocated to Horizon 2020. Art. 19(3) b of the Regulation provides that research activity intended to modify the genetic heritage of human beings which could make such changes heritable will not be financed. Through a question answered in the European Parliament, the Commission took cognizance of the fact that firstly, research using CRISPR/Cas9 to make heritable genetic changes is not permitted in any Member State. Secondly, there is a difference in the national laws of the Member States when it comes to allowing research on embryos – wherein 16 Member States allow research on surplus embryos (up to a 14 days limit), 4 Member States forbid it and 8 Member States leave it unaddressed. As such, the EU remains bound in that it will neither allow funding for research on heritable genetic changes through CRISPR/Cas9, nor for research which leads to the destruction of embryos.⁸⁴

The second area is patentability of biotechnology related inventions wherein certain competences are allocated to the EU. The European Patent Convention (EPC)⁸⁵ represents a bunch of national patents which are independently enforceable and are nationally revocable. Directive 98/44/EC⁸⁶ harmonises aspects of patent law encompassed under Union law pertaining to the internal market.⁸⁷ Concerning biotechnological inventions, the Directive 98/44/EC harmonises aspects of legal protection of biotechnological inventions so as to ensure that their haphazard development does not lead to further disincentives to trade, to the industrial development of such inventions and of the smooth operation of the internal market.⁸⁸ It contains *inter alia* rules on which inventions will be deemed unpatentable. In particular, according to Art. 5(1), the patentability of the human body at various stages of formation and development is prohibited. Accordingly, any technique involving human embryos/ heritable genome editing should not be patentable.

82 Regulation 1291/2013 of the European Parliament and of the Council of 11 December 2013 establishing Horizon 2020 – the Framework Programme for Research and Innovation (2014–2020) and repealing Decision No 1982/2006/EC.

83 Regulation No. 1291/2013, Recital 2.

84 Question reference E-003329/2016, Answer given by Ms. Moedas on behalf of the Commission, available at: [https://www.europarl.europa.eu/doceo/document/E-8-2016-003329-ASW_DE.html?redirect\(15.2.2021\)](https://www.europarl.europa.eu/doceo/document/E-8-2016-003329-ASW_DE.html?redirect(15.2.2021)).

85 In pursuance of a multilateral treaty also known as the Convention on the Grant of European Patents signed on 5 October 1973.

86 Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.

87 *Aerts*, Journal of Intellectual Property Law & Practice 2018/10, p. 801.

88 See Recital 7 of the Biotechnology Directive, 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.

The Court of Justice of the European Union (CJEU) acknowledged that the meaning given to the concept of human embryo in Art. 6(2) of the Directive is a sensitive issue in many Member States.⁸⁹ The court noted that the legal interpretation of the term would be done in accordance with the context of the Directive. Specifically, the court took note that the Directive, while promoting investment in the field of biotechnology, postulates that the use of biological material be done in a manner consistent with regard for fundamental rights and especially human dignity.⁹⁰ This is further supplemented by Art. 6 of the Directive, which deems processes for cloning human beings, processes for modifying the germ line genetic identity of human beings and uses of human embryos for industrial or commercial purposes contrary to *ordre public* or morality.⁹¹ Deriving from the above, the court concluded that the term “embryo” must be given a wide meaning in consonance with human dignity. Thereby the court held that “embryo” must mean any human ovum as soon as fertilised and thus be regarded as a “human embryo” under Art. 6(2) of the Directive.⁹² Also, a non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted would be considered an “embryo”.⁹³ So would a non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis.⁹⁴ In addition, only inventions pertaining to use for therapeutic or diagnostic purposes applied to human embryos are patentable.⁹⁵ In the context of patent law which concerns inventions susceptible to industrial application, the dilemma was to avoid a narrow definition of embryo which would be easy to sidestep and create markets for human reproductive material, embryos and resultant stem cells.

Another area where the EU has competences is public health. According to Art. 168 (4)(c) TFEU, the EU has competence to set high standards of quality and safety for medicinal products and devices for medical use. Accordingly, Regulation 536/2014 (which replaced Directive 2001/20/EC) contains provisions on clinical trials on medicinal products for human use. Art. 90 of the Regulation states that no gene therapy clinical trials may be carried out which result in modifications to the subject’s germ line genetic identity.

