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A NEW GOVERNANCE APPROACH TO REGULATING HUMAN GENOME EDITING

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For years, genomic medicine—medicine based on the growing understanding of the genetic contribution to many diseases and conditions—has been hailed as the future of medical treatment, but it has thus far had limited effect on day-to-day medical practice. The ultimate goal of genomic medicine has always been the ability not just to identify dangerous gene mutations, but to fix them. Now CRISPR and related genome-editing technologies may have the potential to provide a safe and effective way to repair dangerous mutations.

In the wake of ethically dubious experiments with human embryos in China, the international governance of human genome editing is emerging as an urgent topic for scientists, regulators, and the public. Efforts to develop a governance model are

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underway at national and international levels. These efforts are the subject of multiple initiatives by national and international health and science organizations and are topics of discussion at scientific conferences, summits, and meetings.

This Article reports on the Authors' multi-year, interdisciplinary project to identify and investigate the practical, ethical, and policy considerations that are emerging as the greatest concerns about human genome editing, and ultimately to develop policy options. The project involves monitoring the discussions of groups, both government-sponsored and private, that are considering how genome editing should be governed; observing conferences where the topic is discussed; analyzing emerging policy reports by national and international bodies; and interviewing a wide range of stakeholders, including scientists, ethicists, and those who make and comment on public policy. The Article identifies several stakeholder concerns that are especially prominent in the research to date and begins to explore the implications of these concerns for alternative models of governance. There are current indications that, for practical purposes, a focus on "soft," hybrid forms of governance based on networks of multiple public and private stakeholders may turn out to be the most promising course to pursue. The "new governance" paradigm developed in the corporate and financial sectors offers a useful model for understanding the dynamics of this approach.

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I. INTRODUCTION

The first reports of human genome editing—altering the genetic code of a human being—in nonviable embryos in China in 2015 ignited a wave of ongoing policy discussions about the appropriate limits of such research in today's globalized scientific environment.[1] Chinese scientist He Jiankui's 2018 claim to have edited the embryonic genome of living twin baby girls[2] (for which he was reportedly imprisoned for "illegal medical practices"),[3] followed by a Russian geneticist's announcement of similar plans,[4]

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[1] *See* Carolyn Brokowski, *Do CRISPR Germline Ethics Statements Cut It?*, 1 CRISPR J. 115, 115–23 (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6694771/ [https://perma.cc/WYQ9-CTN6].

[2] Dennis Normile, *CRISPR Bombshell: Chinese Researcher Claims to Have Created Gene-Edited Twins*, SCI. (Nov. 26, 2018), https://www.sciencemag.org/news/2018/11/crispr-bombshell-chinese-researcher-claims-have-created-gene-edited-twins [https://perma.cc/JYC7-DSH9].

[3] Dennis Normile, *Chinese Scientist Who Produced Genetically Altered Babies Sentenced to 3 Years in Jail*, SCI. (Dec. 30, 2019), https://www.sciencemag.org/news/2019/12/chinese-scientist-who-produced-genetically-altered-babies-sentenced-3-years-jail [https://perma.cc/7FCZ-QT2B].

[4] *See* Jon Cohen, *Embattled Russian Scientist Sharpens Plans to Create Gene-Edited Babies,* SCI. (OCT. 21, 2019), https://www.sciencemag.org/news/2019/10/embattled-russian-scientist-sharpens-plans-create-gene-edited-babies [https://perma.cc/B5M9-GPTC]. The Russian scientist has not abandoned his plans, even after the controversy in China. *See* Michael LePage, *Russian Scientist Still Aims to Make CRISPR Babies Despite the Risks*, NEW SCIENTIST (Sept. 3, 2020), https://www.newscientist.com/article/2253688-russian-biologist-still-aims-to-make-crispr-babies-despite-the-risks/ [https://perma.cc/FWM8-4A63].

gave new urgency to those discussions.[5] Current human genome editing governance consists of a patchwork of national, local, and institutional regulations and scientific and professional policy statements; some of those statements aim at international status, but few offer specific prescriptions for oversight.[6] In the wake of the developments in China, efforts to harmonize this patchwork across jurisdictions and stakeholder groups have been the topic of multiple conferences, declarations, and publications, involving both scientists and policymakers.

The Authors are engaged in a multi-year, interdisciplinary project to identify and investigate the practical, ethical, and policy considerations that are emerging as the greatest concerns about human genome editing, and ultimately to develop policy options for governance of this rapidly evolving science. The project uses the term *governance* rather than such alternatives as "government," "regulation," or "control" in order to be open to all oversight possibilities, in whatever form and from all possible sources of authority or influence. The project involves, among other research, monitoring the publicly accessible discussions of groups, both government-sponsored and private, that are considering how genome editing should be governed; observing conferences where the topic is discussed; analyzing emerging policy reports by national and international bodies; and interviewing a wide range of stakeholders, including scientists, ethicists, and those who make and comment on public policy. This Article identifies several stakeholder concerns that are especially prominent in the research to date and begins to explore the implications of these concerns for alternative models of governance. There are current indications that, for practical purposes, a focus on "soft," hybrid forms of governance based on networks of multiple public and private stakeholders may turn out to be the most promising course to pursue.[7] The "new governance" paradigm developed in the

[5] *See* Henry T. Greely, *He Jiankui, Embryo Editing, CCR5, the London Patient, and Jumping to Conclusions,* STAT (Apr. 15, 2019), https://www.statnews.com/2019/04/15/jiankui-embryo-editing-ccr5/ [https://perma.cc/HTU3-R7XT].

[6] *See* Brokowski, *supra* note 1.

[7] *See infra* Part VI.C.

corporate and financial sectors offers a useful model for understanding the dynamics of this approach.[8]

Part II of the Article describes the basic science of genome editing. Part III explains the various categories of genome editing and the need for governance across these categories. Part IV presents the research project in more detail and reports some of its significant findings to date. Part V uses these findings to analyze the possible approaches to genome editing governance that are being proposed, with specific reference to the concerns that seem to be motivating the various proposals. Part VI evaluates each approach in terms of its potential to meet these concerns, and Part VII offers a brief conclusion.

II. GENOME EDITING TECHNOLOGY

A. Genes and the Genome

An organism's genome is the entirety of the DNA in its cells.[9] Genes are the subset of the genome that perform the function of building, or coding for, proteins.[10] The details of the protein-building function depend on the specific DNA that is present in the organism's cells. DNA, the chemical responsible for inheritance, is a double-stranded molecule containing long strings of four chemicals called bases (abbreviated A, T, C, and G); because DNA is double-stranded, they appear as base pairs, one on each strand. The order of the base pairs in an organism's genome is its DNA sequence. It is this sequence that determines what proteins an organism's cells build, and when. Genes account for only a

[8] *See generally* John M. Conley & Cynthia A. Williams, *Global Banks as Global Sustainability Regulators?: The Equator Principles*, 33 J.L. & POL'Y 542 (2011) (presenting case study of new governance approach to global banking problem).

[9] The brief overview of genome editing in this section is based on John M. Conley, *Introduction: A Lawyer's Guide to Crispr,* 97 N.C. L. REV. 1041, 1042–47 (2019). Readers interested in more detail about the underlying science should consult that reference and the sources cited therein.

