International Standard Setting in Biomedicine – Foundations and New Challenges

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ABSTRACT: This article examines current challenges for a normative framework regulating biomedicine, including those arising from the use of big data and machine learning tools, and from the use of the CRISPR/Cas-9 technology, as for instance gene drives. The article focusses on the question of legitimate standard setting and takes into account both "hard" and "soft" law as well as private rule making. This includes international treaties and declarations in the area of human rights law and environmental law, such as the International Covenant on Civil and Political Rights, the Cartagena Protocol on Biosafety to the Convention on Biological Diversity, the Rio Declaration on Environment and Development, and, more specifically, the UNESCO Declaration on Bioethics and Human Rights. The author argues that, as instruments of biotechnology and biomedicine merge, international environmental law has to be interpreted in the light of human rights law. In order to adapt to new challenges, the article calls for a humanisation of international environmental law and, because of the ongoing disruptive technological development, argues that further legitimate standard setting is required.

KEYWORDS: Biomedicine, Biotechnology, Gene Drives, Standard Setting, CRISPR/Cas-9, Artificial Intelligence

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I. Introduction

If we think about global health law in specific contexts, there exists a need to shed some light on the problem of international standard setting in biomedicine. How much is at stake in the area of biomedicine became apparent again in November 2018, when a Chinese researcher informed the world of the birth of twins whose embryonic genomes had been edited. The researcher claimed that he edited two human embryos by using the CRISPR-Cas9 genome-editing technique and implanting them in a woman.[1]

The outcry not only of the scientific community about the irresponsibility of the procedure could not be missed.[2] Besides, in the aftermath, the need for the development of international norms and standards on setting limits for this kind of germline research and for creating effective oversight of germline editing was acknowledged even by some State officials.[3] This seems to be an obvious example of an area where we need international standard setting in biomedicine. Before I discuss those current and pressing problems (below V.), I will spell out in the first part (II.-IV.) aspects about international standards that are in place already, how they frame the area of biomedicine, how they relate to each other, and whether there is a way to overcome frictions and fragmentation in order to achieve legitimate standard setting in

[1] The researcher He Jainkui stated that the *CCR5* gene in the embryos was modified; this gene encodes a protein that some common strains of HIV use to infect immune cells. See David Cyranoski, *First CRISPR babies: six questions that remain*, 30 November 2018, available at https://www.nature.com/articles/d41586-018-07607-3.

[2] See for instance Organizing Committee of the Second International Summit on Human Genome Editing, *Statement, On Human Genome Editing II*, 29 November 2018: '[...] At this summit we heard an unexpected and deeply disturbing claim that human embryos had been edited and implanted, resulting in a pregnancy and the birth of twins. We recommend an independent assessment to verify this claim and to ascertain whether the claimed DNA modifications have occurred. Even if the modifications are verified, the procedure was irresponsible and failed to conform with international norms. Its flaws include an inadequate medical indication, a poorly designed study protocol, a failure to meet ethical standards for protecting the welfare of research subjects, and a lack of transparency in the development, review, and conduct of the clinical procedures. [...]', available at http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=11282018b.

[3] United States National Institutes of Health, Director Francis S. Collins, *Statement on Claim of First Gene-Edited Babies by Chinese Researcher*: 'The need for development of binding international consensus on setting limits for this kind of research, now being debated in Hong Kong, has never been more apparent', available at https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-claim-first-gene-edited-babies-chinese-researcher. Quoted by David Cyranoski, *First CRISPR babies: six questions that remain*, *supra* note 1.

biomedicine. I will differentiate between international law, hard law and so-called soft law, and private rule making by non-State entities, such as non-governmental organisations (NGOs) and private companies.

If we try to shed some light on the notion of biomedicine, it seems important not to define biomedicine too narrowly, as many of the chances, benefits, challenges, and risks that will come in the next years and decades will arise from the merger of biotechnology, computer sciences, even artificial intelligence, the use of big data tools,[4] and medicine. Hence, in this paper I understand biomedicine as a broad term. It covers the whole area of so-called life sciences (including biotechnology,[5] gene therapy, neuroscience, virology etc.) with respect to their application to medicine and includes the use of biotechnical tools.[6] The notion of biomedicine covers as diverse and disputed topics as – for instance – cloning of human beings, gene editing of humans, using living organisms as vectors to spread drugs and even human brain-computer interfaces, if the latter are used for medical reasons, for instance to help people with disabilities. Nevertheless, the notion of biomedicine has reasonable limits and boundaries. It does not cover the area and products of consumer devices, even if they are health-related wearables and if there are overlapping areas of preventive medicine.

Looking at these different fields of biomedicine, it already seems obvious that international standard setting in biomedicine will mean multilayer standard setting by various actors and in various fields of medicine. And it is obvious that in this science and technology-driven area of medicine, the legal rules and private norms face the challenge of adapting to a fast-moving field and even 'disruptive' new scientific and technical developments in order to not become outdated and irrelevant. I will elaborate on whether the international order is flexible enough to adapt but can

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[4] Cf. for instance Ivan Glenn Cohen et al. (eds.), *Big Data, Health Law, and Bioethics* (2018).

[5] The Charter of Fundamental Rights of the European Union (CFREU) 2007, OJ 2007 C 303/01, differentiates in its Art. 3 para. 2 between the fields of medicine and biology, but states that the same rules have to be applied for both fields, especially the free and informed consent of the person concerned.

[6] For a discussion of the notion cf. Jelena von Achenbach, *Demokratische Gesetzgebung in der Europäischen Union* (2014), at 73-77. For a use of the notion in an international legal (regional) framework cf. the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Convention of Human Rights and Biomedicine) 1997, ETS 164.

nevertheless give guidance. For this I will give an overview of some of the most relevant rules and norms as well as of some actors.

