BRILL
NIJHOFF

EUROPEAN JOURNAL OF HEALTH LAW (2022) 1–22

European Journal of Health Law

brill.com/ejhl

Transformation of Medical Care through Gene Therapy and Human Rights to Life and Health – Balancing Risks and Benefits

Anne Kjersti Befring | ORCID: 0000-0003-3327-4692
Legal Department, University of Oslo, Kristian Augusts gate 17, 0164 Oslo, Norway
a.k.befring@jus.uio.no

Abstract

This article is about how somatic gene therapy can be legally regulated and risk assessed as medical treatment when taking the following international human rights conventions into consideration: the right to life in Article 2 of the ECHR and the right to health in Article 12 of ICESCR. The right to life can involve both protection against risky genetic methods and access to necessary health care. In this context, human rights can be a basis for identifying interests that must be considered in a rapid technological development. Focusing mainly on human rights to life and to health, it is argued (1) against a total ban or general moratoriums on gene editing; (2) that regulations should be based on international cooperation and consensus; and that (3) rights to health may involve obligations to provide access to genetic methods.

Keywords

personalized medicine – gene therapy – right to life – right to health – medical care – research

1 Introduction

The significant changes in medicine from the last century can be illustrated with a quote from 1892:

> if it were not for the great variability among individuals, medicine might as well be a science and not an art.
>
> SIR WILLIAM OSLER, John Hopkins School of Medicine, Baltimore, MD, USA, 1892

The development has been even faster in the last decade. Genetic factors play a role in most human diseases, with gene variations contributing to their incidence or course.

Today, it is the knowledge of the significance of the variations that leads to a paradigm shift in medical treatment and science. The mapping of the Genome was a scientific breakthrough at the beginning of our millennium. Gene therapy by CRISPR technology was a similar breakthrough and developed since 2012.[1] The CRISPR method has been a controversial method. One of the scientists who had developed it, Jennifer Doudna, warned against the method.[2] The method can today be used in different contexts with different definitions.[3] CRISPR technology, and in particular the system called CRISPR-Cas9 has revolutionized the possibilities of medicine and can increasingly become an important part of personalized medicine.[4] "Personal medicine" refers to an emerging approach to medicine that uses scientific insights or methods in the genetic and molecular basis of health and disease. While knowledge of genetics can be used to predict, prevent and treat disease, gene therapy can be used as tailored medical treatment.[5]

---

1 M. Angrist, R. Barrangou, F. Baylis, C. Brokowski, G. Burgio, A. Caplan, C. Riley Chapman, G.M. Church, R. Cook-Deegan, B. Cwik, J.A. Doudna, J.H. Evans, H.T. Greely, L. Hercher, J. Benjamin Hurlbut, R.O. Hynes, T. Ishii, S. Kiani, L. Hoskins Lee, G. Levrier, D.R. Liu, J.E. Lunshof, K.L. Macintosh, D.J.H. Mathews, E.M. Meslin, P.H.R. Mills, L. Montoliu, K. Musunuru, D. Nicol, H. O'Neill, R. Qiu, R. Ranisch, J.S. Sherkow, S. Soni, S. Terry, E. Topol, R. Williamson, F. Zhang and K. Davies, 'Reactions to the National Academies/Royal Society Report on *Heritable Human Genome Editing*', *The CRISPR Journal* 3 (2020) 332–349, doi: 10.1089/crispr.2020.29106.man.

2 H. Devlin and J. Doudna, 'I have to be true to who I am as a scientist.' *The Guardian* (2 July 2017); J. Doudna and E. Charpentier, 'Genome Editing. The new frontier of genome engineering with CRISPR-Cas9', *Science* 346 (6213) (2014) 1258096, p. 28. When the first Chinese experiment was published, Doudna and a group of scientists and philosophers asked that scientists for the time being refrain from using CRISPR to modify human fetuses.

3 N. Bostrom, 'A history of transhumanist thought', *Journal of Evolution and Technology* 14 (2005), 1–25, p. 18, available online at http://jetpress.org/volume14/bostrom.html. A. Nordberg, 'Patentability of human enhancement: from ethical dilemmas to legal (un)certainty', In: T. Pistorius (ed.), *Intellectual Property Perspectives on the Regulation of New Technologies* (Cheltenham: Edward Elgar, 2018), 54–92. p. 55, doi: 10.4337/9781786436382.00009.

4 K. Maxson Jones, R.A. Ankeny and R. Cook Deegan. 'The Bermuda Triangle: The Pragmatics, Policies, and Principles for Data Sharing in the History of the Human Genome Project', *Journal of the History of Biology* 51 (2018) 693–805, doi: 10.1007/s10739-018-9538-7.

5 N. Scholz, Personalised medicine, 'The right treatment for the right person at the right time', *European Parliament Briefing* (2015). A.K. Befring, *Persontilpasset medisin. Rettslige perspektiver* (Gyldendal, Oslo, 2019), Chapters 1 and 3.

The use of genetic methods has transformed medical treatment in recent years and is regulated in a fragmented legal landscape. The term "genetic methods" is used as a common term for genome sequencing, gene therapy and gene editing, although the legal considerations may vary with the method used. Gene editing is a collective term for methods that change the genetic material and is understood as the ability of genetic improvement through the correction of altered (mutated) genes or site-specific modifications that target therapeutic treatment.[6] Legally, there is a distinction between gene therapy that modifies a person's genes to treat or cure a disease and when this therapy leads to changes in the human germ line, and which involves "rewriting the gene pool for future generations."[7]

This article examines, if – and if so to what extent – states might be obliged to implement and use gene therapy and what these obligations may entail, on the basis of the right to life in Article 2 of the ECHR[8] and the right to health in Article 12 of the ICESCR.[9] The article analyses the content of these provisions and the collisions and ambiguities that arise between these human rights in a situation when further regulations of gene therapy in national law or as international standards are to be further developed, for example in the Biomedicine Convention.[10] Somatic gene editing can affect the genes in the targeted cells of existing patients without effecting future generations. To modify the human germline is in most legal orders, either prohibited or severely restricted. A brief analysis is given of the ban on gene therapy that affects the legacy of the next generation in Article 13 of the Biomedicine Convention and how the ban may have implications for the ECHR, Norwegian legislation and EU law. Challenges arise with how international regulations are to be applied, and how the clear distinction in regulations of health research and medical treatment is to be understood. The article derives and points out what will be relevant assessment themes and factors when the two mentioned human rights are to be applied in connection with gene therapy. This is particularly relevant when gene therapy

6 G.A. Rangel Gonçalves and R.de Melo Alves Paiva. 'Gene therapy: advances, challenges and perspectives Advances, challenges and perspectives.' *Einstein* 15 (3) (2017) 369–375, doi: 10.1590/S1679-45082017RB4024.