Moreover, EU Directive 2004/23/EC concerns setting high standards of quality and safety when handling human tissue and cells. This competence basis is found under Art. 168(4)(a), which pertains to setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives. The Directive recognises that it does not interfere with decisions made by Member States concerning the use or non-use of germ cells and embryonic stem cells, however, the provisions of the Directive will apply.⁹⁶

89 ECJ, *Oliver Brüstle v. Greenpeace e.V.*, ECLI:EU:C:2011:669, para 30.

90 Ibid.

91 Ibid., para 33.

92 Ibid., para 35.

93 Ibid., para 36.

94 Ibid.

95 Ibid, para 46.

96 Recital 12.

The Directive 2004/23/EC became the overarching framework, together with the Directive 2006/17/EC, which contains the technical requirements pertaining to donation, procurement and testing of human tissues and cells, and Directive 2006/86/EC, which contains traceability requirements, notification of serious adverse reactions, etc.⁹⁷ The Directive 2006/17/EC in turn supplements Directive 2004/23/EC by laying down quality and safety requirements for all tissues and cells to be used in the human body or in the manufacture of medicinal products.⁹⁸

Furthermore, the use of genome editing techniques to manufacture medicinal products is subject to Regulation 1394/2007. There is an overall authorized system which is managed by the Committee for Advanced Therapies at the European Medicines Agency.⁹⁹

Accordingly, whether or not Member States allow research on germline modifications on supernumerary embryos, these must comply with the technical requirements outlined above.

If there is a question of EU law providing for genome editing, it would have to pass the compatibility test under Art. 1, 2 and 3 of the Charter. Art. 52(3) of the Charter provides that “[i]n so far as this Charter contains rights which correspond to rights guaranteed by the Convention for the Protection of Human Rights and Fundamental Freedoms, the meaning and scope of those rights shall be the same as those laid down by the said Convention. This provision shall not prevent Union law providing more extensive protection.” Thus, the CJEU might be poised to follow the ECtHR where there is a corresponding provision.¹⁰⁰ Accordingly, the CJEU might say that while embryos do not possess a “right to life”, interventions involving embryos must be carried out in a way compliant with human dignity.¹⁰¹

Art. 3 of the EUCFR expressly prohibits eugenic practices in the field of medicine and biology.¹⁰² This indicates that it would not be compatible with Art. 3 to carry out gene editing law providing for selecting desirable traits attaining a minimum level of threshold.¹⁰³ It must be noted that this protection can be raised against states and strictly voluntary programmes to eliminate hereditary diseases are not prohibited.¹⁰⁴

97 *Marazuela/Garrido/Matesanz*, Transplantation Proceedings 2009/6, p. 2045.

98 Recital 3.

99 Parliamentary Question, 29.1.2019, Answer given by Ms. Andriukaitis on behalf of the European Commission, P-006073/2018, available at: https://www.europarl.europa.eu/doceo/document/P-8-2018-006073-ASW_EN.html (27.2.2021).

100 Please see section D.II.2 of this paper.

101 *Becchi*, in: *Becchi/Mathis* (eds.), p. 28 f.

102 Art. 3 Charter of Fundamental Rights of the European Union. Also see *De Miguel Beriain*, *Regenerative Medicine* 2017/6, p. 672. See, *Heselhaus*, in: *Becchi/Mathis* (eds.), p. 958.

103 While there is currently no case law of the CJEU in this regard, the possibility of eugenic practices for instance towards selecting the sex of the child was raised regarding the voluntary interruption of pregnancy (Abortion and Contraception Act passed on 30 May 2001) in France. The French Conseil Constitutionnel, in its decision 2001-446 DC did not find a risk of eugenic practices material to this case.