[10] The distinction between genome and genes, and thus between genome editing and gene editing, is important to scientists but rarely of interest to other audiences. The policy literature tends to use genome and gene editing interchangeably, as the authors do on occasion in this Article.

small portion of the DNA in the genome.[11] Other portions of the genome have regulatory functions, such as controlling when particular genes switch on and off, while other large portions of the genome have no currently known function.[12] RNA is a single-stranded cousin of DNA that performs many functions in the cell.[13] By coding for proteins in particular ways, DNA provides a template for life; it determines the identities of different species, and influences some of the differences between individuals within a species. Some DNA variants, or mutations—changes in the sequence from the organism's usual pattern—can contribute to, or, in some cases, cause a disease or disability. Still, other variants may be beneficial in the sense offering special protections from disease or disability.

B. CRISPR Gene Editing

To edit the genome is to intervene in a cell and change its DNA sequence. This can be done in a variety of ways: by excising one or more bases, by turning particular bases on or off, or even by substituting one sequence for another. This latter possibility represents the ultimate promise of genomic medicine: the ability not just to identify dangerous gene mutations, but to *fix* them, to go into a patient's cells and change a dangerous DNA sequence to a non-pathogenic one.

Gene editing technologies have been around for more than twenty-five years. Earlier approaches include Zinc-Finger Nucleases (ZFNs) and Transcription Activator-Like Effector Nucleases (TALENs).[14] The current focus is on a technology called CRISPR, which stands for Clustered Regularly Interspaced

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[11] *See* Jonathan Henninger, *The 99 Percent . . . of the Human Genome*, HARV. UNIV.: SCI. IN THE NEWS (Oct. 1, 2012), http://sitn.hms.harvard.edu/flash/2012/issue127a/ [https://perma.cc/ECM6-4HV9].

[12] *See id.*

[13] *See* Carl Zimmer, *Breakthrough DNA Editor Born of Bacteria*, QUANTA MAG. (Feb. 6, 2015), https://www.quantamagazine.org/crispr-natural-history-in-bacteria-20150206/ [https://perma.cc/3Q9J-D2CE].

[14] *See* Conley, *supra* note 9, at 1046.

Palindromic Repeats.[15] These are short repeating sequences in the DNA of *E. coli* and other bacteria that were discovered by Japanese researchers in the 1980s.[16] Their function was unknown for about twenty years, until food scientists using bacteria to make yogurt figured out that they are part of the bacteria's immune system.[17] These scientists realized that the CRISPR sequences resemble the DNA of viruses.[18] In fact, the CRISPR sequences are taken from viral DNA that the bacteria has captured during past viral invasions.[19] When a new viral attack occurs, the bacteria's immune system compares the virus's genetic material to the sequences stored in CRISPR; if it detects a match, it launches enzymes (a class of proteins that facilitate chemical reactions) to cut up the incoming viral DNA and repel the invasion.[20]

The bacterial CRISPR sequences are always accompanied by genes that code for enzymes that can cut DNA.[21] The original CRISPR scientists called them Cas (for CRISPR-associated) genes.[22] Later research revealed that when viruses invade a bacterial cell, the CRISPR regions produce single-stranded RNA versions of the viral DNA sequences that it has captured and stored.[23] These RNA sequences are cradled by the Cas enzymes and carried around the cell.[24] When an RNA sequence encounters its viral DNA counterpart it latches on and the Cas enzyme cuts the DNA, which stops the virus from replicating.[25]

Current CRISPR gene-editing technology mimics this natural process. Researchers at the University of California-Berkeley

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[15] Brad Plumer et al., *A Simple Guide to CRISPR, One of the Biggest Science Stories of the Decade*, VOX (Dec. 27, 2018), https://www.vox.com/2018/7/23/17594864/crispr-cas9-gene-editing [https://perma.cc/N6AM-MBMA].

[16] *Id.*

[17] *Id*.

[18] *Id.*

[19] *Id.*

[20] *Id.*

[21] Plumer et al., *supra* note 15.

[22] *Id.*

[23] *Id.*

[24] *Id.*

[25] *Id.*

chose a pair of Cas enzymes called Cas9.[26] They supplied the enzymes with the RNA counterpart of the genetic sequence they wanted to edit—the target gene.[27] The RNA finds and binds to the target DNA and the Cas9 enzymes cut it at its two ends.[28] With the target gene excised, the cell can be induced to make a new one.[29] In the simplest application, the CRISPR mechanism finds and cuts out a "defective" gene—for example, one that causes a single-gene disease such as cystic fibrosis, hemophilia, or sickle cell disease—and the cell replaces it with a normal one.[30] CRISPR technology can also be used to introduce a new gene into the space.[31]

CRISPR represents a major advance over previous editing technologies in terms of efficiency and accuracy.[32] CRISPR was used in the ethically contentious Chinese experiments and is now a primary tool in a global research effort, with projects ranging from basic science to plant and animal research to early efforts to apply it in human medicine. To illustrate, a recent survey of published CRISPR developments by a Spanish research institute lists the correction of a gene responsible for Duchenne muscular dystrophy in humans and mice, and—all in mouse models—improvements in progeria (premature aging disease), correction of a gene that causes obesity, and the development of a new cancer strategy that uses CRISPR and immunotherapy (stimulating the body's natural defenses).[33] Similarly, at a July 2020 virtual conference of genome editing scientists, industry representatives, and government regulators organized by the Genome Writers Guild, a

[26] Plumer et al., *supra* note 15.
[27] *Id.*
[28] *Id.*
[29] *Id.*
[30] *Id.*
[31] *See* Zimmer, *supra* note 13.
[32] *See* Conley, *supra* note 9, at 1047.
[33] Lucia Gomez-Tatay, *CRISPR Promises: Some of the Most Recent Developments in Gene Editing*, BIOETHICS OBSERVATORY (Feb. 4, 2020), https://bioethicsobservatory.org/2020/02/crispr-promises-some-of-the-most-recent-advances-in-gene-thera/34049/?at_a_glance_summer_issue [https://perma.cc/NQ69-NR95].

self-described "genome engineering society"[34] (which members of the research group attended), the use of CRISPR was discussed in sessions on animal and plant editing developments, editing repair, gene and cell therapies, many of which are now in human use, and the use of oncolytic (cancer-cell-killing) viruses.[35]

A final and highly important technical point is the distinction between germline and somatic cell editing. The genetic information in somatic cells—the cells that make up nonreproductive organs and tissues—cannot be passed down to future generations. Germline cells are the reproductive cells (eggs and sperm) in adults, which do pass along parental genetic information, and the cells in undifferentiated early embryos, which provide the genetic instructions for all the subsequent cells in the body, including the reproductive cells. Thus, germline edits, like natural mutations, are transmitted to future generations. For this reason, while concerns about editing somatic cells are focused on the individual patient, germline edits also raise concerns for future generations.

III. THE CATEGORIES OF GENOME EDITING AND THE NEED FOR GOVERNANCE

As noted above, current genome-editing governance is, at most, a patchwork of national and local laws, many of which apply only by implication, together with initiatives of many advisory and advocacy groups.[36] Across this patchwork, one widespread point of early consensus is that gene editing research should prioritize medical applications over attempts to enhance human traits, given the moral concerns—such as exacerbating background social injustices—the latter would raise.[37] Underlying this consensus is a broadly accepted distinction between gene editing for treatment or prevention of disease and disability, on the one hand, and

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[34] GENOME WRITERS GUILD, https://www.genomewritersguild.org/ [https://perma.cc/59YQ-YFDM].