7 D. Cyranoski, 'The CRISPR-Baby Scandal: What's Next for Human Gene-Editing'. *Nature* 566 (7745) (2019) 440–442.

8 The Convention of 4 November 1950 for the Protection of Human Rights and Fundamental Freedoms.

9 The International Covenant of 16 December 1966 on Economic, Social and Cultural Rights. The right to health as a universal human right was first declared by the World Health Organization (WHO) in the preamble to WHO's constitution in 1946.

10 Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, 1997, ETS No. 164 (hereinafter referred to as the Biomedicine Convention).

is of great importance in order to provide medical treatment at the same time as it can lead to changes in the human germ line and heredity.

2 The Right to Life and Health as a Basis for Balancing Risk and Opportunity

2.1 *The Right to Life and Health as a Positive and Negative Commitment*

Analysis of whether the basic human rights are complied with in the regulation of gene therapy presupposes factual descriptions of gene therapy, opportunities, risks, and scenarios. The fundamental human right to life in Article 2 of the ECHR and rulings of the European Court of Human Rights (ECtHR) are relevant in order to identify and consider fundamental considerations and perspectives on when genetic methods can be used. The Court has also found the allegations from persons suffering from serious illnesses when not receiving sufficient health treatment to fall under Article 2 of the Convention when the circumstances potentially engaged the responsibility of the State.[11]

The right to life is called *the supreme value in the hierarchy of human rights*.[12] The obligation for states to fulfil this right can be divided into a negative obligation, which means that interventions must not be made that can take lives, as well as protection against interference from others that involves a similar risk, and a positive obligation to meet the necessary needs to sustain life. The state shall actively protect life and shall refrain from taking life, with some exceptions set forth in the provision.

Article 12 of the International Covenant on Economic, Social and Cultural Rights (ICESCR), formulates the right to 'the highest attainable standard of health'.[13] The right to health is a fundamental part of the right to life in article 2 of the Convention for the Protection of Human Rights and Fundamental Freedoms. The human right to health has the greatest significance in that it obliges the states to offer a medical treatment of sufficient quality. The right to a high standard entails an obligation to develop the health service in line with medical developments. Legal standards are dynamic and must be complemented in the light of medical technological developments and must therefore be elaborated in the context of genetic methods and the corona pandemic. The

11 L.C.B. v. the United Kingdom, paras 36–41, concerning an applicant suffering from leukaemia (G.N. and Others v. Italy), concerning applicants suffering from a potentially life-threatening disease, hepatitis; Hristozov and Others v. Bulgaria, concerning applicants suffering from different forms of terminal cancer; Oyal v. Turkey.

12 Streletz, Kessler and Krenz v. Germany (para. 94).

13 The Covenant was adopted by the United Nations General Assembly in its resolution 2200A (XXI) of 16 December 1966. It entered into force in 1976.

right to health is described *as a universal standard and as a minimum standard* that must be seen in the context of the state's wealth.[14] Assessments of proportionality, benefit and risk must be based on individual and collective aspects.

In recent years, increasing attention has been paid to the contents of "the highest attainable standard of health." Article 14 of the UNESCO Universal Declaration on Bioethics and Human Rights (2005) states that "the highest attainable standard of health" is a fundamental right of every human being, which means in the present context access to the highest available healthcare.

The content of this standard and the requirements for quality can provide a basis for deriving an expectation that medical methods will be used. On this basis, the standard can be considered to contain a right to benefit from new methods when these are crucial to be able to provide effective medical treatment with the necessary quality. In this context, the standard is assessed in the light of new genetic methods and implementing new and effective medical methods.[15]

> The concept of human dignity, which is also highlighted, constitutes the essential value to be upheld. It is at the basis of most of the values emphasised in the Convention.[16]

The right to health must be seen in the context with article 15 in ICESCR and of the Universal Declaration of Human Rights which formulates a right to health and to enjoy scientific progress (article 25 and 27). What can be expected is elaborated in a General comment from the Committee on Economic, Social and Cultural Rights:

> scientific progress creates medical applications that prevent diseases, such as vaccinations, or that enable them to be more effectively treated. The right to participate in and to enjoy the benefits of scientific progress and its applications is therefore instrumental in realizing the right to health.[17]

14 K.H. Søvig, 'Minstestandarder og universalitet i norsk helse-og sosialrett, sett i lys av FNs konvensjon om økonomiske, sosiale og kulturelle rettigheter', *Jussens Venner* 41 (1) (2006) 36–56.

15 Committee on Economic Social and Cultural Rights (CESCR), General Comment No. 25 (2020) on science and economic, social and cultural rights (article 15 (1) (b) (2) (3) and (4) of the Covenant), para. 70.

16 Explanatory Report (1997), p. 3.

17 Para. 67 in General Comment No. 25 (2020) on science and economic, social and cultural rights (article 15 (1) (b) (2) (3) and (4) of the Covenant), Committee on Economic Social and Cultural Rights (CESCR).

It is stated in the same section that the states shall take an active role in promoting "scientific research, through financial support or other incentives, to create new medical applications and make them accessible and affordable to everyone."