II. Foundations and Current Questions of Legitimate Standard Setting

Arguing from the sphere of public international law, a first level of rules that act as the bases of international standard setting in biomedicine are rules laid down in universal international law treaties and secondary[7] international soft law rules that are drafted by the States parties of those treaties. However, there is no sector-specific comprehensive international treaty on biomedicine and new grey areas develop with the use of biotechnological tools to fight diseases.

A. Human Rights Treaties

Although the field of biomedicine is very fast-moving, the general human rights treaties bind State parties at the global and regional level, such as for instance, first and foremost, the 1966 International Covenant on Civil and Political Rights (ICCPR),[8] the 1966 International Covenant on Social, Economic and Cultural Rights,[9] and the

[7] International soft law is defined as rules and principles that cannot be attributed to a formal legal source of public international law and that are, hence, not directly legally binding, but that have been agreed upon by subjects of international law (States, International Organisations) that could, in principle, establish international hard law; for a similar definition see Daniel Thürer, 'Soft Law', in Rüdiger Wolfrum (ed.), *Max Planck Encyclopedia of Public International Law*, Vol. IX (2012) 269, at 271, para. 8. The discussion about international soft law rules, their impact and conditions of validity becomes clearer if we differentiate – inter alia – *on the one hand*, between soft law norms that are agreed upon by States parties of a treaty in order to spell out in more detail the content of the existing (hard law) international treaty law norms. As a general rule, those *secondary international soft law norms* must not be incoherent with the (primary and hard law) treaty rules. On the *other hand*, there are soft law norms that are agreed upon by States outside a specific hard law treaty framework; they can be called *primary international soft law norms.* As examples for the latter see below for instance the United Nations Educational, Scientific and Cultural Organization (UNESCO) Declarations in the area of biomedicine, *infra* notes 47-49, and the Rio Declaration, *infra* note 26.

[8] International Covenant on Civil and Political Rights (ICCPR) 1966, 999 UNTS 171.

[9] International Covenant on Social, Economic and Cultural Rights (ICESCR) 1966, 993 UNTS 3. It is important to note that more than 20 member States of the United Nations have not ratified one of the Covenants; for this and an argument that even the ICCPR and the ICESCR as so-called core human rights treaties do not provide a standard of international legitimacy, see Gerald L. Neuman,

1950 European Convention on Human Rights (ECHR).[10] Especially the ECHR is an important element of international – not global, but regional – standard setting and the European Court of Human Rights has issued judgments on biomedical questions, such as for instance on reproductive rights and medically assisted procreation as well as prenatal medical tests.[11] These universal human rights treaties and the regional human right treaty include several health-related norms, as the right to life[12] and bodily integrity, the right to health,[13] and the right to privacy.[14] Any restriction of these rights must have a legitimate aim and must be proportionate. These human rights are cornerstones of a rights-based framework of international standard setting in biomedicine.

The Covenants and the ECHR do not include a human dignity clause[15] that is similar to Article 1 German Basic Law stating 'Human dignity shall be inviolable. To respect and protect it shall be the duty of all state authority', and only the preambles to the two human rights Covenants mention the inherent dignity of the human person.[16] Nevertheless, there is a 'red line' for any medical research or treatment (biomedical or other) that is laid down in Article 7 ICCPR: '[...] In particular, no one shall be subjected without his free consent to medical or scientific experimentation.'

'Human Rights, Treaties, and International Legitimacy', in Silja Voeneky and Gerald L. Neuman (eds.), *Human Rights, Democracy, and Legitimacy in a World of Disorder* (2018) 51, at 54 et seq.

[10] Convention for the Protection of Human Rights and Fundamental Freedoms 1950, 213 UNTS 221.

[11] For an overview cf. European Court of Human Rights, *Factsheet – Reproductive Rights* (2018), available at https://www.echr.coe.int/Documents/FS_Reproductive_ENG.pdf.

[12] For a current analysis cf. Human Rights Committee (HRC), General Comment No. 36 (2018) on article 6 of the International Covenant on Civil and Political Rights, on the right to life, UN Doc. CCPR/C/GC/36, 30 October 2018.

[13] For an analysis of an enforceable right to health, see Alicia Ely Yamin, 'Democracy, Health Systems, and the Right to Health: Narratives of Charity, Markets, and Citizenship', in Silja Voeneky and Gerald Neuman (eds.), *Human Rights, Democracy, and Legitimacy in a World of Disorder* (2018) 185, at 198 et seq.

[14] For a detailed analysis of these human rights with regard to biotechnology research that is dual use research of concern cf. Constantin Teetzmann, 'Schutz vor Wissen? Forschung mit doppeltem Verwendungszweck zwischen Schutzpflichten und Wissenschaftsfreiheit' (forthcoming 2019) (PhD thesis on file at Freiburg University), Chapter 3, A, B.

[15] Different, however, Art. 1 Convention of Human Rights and Biomedicine.

[16] Niels Petersen, 'Human Dignity, International Protection', in Rüdiger Wolfrum (ed.), *Max Planck Encyclopedia of Public International Law*, vol. IV (2012) 1013, at 1016.

This prohibition could be seen as ius cogens[17] and is a decisive basis of international standard setting in biomedicine not only for the 20th century but for current questions in biomedicine as well. We might think for instance about the proposal to use insects to spread vaccines.[18] With regard to Article 7 ICCPR, one could argue that there exists a need for free (and informed)[19] consent from every individual who could be vaccinated by these insects if we do not limit the content of this rule to cases of torture-like misuse of individuals.[20] For this red line, there is no need for new international standard setting in biomedicine, because legally binding human rights based on the principles of human dignity and autonomy, as spelled out by the binding human right norms, already are an important limitation. Or to put it differently: new and – maybe – disruptive technologies in the area of biomedicine need non-disruptive standard setting, and there are core minimum human right standards in the area of biomedicine that must not be violated.