104 See, *Heselhaus*, in: *Becchi/Mathis* (eds.), p. 958.

Lastly, as to the question of whether genome editing practices are deemed compliant with human dignity, this may be explored under Art. 1 of the Charter, which declares human dignity inviolable. It is under Art. 4 of the Charter that human dignity has been discussed more comprehensively.¹⁰⁵ When affording protection of human dignity under Art. 1, the CJEU has taken account of the uniqueness and equality of human beings.¹⁰⁶ While the CJEU has not yet pronounced clarification of what human dignity under Art. 1 in the context of genome editing entails, it is likely to be done conservatively with a view to keeping account of the wide variance of Member State practices.¹⁰⁷

E. Comment

Health values rest upon legally binding general EU values such as respect for human dignity and freedom. These values are highly relevant in medicine, healthcare and public health ethics.¹⁰⁸ The Oviedo Convention is the first international legally binding text to preserve human dignity against misuse in genetic advances. It therefore puts human beings before the interests of science or society. As such, there is no unbridled right to proceed with “science” either. It has been argued that there ought to be ethical accountability in compliance with human dignity to the progress of science.¹⁰⁹

I have so far sought to determine whether the laws provide us with concrete answers when it comes to applications of gene editing in humans in the area of research as well as in the clinic. While it can safely be said that the Oviedo Convention allows research with conditions, it bans clinical use. The ECHR, on the other hand, does not explicitly address the research scenario, but it may be said that gene editing on human embryos in the context of research (i.e. not used to initiate pregnancies) may be considered permissible since it does not collide with right to life guaranteed under Art. 2. As to the second scenario, a joint reading of Art. 2 and 3 of the ECHR does not permit gene editing on embryos to initiate pregnancies unless it is for a rare genetic disease for which there are no alternatives and gene editing provides reasonable guarantees of success.

As such, the scientists who wish to proceed with the use of gene editing for enhancement will have to battle the question whether such interventions are compliant with human dignity. Indeed, with advancements in this technology, it is being looked at to be applied in treatments of cancer, atherosclerosis, Duchenne muscular dystrophy, progeria and others.¹¹⁰

105 The question of human dignity has been tackled more comprehensively under Art. 4 of the Charter for instance in the context of absolute protection against torture, inhuman and degrading treatment under Art. 4 EUCFR. In this regard, see, *Heselhaus*, in: Becchi/Mathis (eds.), pp. 959, 954 f.

106 See, *Heselhaus*, in: Becchi/Mathis (eds.), p. 960.

107 We already know from the case *Oliver Brüstle v. Greenpeace e.V.* ECLI:EU:C:2011:669, paras 33 f. that the CJEU interprets the term “embryo” broadly so as to exclude patentability. According to the CJEU, this interpretation is in line with human dignity.

108 *Frischhut/Werner-Felmayer*, *Medicine* 2020/10.

109 *Starck*, *Isr. L. Rev.* 2006/39, pp. 114 f.

110 <https://www.theguardian.com/science/2021/feb/21/after-the-nobel-what-next-for-crispr-gene-editing-therapies> (23.2.21).

The ECHR does not mention the word “dignity” but contains a conceptualisation of it under Art. 3 which prohibits torture, inhuman or degrading treatment.¹¹¹

When it comes to the use of gene editing for enhancement, arguments based on human dignity have been raised on both sides. Those for enhancement argue that because human dignity is a vague concept, it should not come into play while making this decision.¹¹² Anti-enhancers argue that allowing enhancement would not be in compliance with human dignity.¹¹³ In both of these cited examples, neither side attempts defining what human dignity is, and why exactly gene editing for the purposes of enhancement would lead to its violation.

It is indeed difficult to get into a discussion about what dignity means, and what normative field it occupies. There are few cases where judges venture to define it or decide cases on the basis of human dignity alone.¹¹⁴ Without getting into the nitty gritty of human dignity, I will attempt to present the most crucial arguments pertinent to genome editing.

From one post, it has been argued with much force that genes are common heritage of humankind and are not at the individual’s disposal to alter. They are common heritage as has also been recognised by forbidding their patentability.¹¹⁵ This means that while all human beings are repositories of genetic codes, we are as such not free to make unbridled alternations and allow it to pass into the gene pool through our progeny.¹¹⁶ This however does not mean that the human gene pool as it stands is to be treated as sacred, for it contains horrible mutations like sickle cell anemia. But this argument becomes clear when seen in conjunction with the Habermasian ethics which posit that genetic reprogramming would preclude a symmetrical relationship between “the editor” and their child.¹¹⁷ As such, by reprogramming, the editor takes away the autonomy of the child to not have those edits. Ultimately, one cannot make a call about the dignity of the child before it is born.