Article 12 and Article 15 must be seen in context, cf. also a general comment from the committee. Quality in terms of including research will be a common criterion for how life and health can be safeguarded. The content of the rights to necessary health care based on a universal standard and gene editing means that the obligation for states to develop high-quality medical treatment regimens may include medical treatments with elements of research. The content of the right to health can, with genetic methods, be based on presumed evidence which replaces evidence-based medicine. There is no doubt that access to new genetic methods can be crucial for public health and for the individual health situation and crucial to sustaining life. Increased use of gene therapy could have been an effective tool. Furthermore, parties of the State should "prioritize the promotion of scientific progress to facilitate better and more accessible means for the prevention, control and treatment of *epidemic*, endemic, occupational and other diseases (Article 12 (2) c)."

The obligation for states includes to safeguard positive and negative rights. The state shall both fulfil the rights to have basic needs and services covered, and to refrain from using methods that may harm, or to intervene unnecessarily in people's lives. The use of gene therapy can be crucial in saving lives and can lead to injuries and it must be assessed whether it is part of the necessary and the standard health care we should require. This may be an argument that it is forbidden to use medical methods that can harm people or that can have unintended effects as a result of changes in genetics.

2.2 *Balancing Risks and Benefits and Assessment Topics*

Compliance with fundamental rights to life and health are part of the considerations which must be included when risk and opportunities are to be balanced in connection with the regulation of gene therapy.

First, the authorities must have a "regulatory framework" in place and implement preventive operational measures that are "necessary and sufficient" to avert the danger.[18]

The obligation to take measures to avert external risk may arise when the state knew or should have known about it (Osman v. The United Kingdom (para. 116)). Accordingly, not every claimed risk to life can entail for the authorities a Convention requirement to take operational measures to prevent that

18 Öneryildiz v. Turkey (para. 101).

risk from materializing. This positive obligation means that the state should take appropriate steps to safeguard the lives of those within its jurisdiction, (a) to provide a regulatory framework; and (b) to take preventive operational measures.[19] The obligation also applies in the context of health care.[20]

When assessing whether a method should be permitted, several considerations must be considered, including the benefit that others may have from the research. The precondition for such medical experiments to be carried out is nevertheless that the risk and strain on the subject is minimal, cf. Article 17 (2) (i) of the Biomedical Convention and Article 6 (2) of the Additional Protocol CETS 196. By minimal risk and strain is meant research that in the worst-case results in a very small and transient negative impact on the health status of the subject. See also Article 5 (e) of the 1997 UNESCO Declaration and Article 28 of the Helsinki Declaration. The obligation for the authority will include legal regulations, clarity in the placement of responsibilities and legal liability. The state has the burden of proving that it has provided "effective protection."[21] The closer choice of measures belongs to the state's margin of discretion.[22]

Secondly, the legislation must allow for the rapid development of genetic methods, but with time to assess the developments. Human rights have historically been about protecting the individual also in such situations. The principle is that in such situations Article 2 applies either if (a) the activity at issue was dangerous by its very nature and put the life of the people concerned at real and imminent risk, or if (b) the injuries suffered by them were seriously life-threatening. In germline-based gene therapy, precautionary considerations are important, as well as that the burden of justifying restrictive regulation must lie with the state in the event of uncertainty. Risk assessments are used both in order to prevent hazards and to contribute to the balancing between the material goals to be achieved and risks to be avoided. In germline-based gene therapy, precautionary considerations are important, as well as that the burden of justifying restrictive regulation must lie with the state in the event of uncertainty, but with the reservation that it takes time to assess new forms of treatment and a limitation for the costs.[23] The principle of proportionality is

19 Centre for Legal Resources on behalf of Valentin Câmpeanu v. Romania [GC], para. 130.

20 Calvelli and Ciglio v. Italy [GC]; Vo v. France [GC].

21 Öneryildiz v. Turkey (para. 89), Budayeva and Others v. Russia (para. 132), Brincat and Others v. Malta (para. 110).

22 Brincat and Others v. Malta (para. 101).

23 R. Yotova. 'Regulating genome editing under international human rights law', *International & Comparative Law Quarterly* 69 (3) (2020) 653–684, p. 666, doi: 10.1017/S0020589320000184.

used to balance different interests, even when human rights collide and some obligations can be deduced in connection with the application of gene therapy when such therapies are sufficiently safely developed in order to be part of the health care.

Assessments of the risk with the method must be based on actual descriptions of how the method works and legal factors.[24] The margin of discretion seems to be narrower where the risk is of "man-made origin" such as gene therapy, compared to life-threatening situations that are "beyond human control."[25] The expectations of the state must be reasonable. This means that they will vary according to the possibilities for averting risk, the seriousness of the situation, investment needs and the possibilities for a fair distribution of health benefits.

Third, the risk must be seen in connection with the right to health and in the context of the possibilities for medical treatment that the genetic method can provide. In gene therapy in medical treatment, several aspects must be considered, the consequences for those who have a disease and where there are no other effective methods, and consequences for others. It must be considered whether a higher risk may be acceptable and necessary to meet the need for medical treatment for patients with life-threatening conditions. The state's obligations to further develop medical treatment regimens in line with genetic development, and quality requirements, may be an argument that certain genetic methods must be made available. This means that the proportionality assessment must include the risk of using the method, the possible benefits of the method and the consequences of not using the genetic method.

In connection with gene therapy, both the benefits and risk to the individual and the risk to humanity must be considered. On the one hand, the state's has the burden of proving that "effective protection" has been provided.[26] The system must actively consider new genetic methods, for the purpose of making methods available or to prevent methods that do harm. New opportunities with gene editing, and risk-reducing measures, at the same time increase the state's responsibility to ensure access to gene methods and that it takes place step by step in accordance with what is justifiable.