However, I will argue that the international norms have to adapt to the new technologies, which means that the merging of technologies, especially biomedicine and biotechnology, needs the merging and convergence of standards and standard setting. More specifically, I will propose a kind of 'humanisation' of international

[17] For a discussion which human rights norms are ius cogens, see Gerald L. Neuman, 'Human Rights, Treaties, and International Legitimacy', in Silja Voeneky and Gerald L. Neuman (eds.), *Human Rights, Democracy, and Legitimacy in a World of Disorder* (2018) 51, at 59 et seq. For the work of the International Law Commission (ILC) and its Special Rapporteur on the foundations of ius cogens without a list on rules or principles that can be considered ius cogens, cf. ILC, Third report on peremptory norms of general international law (jus cogens) by Dire Tladi, Special Rapporteur, UN Doc. A/CN.4/714, 12 February 2018.

[18] For research with regard to this, see Daisuke S. Yamamoto, Hiroshi Nagumo, and Shigeto Yoshida, 'Flying Vaccinator; A transgenic Mosquito Delivers a Leishmania Vaccine via Blood Feeding', 19 *Insect Mol Biol* (2010) 391.

[19] For the free and informed consent standard cf. Art. 3(2) CFREU.

[20] It seems generally acknowledged that the notion *medical experimentation* has to interpreted in a narrower way than the notion *medical treatment*. However, even non-experimental medical treatment that reaches a certain level of severity – if there is no consent by the patient – can violate Art. 7 ICCPR, cf. Sarah Joseph, Jenny Schultz, and Melissa Castan (eds), *The International Covenant on Civil and Political Rights – Cases, Materials, and Commentary* (2nd ed., 2004) 254, at para. 9.101. This seems convincing, as the ICCPR has no rule in the operative part that includes human dignity per se; this is a reason not to interpret Art. 7 ICCPR in too narrow a way, as the purpose of this fundamental norm is to protect human dignity.

environmental law, which means that international environmental law treaties must be interpreted in the light of human right norms and principles.[21]

B. International Environmental Law: Treaties, Soft Law Rules, and a Proposal for a 'Humanisation' of International Environmental Law

If the notion of biomedicine is understood in even broader terms such as including biotechnical tools, even treaties of public international environmental law may become relevant, as for instance the 1992 Convention on Biological Diversity (CBD),[22] the 2000 Cartagena Protocol on Biosafety to the Convention on Biological Diversity (Cartagena Protocol),[23] and the 2010 Kuala Lumpur Liability Protocol,[24] which are applicable to important areas of biotechnology. They do not apply to the modification of human beings but they do govern questions of genetic modification of organisms that might be used to fight certain diseases which can affect human beings. At the universal level, the Cartagena Protocol on Biosafety is the decisive international treaty containing binding rules for living modified organisms that may have adverse effects on biological diversity and expressly includes risks to human health. Article 1 Cartagena Protocol reads: '[...] [T]he objective of this Protocol is to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also *into account risks to human health*, and specifically focusing on transboundary movements.' This aim is expressly in line with the precautionary principle – as a legal or soft law principle – which states according to the version of the 1992 Rio Declaration on Environment and Development that where 'there are threats of serious or

[21] For this approach, with regard to the right to life, see as well HRC, General comment No. 36, *supra* note 12, para. 62: '[T]he obligation of States parties to respect and ensure the right to life should also inform their relevant obligations under international environmental law.' This approach is similar to the 'greening' of human rights law, which means that the interpretation of human rights, especially the right to life, should be informed by the obligations under international environmental law.

[22] Convention on Biological Diversity 1992, 1760 UNTS 79.

[23] Cartagena Protocol on Biosafety to the Convention on Biological Diversity (Cartagena Protocol) 2000, 2226 UNTS 208.

[24] Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety 2010, UN Doc. UNEP/CBD/BS/COP-MOP/5/17, 15 October 2010.

irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.'[25] Having more than 170 parties, States (including Germany) and the European Union,[26] the Cartagena Protocol is an important international agreement for the regulation of living modified organisms, even though relevant State actors have not signed or ratified the treaty.[27] If, for instance, a mosquito is modified to fight malaria (via a so-called gene drive)[28] and foreign DNA is integrated into the target organism`s genome, the Cartagena Protocol is applicable. Nevertheless, there are lacunae: States that are not Parties to the Cartagena Protocol, such as the United States, are not governed by these specific international legal standards and these standards are not part of customary law.[29] Hence, the Cartagena Protocol on Biosafety sets an international standard, but does not bind every State.[30] And it is part of international environmental law, not sector-specific international biomedicine law.

That the latter is of relevance is shown by the principle of informed consent, which is a key element of international biomedicine standard setting. The question is what exactly this principle means in regard to a certain biotechnology, such as gene drives,

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[25] See Principle 15 of The United Nations Conference on Environment and Development, Rio Declaration on Environment and Development, UN Doc. A/CONF.151/26 (Vol. I), 12 August 1992, adopted by the United Nations General Assembly (UNGA) Res. 48/190, 21 December 1993. There are, however, different definitions of the precautionary principle as a legal and an *ethical* principle, and it is discussed which scenarios should be governed, see for instance Daniel Steel, *Philosophy and the Precautionary Principle – Science, Evidence, and Environmental Policy* (2015), at 44 et seq., and for a critical approach Cass R. Sunstein, *Laws of Fear – Beyond the Precautionary Principle* (2005), at 109 et seq.

[26] Accession of the European Community in 2002; cf. Council Decision 2002/628/EC of 25 June 2002, OJ 2002 L 201/48.

[27] Cf. list of parties, available at http://bch.cbd.int/protocol/parties/.