But why would a child want to inherit genes which cause cystic fibrosis or Huntington’s or deafness? More often than not, most people would prefer a healthier life over a diseased one. But this value judgment works well for severe rare diseases and not so well for others.¹¹⁸ For example, eradicating children with Down’s syndrome or allowing abortions for cleft palate would be such value judgments.

111 In *Pretty v. United Kingdom*, (1997) 35 EHRR 423, para 65, the court held that “the very essences of the Convention is respect for human dignity and human freedom”.

112 See for instance, *Sykora/Caplan*, Germline gene therapy, EMBO Reports 2017, p. 2086.

113 See for instance, *Baylis/Ikemoto*, EMBO Reports 2017, pp. 2084 f.

114 On certain activities which have been decried by the courts as being dignity degrading, see on peepshows (BVerG, 16.5.1990 – 1 BvR 450/90), on dwarf-tossing (*Wackenheim v. France*, Communication No. 854/1999), “Gotcha-Game” (CJEU, C-36/02, *Omega*, ECLI:EU:C:2004:614). As such, dignity mostly acts in support or in foundation of other rights. For an analysis of case law on dignity on the European Convention of Human Rights, as well as jurisprudence of the Court of Justice of the European Union, see, *Di Stasi*, Judicial Power in a Globalized World 2019, pp. 115–130.

115 See for instance, Art. 6(2) b and c of Directive 98/44/EC.

116 *Sturges*, Am. U. Int’l L. Rev. 1997, p. 219.

117 *Habermas*, pp. 29, 37–44. Also see *Segers/Mertes*, Bioethics 2020, p. 37.

118 *Segers/Mertes*, Bioethics 2020/1, p 37.

This is also the appropriate juncture to address why autonomy alone, i.e. respecting people's wishes and desires alone, does not present the complete picture. While autonomy is significant in determining whether an intervention is dignity conformant, it alone is not the key.¹¹⁹

Its inadequacy is established in many activities which may be considered dignity degrading but finds willing participants nonetheless. Case in point-dwarf tossing, peep shows as well as Gotcha games.¹²⁰ Similarly, if autonomy being an element of dignity alone was the answer, the only criterion would be to see if an individual provides informed consent for gene editing to their germ cells. Autonomy alone is insufficient to derive unconditional support for making this call since the effects will transcend the individual whose germ cells are edited. As such, inalienable autonomy may persist both in enhanced and non-enhanced situations. By making this call, one takes away the autonomy of an individual who will result from such enhanced or experience unintended effects thereof. Those individuals will be prevented from exercising autonomy with respect to exercise dignity in enhanced or non-enhanced scenarios. Even those enhancements which are most likely dignity enhancing are ridden with this problem. Human dignity is indeed conformant with pursuits which enable human beings to thrive.¹²¹ But these instances are immensely difficult to even identify, let alone successfully predict outcomes in individual cases.¹²² Our understanding of interventions and their outcomes may also evolve over time.¹²³

Time and again, the difficulty of these decisions is drawn to the vagueness of the concept of human dignity. Indeed, what may be dignity enhancing in one context may not be so in another. This is, however, not due to the weakness of the concept but people's different ways of living, no matter what construction of human dignity is bound to leave out or exclude.¹²⁴ In effect, dignity may reside in a variety of situations, even with the most constraining of physical and health situations.

In summary, at present one may not proceed to make changes to the human gene pool as desired by oneself because it affects the autonomy and dignity of the future generation.¹²⁵

119 *Foster*, p. 3 f.

120 On peepshows, BVerG, 16.5.1990 – 1 BvR 450/90, on dwarf-tossing, *Wackenheim v. France*, Communication No. 854/1999, on “Gotcha-Game”, CJEU, C-36/02, *Omega*, ECLI:EU:C:2004:614.

121 *Foster*, p. 31 f.

122 As such, decisions on whether an enhancement is dignity enhancing or not is complex. Consider for instance the example of whether an achondroplastic child should be enhanced to provide them with a taller body. These value judgments are very difficult to make in advance. In this regard, see *Foster*, pp. 150–153.