It is unclear what significance this human right has in terms of the states' obligation to offer methods that involve elements of research to reduce the risk of loss of life, and to what extent costs of the method should be taken into account. The right entails on the one hand a duty to protect lives through

24 Nicolae Virgiliu Tănase v. Romania [GC] (paras 139–145).

25 Budayeva and Others v. Russia (paras 134, 135 and 137).

26 *Supra* note 21.

access to medical research such as to new genetic methods, and on the other hand a protection against gene editing that can harm man and humanity. A reservation must be made that the right can be limited in this context, among other things in order to be able to distribute access to medical treatment methods in a fair way.

3 Gene Therapies as Medical Treatment and Research

3.1 *Rights to Access Genetic Therapy in Clinical Trials*

A characteristic of the use of genetic methods is that medical treatment will include clinical trials with a primary purpose of providing effective medical treatment and a secondary goal of gaining knowledge that may be of general interest.[27] There are clear distinctions in how medical treatment and research are regulated. Declaration of Helsinki and CETS 196. Many countries, including Norway, have their own law on health research.

Such a distinction between regulations of health research and medical treatment cannot be inferred from the right to life in Article 2 of the ECHR and Article 13 of the Biomedical Convention, and the ban on using germline-based gene therapy. Genetic methods can be crucial in securing life and can lead to damage that can affect several generations and unintended effects.

The right to health is *traditionally* understood as the right to methods based on medical knowledge and science, and not a right to take part in clinical trials as part of medical treatment. The genetic methods challenge the distinction between medical care and health research and provides new assessment topics about the content of the universal standard in ICESCR Article 12. On the one hand, the offer of medical treatment must be distributed in a fair way. The distribution of health must consider that suffering from an illness can be an injustice and that a rare illness can limit the treatment options. On the other hand, there is no medical treatment for all diseases, and there may be other forms of restrictions, for example that the person will not tolerate such treatment or that it is too expensive in connection with the effect. In determining the content of the right to health, a distinction must be made between

27 Summary of the Norwegian Strategy for Personalised Medicine in Health Care.pdf (helsedirektoratet.no), available online at https://www.helsedirektoratet.no/rapporter/strategi-for-persontilpasset-medisin-i-helsetjenesten/Summary%20of%20the%20Norwegian%20Strategy%20for%20Personalised%20Medicine%20in%20Health%20Care.pdf/_/attachment/inline/5a6c511c-b245-4546-8dfa-daa057f275dc:f0a88b9e56ddd839001639bea4de5c04919bf407/Summary%20of%20the%20Norwegian%20Strategy%20for%20Personalised%20Medicine%20in%20Health%20Care.pdf.

pure improvements of human beings and medical treatment of illness. Risk assessments and access to gene therapy must be seen in relation to the disease's severity, rarity, and consequences of not having access to gene therapy. Otherwise, risk assessments may limit the possibilities for medical treatment for some groups of diseases, such as rare diseases. There may be an argument that the right to health will apply to methods that include research when this is the only method that provides an effective health service developed in line with medical knowledge. Overall, these may be arguments that there may be a right to certain methods when these methods are crucial to fulfil the right to health.[28] When more of the medical treatment is offered through clinical trials, the question arises of a fair distribution of who should be offered to participate in such trials.

The patient is at the same time a research subject for whom consent and the conditions for research and medical treatment will be linked. At the same time, rights as a patient will be important during research. When using gene therapy can risk assessments that do not take sufficient account of the need for *medical treatment* may limit the possibilities for safeguarding life and health in accordance with Article 2 of the ECHR and Article 12 of the ICESCR. The accumulation of new knowledge nevertheless becomes an *outcome and a secondary purpose*.

The necessity of defining the consideration for the patient as the primary purpose can be deduced from the restrictions that currently exist in the Biomedicine Convention. Article 1 emphasizes the consideration for human dignity and that human beings have an intrinsic value that is important for the legality of using biomedical methods in research and health care.

These considerations take precedence over the consideration of gaining knowledge using gene therapy, see Article 2 of the Convention. Humans should not be made a means of biomedical treatment, but it can be discussed how far it is legal to go by using humans in research. Corresponding regulations are found in Article 8 of the Helsinki Declaration.[29]

In assessing whether gene therapy should be offered, consideration must be given to others, for example if the method leads to lasting changes in the significance for humanity and whether others benefit from the research. These considerations and the need to minimize risk must include the generation and verification of data from clinical trials, treatment measures and how the effect of treatment is controlled.

28 Befring, *supra* note 5, pp. 374–377.

29 Article 10 of the UNESCO Declaration (1997) and Article 3 (2) of the UNESCO Declaration (2005).

This means at the same time that the patient must accept conditions for receiving the treatment offer, which may include the processing of data and examinations after the medical treatment has ended. Conditions must be set prior to the medical treatment, to meet requirements that apply in the research, and which will include the agreeing to examinations that can go over a longer period to get an overview of effects and side effects. Genetic methods will require new forms of participation as the changes will affect more than those who are patients. The opportunities to use these methods depend on more people contributing data and the data obtained can be crucial in satisfying other people's needs for medical treatment.

The implementation of genetic methods and the element of research will change the course of patient treatment, in the sense that it becomes more circular than the traditional linear approach with a clear start and end.[30] While a traditional course of treatment starts with a diagnosis, then medical treatment and the end of the treatment, i.e., a linear course, a course of treatment with clinical trials will be more circular. It may be necessary to maintain contact with the patient over time.

These changes in the medical care implies a different approach from that in ordinary research and will affect the content of obligations and patient rights. In any case, the purpose and method must be made clear in advance, and the rules must be applied based on these descriptions. It must be considered what is the state of art when there is only one method that can give the necessary effect and when it involves elements of clinical trials. If standard procedures are introduced that involve an alternation between documented medical treatment and clinical trials, a decision must also be made as to whether these standards are included as part of the right to health care.