[35] *GWG 2020 Conference Program*, GENOME WRITERS GUILD, https://www.genomewritersguild.org/gwgcon2020program [https://perma.cc/FU97-Z8FD].

[36] *See* Brokowski, *supra* note 1 and accompanying text.

[37] *See* Brokowski, *supra* note 1.

enhancement of traits generally regarded as "normal," on the other.[38]

On the whole, genetics professionals[39] and the public[40] seem to concur with this consensus. However, some policy statements have expanded the definition of "medical applications" beyond the categories of disease treatment or prevention, further complicating the issue.[41] Moreover, few of the policy initiatives have offered specific suggestions for how science policy should deal with research governance issues.

Other forms of biomedical enhancement already illuminate multiple ways in which using human gene editing to prevent disease could open the door to enhancement applications. For example, compensatory enhancements like immunizations intentionally strengthen particular human functions beyond a typical baseline in order to counteract pathogenic threats.[42] They are generally not controversial, but can become so if used in such

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[38] The consensus about this distinction has its origins in the governance of pre-gene editing human gene therapy. *See generally* Eric Juengst, *The NIH "Points to Consider" and the Limits of Human Gene Therapy*, 1 HUMAN GENE THERAPY 425 (1990); Eric Juengst & LeRoy Walters, *Ethical Issues in Human Gene Transfer Research,* THE DEVELOPMENT OF HUMAN GENE THERAPY 691, 691–713 (Theodore Friedmann ed., 1999) (both sources illustrating the development of the consensus in the pre-gene editing environment).

[39] *See* Alyssa Armsby et al., *Survey Results: Genetics Specialists' Views on Genome Editing*, EUREKALERT (Oct. 19, 2017), https://www.eurekalert.org/pub_releases/2017-10/asoh-srg101117.php [https://perma.cc/6WF3-FQD7].

[40] *See U.S. Public Opinion on the Future Use of Gene Editing*, PEW RSCH. CTR. (July 26, 2016), https://www.pewresearch.org/science/2016/07/26/u-s-public-opinion-on-the-future-use-of-gene-editing/ [https://perma.cc/VY6U-TY6X].

[41] *See generally, e.g.,* NETHERLANDS COMM'N ON GENETIC MODIFICATION, EDITING HUMAN DNA: MORAL AND SOCIAL IMPLICATIONS OF GERMLINE GENETIC MODIFICATION (2017), https://cogem.net/app/uploads/2019/07/Germline-Modification1.pdf [https://perma.cc/R35E-T88E]; *Genome Editing and Human Reproduction: Social and Ethical*, NUFFIELD COUNCIL ON BIOETHICS (2018), https://www.nuffieldbioethics.org/publications/genome-editing-and-human-reproduction [https://perma.cc/VK5K-FGKV] (both sources reflecting an expanded definition of "medical" applications).

[42] *See* Anita Silvers, *Meliorism at the Millennium: Positive Molecular Eugenics and the Promise of Progress without Excess, in* MUTATING CONCEPTS, EVOLVING DISCIPLINES: GENETICS, MEDICINE, AND SOCIETY 215–34 (L.S. Parker & Rachel A. Ankeny eds., 2002).

practices as the U.S. military's efforts to produce a "[m]etabolically [d]ominant [s]oldier" who can go "for days with little or no food[.]"[43] Another category, secondary enhancements, is illustrated by the efforts of biogerontologists to develop ways of controlling human senescence in order to prevent late-life diseases.[44] Once again, the basic uses are noncontroversial, but those efforts could also extend the healthy human life span beyond its historical limits, raising concerns about the value of the traditional human life cycle.[45] In other cases, interventions that could forestall disease in at-risk patients might also be used off-label to enhance functional traits in healthy individuals.[46] For example, synthetic human growth hormone was developed to help prevent extreme short stature due to hormonal deficiencies, but ethical questions arose about its use to enhance the height of hormonally typical young people.[47] Finally, interventions designed to enhance particular traits are sometimes rationalized as therapeutic or preventive—that is, medicalized—in order to justify their development as biomedical tools; the medical rationale for purely cosmetic breast enhancement surgery is a classic example.[48]

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[43] *See* William Matthews, *Supersoldiers: Can Science and Technology Deliver Better Performance?*, ARMY MAG. (Apr. 20, 2015), https://www.ausa.org/articles/supersoldiers-can-science-and-technology-deliver-better-performance [https://perma.cc/7G7P-DQ39].

[44] *See* James L. Kirkland, *The Biology of Senescence: Potential for Prevention of Disease*, 18 CLINICS GERIATRIC MED. 383, 394 (2002).

[45] *See generally* A WORLD GROWING OLD: THE COMING HEALTH CARE CHALLENGES (DANIEL CALLAHAN, RUUD H. J. TER MEULEN & EVA TOPINKOVÁ EDS., 1995) (describing the cross-disciplinary challenges and issues of an aging population).

[46] For a discussion of this issue in a non-genetic context, see Lisa E. Smilan, *The Off-Label Loophole in the Psychopharmacologic Setting: Prescription of Antipsychotic Drugs in the Nonpsychotic Patient Population*, 30 HEALTH MATRIX: THE J. OF L. MED. 233 (2020).

[47] *See* SHEILA M. ROTHMAN & DAVID J. ROTHMAN, THE PURSUIT OF PERFECTION: THE PROMISE AND PERILS OF MEDICAL ENHANCEMENT 16–17 (2003). Ethical questions have also been raised about the use of growth hormone to prevent extreme short stature because of the normative implications of "heightism." In that case, however, the concern is less with enhancement than with the underlying social norms themselves.

[48] *See* Linda F. Hogle, *Enhancement Technologies and the Body*, 34 ANN. REV. ANTHROPOLOGY 695, 700 (2005).

Since the 1980s, bioethicists have used cases of enhancement like these to mount or refute arguments about whether enhancement interventions can ever be meaningfully distinguished from medical applications.[49] They have asked whether these cases raise any moral concerns,[50] and what societal responses they warrant.[51] But however one resolves these ethical debates, they leave unanswered another question at the level of research governance: even if stakeholders generally accept both the conventional treatment-enhancement boundary and the endorsement of prevention as a legitimate goal for gene editing, how should governance policy deal with the resulting incidental enhancement concerns? More specifically, how should policymakers deal with apparent enhancements that are unintended side effects—"off-label" uses that are compensatory in one context but not in another—or otherwise tread the line between prevention, treatment, and enhancement? To answer this, those engaged in developing responsible governance for gene editing research need to know more about the contexts of this research, the moral meaning of enhancement in those contexts, and its salience as a boundary marker for gene editing research. It is to such issues that the research project and this Article are addressed.

IV. THE RESEARCH PROJECT

The Authors began their collaborative research in 2018, and in May 2020 they received a four-year grant from the National Human Genome Research Institute (part of the National Institutes of Health) to support an intensive, multidisciplinary research effort.[52] The research group's members come from bioethics,

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[49] *See* Eric T. Juengst, *Can Enhancement Be Distinguished from Prevention in Genetic Medicine?,* 22 J. MED. & PHIL. 12, 134–36 (1997).