[28] Gene drives systems promote the spread of genetic elements through populations by ensuring that they are inherited more frequently than Mendelian inheritance would predict, cf. Nuffield Council on Bioethics, *Genome editing: An Ethical Review* (2016), available at http://nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf, at 79. Natural populations of species with short intervals between generations, such as malaria-carrying types of mosquitoes, could be changed or wiped out through gene drives within short periods of time. Hence genetically modified mosquitoes have emerged for some as a promising new tool to combat vector-borne diseases like malaria and dengue, see World Health Organization (WHO), *Guidance Framework for Testing Genetically Modified Mosquitoes* (2014), available at http://www.who.int/tdr/publications/year/2014/guide-fmrk-gm-mosquit/en/.

[29] Silja Vöneky and Felix Beck, 'Umweltschutz und Menschenrechte', in Alexander Proelß (ed.), *Internationales Umweltrecht* (2017) 133, at 141.

[30] *Ibid*., at 178.

that aims to fight a disease by killing[31] or modifying insects. Whether the consent of the individuals who live in the area where the modified insects are released needs to be given for the use of this technology remains unclear. To answer this question is not only of theoretical relevance but has important practical implications, as in 2018 it was reported that researchers and an NGO will release genetically engineered mosquitoes in Africa for the first time.[32] The legal basis for this experiment seems to be that the national biosafety authority of the African State where the tests take place, Burkina Faso, granted scientists permission to release up to 10,000 genetically engineered mosquitoes.[33]

The experiments were one reason for a debate at the Conference of the Parties to the CBD in 2018 about whether there should be a (legally non-binding, hence soft law) moratorium that should stop these experiments and that should bind at least those States that are party of the CBD. However, no consensus was reached by the States parties of this Convention for such a moratorium.[34] The relevant Working Group[35] made a decision that seems to spell out a leeway on how to proceed with gene drive experiments without violating international standards. This decision stressed

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[31] Kyros Kyrou et al., 'A CRISPR-Cas9 gene drive targeting doublesex causes complete population suppression in caged Anopheles gambiae mosquitoes', 36 *Nature Biotechnology* (2018) 1062, available at https://www.nature.com/articles/nbt.4245: 'A CRISPR-Cas9 gene drive construct targeting this same sequence spread rapidly in caged mosquitoes, reaching 100% prevalence within 7-11 generations while progressively reducing egg production to the point of total population collapse.'

[32] Cf. Scientific American, *Researchers to Release Genetically Engineered Mosquitoes in Africa for First Time* (2018), available at https://www.scientificamerican.com/article/researchers-to-release-genetically-engineered-mosquitoes-in-africa-for-first-time/.

[33] *Ibid*., quoting the director of stakeholder engagement for the NGO Target Malaria Project, which runs the Burkina Faso test and coordinates the research across three African countries. It is important to note that these experiments do not yet include gene drive mosquitoes but are a first step to use even gene drives mosquitos in order to fight malaria at a later stage.

[34] Cf. Jonathan Watts, The Guardian, *GM mosquito trial sparks 'Sorcerer's Apprentice' lab fears*, 25 November 2018, available at https://www.theguardian.com/world/2018/nov/25/gm-mosquitoes-released-burkina-faso-malaria-gene-drive. According to this, the International Union for Conservation of Nature has been asked by its members to refrain from supporting research into gene drives until it completes an ongoing assessment of the technology, *ibid*. Some non-governmental organisations (NGOs) are supporting the tests, as for instance *Island Conservation*, and others are opposed to it, as Terre a Vie and African Centre for Biodiversity, *ibid*.

[35] Conference of the Parties to the Convention on Biological Diversity, Synthetic Biology, Draft decision submitted by the Chair of Working Group II, UN Doc. CBD/COP/14/L.31, 28 November 2018.

that States should apply a precautionary approach with regard to gene drives. But more specifically, it states that it

> [...] also calls upon Parties and other Governments to only consider introducing organisms containing engineered gene drives into the environment, including for experimental releases and research and development purposes, when:
>
> (a) Scientifically sound case-by-case risk assessments have been carried out;
>
> (b) Risk management measures are in place to avoid or minimize potential adverse effects, as appropriate;
>
> (c) Where appropriate, the "prior and informed consent", the "free, prior and informed consent" or "approval and involvement"[36] of potentially affected indigenous peoples and local communities is sought or obtained, where applicable in accordance with national circumstances and legislation [...].[37]

The last paragraph spells out and proposes some criteria for a valid consent under the umbrella of the CBD, as it was interpreted by the Working Group. From a human rights point of view, however, could one argue that because '[...] (n)o one shall be subjected without his free consent to medical or scientific experimentation' according to Article 7 ICCPR, free consent is necessary by every individual who lives in the region and who could be affected by the released insects? This interpretation certainly would stress the principle of autonomy and the value of human dignity of every human being. On the other hand, it seems reasonable to argue as well that the persons living in the area are not 'subjected' to medical or scientific experimentation as long as the mosquitos are modified not in order to transfer any drug[38] to human beings, but only to suppress the population of certain mosquitoes, and as long as the insects cannot be the vector of a disease.

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[36] Conference of the Parties to the Convention on Biological Diversity, Decision adopted by the Conference of the Parties to the Convention on Biological Diversity, UN Doc. CBD/COP/DEC/XIII/18, 17 December 2016.

[37] Conference of the Parties to the Convention on Biological Diversity, *supra* note 35, at para. 9. See also paras. 10 and 11, which state: '10. Recognizes that, as there could be potential adverse effects arising from organisms containing engineered gene drives, before these organisms are considered for release into the environment, research and analysis are needed, and specific guidance may be useful, to support case-by-case risk assessment; 11. Notes the conclusions of the Ad Hoc Technical Expert Group on Synthetic Biology that, given the current uncertainties regarding engineered gene drives, the free, prior and informed consent of indigenous peoples and local communities might be warranted when considering the possible release of organisms containing engineered gene drives that may impact their traditional knowledge, innovation, practices, livelihood and use of land and water; [...]'.