3.2 *Possible Conflicts of Interest between Public and Commercial Actors*

Access to gene therapy and new methods can be hindered by the country's legislation, cf. Norwegian law in the next chapter, economy, and various forms of ownership. Common denominators in the basic principles include several aspects of the implementation of new genetic methods.[31] The distribution of new methods shall be safeguarded and be based on principles of equality, and the protection of the individual's integrity – in a broad sense – as well as voluntariness. International law can contribute to common practice and that can limit harmful methods that apply to humanity, i.e., methods that lead to lasting and harmful changes in the human genome. Ownership of methods

30 Befring, *supra* note 5, pp. 241–247.

31 *Ibid.*, Chapters 5 and 11.

that provide knowledge about genes were put at the forefront by American researchers (the American Civil Liberties Union (ACLU)) when they launched a lawsuit against Myriad Genetics. In the decision of the US Supreme Court in 2013 (Association for Molecular Pathology against Myriad Genetics) it was decided that it is not possible for the company to patent human genes.[32] The US Supreme Court ruled in 2013 and ruled that naturally occurring DNA sequences are not patentable. This decision has had ripple effects throughout the scientific community and the biotechnology industry.

Patients' access to genetic methods can be hindered by protected intellectual property protection. Jorge Contreras proposes that patent schemes must be developed for rapidly evolving genetic technologies that must be used in connection with medical treatment.[33] There is a close relationship between patient rights and patent rights. As stated in the World Trade Organization Doha Declaration, the intellectual property regime should be implemented in a manner supportive of the duty of States "to protect public health and, in particular, to promote access to medicines for all."[34] The right to participate in and to enjoy the benefits of scientific progress and its applications assists States in making sure that these property rights are not realized to the detriment of the right to health.[35] This right becomes a significant mediator between a human right – the right to health – and a property right.[36] Thus, State authorities should use, when necessary, all the flexibilities of the TRIPS Agreement, such as compulsory licences, to ensure access to essential medicines, especially for the most disadvantaged groups. State authorities should also refrain from granting disproportionately lengthy terms of patent protection for new medicines in order to allow, within a reasonable time, the production of safe and effective generic medicines for the same diseases. Models must be developed for collaboration between public health enterprises and commercial actors and ownership of methods.

32 Supreme Court Of The United States: *Association for Molecular Pathology et al. v. Myriad Genetics*. No. 12-398. Argued 15 April 2013. Decided 13 June 2013.

33 J. Contreras, 'Association for Molecular Pathology v. Myriad Genetics: A Critical Reassessment', *Michigan Technology Law Review* 27 (2020–2021) 1–54, doi: 10.36645/mtlr.27.1.association; J. Contreras, *The Genome Defense: Inside the Epic Legal Battle to Determine Who Owns Your DNA* (New York, NY: Algonquin Books, 2021), available online at https://www.booktopia.com.au/the-genome-defense-jorge-l-contreras/book/9781616209681.html.

34 WTO: Declaration on the TRIPS agreement and public health (DOHA), 20. November 2001.

35 O. Feeney, O.J. Cockbain and S. Sterckx, 'Ethics, Patents and Genome Editing: A Critical Assessment of Three Options of Technology Governance', *Frontiers in Political Science* 3 (2021) 731505, p. 3, doi: 10.3389/fpos.2021.731505.

36 Para. 69, General Comment No. 25 (2020) on science and economic, social and cultural rights (Article 15 (1) (b) (2) (3) and (4) of the Covenant).

4 Biomedicine Convention, EU-Law, and Norwegian Laws

4.1 *Biomedicine Convention and EU Rules*

The content of the ban on gene therapy that can lead to hereditary changes must be considered further, in light of the fact that such changes may be necessary in medical treatment. Article 13 of the Biomedicine Convention limits the modification of the human genome for diagnostic, preventive, and therapeutic purposes, and prohibits germline-based gene therapy:

> An intervention seeking to modify the human 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.

The ban on interventions that are intended to alter the human genome in a way that inherited was justified during the preparatory work of the convention by the scientific uncertainty as presented, and the unpredictable effects such an intervention would have on future generations.[37] The restriction imposed by article 13 of the Biomedicin Convention entered into force on 1 December 1999. It is not clear how this ban will be applied. When changing the CRISPR technology so that it is possible to see the risk and achieve the benefit, it must be considered whether the prohibitions against germline-based gene therapy and human improvement will be maintained, and how rules are to be applied and developed.[38]

Nordberg and other researchers have emphasized that the wording of Article 13 is "only if its aim is not to introduce any modification," and that the Convention therefore does not prohibit any actual modification of the germ line, but only interventions that have such a modification intended.[39] This means that Article 13 can be understood as a general ban on interventions that can change the germ line, but with the exception cf. "modification" as an

37 Preparatory Work on the Convention on Human Rights and Biomedicine (2000) p. 63. Only 28 countries have ratified (out of 47 member states). Absences include, e.g., the EU as an institution, Germany, Ireland, Italy, The Netherlands, Poland, Sweden, UK, Israel, and the Russian Federation.

38 B.C. van Beers, 'Rewriting the human genome, rewriting human rights law? Human rights, human dignity, and human germline modification in the CRISPR era', *Journal of Law and the Biosciences* 7 (1) (2020), 1–36, p. 18, doi: 10.1093/jlb/lsaa006.

39 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, p. 54. https://doi.org/10.1093/jlb/lsx043.

exception for therapeutic methods.[40] Formulations of this ban can be interpreted so that somatic gene therapy that may have an effect on germ line as a side effect, is allowed.[41]

In connection with the legislative changes in Norway in 2020, the parliament (Stortinget) discussed whether mitochondrial donation is legal vis-à-vis the Biomedical Convention as there is no manipulation of genes as the genetic material in the egg nucleus does not change.[42] A proposal was made that the government amend the Biomedical Convention to ensure that mitochondrial donation can be allowed in Norway when the method is safe and professionally sound.

It must be added that it is assumed that the Convention must be amended in line with new scientific discoveries and developments.[43] The Biomedicine Convention can be interpreted dynamically in the light of the Convention preparatory work and subsequent practices and agreements between convention countries, cf. the Vienna Convention Articles 31 and 32.

Neither the directive on biotechnological inventions nor the regulation on clinical trials provides basis for a general regulation of germline-based gene therapy at EU level.