123 Mass operations to “fix” intersex persons at birth have later been recognised as violations of human dignity. See for instance *Reis*, *Medical Law Review* 2019/4, pp. 658–674.

124 BGE 143 IV 77, para. 4.1 pp. 82 f., cited in *Heselhaus/Hemsley*, in: Becchi/Mathis(eds); Also see FCC Judgment of 14 December 1965 – 1 BvR 413, 416/60 = BVerfGE 19, 206 (216); FCC Judgment of 24 September 2003 – 2 BvR 1436/02, para. 42 = BVerfGE 108, 282 (299).

125 On the aspect of human nature, also see *Fukuyama*. *Our posthuman future: Consequences of the biotechnology revolution*. New York: Farrar, Straus, and Giroux.

F. Conclusion

Gene editing is an exciting technology full of promise of a healthier world. It is, however, also a big step for humankind. It is unlike any other advance in gene therapy and clinical interventions. It must thus be concluded that we must proceed with caution in this area, if at all. The current regulations including the Oviedo Convention and the ECHR rightly prohibit gene editing with heritable effects in human beings because the safety and efficacy of this technique has not yet been established. Moreover, the most intriguing argument forces scientists and lawyers to dissect whether this would be compatible with human dignity. As noted above, this understanding might evolve in the future. At present, however, the extent of control this technique can allow human beings over themselves for the purpose of enhancement is worrying. The only consensus seems to be that the ethical pluralism and underlying biological complexity is difficult to translate in legalese.¹²⁶

Bibliography

- AERTS, ROB J., *The European Commission's notice on directive 98/44 and the European Patent Organization's response: the unpredictable interaction of EU and EPC law*, *Journal of Intellectual Property Law & Practice*, 2018, Vol. 13(10), pp. 800–805
- ARAKI, MOTOKO, ISHII, TETSUYA, *International regulatory landscape and integration of corrective genome editing into in vitro fertilization*, *Reproductive biology and endocrinology*, 2014, Vol. 12(1), pp. 108–120
- BAYLIS, FRANÇOISE, *Altered inheritance: CRISPR and the ethics of human genome editing*, Cambridge, 2019
- BAYLIS, FRANÇOISE, *Human genome editing: Our future belongs to all of Us*, *Issues in Science and Technology*, 2019, Vol. 35(3), pp. 42–44
- BAYLIS, FRANÇOISE; IKEMOTO, LISA, *The Council of Europe and the prohibition on human germline genome editing*, *EMBO Reports*, 2017, Vol. 18(12), pp. 2084 f.
- BELOVA, GABRIELA, *Some Remarks on the Legal Status of Human Embryo*, *Kutafin University Law Review*, 2019, Vol. 6(1), pp. 2–12
- BONAWITZ, NICHOLAS D, et al., *Zinc finger nuclease-mediated targeting of multiple transgenes to an endogenous soybean genomic locus via non-homologous end joining*, *Plant Biotechnology Journal*, 2019, Vol. 17(4), pp. 750–761
- CHNEIWEISS, HIRSCH, et al, *Fostering responsible research with genome editing technologies: a European perspective*, *Transgenic Research*, 2017, Vol. 26(5), pp. 709–713

126 *Walsh*, *European Journal of Health Law* 2007, p. 147.