[38] This is different from the example that insects that are used in order to vaccinate individuals, see *supra* note 31.

By this I am not arguing that a State should permit such experiments without the consent of the population or the people who could be affected. But I would like to discuss the question of whether the *free* consent of *every single* individual is necessary, or whether it is sufficient that the following conditions have to be met:

- Firstly, a scientifically sound case-by-case risk assessment has to take place that leads to the conclusion that the health benefits for the population outweigh the health risks and other risks (as for instance risks to the environment) (1), *and*
- secondly, a transparent consultation process has to take place taking into account the case-by-case risk assessment (2), *and*
- thirdly, a general prior, free and informed consent given by a representative of a group of the part of the population that is potentially affected has to be given (3).

I would argue that these conditions have to be fulfilled cumulatively for a valid general consent. This is the case because they combine bioethical (utilitarian) risk-benefit reasoning (precondition 1) with elements that are human rights-based (preconditions (2) and (3)) and elements for the protection of the environment (precondition 1) that reflect the aims of the CBD and public international environmental law. These preconditions seem to be necessary to enhance *procedural and substantive legitimacy* that must be given before an experiment (or trial) is permitted, if the experiment might affect human beings but does not constitute medical research involving human subjects *strictu sensu*. They are in line with human rights law, as a human rights-based approach requires procedural rights for individuals to participate in the making of decisions that affect them. According to this, a mere government approval is not sufficient to legitimise experiments that fall in the grey area of biomedicine and biotechnology; this is even more true if the experiments take place in a non-democratic State.

This example may show that the more the tools of biomedicine and biotechnology merge, the more international law scholars have to think about how to merge the rules of human rights law, bioethical principles and environmental law. And this does not mean to argue in the formal way of *lex specialis* or *lex posterior* only. It means to think about the question of whether there are reasons that human rights treaties form the

basis of any method or means that could affect human dignity and human rights that are so fundamental as the rights to life, bodily integrity, and health.

C. Key Elements of *Legitimate* Standard Setting in Biomedicine

It is beyond the scope of this article to spell this argument out in more detail, but my argument is that if we discuss problems of standard setting in biomedicine, we have to think about the criteria of *legitimate* standard setting in biomedicine. I argued above that with regard to areas of biomedicine, we have to interpret the relevant environmental law in the light of human rights law and that environmental law does not *per se* have priority only because a treaty or norm developed after a human rights treaty or norm did. Rather, the global order can and should be understood as an order with legally-enshrined values whereby the values enshrined in human rights have primacy. This is even more true in those contexts, as biomedicine, that have a close connection to fundamental human rights, human dignity, and the existence of humankind.[39] This is part of the legal and ethical bases of what I called the 'humanisation' of international environmental law.

These arguments rely on the reasoning – which I have spelled out in an earlier article[40] – that *legitimate* standard setting means that the relevant standards have to be justifiable in a supra-legal way, in the sense that they possess rational acceptability.[41] Hence, if we think about the current and future *legitimate* international standard setting in biomedicine, the guiding norms and standards of rulemaking in biomedicine have to be coherent with existing international law insofar as the international law reflects justified values. There are different ethical paradigms (or normative ethical theories) that are able to justify standards in a supra-legal way. Before, I men-

[39] For arguments of a human rights-based approach with regard to the governance of global catastrophic risks that endanger humankind, cf. Silja Vöneky, 'Human Rights and Legitimate Governance of Existential and Global Catastrophic Risks', in Silja Voeneky and Gerald L. Neuman (eds.), *Human Rights, Democracy, and Legitimacy in a World of Disorder* (2018) 139, at 151-160.

[40] For the criteria of legitimate standard governance, see *ibid.*, at 149-151.

[41] Convincing criteria of rational acceptability are coherence, consistency, and relevance. Here I follow the position of the philosopher Hilary Putnam; he shows and argues that the notions of fact and truth and rationality are interdependent, but nevertheless no neutral understanding of rationality exists as the criteria 'rest on and presuppose our values': the 'theory of rationality (...) presupposes our theory of good', see Hilary Putnam, *Reason, Truth, and History* (1981), at 198, 201, 215.

tioned the human rights-based approach that can be considered a deontological concept, as the rightness or wrongness of conduct is derived from the character of the behavior itself.[42] Another approach mentioned before is utilitarianism, which is a doctrine stating that among the acts with available evidence, one should perform the act that will most probably maximise benefits.[43] I argue that a legitimate international standard setting in biomedicine should be based on human rights, more precisely on legally binding human rights. This does not mean that other ethical approaches to solve biomedical problems are ruled out as far as they are compatible with human rights. But I do not agree with those who argue that utilitarian arguments should be the primary standard to measure the legitimacy of a governance regime or standard setting in biomedicine. There are several arguments that could be brought forward to support this claim, even the pragmatic one that human rights are not only justified values, but part of the existing international legal order. An additional argument concerning standard setting in the area of biomedicine is that the problems that have to be solved in the area of biomedicine are so closely related to the dignity of human beings, and biomedical experiments might easily undermine this dignity – or at least have the potential to undermine it;[44] hence the convincing standard seems to be the one that is based on the value of human dignity and aims to spell out and to preserve this dignity, as human rights do.[45]

D. UNESCO Soft Law

Apart from the international treaties, primary soft law rules are relevant for standard setting in the area of biomedicine. There are specific soft law norms and rules that cover areas of biomedicine, most importantly the 1997 United Nations Educa-

[42] A deontological theory of ethics is one which holds that at least some acts are morally obligatory regardless of their consequences, see Robert G. Olson, *The Encyclopedia of Philosophy*, Vol. 1-2 (1997), at 343.