Article 2 (5) of Regulation (EC) No. 1394/2007 specifies that gene therapy is both a gene therapy medicinal product and a 'somatic cell therapy medicinal product' or a 'medicinal product derived from engineered tissue'. Gene therapy can be carried out without gene editing, with the addition of genetic material where the patient's own genome is untouched. Such treatment will only have a temporary effect.

Clinical trials of gene therapy require approval in accordance with the rules in EU Regulation No. 536/2014 on clinical trials of medicinal products for human use. Pursuant to Article 90 of the Regulation, other paragraph is prohibited with clinical trials of gene therapy "which result in modifications to the subject's germ line genetic identity." Procedures for genetic modification of human germ cells are not patentable, cf. Article 6 no. 2 b) in EU Directive 1998/44/EC on legal protection of biotechnological inventions. EU consensus on a ban on germ-based gene therapy is also reflected in point 40 of the preamble to the Directive: "[T] here is a consensus within the Community that

40 A. Nordberg, 'Patentability of human enhancement: From ethical dilemmas to legal (un) certainty.' In T. Pistorius (eds.). *Intellectual Property Perspectives on the Regulation of New Technologies* (Edward Elgar Publishing, 2018), p. 77. https://doi.org/10.4337/9781786436382.00009.

41 *Supra* note 37, p. 65.

42 Innst. 296 L (2019–2020) p. 18.

43 *Supra* note 37, pp. 65, 124.

interventions in the human germ line and the cloning of human beings offends against ordre public and morality […]."

The EU Charter of Fundamental Rights has a scope that is limited to "the institutions, bodies, offices, and agencies of the Union" and to the Member States "only when they are implementing Union law," cf. Article 51. Article 3 of the EU Charter sets out several bioethical requirements, including the ban on "eugenic practices" in No. 2 b). In the explanations of the Charter (2007/C 303/02) states that the principles set out in Article 3 are already enshrined in the Council of Europe's Biomedicine Convention, and that the Charter does not intend to depart from these principles. One conclusion is that EU rules do not contain a general ban on germline-based gene therapy, except when it is aimed at eugenics.[44] Such a ban must in any case have been formulated more clearly.[45]

The distinction between therapy and eugenics can be difficult to draw, for example, it is discussed whether the improvement of immunological systems is eugenics, and thus prohibited, or medical treatment that is legal.[46] In this context, the purpose of applying the method and effects will be factors that can determine whether it is legal.

4.2 *Norwegian Legislation: From Bans to Modifications, Pre-Approvals, and Legal Standards*

In Norway, several laws must be used to get an overview of how somatic gene therapy is regulated and patient rights. The Biotechnology Act of 1994 regulates which genetic methods can be used. The Patient and User Rights Act of 1999 regulates rights to medical treatment.[47] Clinical research and other health research are regulated by the Health Research Act of 2008.

The Biotechnology Act does not contain a ban on somatic gene therapy. Changes in the human germline have been prohibited in the Norwegian Biotechnology Act since it came into force in 1994, and in para. 7-1 (2) and later in para. 6-1 (2) of the current 2003 Act.[48] In Norway, increased opportunities were provided for gene editing through amendments to the Biotechnology Act

44 van Beers, *supra* note 38.

45 Yotova, *supra* note 23, pp. 670–671.

46 N. Bostrom and R. Roache, 'Ethical issues in human enhancement.' In J. Ryberg, T. Petersen, and C. Wolf (eds.) *New Waves in Applied Ethics*. (Basingstoke: Palgrave Macmillan, 2008), pp. 120–152.

47 Act of 2 July 1999 no. 63.

48 Act of 5 December 2003 no. 100.

in 2020.[49] Before the law was changed, gene therapy was only allowed for "serious" diseases.[50]

The reason is that Gene therapy can be crucial in preventing all genetic diseases. In the Biotechnology Act para. 6-2 (2) Gene therapy is prohibited except for the treatment of disease or to prevent disease from occurring. In the preparatory work, it is stated that gene therapy and other transmission of genetic material to human cells, fetuses and fertilized eggs that cause genetic changes that are inherited in gametes are prohibited.[51] There are still some ambiguities in the law, including whether the exception that applies to medical treatment applies to all forms of gene therapy. The preparatory work for an amendment law points out that there are several medical treatments that can lead to changes in gametes and emphasizes that the CRISPR method cannot be used to treat hereditary genetic defects in gametes, but that it can be used in treatment of somatic cells, for example in cancer treatment.[52] Amendments to the law have led to the ban being clarified to apply to "genetic changes that are inherited in germ cells," shall be understood as meaning that gene therapy shall be prohibited if it is "predominantly probable" that the treatment causes hereditary genetic changes.[53]

The ban has been elaborated in the previous preparatory work. Emphasis is placed on three considerations, that prudential considerations justify a ban on methods that influence future generations, and that the rules must be seen in the context of international cooperation and international consensus.[54] The technological development and the development of the international regulations will thus be factors when ambiguities in the law are to be interpreted.

The definition of gene therapy has been changed so that it is in line with relevant EU regulations to ensure simplification and harmonization with international regulations (para. 6-1) and the approval scheme for gene therapy was simultaneously removed.

4.3 *General and Individual Decisions*

In legal theory and in the public debate, it is discussed how far *general decisions* can limit fundamental individual rights to health care and the content of

49 Legislative change 19th of June 2020 no. 78.
50 Prop. 34 L (2019–2020).
51 Innst. 296 L (2019–2020) pp. 18 and 19.
52 Prop 34 L (2019–2020) p. 58.
53 Innst. 296 L (2019–2020) p. 18.
54 Ot.prp. nr. 37 (1993–1994) pp. 41–42. Ot.prp. nr. 64 (2002–2003) pp. 16 and 115. Halvorsen, M. Rettslig grunnlag for medisinsk behandling, 1998, p. 101.

the right.[55] Although the approval scheme for gene therapy has been removed, the Norwegian law includes a general requirement for approval of all medical methods used in hospitals, by the owner of the hospitals, the regional health authorities, cf. the Specialist Health Services Act para. 4-4. This provision does not apply to health research but will be a legal barrier to using non-research gene therapy. The approval scheme is justified by the need to prioritize methods based on cost and benefit, and not to protect the population from harmful methods. In regulations of the right to necessary health care, in the Patient and User Rights Act para. 2-1b, it is pointed out that the right is limited by the general decisions on new methods. This means that gene therapy must both be considered justifiable in accordance with the Specialist Health Services Act para. 2-2 and must be pre-approved by the owner of the hospitals.