[50] *See* JOHANNN A.R. RODUIT, THE CASE FOR PERFECTION: ETHICS IN THE AGE OF HUMAN ENHANCEMENT 71–86 (2016).

[51] *See* MAXWELL J. MEHLMAN, THE PRICE OF PERFECTION: INDIVIDUALISM AND SOCIETY IN THE ERA OF BIOMEDICAL ENHANCEMENT 185–210 (2009).

[52] *Project Information: 1R01HG010661-01A1,* NAT'L INST. HEALTH, https://projectreporter.nih.gov/project_info_description.cfm?aid=9967484&icde=52225919&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC&pball= [https://perma.cc/AZ7A-MTN7] (last visited Nov. 2, 2020).

anthropology, sociology, law, philosophy, and public policy. A major component of the method is ethnographic, relying on interviews, participant observation at relevant events, and monitoring the public activities of governmental bodies and nongovernmental interest groups. The research also includes ongoing Internet and literature research and policy analysis.

In order to ground the project's understanding of the critical ethical and policy issues in a scientific perspective, the researchers have begun to identify and interview scientists whose work is relevant to gene editing. They are identifying scientists through monitoring the emerging literature as well as websites, email listservs, and other online sources; participant observation[53] at conferences and meetings; opportunistic follow-up with colleagues and associates of people being interviewed; and consultation with a group of global advisors to the project. Using both quantitative and qualitative interpretive analytical methods, the research group is seeking to identify the conceptual points, ethical arguments, and policy considerations that are emerging as the greatest concerns in the scientific community.

At the same time, the research is also focusing on groups that are beginning to consider how gene editing should be governed. These include government-sponsored organizations such as the National Academies of Sciences, Engineering, and Medicine's Human Genome Editing Initiative in the United States and its international counterparts;[54] government-sponsored international groups such as the World Health Organization;[55] and private, voluntary groups advocating for various kinds of self-governance, such as the Association for Responsible Research and Innovation

[53] Participant observation is an anthropological method. As the phrase suggests, it involves immersing oneself to the maximum extent possible in the activities of the group being studied, simultaneously observing and participating in those activities. For a fuller explanation and an example of the method used in another bioethical context, see John M. Conley et al., *Is Real-Time ELSI Realistic?*, 11 AM. J. BIOETHICS EMPIRICAL 134, 136–37 (2020), https://doi.org/10.1080/23294515.2020.1722289 [https://perma.cc/AD9E-KEUY].

[54] *See infra* notes 64–72 and accompanying text.

[55] *See infra* notes 78–79, 129–31 and accompanying text.

in Genome Editing (ARRIGE) and the Genome Writers Guild.[56] For such groups, the researchers are collecting relevant information from websites, published documents, and listserv emails; and engaging participant observation of their meetings and conferences. In the analysis of their respective views and approaches, the primary focus is on governance proposals relevant to the scientific issues identified above. The project's ultimate objective is to develop useful guidance for governance that is particularly attentive to the policy trade-offs between preventive benefits and enhancement concerns.

In the sections that follow, the Authors outline some of the major themes that are emerging in the research to date and map these themes onto some of the relevant governance literatures. The Article concludes with some preliminary recommendations about policy.

V. APPROACHES TO GOVERNING HUMAN GENOME EDITING RESEARCH

In the relevant literatures and the project's research to date, governance discussions have centered on some combination of four basic approaches to regulating or guiding gene editing research. One possibility is self-regulation, in this case by the scientific community—the loosely connected network of scientists who are working, directly or indirectly, on genome editing and its applications. Self-regulation can rely on nothing more than advisory or aspirational ethical codes or—as in the case of the traditional professions like medicine or law—can involve the authority, delegated by government, to create barriers to entry (licensing requirements, for example) and discipline noncompliant members. Two other approaches involve "hard" regulation, defined as rules of law imposed by and enforceable by governments. The imposition of hard regulation can take place at the level of the individual nation-state or at the international level. In the latter case, national governments, usually acting by treaty, can imbue an existing supranational organization with regulatory power or create a new one for a specific purpose. As the Authors

[56] *See infra* notes 74–76, 99–100 and accompanying text.

will argue, the success of any international regime always comes down to the will of the participating states. The last approach is a hybrid. Called variously soft, polycentric, anticipatory, or new governance (perhaps the most widely used term, which this Article uses), its hallmark is a diffusion of rights and responsibilities among networks of state and non-state stakeholders—governments, corporations, non-governmental organizations ("NGOs"), and others—that transcend national boundaries.

In the presentation and discussion of these governance approaches in the ongoing wave of declarations and reports on human genome editing, three sets of stakeholder concerns emerge as particularly prominent: (1) threats to the gene editing scientific community's privileged standing as a self-governing professional community; (2) worries about developing hard forms of governance having the force of law at the international level; and (3) anxieties about public support for, and trust in, the human genome editing research enterprise. When these concerns are mapped onto each of the main governance approaches, the reasons for its widespread endorsement as an approach to gene editing governance become apparent.

A. Threats to Scientific Self-Governance

Genome scientists, like other technical experts and members of traditional professions, have enjoyed wide latitude in governing their own work in exchange for voluntary adherence to expected norms of behavior.[57] The rationale for this "grand bargain" between science and society is that socially beneficial knowledge is produced and applied more efficiently if scientists are granted professional autonomy.[58] That model is under pressure today, however, as the professional role of scientists in high-income countries becomes more market-oriented.[59] At the same time,

[57] For an early overview, see ANDREW ABBOTT, THE SYSTEM OF PROFESSIONS: AN ESSAY ON THE DIVISION OF EXPERT LABOR (1988).

[58] The "grand bargain" theory is explained and criticized in RICHARD SUSSKIND & DANIEL SUSSKIND, THE FUTURE OF THE PROFESSIONS: HOW TECHNOLOGY WILL TRANSFORM THE WORK OF HUMAN EXPERTS 9–45 (2015).

[59] As evidence of this shift, one need to look no further than the proliferation of technology transfer offices in U.S. universities, designed in part to help university

especially in China, the alleged role of scientists as agents of the state presses the grand bargain model from the other direction, raising concerns about nationalistic influences on research.[60]

Concerns about threats to scientific self-governance have emerged in the discussion of human genome editing since the initial calls for moratoria on human germline interventions by groups of individual scientists.[61] Thus, some prominent senior scientists who were active in recombinant DNA research in the 1970s have tried to frame the current debate as one best managed by the scientific community itself.[62] They sometimes invoke the iconic 1974 Asilomar Conference, where scientists, physicians, and lawyers discussed the potential risks of early recombinant DNA technology and produced a set of voluntary guidelines.[63]

These concerns have also surfaced in the initiatives organized by national science academies. For example, the revelation of human embryo editing experiments in China came just before the 2018 Second International Summit on Human Gene Editing in Hong Kong, which was sponsored by the U.S. National Academies of Science, Engineering and Medicine (NASEM) and its counterparts in the U.K. and Hong Kong.[64] He Jiankui, the Chinese scientist who conducted those experiments, had been scheduled to

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scientists bring their invention to the for-profit private sector. At UNC-CH, for example, this office is called the Office of Technology Commercialization. UNC OFFICE OF TECH. COMMERCIALIZATION, https://otc.unc.edu/ [https://perma.cc/P5BX-7ED6] (last visited Oct. 13, 2020).