[43] See Richard B. Brandt, *Facts, Values, and Morality* (1996), at 142.

[44] For a philosphical argument speaking of the dignity of humankind, cf. Jürgen Habermas, *Die Zukunft der menschlichen Natur – Auf dem Weg zu einer liberalen Eugenik* (2001); for a discussion of the linkage between human dignity and human cloning, cf. Silja Vöneky and Rüdiger Wolfrum (eds.), *Human Dignity and Human Cloning* (2004).

[45] The HRC in its General comment No. 36 Art. 6 ICCPR, on the right to life, states: 'The right to life is a right which should not be interpreted narrowly. It concerns the entitlement of individuals [...] to enjoy a life with dignity. [...]', *supra* note 12, at para. 3.

tional, Scientific and Cultural Organization (UNESCO) Declaration on the Human Genome and Human Rights;[46] the 2003 UNESCO Declaration on Human Genetic Data;[47] and the 2005 Universal Declaration on Bioethics and Human Rights.[48] They are part of international soft law, meaning that they are not binding as law in the strict sense but they nevertheless have a normative force since States parties to the UNESCO agreed on these principles and with this declared that they will not violate these principles.[49] These soft law declarations are relevant if we discuss international standard setting today in two ways. They are relevant from a procedural and from a substantive point of view, even if they do not answer every pressing question of biomedicine law.

1. Procedural Aspects

They are relevant from a procedural point of view since they can be seen as effective tools to bridge the bottom up/top down norm creation gap, i.e. the gap that might result from rule creating by private entities (bottom up) and by States (top down). This can be shown with regard to the drafting of the UNESCO Declaration on Bioethics and Human Rights.[50] In 1993, UNESCO established the International Bioethics Committee (IBC), an expert body that consists of 36 members that are independent experts in the field of bioethics. The IBC can give advice and issue recommendations. Five years later, in 1998, the Intergovernmental Bioethics Committee (IGBC) was established as a counterbalance for the IBC as the IGBC members are State representatives. Nevertheless, it was the IBC – the expert body – that was decisive in drafting the UNESCO Declaration on Bioethics and Human Rights. The

[46] UNESCO, Records of the General Conference, 29th session, Paris, 21 October to 12 November 1997, v. 1: Resolutions (1998), UNESDOC 29 C/Resolutions + CORR, at para. 16.

[47] UNESCO, Records of the General Conference, 32nd session, Paris, 29 September to 17 October 2003, v. 1: Resolutions (2004), UNESDOC 32 C/Resolutions, para. 22.

[48] UNESCO, Records of the General Conference, 33rd session, Paris, 3 to 21 October 2005, v. 1: Resolutions (2005), UNESDOC 33 C/Resolutions + CORR. + CORR.2 + CORR.3 + CORR.4 + CORR.5, at para. 36.

[49] For a categorisation of primary and secondary international soft law rules, see *supra* note 7.

[50] For this see Silja Vöneky, *Recht, Moral und Ethik* (2010), at 359-377; Fruzsina Molnár-Gábor, *Die internationale Steuerung der Biotechnologie am Beispiel des Umgangs mit genetischen Analysen* (2017), at 218 et seq.

drafting process took less than two years (starting in January 2004) and State representatives negotiated from January 2005 to October 2005 after the working group of the IBC presented its draft.[51] The Universal Declaration on Bioethics and Human Rights is still a model for future developments in international standards setting in biomedicine because it combines State-based regulation and norm creation by experts. The drafting of this Declaration shows that an international document can be created that comprises of an overlapping consensus of experts in the field and State representatives in a short period of time.

2. Substantive Rules

The substance of the 28 Articles of the UNESCO Declaration on Bioethics and Human Rights entails key elements of biomedical and bioethical standards. It stresses human dignity and human rights, the principle of maximising benefits and minimising harm; the principle of prior, free, and informed consent; the respect for human vulnerability; the principles of personal integrity, privacy, equality, justice and equity, non-discrimination, respect for cultural diversity, and the principles of solidarity and cooperation, social responsibility, sharing of benefits, and protection of the environment (Articles 1-17).[52]

Looking at the drafting history, one has to remark that – although it is sometimes written this way – it would be incorrect to say that during the drafting process, a bioethical (and utilitarian) document was changed into a human rights document because of and by the State representatives. The key elements, which are human rights-based, were already part of the IBC draft version of the Declaration (human dignity, Article 3; autonomy, Article 5; informed consent, Article 6, integrity, Article 8; privacy, Article 9; non-discrimination; Articles 10, 11).[53] State representatives did change the declaration, but in a different way than is sometimes stated. They softened the soft law by changing 'shall' into 'should'; and they lowered the standards for privacy protection (Article 9). Besides, State representatives broadened the realm to

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[51] Silja Vöneky, *Recht, Moral und Ethik*, *supra* note 50, at 369 et seq.

[52] Henk ten Have, 'Bioethics and Human Rights – Wherever the Twain Shall Meet', in Silja Vöneky et al. (eds.), *Ethics and Law – The Ethicalization of Law* (2013) 149, at 163-167.

[53] Silja Vöneky, *supra* note 50, at 371 et seq.

limit the principles of the declaration (Article 27): If the application of the principles of this declaration is to be limited, legitimate aims are: 'interests of public safety', 'protection of public health'. In a narrower way, the IBC, as an expert body, argued that restrictions have to be necessary 'in a democratic society'.[54] As UNESCO consists of 193 member States, this Declaration could be seen as the basic law of bioethics and human rights, even if the United States (again) will no longer be a UNESCO member starting in January 2019.[55] Therefore, any progress in the area of biomedicine should at least not violate this Declaration and human rights norms.