Criticism of this system is strong mainly because ownership decisions are not without conflicts of interest and because it takes a long time to obtain prior approval. The national approval scheme reduces access to new genetic methods, which is particularly important for people with rare diseases. Norway is the only country in Europe that has such a scheme. Other countries, including England, have independent committees that make recommendations.

There is little doubt that this scheme may at the same time conflict with the human right to health and the duty to make individual assessments of benefit and risk.

In The Human Rights Act (Act relating to the strengthening of the status of human rights in Norwegian law) in section 2, the ECHR and the ICESCR are included among three other conventions.[56] It appears from section 3 of this Act that national laws give way if they conflict with a provision in one of the enumerated conventions.

The rapid development of gene therapy forms means that the laws are generally formulated with legal standards. The use of gene therapy that does not affect the next generation is mainly regulated by a general standard of soundness: "State of the art," cf. Health Personnel Act para. 4, the Specialist Health Services Act para. 2-2 and the Health Research Act para. 5.

55 PROBA, Evaluering av systemet for Nye metoder i spesialisthelsetjenesten, *Rapport 2021/16. Projekt nr. 20048*.

56 Act of 5 May 1999 no. 30. The other conventions are The International Covenant of 16 December 1966 on Civil and Political Rights, The Convention of 20 November 1989 on the Rights of the Child, The Convention of 18 December 1979 on the Elimination of All Forms of Discrimination against Women with Optional Protocol of 6 October 1999.

In the preparatory work for the laws, it is specified that soft law is important when the content of the standards is to be determined.[57] When this standard is to be interpreted, soft law, including recommendations from the WHO, will be of great importance in identifying and analysing the legal issues, and when the legislation is to be applied. The two publications from the WHO Expert Advisory Committee on Developing Global Standards for Governance and The Oversight of Human Genome Editing are the first framework that can contribute to common global standards and a common understanding of how the field should be governed.[58] The recommendations of the WHO Committee include both somatic and hereditary human genome editing and apply to the state's improvements to create capacity for the genetic methods.

In this perspective, human rights to life and health will be a barrier to replacing individual rights with general considerations. This follows both from the fact that Norway has ratified these conventions and from the fact that Norway has its own law that can be used when national laws conflict with human rights conventions.

5 Assessments of Fulfilment of Rights and Obstacles, Global Standards

Allowing genetic methods and giving the right to such methods can be described as different legal levels and where the law is based on the fact that it is allowed. *Prohibition* of the use of gene therapy may apply to the development and application of these methods, although there are different rules for health research and medical treatment. When the method *is allowed*, it can be offered either as clinical trials or medical treatment, or in combination. This raises the question of several rights, equal access to the method, regardless of ability to consent, assessments of the significance of the consent, and whether the right to medical treatment applies when gene therapy is used as research. The use of gene editing methods and measures must be based on more than the individual's voluntariness, as common interests must be considered. The individual will

57 Ot. prop. nr. 13 (1998–1999) comments to para. 4. Ot.prp.nr.74 (2006–2007) comments to para. 5.

58 WHO, 'Human Genome Editing: Recommendations', *World Health Organization* (2021), available online at https://apps.who.int/iris/handle/10665/342486 (accessed 10 January 2022); WHO, Human Genome Editing: A Framework for Governance, 2021. World Health Organization, 'Human Genome Editing: Position Paper', *World Health Organization* (2021), available online at https://apps.who.int/iris/handle/10665/342485 (accessed 10 January 2022).

have limited opportunities to gain insight into the method and its effects. This means that a clear distinction must be made between risk assessments of the method and the legal responsibility that is to safeguard an integrity protection, and the permission for it to be used.[59]

With new technology, it is necessary that the legal responsibility for the medical treatment is clearly placed and that errors that arise because of the method not being of sufficient quality are not to be explained with the patients' position. Volunteering for the individual, on the other hand, is of great importance in connection with medical treatment to maintain trust. It can be difficult to clearly distinguish between ethical and legal aspects when determining the content of fundamental human rights. In this context, the risk for the next generations and precautionary assessments must be considered.

Global perspectives on the right to life and health are about what expectations are justified towards countries, and about cooperation. UNESCO have provided guidelines for the processing of the genome or genetic data in three declarations.[60] In the Universal Declaration of Human Genome and Human Rights the human genome presented as a symbolic 'human heritage'.[61] IBC (UNESCOs International Bioethics Committee) to 'provide advice on the follow-up of this statement especially with regard to genetic methods of importance to the next generations.[62] This applies to the consequences of eugenic methods. At the same time, it is understood that a ban on access to therapeutic intervention may conflict with the right to health.' In 2017, the IBC published a report on the human genome and human rights that recommends a moratorium on genome editing of the human germ line.[63] IBC emphasizes, on the one hand, that there are crucial differences between medical and non-medical use of gene therapy and that there is a need for greater security. Then it is pointed out that the right to health should include precision and personalized medicine on the grounds that every human being should have the opportunity to have the highest possible standard of health. The importance of global responsibility and governance regarding scientific and technological advances

59 Befring, *supra* note 5, pp. 291–293.

60 UNESCO 1997/1998, 2003 and 2005.

61 Article 1 and 24 in The Universal Declaration on the Human Genome and Human Rights, adopted by the UNESCO General Conference, 1997/1998.