[60] *See, e.g.,* Nidhi Subbaraman, *US Investigations of Chinese Scientists Expand Focus to Military Ties*, NATURE (2020), https://www.nature.com/articles/d41586-020-02515-x [https://perma.cc/PBK3-8W3D].

[61] *See infra* note 76 and accompanying text.

[62] *See, e.g.,* Comm. on Sci., Tech., & L. Pol'y & Glob. Affairs, *International Summit on Human Gene Editing: A Global Discussion*, NAT'L ACADS. PRESS 4–6 (Dec. 1–3, 2015), https://www.nap.edu/read/21913/chapter/1 [https://perma.cc/SH9R-279M].

[63] *See e.g.,* Paul Berg et al., *Summary Statement of the Asilomar Conference on Recombinant DNA Molecules*, 72 PROC. NAT'L. ACADS. SCI. 1981 (1975).

[64] *See* Nat'l Acads. of Sci., Eng'g, & Med., *Second International Summit on Human Genome Editing: Continuing the Global Discussion*, NAT'L ACADS. PRESS (Jan. 10, 2019), https://www.nap.edu/read/25343/chapter/1 [https://perma.cc/K8UV-AYT4].

speak on different work.[65] When the embryo editing came to light, He was given his own session, which played out amid great tension and critical questioning from the audience.[66] In the aftermath of this drama, the organizing committee nonetheless put out a statement that attempted to straddle the line between regulation and scientific freedom. On the one hand, it labeled the human germline genome-editing experiments as "unexpected and deeply disturbing," with "flaws" ranging from study design to "failure to meet ethical standards," echoing a rogue science theme; on the other hand, it defended professional autonomy by arguing for the creation of "a rigorous, responsible translational pathway toward [germline genome-editing] trials."[67]

The organizing committee also called for "an ongoing international forum" to address genome-editing governance, which was launched as the International Commission on Clinical Use of Heritable Human Genome Editing.[68] The Commission released its report, *Heritable Human Genome Editing*, at a webinar on September 3, 2020.[69] The members of the Commission stressed

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[65] *Id*.

[66] *See id.* One of the co-authors attended and observed.

[67] *Statement by the Organizing Committee of the Second International Summit on Human Genome Editing,* NAT'L ACADS. SCI., ENG'G, & MED. (Nov. 28, 2018), https://www.nationalacademies.org/news/2018/11/statement-by-the-organizing-committee-of-the-second-international-summit-on-human-genome-editing#:~:text=to%20main%20content-,Statement%20by%20the%20Organizing%20Committee%20of%20the,Summit%20on%20Human%20Genome%20Editing&text=The%20committee%20also%20stated%20that,germline%22%20editing%20at%20that%20time [https://perma.cc/QKD8-TFDE].

[68] *Id.*; *see International Commission on Clinical Use of Human Germline Genome Editing*, NAT'L ACADS. OF SCI., ENG'G, & MED, http://www.nationalacademies.org/gene-editing/international-commission/index.htm?_ga=2.267074126.1919016442.1562599670-715002107.1562599670 [https://perma.cc/E3CF-FKTD] (last visited Sept. 25, 2020).

[69] NAT'L ACADS. OF SCI., REPORT SUMMARY: HERITABLE HUMAN GENOME EDITING (2020), https://www.nap.edu/resource/25665/Heritable%20Human%20Genome%20Editing%20Report%20Summary%20-%20FINAL%2020200903.pdf [https://perma.cc/96TK-PSLJ]. The webinar is available at the International Commission on the Clinical Use of Human Germline Genome Editing webpage. *International Commission on Clinical Use of Human Germline Genome Editing*, NAT'L ACADS. OF SCI., ENG'G & MED., https://www.nationalacademies.org/our-work/international-commission-on-the-clinical-use-of-human-germline-genome-

that no applications should be undertaken until scientists can "efficiently and reliably" edit human embryos without off-target effects, and that science is not yet at that point.[70] Looking ahead, the Commission members proposed a ranking system for potential uses, with the highest priority being serious monogenic (caused by a single gene) conditions for people who could not have a healthy biological child through current embryo selection technology and the lowest being enhancement addressed to non-disease traits, using HIV resistance as an example. Although the report offers recommendations for a "translational pathway" to heritable human genome editing ("HHGE") that have significant legislative and regulatory implications for both nations and international bodies, the International Commission is at pains to present itself as primarily an exercise in professional self-governance by the scientific community.[71] As the report says, while "the decision to permit the clinical use of HHGE and, if so, for which specific applications, must ultimately rest with individual countries following informed societal debate of both ethical and scientific considerations," the goal is "to elaborate national and international mechanisms necessary for appropriate *scientific* governance of HHGE, while recognizing that additional governance mechanisms may be needed to address societal considerations that lie beyond the Commission's charge."[72]

B. Hopes and Fears for Hard Approaches to International Governance

There is currently no international hard (imposed by governments and having the force of law) regulation of human genome editing or its medical applications.[73] One organization that

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editing (last visited Nov. 16, 2020). Some of the co-authors attended the webinar.

[70] NAT'L ACADS. OF SCI., REPORT SUMMARY: HERITABLE HUMAN GENOME EDITING, *supra* note 69, at 3.

[71] *Id.* at 1–2.

[72] *Id*.

[73] For a survey of the regulatory landscape, see R. Alta Charo, *The Legal and Regulatory Context for Human Gene Editing*, ISSUES SCI. & TECH., https://issues.org/the-legal-and-regulatory-context-for-human-gene-editing/ [https://perma.cc/FY2P-D79Y].

has advocated an international law approach is ARRIGE, mentioned above.[74] ARRIGE is a nongovernmental organization founded in France in 2018 whose objectives include "promot[ing] a global governance of genome editing through a comprehensive setting for all stakeholders" and "foster[ing] the development of genome editing technologies within a safe and ethical framework."[75] It has also advocated an international law approach. In December 2018, ARRIGE proposed:

> [T]he modification of any UNESCO universal declarations, such as the Declaration on the Human Genome, to include a simple additional point clearly stating that the application of human genome edited technologies should not be permitted nor authorized until deemed safe and effective for human beings, with precise therapeutic applications justified after a broad and open debate.[76]

In a comparable but narrower initiative, a group of fifteen individual international researchers argued for a moratorium on germline genome editing in *Nature* in March 2019, calling "for the establishment of an international framework in which nations, while retaining the right to make their own decisions, voluntarily commit to not approve any use of clinical germline editing unless certain conditions are met."[77]

Another initiative that may point in the direction of harder forms of governance at the international level is the aspiration of the Expert Advisory Committee of the World Health Organization to develop global standards for governance of genome editing that could ultimately be turned into law. In 2019, the Expert Committee proposed a central, worldwide registry of ongoing human genome

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[74] *About Us*, ASS'N FOR RESPONSIBLE RSCH. & INNOVATION IN GENOME EDITING, https://arrige.org/aboutus.php [https://perma.cc/H3DD-7APS].