3. UNESCO as Future Actor

One might ask whether the UNESCO will be able to be a main actor for international standard setting in biomedicine in the years to come. In 2015, the IBC stated that States should '[r]enounce the possibility of acting alone in relation to engineering the human genome and accept to cooperate on establishing a shared, global standard for this purpose, building on the principles set out in the Universal Declaration on the Human Genome and Human Rights and the Universal Declaration on Bioethics and Human Rights'.[56] However, the Work Programme of the IBC for the years 2018-2019 states that: 'The Committee will elaborate on the principle of individual responsibility for health as part of its reflection on Article 5 (Autonomy and Individual Responsibility) of the Universal Declaration on Bioethics and Human Rights.' And even if there was an 'opportunity to further reflect on some of the issues raised on its work concerning big data and health', this does not seem to be a clear sign which shows that the IBC and UNESCO want to further develop rules for the challenges and chances of biomedicine. If UNESCO wants to be an important actor, the organisation and the IBC could think about drafting new declarations that cover pressing problems of international standard setting in biomedicine in the 21st century, such as for instance the merger of biomedicine and biotechnology and the merger of biomedicine and artificial intelligence (AI).

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[54] *Ibid*., at 372 et seq.

[55] In 2017 the United States withdrew from UNESCO; cf. list of parties, available at http://www.unesco.org/eri/cp/ListeMS_Indicators.asp.

[56] International Bioethics Committee, Report of the IBC on updating its reflection on the Human Genome and Human Rights, UNESDOC SHS/YES/IBC-22/15/2 REV.2, 2 October 2015.

III. First Results and Open Questions

As a first result, one can conclude that there are human rights treaties that are the relevant basis for legitimate standards in biomedicine. Even some international environmental treaties with regard to biotechnological aspects are decisive. I argue above that with regard to areas of biomedicine, we have to interpret the relevant environmental law in the light of human rights law – a 'humanisation' of international environmental law – and that environmental law does not per se have priority only because a treaty or norm developed after a human rights treaty or norm. Additionally, the UNESCO declarations with more specific rules merge bioethical principles and human rights. But there is no sector-specific comprehensive international treaty on biomedicine and new grey areas develop with the use of biotechnological tools to fight diseases.

Problems like research with human beings, cloning of human beings, genome editing, etc. remain only partially covered by already-existing norms in a fragmented way or by rules that are only soft law or norms of codes of conducts. Standards that could be mentioned here as well are, for instance, the UN Commission on Human Rights Resolution 69 on Human Rights and Bioethics (2003)[57] or the Resolution of the World Health Organization on ethical, scientific and social implications of cloning in human health of 1998;[58] there is a UN General Assembly resolution of March 2008 on Human Cloning[59] that prohibits 'all forms of human cloning inasmuch as they are incompatible with human dignity'. The last example shows very clearly that in some areas, clear international standard setting is not possible because States could not reach consensus on the specific content of a prohibition or limitation.

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[57] UN Commission on Human Rights, Res. 2003/69: *Human Rights and Bioethics,* UN Doc. E/CN.4/RES/2003/69, 25 April 2003.

[58] WHO, Ethical, scientific and social implications of cloning in human health, UN Doc. EB101.R25, 27 January 1998.

[59] UNGA Res. 59/280, 8 March 2005.

IV. Private Rule-Making and Codes of Conduct

As in other areas of international law, grey areas and lacunae might be governed by codes of conduct that are drafted by private entities. In the area of biomedicine, there are examples for important private rules and codes of conduct which have largely influenced specific fields of research in a sustainable and global way, first and foremost the Declaration of Helsinki of the World Medical Association on Ethical Principles for Medical Research Involving Human Subjects.[60] This is an example of private rule making that still has a major impact on framing and limiting a specific area of biomedical research. It is another part of a complex multi-layer governance that consists of rules of international law, supranational and national law, private norm setting, and even hybrid forms that combine elements of international and national law as well as private norm setting. However, if we think about *legitimate* international standard setting in biomedicine, the Helsinki Declaration as well as other standards in biomedicine have to be coherent with existing international law, especially with binding human rights, as they reflect justified values.[61]

V. Pressing Problems in Biomedicine – the Need for New International Legitimate Standard Setting

Two main challenges for biomedicine are developments – on the one hand – in the field of big data, machine learning, and AI and – on the other hand – the famous CRISPR-Cas9 gene editing and genome engineering technology.[62] With this method, it is possible to 'edit' DNA more easily and precisely than before, as the CRISPR

[60] See World Medical Association, *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects,* 19 October 2013, available at http://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/; for a critical analysis of the Declaration see Mira Chang, *Ungerechtfertigte Ethik* (2017); Sigrid Mehring, *First Do No Harm: Medical Ethics in International Humanitarian Law* (2015), at 360-417.

[61] See part II.C. of this paper.

[62] CRISPR (clustered regularly-interspaced short palindromic repeats) are segments of bacterial DNA that, when paired with specific guide protein such as Cas9 (CRISPR-associated protein 9), can be used to make targeted cuts in an organism's genome; Cas9 is an enzyme that can be programmed with RNA guides to target site-specifically any DNA sequence of interest, see National Academies of Sciences, *Gene Drives on the Horizon: Advancing Science, Navigating Uncertainty, and Aligning Research with Public Values* (2016), summary available at http://nas-sites.org/gene-drives/, at 1.

molecule unzips the twisted DNA strands of a living organism (this can be a plant or an animal) or a human being and cuts the targeted DNA sequence with its molecular 'scissors'. The organism can just repair itself on its own or scientists can include a corrected sequence.[63] Obviously the genome editing holds great promise for future biotechnical and biomedical applications, but there are concerns that the discovery gives the power to rewrite the codes of life and that so-called off-target effects cannot be excluded.[64] Usages of this tool that change the DNA of unborn human beings, as is the case with human germline editing (or: human germline therapy), are most controversial. Although it is prohibited inter alia in Germany[65] by national laws, and according to Article 13 Convention on Human Rights and Biomedicine of the Council of Europe[66] (binding only 35 States parties), i.e. a regional international treaty norm, there does not exist a universal international law-based prohibition of human germline editing; even the soft law UNESCO Declarations mentioned above do not prohibit this type of gene editing.