- CHOI, PETER S; MEYERSON, MATTHEW, *Targeted genomic rearrangements using CRISPR/Cas technology*, Nature Communications, 2014, Vol. 5(1), pp. 1–6
- DE LECUONA, ITZIAR, et al., *Focus: genome editing: gene editing in humans: towards a global and inclusive debate for responsible research*, The Yale Journal of Biology and Medicine, 2017, Vol. 90(4), pp. 673–681
- DE MIGUEL BERIAIN, IÑIGO, *Legal issues regarding gene editing at the beginning of life: an EU perspective*, Regenerative Medicine, 2017, Vol. 12(6), pp. 669–679.
- DE MIGUEL BERIAIN, IÑIGO, *Should human germ line editing be allowed? Some suggestions on the basis of the existing regulatory framework*, Bioethics, 2019, Vol. 33(1), pp. 105–111
- DISTASI, ANGELA, *Human Dignity as a Normative Concept. “Dialogue” Between European Courts (ECtHR and CJEU)?*, in: Pinto de Albuquerque, Paulo; Wojtyczek, Krzysztof (eds.) *Judicial Power in a Globalized World Liber Amicorum Vincent De Gaetano*, Switzerland, 2019, pp. 115–130
- DICKENSON, DONNA; DARNOVSKY, MARCY, *Did a permissive scientific culture encourage the ‘CRISPR babies’ experiment*, Nature Biotechnology, 2019, Vol. 37(4), pp. 355–357.
- DOUDNA, JENNIFER A; CHARPENTIER, EMMANUELLE, *The new frontier of genome engineering with CRISPR-Cas9*, Science, 2014, Vol. 346, No. 6213, pp. 1077–1086
- DUCKWORTH, DONNA H; GULIG, PAUL A, *Bacteriophages*, BioDrugs, 2002, Vol. 16(1), pp. 57–62
- FOGLEMAN, SARAH, et al, *CRISPR/Cas9 and mitochondrial gene replacement therapy: promising techniques and ethical considerations*, American Journal of Stem Cells, 2016, Vol. 5(2), pp. 39–52.
- FOSTER, CHARLES, *Human dignity in bioethics and law*, Bloomsbury, 2011
- FRISCHHUT, MARKUS; WERNER-FELMAYER, GABRIELE, *A European perspective on medical ethics*, Medicine, 2020, Vol. 48(10), pp. 634–636
- FUKUYAMA, FRANCIS, *Our posthuman future: Consequences of the biotechnology revolution*, New York, 2003
- GUNNING, JENNIFER, *Article 18 of the European Biomedicine Convention: What Impact on Assisted Reproduction*, European Journal of Health Law, 1999, 6, pp. 165–171
- HABERMAS, JÜRGEN, *The future of human nature*, Cambridge, 2003
- HARRISON, PATRICK T; HART, STEPHEN, *A beginner's guide to gene editing*, Experimental Physiology, 2018, Vol. 103(4), pp. 439–448
- HESELHAUS, SEBASTIAN, *Human Dignity in the EU*, in: Becchi, Paolo; Mathis, Klaus (eds.), *Handbook of Human Dignity in Europe*, New York, 2019, pp. 943–967

- HYUN, INSOO, et al., *Toward guidelines for research on human embryo models formed from stem cells*, *Stem Cell Reports*, 2020, Vol. 14(2), pp. 169–174
- KIM, YANG-GYUN, et al., *Hybrid restriction enzymes: zinc finger fusions to Fok I cleavage domain*, *Proceedings of the National Academy of Sciences*, 1996, Vol. 93(3), pp. 1156–1160
- KOMAROVA, TETYANA V, *The Patentability of Biotechnological Inventions in the Eu: an Impact on Therapeutic Practice*, *Wiadomosci Lekarskie*, 2020, Vol. 73(8), pp. 1747–1751
- LANDER, ERIC, et al., *Adopt a moratorium on heritable genome editing*, *Nature*, 2019, Vol. 567, pp. 165–168
- LE RHUN, ANAÏS, et al., *CRISPR-Cas in Streptococcus pyogenes*, *RNA Biology*, 2019, Vol. 16(4), pp. 380–389.
- LEDFORD, HEIDI, *CRISPR gene editing in human embryos wrecks chromosomal mayhem*, *Nature*, 2020, Vol. 583, No. 7814, pp. 17 f.
- LI, JINHUAN, et al., *Efficient inversions and duplications of mammalian regulatory DNA elements and gene clusters by CRISPR/Cas9*, *Journal of Molecular Cell Biology*, 2015, Vol. 7(4), pp. 284–298.
- LWOFF, LaURENCE, *Council of Europe adopts protocol on genetic testing for health purposes*, *European Journal of Human Genetics*, 2009, Vol. 17(11), pp. 1374–1377
- LWOFF, LaURENCE, *New Technologies, New Challenges for Human Rights? The Work of the Council of Europe*, *European Journal of Health Law*, 2020, Vol. 27(3), pp. 335–344
- MARAZUELA, RAFAEL; GARRIDO, GREGORIO; MATESANZ, ROSARIO, *European union and Spanish regulations on quality and safety of tissues and cells: Overview and biovigilance*, *Transplantation Proceedings*, 2009, Vol. 41(6), pp. 2044–2026
- MILLER, JEFFREY C, et al., *A TALE nuclease architecture for efficient genome editing*, *Nature Biotechnology*, 2011, Vol. 29(2), pp. 143–148
- NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE, *Human Genome Editing: Science, Ethics, and Governance*, Washington, 2017
- NOVAK, STEPHEN, *Plant Biotechnology Applications of Zinc Finger Technology*, in: Kumar, Sandeep; Barone, Pierluigi; Smith, Michelle (eds.) *Transgenic Plants. Methods in Molecular Biology*, Vol. 1864, New York, 2019, pp. 295–310
- PENNISI, ELIZABETH, *The CRISPR craze*, *Science*, 2013, Vol. 341, pp. 833–836
- POLI, LUDOVICA, *Regulation of Human Germline Genome Modification in Italy*, in: Boggio, Andrea; Romano, Cesare; Almqvist, Jessica (eds.), *Human Germline Genome Modification and the Right to Science: A Comparative Study of National Laws and Policies*, Cambridge, 2020, pp. 335–357