[75] *Id.*

[76] ASS'N FOR RESPONSIBLE RSCH. & INNOVATION IN GENOME EDITING, STATEMENT FROM ARRIGE STEERING COMMITTEE ON THE POSSIBLE FIRST GENE-EDITED BABIES (Dec. 3, 2018), https://arrige.org/ARRIGE_statement_geneeditedbabies.pdf [https://perma.cc/Z69V-VQZ3]. ARRIGE's current president, Lluis Montoliu, has recently elaborated on this position. *See infra* note 91 and accompanying text.

[77] Eric Lander et al., *Adopt A Moratorium on Heritable Genome Editing*, 567 NATURE 165, 165 (2019), https://media.nature.com/original/magazine-assets/d41586-019-00726-5/d41586-019-00726-5.pdf [https://perma.cc/7LCH-M47P].

editing research.[78] But, more recently, the Expert Committee has published a draft framework for governance.[79] As the Authors will discuss below, the draft has turned toward a new governance approach that includes an array of governmental and nongovernmental stakeholders.[80]

Given the difficulties of developing and implementing hard governance approaches at the international level, some country-based policy efforts have focused on articulating hard rules at the national level. In the United States, much of the discussion on new hard regulatory approaches to genome editing has been driven by NASEM, a co-sponsor of the 2018 Hong Kong conference discussed above.[81] Although the National Academies are private nonprofit organizations, they date back to a congressional charter signed by Abraham Lincoln and are in that sense government-related public organizations. In its 2017 report, Human Genome Editing: Science, Ethics, and Governance, NASEM recommended that existing regulatory processes be applied to basic laboratory research and to somatic human genome editing to treat or prevent disease or disability.[82] It further recommended against permitting human genome editing for enhancement purposes, defined as "purposes other than treatment or prevention of disease and disability."[83] Finally, NASEM recommended that clinical trials of germline gene editing be permitted, but "limited to only the most compelling circumstances

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[78] *WHO Expert Panel Paves Way for Strong International Governance on Human Genome Editing*, WORLD HEALTH ORG. (Mar. 19, 2019), https://www.who.int/news-room/detail/19-03-2019-who-expert-panel-paves-way-for-strong-international-governance-on-human-genome-editing [https://perma.cc/6FDS-TCET].

[79] Expert Advisory Comm. on Developing Glob. Standards for Governance and Oversight of Hum. Genome Editing, *Human Genome Editing: A DRAFT Framework for Governance*, WORLD HEALTH ORG. 1 (Jan. 2020), https://www.who.int/ethics/topics/human-genome-editing/Governance-framework-for-HGE-Jan2020.pdf?ua=1 [https://perma.cc/NWX4-AQT6].

[80] *See infra* notes 128–30 and accompanying text.

[81] *See supra* notes 64–66 and accompanying text.

[82] NAT'L ACADS. OF SCI., ENG'G, & MED., HUMAN GENOME EDITING: SCIENCE, ETHICS, AND GOVERNANCE 185 (2017). For a regulatory survey, see Brokowski, *supra* note 1, at 116–20.

[83] NAT'L ACADS. OF SCI., ENG'G, & MED., *supra* note 82, at 192.

and subject to a comprehensive oversight framework."[84] that satisfies ten rigorous criteria.[85] Immediate reactions to the report focused on this final recommendation, which one journalist characterized as a "yellow light to human embryo editing."[86]

Conferences representing the broader scientific community reflect a more skeptical view of top-down governance, with governmental authorities imposing binding rules. For example, at the 2018 CRISPRcon conference (which members of the research group attended), where "a broad selection of diverse voices [came] together to discuss the future of CRISPR and related gene editing,"[87] real-time audience polling indicated that the audience viewed international regulation (presumably of the hard variety) of germline editing as having high importance but low feasibility. Various speakers emphasized the difficulties of making and enforcing treaties and the fragmentary, often ill-suited nature of existing national regulations; instead, many stressed local regulation, voluntary attention to local communities, and scientific guidelines. A significant theme was the danger of regulatory arbitrage: in a world that relies on government regulation, risky research will seek out the least-regulated environment—at the moment, China.[88]

At the 2018 Genome Writers Guild conference,[89] project members in attendance heard a speaker argue that "regulation will

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[84] *Id*. at 189.

[85] *Id.* at 189–90.

[86] Jocelyn Kaiser, *U.S. Panel Gives Yellow Light to Human Embryo Editing*, SCI. MAG. (Feb. 14, 2017, 11:00 AM), https://www.sciencemag.org/news/2017/02/us-panel-gives-yellow-light-human-embryo-editing [https://perma.cc/36Z5-KWDG].

[87] CRISPRCON, https://crisprcon.org/crisprcon-2018/ [https://perma.cc/85PS-CQW3] (last visited Sept. 25, 2020).

[88] *Recent Events Highlight an Unpleasant Scientific Practice: Ethics Dumping*, ECONOMIST (Feb. 2, 2019), https://www.economist.com/science-and-technology/2019/02/02/recent-events-highlight-an-unpleasant-scientific-practice-ethics-dumping [https://perma.cc/6UZV-6BAG].

[89] *GWG 2018 Conference*, GENOME WRITERS GUILD, https://www.genomewritersguild.org/gwg-2018-conference [https://perma.cc/ZX7B-LBNU] (last visited Sept. 8, 2020). Here and elsewhere, unless otherwise indicated (such as where presentations were recorded and are available online), quotes from speakers at conferences that members of the research group attended are taken from the researchers' notes.

drive creative people underground." Another suggested that efforts to increase consumer confidence in genome editing might lead to "reducing regulatory barriers." At the same conference in 2020, speakers continued the theme that research might gravitate toward countries with minimal regulation. Lluis Montoliu, the current president of ARRIGE, stated that in the European Union ("EU"), "unfortunately," edited organisms are treated as genetically modified organisms ("GMOs") and are thus presumptively forbidden; with "progress blocked" in the EU, research goes elsewhere.[90] In a different vein, at the 2020 World Congress of Bioethics, a bioethicist from the National University of Singapore noted that lax regulation can lead to gene editing "tourism."[91] Consequently, he stressed, there is a strong need for global governance to overcome narrow national interests. Nonetheless, "national interest can be leveraged in global governance"—being saddled with a "rogue" reputation can be a meaningful sanction, as China has learned from the He experiments.[92]

C. New Governance and Public Trust

A third dominating theme from these early discussions has been the importance of transparent and publicly engaged approaches to governance to encourage wider trust in genomic science. Almost all the major policy declarations, organizational platforms, and promotional conference rhetoric reflect a deep concern for public opinion, by advocating increased public engagement and seeing a need for societal consensus in any governance development process.[93] For example, one of the first

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[90] Genome Writers Guild, *GWGCON2020 Session 7*, YOUTUBE (Aug. 11, 2020) https://www.youtube.com/watch?v=BAG7sTapFUM&list=PLPxVuE44an0BWlcRT9TbunE2hJ6jOjHIC&index=2 [https://perma.cc/K8R3-W3G7] (broadcasting the address of Lluis Montoliu, president of ARRIGE, at the 2020 Genome Writers Guild).