62 UNESCO, *Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights*, SHS/YES/IBC-22/15/2REV.2 (Paris, Oct. 2, 2015), at pp. 127–128.

63 UNESCO, *Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights* (2015), available online at http://unesdoc.unesco.org/images/0023/002332/233258E.pdf.

in genomics was emphasized.[64] Different regulations will lead to the liberal countries being used for research and commercialization regarding genetic methods with potential for harm.

There will be differences in what can be expected of the states. In addition to safeguarding their own populations, the rich states can be expected to contribute to the global community and to poor countries, for example with CRISPR technology, medical knowledge, and logistics for a more equitable distribution of health benefits. When Article 2 (1) of the ICESCR stipulates that the States Parties are obliged to implement these rights "individually and through international assistance and co-operation, especially economic and technical," it was made clear that the achievement of a reasonably good standard of health in poor countries demands development assistance and cooperation on the part of rich countries. WHO has pointed out that the justification for international health regulations lies in the fact that in today's globalized world, disease can spread swiftly and widely due to international travel and trade. Global perspectives on the right to life and health are about what expectations are justified towards countries, and about cooperation.

6 Conclusions and the Way Forward

In the next decades, gene editing technologies are expected to be used in the treatment and prevention of human diseases as personalized medicine.[65] Van Beers, raises the question of whether changes in the genome lead to changes in human rights.[66] Human rights are dynamic in the sense that legal issues and perspectives can be deduced when the actual possibilities for medical methods change. The European Court of Human Rights has on several occasions ruled that the European Convention on Human Rights is a "living instrument" that is subject to dynamic interpretation. The rapid changes and benefit of gene therapy are having an impact on how gene therapy can and should be regulated to comply with human rights.[67] Some conclusions on how the right to life and the right to health should be used in gene editing can be drawn:

64 *Ibid*., pp. 115–122.

65 L.F. Moutinho Rocha, L.A. Maciel Braga and F. Batista Mota. 'Gene Editing for Treatment and Prevention of Human Diseases. A Global Survey of Gene Editing-Related Researchers', *Human Gene Therapy* 31 (15–16) (2020) 852–862, doi: 10.1089/hum.2020.136.

66 van Beers, *supra* note 38.

67 Nordberg, supra note 40, p. 60; F. Fukuyama, *Revolution* (New York, NY: Farrar, Straus and Giroux, 2002), pp. 6–10, 98, 100–102 and 173.

First, the State's obligations to protect life in Article 2 (ECHR) and safeguard health in Article 12, are increasing with new genetic knowledge. The right to health is a fundamental part of the right to life, and the understanding of a life in dignity. And vice versa, the right to life can be a central part of the right to health. The universal standard in Article 12 can be further defined by the requirement to allow the population to take part in scientific advances and methods, and which will include new genetic method. The right to life and health may provide a basis for states to have a system that can actively take a position on new genetic methods. Balancing the health benefits of genetic methods with basic human rights requires rethinking the way healthcare is organized and regulated. Further development of legislation and governance of new genetic knowledge should take place based on the basic concepts and principles. On the other side the expectations of the state must be reasonable and the choice of measures belongs to the state's margin of discretion.[68] Although it is unclear how far the obligations to fulfil the right to life extend in this context, an obligation to establish a transparent system of governance can be deduced.

Nordberg and several others have pointed out that a moratorium on germline-based gene therapy may make other forms of use of CRISPR technology seem legitimate and acceptable.[69] The World Health Organization has stated that over 10 000 monogenic diseases are caused by a defect in a single gene of DNA, which occurs in 1% of births.[70] The application of gene therapy must be based on balancing risk and benefits. Harmful diseases cannot be met with harmful genetic methods. Gene therapy can be of great importance to reduce serious and rare diseases. An example could be the ban of the treatment of a rare disease due to lack of sufficient risk assessment and as a consequence persons having the disease not receiving the necessary health care. New questions arise about equal access to medical treatment methods for people with rare diseases and disabilities, for example whether genetic mutations that cause disease can be reversed. The legislation must consider the rapid development of The CRISPR method. This argues for that the ban against germline-based gene therapy should be nuanced. Common standards can be to achieve a desired development of how gene therapy should be used. These must be developed continuously in line with the development in supplementary regulations in the form of soft law.

68 Brincat and Others v. Malta (para. 101).

69 Nordberg et al., *supra* note 39, p. 75.

70 http://www.who.int/genomics/public/geneticdiseases/en/index2.html.

Secondly, gene editing will lead to changes in the State's obligations to further develop the health service also entail a further development of patient rights. Regulations of health research will cover a wide range of considerations, in which medical treatment of a patient may be a primary – and not a secondary purpose, as is usually the case in research. The clear distinction between medical treatment and health research is becoming less clear and the diversity of interests must be safeguarded, including health justice. Patient rights must be rewritten to include the consequences of medical treatment containing elements of research and changes in the course of treatment. Some argue that it should be left to the individual to assess how much risk one wants to take with regards to medical treatment – like an individual voluntary risk taking in sports and leisure activities. Such an approach could disrupt the possibilities for a clearly placed legal responsibility for the genetic method. If the patient is to take greater responsibility for risk assessments, and with an opportunity to take over responsibility, this will have consequences for trust in research and the health service. This approach will also lead to different offers of health services to people with and without consent competence, which can have unpredictable effects when the health service and health research are used towards people who lack consent. A clear distinction must be made between liability principles and formal requirements for consent.

Finally, Gene therapy represents a significant transformation of medical treatment that requires global regulation and standards for achieving common practice. International law provides guidance on both rights and assessment topics when gene therapy is to be used and when we are faced with technologies that can change mankind and affect the future of humanity. Models for cooperation between countries, and between public health services and commercial actors, must be further developed in order to achieve new genetic methods and fair access to these methods. For this reason, the distinction between gene therapy that is important for next generations and somatic gene therapy must be maintained and at the same time, it must be further developed. The rapid development of complex technologies requires both international exchange, cooperation and a dynamic development of rules in order to be sustainable.