- RAPOSO, VERA LUCIA, *The First Chinese Edited Babies: A Leap of Faith in Science*, JBRA Assisted Reproduction, 2019, Vol. 23(3), pp. 197–199
- RATH, JOHANNES, *Safety and security risks of CRISPR/Cas9*, in: Schroeder, Doris, et al (eds.), *Ethics Dumping*, New York, 2018, pp. 107–113
- REIS, ELIZABETH, *Did Bioethics Matter? A History of Autonomy, Consent, and Intersex Genital Surgery*, *Medical Law Review*, 2019, Vol. 27(4), pp. 658–674
- SANDOR, JUDIT, *Editing human reproduction? Legal and ethical aspects*, in Sills, Scott; Palermo, Gianpiero (eds.), *Human Embryos and Preimplantation Genetic Technologies, Ethical, Social, and Public Policy Aspects*, Cambridge, 2019, pp. 185–197
- SEGERS; SEPPE; MERTES, HEIDI, *Does human genome editing reinforce or violate human dignity?*, *Bioethics*, 2020, Vol. 34(1), pp. 33–40
- SMOLENSKI, JOANNA, *CRISPR/Cas9 and germline modification: New difficulties in obtaining informed consent*, *The American Journal of Bioethics*, 2015, Vol. 15(12), pp. 35–37
- STARCK, CHRISTIAN, *Freedom of Scientific Research and Its Restrictions in German Constitutional Law*, *Israel Law Review*, 2006, Vol. 39, pp. 110–126
- STURGES, MELISSA L, *Who Should Hold Property Rights to the Human Rights Genome – An Application of the Common Heritage of Humankind*, *American University International Law Review*, 1997, Vol. 13, pp. 219–261
- SYKORA, PETER; CAPLAN, ARTHUR, *Germline gene therapy is compatible with human dignity*, *EMBO Reports*, 2017, Vol. 18(12), p. 2086
- SYKORA, PETER; CAPLAN, ARTHUR, *The Council of Europe should not reaffirm the ban on germline genome editing in humans*, *EMBO Reports*, 2017, Vol. 18(11), pp. 1871 f.
- TORRES, RAUL, et al, *Engineering human tumour-associated chromosomal translocations with the RNA-guided CRISPR–Cas9 system*, *Nature Communication*, 2014, Vol. 5(1), pp. 1–8
- VIVILLE, STEPHANE; NISAND, ISRAËL, *Legal aspects of human embryo research and preimplantation genetic diagnosis in France*, *Human Reproduction*, 1997, Vol. 12(11), pp. 2341–2342
- VOGEL, GRETCHEN, *Embryo engineering alarm*, *Bioethics*, 2015, Vol. 347, No. 6228, p. 1301
- WALIN, LAURA, *Ambiguity of the embryo protection in the human rights and bio-medicine convention: Experiences from the Nordic countries*, *European Journal of Health Law*, 2007, Vol. 14(2), pp. 131–148
- WANG, YAO, et al., *Specificity profiling of CRISPR system reveals greatly enhanced off-target gene editing*, *Scientific Reports*, 2020, Vol. 10(1), pp. 1–8