[91] G. Owen Schaefer, *Sociopolitical Dimensions of Germline Gene Editing*, 15TH WORLD CONGRESS OF BIOETHICS VIRTUAL CONFERENCE, program available at https://iab2020.org/ [https://perma.cc/D7D4-NTXL] (last visited Sept. 8, 2020).

[92] *Id*.

[93] *See* Eric T. Juengst, *Crowdsourcing the Moral Limits of Human Gene Editing?*, 47 HASTINGS CENTER REP. 15, 15–23 (May 24, 2017), https://pubmed.ncbi.nlm.nih.gov/28543411/ [https://perma.cc/L27N-2Y6G].

scientific declarations (from 2015) about human genome editing concludes that it would be "irresponsible to proceed" with germline or enhancement applications until "there is broad societal consensus about the appropriateness of the proposed application."[94] And, as co-author Eric Juengst has pointed out about the 2017 NASEM Report:

> Fully half of the report's fourteen formal recommendations reiterate the need for public dialogue to drive the policy making process, using a family of phrases variously calling for "broad," "extensive," "inclusive," "transparent," "meaningful," "expanded," "robust," and "ongoing" public "communication," "discussion," "debate," "engagement," "input" and "participation," as a "necessary condition for moving forward" before "any consideration of whether to authorize clinical trials" of either enhancing or inheritable human gene editing interventions. [95]

But others caution that public engagement may not help advance the goal of more harmonized and publicly trustworthy governance, especially internationally, because of the dramatic range of public views about the ethics of genome editing.[96] This diversity of voices and viewpoints was on display at the 2018 CRISPRcon conference, where the moderator of a panel of activists representing indigenous, disability, agricultural, and other constituencies concluded, "we may never reach something that is a consensus. It will fail to satisfy virtually everyone."[97] In a similar vein, at the 2020 Genome Writer's Guild Conference, Lluis Montoliu, the president of ARRIGE, spoke pointedly about the need "to foster public trust and prove we deserve it."[98] Noting ARRIGE's position regarding CRISPR, he counseled attendees to be honest about its current limitations and to be clear with the public about off-target effects (accidentally editing the wrong gene) and heritability concerns.[99] He said—perhaps with

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[94] Lander et al., *supra* note 77, at 166.

[95] Juengst, *supra* note 93, at 16 (quoting NAT'L ACADS. OF SCI., ENG'G, & MED., *supra* note 82, *passim*).

[96] *See id.* at 19.

[97] *See* CRISPRcon, *CRISPRcon 2018 – Whats at Stake?*, YOUTUBE (June 29, 2018), https://www.youtube.com/watch?v=653sn_AmFz0&feature=emb_title [https://https://perma.cc/G2GT-27WT].

[98] Genome Writers Guild, *supra* note 90.

[99] *Id*.

unintended irony, given science's mixed messages during the pandemic—that COVID presents an opportunity to "remind society that science has procedures, that we have timelines, that we have permissions, and that we have protocols. That we need to do one step after the other."[100]

At the 2020 World Congress of Bioethics, a bioethicist from University of Manchester in the United Kingdom pursued the problem of public trust from a somewhat different angle.[101] Starting from the "assumption . . . that we need public discourse," he asked such questions as: "can we get relevant input," "what's relevant," "what are relevant publics," and "how do we get input from them?"[102] He concluded by posing an ultimate dilemma: "what if the public disagrees with bioethicists in the end?" His answer was that "bioethicists should show humility—consensus is rare—let the public decide."[103] But he left unaddressed the problem he started with—discerning the public's will.[104]

Another related set of concerns about public trust emerged in a panel discussion entitled "CRISPR and Human Identity: Governing Germline Gene Editing" at the 2020 ELSI [referring to the Ethical, Legal, and Social Implications of genetics] Virtual Forum.[105] A recurrent theme was the need for humility in dealing with the public. One panelist, Emory University disability scholar Rosemarie Garland-Thomson, warned of "velvet eugenics." In contrast, she urged, the gene editing community needs to "cultivate an attitude of humility" toward others' lives and avoid characterizing mere human variation as "new disease" that gene

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[100] *Id*.

[101] Søren Holm, *Sociopolitical Dimensions of Germline Gene Editing*, 15TH WORLD CONGRESS OF BIOETHICS VIRTUAL CONFERENCE, program available at https://iab2020.org/ [https://perma.cc/EFY5-EMXV] (last visited Sept. 8, 2020).

[102] *Id*.

[103] *Id*.

[104] *Id*.

[105] *ELSI Virtual Forum Video Recordings*, COLUM. U. DEP'T MED. HUMS. & ETHICS, https://www.mhe.cuimc.columbia.edu/our-divisions/division-ethics/elsi-virtual-forum/elsi-virtual-forum-video-recordings [https://perma.cc/46FP-P5M2] (last visited Sept. 8, 2020).

editing can cure.[106] To illustrate the point, she said that "we're already practicing eugenics . . . routinely in reproductive medicine. For example, . . . [we've] already decided that the human variations, [like] Down Syndrome, are unacceptable variations and . . . that kind of person is 'expendable' and 'disposable' . . . . [W]hat a serious disease is, what human suffering might be, we need to look at it quite a bit more closely."[107]

VI. HOW WELL DO THE VARIOUS APPROACHES TO GOVERNANCE MEET THESE CONCERNS?

In mapping these concerns onto relevant theories of governance, the researchers can begin to make some observations about the promise of the various approaches to governance. Table 1 lists five goals that gene-editing stakeholders have begun to identify as desiderata that any effective governance regime should promote: scientific autonomy, international harmonization, and public trust, plus meaningful enforcement and ease of implementation. The table then rates each of four potential approaches to governance—professional self-governance, national laws, international treaty, and new governance—according to its apparent capacity to promote these objectives.

A. Scientific Self-Regulation

The potential efficacy of scientific self-regulation is largely a function of the details of the model chosen. Self-regulation that depends solely on voluntary compliance with ethical precepts is only as effective as participants choose to make it. At the other end of the spectrum, as in the case of law, it can take on many of the attributes of hard regulation if a government defines the profession and delegates to it the power to limit entry, police members' conduct, and expel those who fail to comply with its rules. In the middle ground, a professional group can informally regulate conduct through such measures as public shaming (censure) and, in the

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[106] Rosemarie Garland-Thomson et al., *CRSPR and Human Identity: Governing Germline Gene Editing*, ELSI VIRTUAL FORUM (June 16, 2020), https://www.mhe.cuimc.columbia.edu/our-divisions/division-ethics/elsi-virtual-forum/elsi-virtual-forum-video-recordings [https://perma.cc/46FP-P5M2].

[107] *Id*.

academic world, conditioning publication on ethical warranties.[108] This begins to look like a new governance environment, as will be discussed shortly.

Voluntary professional self-governance obviously maximizes scientists' autonomy and control over the scientific enterprise, and equally obviously does not have sharp teeth. As the model moves in the direction of the harder regulation of the traditional professions, the teeth get sharper, but at the expense of autonomy. International harmonization of voluntary standards is possible, but meaningless without international enforcement mechanisms. Public trust is unlikely to be affected by the mere presence of standards but will depend on how well the scientists behave. Since self-governance is so open-ended, it can be easy to implement. A problem with this approach, however, is that "science" has no clear definition as a profession; the disparate putative members include researchers from many disciplines as well as healthcare practitioners who may already be subject to hard regulation.