The German Ethics Council, a law-based interdisciplinary national ethics committee that shall inform the German parliament, the German government and the public,[67] issued an opinion in September 2017 on this topic and argued that there is a need for global political debate and international regulation as germline intervention on the human embryo 'touches also on the interest on mankind'.[68] However, until now there was no consensus at the UNESCO to do so: In 2015 the UNESCO IBC called on member States to agree on a joint moratorium, but there was no consensus by member States. Besides, there was no consensus at the 2015 International Summit on Human Gene Editing that was organised by national science academies of three States (United

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[63] See Emmanuelle Charpentier and Jennifer A. Doudna, 'Rewriting a Genome', 495 *Nature* (2013) 50, at 50.

[64] Silja Vöneky, 'Human Rights and Legitimate Governance of Existential and Global Catastrophic Risks', in Silja Voeneky and Gerald L. Neuman (eds.), *Human Rights, Democracy, and Legitimacy in a World of Disorder* (2018) 139, at 144.

[65] Act for the Protection of Embryos (*Embryonenschutzgesetz*), 13 December 1990, *Bundesgesetzblatt* (BGBl.) I, 2746, as amended on 21 November 2011, BGBl. I, 2228.

[66] See *supra* note 6.

[67] Silja Vöneky, *supra* note 50, at 234-315.

[68] German Ethics Council, *Germline intervention in the human embryo: German Ethics Council calls for global political debate and international regulation, Ad Hoc Recommendation*, 29 September 2017, available at https://www.ethikrat.org/fileadmin/Publikationen/Ad-hoc-Empfehlungen/englisch/recommendation-germline-intervention-in-the-human-embryo.pdf, at 2.

States of America, United Kingdom, and China).[69] As the experiments with the Chinese twins in 2018[70] showed, we need more international discussion about the risks, benefits, and values, even the 'dignity of humankind',[71] with regard to human germline intervention. However, it is quite unclear, and I am rather pessimistic on whether there will be a chance to agree on a meaningful international consensus.

Another pressing topic is whether there can be agreement on a new declaration on AI and biomedicine. Until now, there is, on the one hand, standard setting by private actors on questions of AI. Google's principles on AI were released in June 2018 as internal guidelines for Google's own AI research and development.[72] The so-called Asilomar AI Principles were drafted in 2017 as guidelines by scientists and stakeholders.[73] They are now endorsed by the State of California.[74] State representatives were not involved in the drafting, meaning that both documents are based on private 'bottom up' rule-making. On the other hand, there exists very powerful top-down regulation at the supranational level. If we think for instance about brain data protection, we have to focus on the European Union General Data Protection-Regulation.[75] Since AI is always data-driven and will be data-driven in the area of biomedicine as

[69] Cf. National Academies of Sciences, Engineering, and Medicine, *On Human Gene Editing: International Summit Statement*, 3 December 2015, available at http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12032015a. In 2017 in the United States, a joint committee convened by the United States National Academy of Sciences and the National Academy of Medicine argued that germline intervention were ethically defensible if this constituted the last reasonable option for a couple to have a healthy biological child, cf. Jocelyn Kaiser, 'U.S. panel gives yellow light to human embryo editing', *ScienceMag*, 14 February 2017, available at http://www.sciencemag.org/news/2017/02/us-panel-gives-yellow-light-human-embryo-editing; see study report by the National Academies of Sciences, Engineering, and Medicine, *Human Genome Editing: Science, Ethics, and Governance* (2017), available at https://www.nap.edu/catalog/24623/human-genome-editing-science-ethics-and-governance.

[70] See *supra* note 2.

[71] Cf. Habermas, *supra* note 44.

[72] Google, CEO Sundar Pichai, *AI at Google: our principles*, 7 June 2018, available at https://www.blog.google/technology/ai/ai-principles/.

[73] Future of Life Institute, *Asilomar AI Principles* (2017), available at https://futureoflife.org/ai-principles/.

[74] Assembly of the State of California, Assembly Concurrent Resolution No. 215, Chapter 206, Relative to the 23 Asilomar Principles, Legislative Counsel's Digest, ACR-215, 7 September 2018, available at http://leginfo.legislature.ca.gov/faces/billTextClient.xhtml?bill_id=201720180ACR215.

[75] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016, OJ 2016 L 119/1.

well,[76] the analysis of rules governing AI requires a look at international, regional, and national data protection norms. Here again there is the need to overcome the dichotomy between 'top-down' and 'bottom-up' rule making. Human rights as part of international law should form the normative basis for legitimate rule making, as all relevant States financing or permitting AI research and development are bound by these rights. A new declaration on 'AI and Biomedicine' should be based on human rights as well, but spell them out in a sector-specific way, as it was done in UNESCO Declarations before. Since 2005, when the last of the decisive UNESCO Declarations was agreed on, the field of biomedicine did change in major ways and it will change even more and even faster in the future. The discussion on rules governing AI and biomedicine should bring together major actors, private entities, and State representatives in order to develop coherent and legitimate rules for one of the most challenging technologies of the 21st century.

[76] Cf. Ivan Glenn Cohen et al. (eds.), *Big Data, Health Law, and Bioethics* (2018).