B. Hard Regulation

Hard regulation on a country-by-country basis has the virtue of strong enforcement potential, and the adoption of rigorous standards that are diligently enforced may engender public trust—or cynicism if enforcement seems lax. But regulations take time and political will to adopt, and international consistency is unlikely on any complex legal issue. Moreover, countries may be tempted to adopt weaker standards to attract research, much like countries have used weaker environmental and labor standards to attract industry.[109]

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[108] The death of research subject Jesse Gelsinger in a trial employing gene therapy, a predecessor to gene editing and still in trials today, provides an example where censure and conditions on publication were imposed as sanctions on researchers and institutions conducting research. *See* Sheryl Gay Stolberg, *The Biotech Death of Jesse Gelsinger,* N.Y. TIMES MAG. (Nov. 28, 1999), https://www.nytimes.com/1999/11/28/magazine/the-biotech-death-of-jesse-gelsinger.html [https://perma.cc/B8UN-258R].

[109] *See Flagging Out*, GREENFACTS, https://www.greenfacts.org/glossary/def/flagging-out.htm [https://perma.cc/M8AB-27A6] (last visited Sept. 25, 2020).

Binding and enforceable international legal regimes—which solve the harmonization problem—are even more difficult to create and maintain. First, all the relevant countries—in the gene editing context, the United States, China, and the EU, at a bare minimum—must negotiate and sign a treaty. Then each signatory must ratify the treaty according to its national law. In some cases, signatory countries must enact national legislation to implement the treaty.[110] Finally, and critically, the signatories must actually carry out the enforcement they have promised. The recent U.S. withdrawal from the Paris Agreement on climate change illustrates these difficulties.[111] The Obama administration signed the Agreement but never submitted it to the U.S. Senate for ratification as a treaty; the Trump administration therefore treated it as a non-binding commitment that it was free to repudiate.[112] Given all these obstacles, a meaningful international law of gene editing seems unlikely for the foreseeable future.

The version of this approach suggested in the *Nature* proposal described above[113]—parallel legal action by individual countries—avoids some of the formal steps required by the NASEM Commission report, *Heritable Human Genome Editing,* with its recommendation of nation-level action guided by its "translational pathway."[114] Leaders of essential countries must come to an agreement on general principles and the manner of implementation,

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[110] Treaties that require implementing legislation are called non-self-executing treaties, in contrast to self-executing treaties, which do not. *See Self Executing Treaties,* LEGAL INFO. INST., https://www.law.cornell.edu/wex/self_executing_treaty#:~:text=A%20self%2Dexecuting%20treaty%20is,through%20the%20implementation%20of%20legislation [https://perma.cc/D88V-UXBS] (last visited Sept. 25, 2020).

[111] *See* Press Statement, Sec'y of State Michael R. Pompeo, On the U.S. Withdrawal from the Paris Agreement (Nov. 4, 2019) (on file with the U.S. Dept. of State).

[112] *See* Eugene Kontrovich, *The U.S. Can't Quit the Paris Climate Agreement, because It Never Actually Joined,* WASH. POST (June 1, 2017), https://www.washingtonpost.com/news/volokh-conspiracy/wp/2017/06/01/the-u-s-cant-quit-the-paris-climate-agreement-because-it-never-actually-joined/ [https://perma.cc/3ZW9-ZSKF].

[113] *See* Lander et al., *supra* note 77 and accompanying text.

[114] *See* NAT'L ACADS. OF SCI., REPORT SUMMARY, *supra* note 69.

and then—at least in democracies—persuade potentially fractious lawmakers to go along.

C. New Governance

This leaves the hybrid approach that combines aspects of self-governance with elements of harder regulation. The still-nebulous proposals for a hybrid approach to governance that the project has encountered can be grouped under the broad heading of new governance.[115] According to new governance theory, the democratic state is in the midst of a shift to a "post-regulatory" model characterized by a weakening of top-down regulation by the all-powerful administrative state—"old" governance—in favor of a diffusion of rights and responsibilities among governments, private companies, NGOs, and other interested parties.[116] New governance approaches involve "transnational private regulation" by coalitions of non-state actors.[117] The essence of the post-regulatory state, captured in the linguistic shift from *government* to *governance*, is the distribution of regulatory power among transnational networks of state and non-state actors that often use market and other private forces to set and enforce standards.[118]

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[115] Recent articles have reviewed new governance theory in a variety of contexts. *See, e.g.*, John Gerard Ruggie, *Global Governance and "New Governance Theory": Lessons from Business and Human Rights*, 20 GLOB. GOVERNANCE 5 (2014); Myrisha S. Lewis, *Innovating Federalism in the Life Sciences*, 92 TEMP. L. REV. 383 (2020); Melanie Hess, *A Call for an International Governance Framework for Human Germline Gene Editing*, 95 NOTRE DAME L. REV. 1369 (2020); Ryan Hagemann, Jennifer Huddleston Skees & Adam Thierer, *Soft Law for Hard Problems: The Governance of Emerging Technologies in an Uncertain Future*, 17 COLO. TECH. L.J. 37 (2018); Jonas J. Monast, *Editing Nature: Reconceptualizing Biotechnology Governance*, 59 B.C. L. REV. 2377 (2018).

[116] *See* John M. Conley & Cynthia A. Williams, *Engage, Embed, and Embellish: Theory versus Practice in the Corporate Social Responsibility Movement,* 31 J. CORP. L. 1, 6, 31–33 (2005) (defining attributes of new governance).

[117] Tim Bartley, *Institutional Emergence in an Era of Globalization: The Rise of Transnational Private Regulation of Labor and Environmental Conditions*, 113 AM. J. SOCIO. 297, 297 (2007).

[118] *See* Conley & Williams, *Engage, Embed, and Embellish, supra* note 116, at 31.

There have been extensive studies of new governance approaches in other areas that are analogous in important respects to gene editing research. One example is the corporate social responsibility movement.[119] In that instance, many corporations have sought to address social and environmental issues by such strategies as voluntary commitments to industry codes and best practice standards, convening multi-stakeholder advisory groups (sometimes adding such constituencies to their boards of directors), and measuring and disclosing social and environmental risks through triple bottom line (financial, social, and environmental) accounting.[120] Such private governance networks sometimes adopt substantive standards promulgated by governmental and quasi-governmental bodies. For example, the biggest global banks collectively adopted the World Bank's social and environmental standards in establishing the "Equator Principles" to govern private lending for large-scale projects in developing countries.[121]

Motivations for participating in new governance regimes can vary.[122] Private actors may perceive a hard regulation vacuum and move to fill it in the sincere belief that standards must be set. But they may also see an opportunity to preempt more onerous governmental regulation by demonstrating, at least superficially, that they have the problem under control. With respect to efficacy, new governance advocates sometimes contend that actors who invest in the creation of standards are more likely to comply than those who have standards imposed on them. Especially where science, technology, and other arcane practices are involved, private actors can plausibly contend that those who know the

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[119] *See generally id.*; John M. Conley, Cynthia A. Williams, Lodewijk Smeehuijzen & Deborah E. Rupp, *Can Soft Regulation Prevent Financial Crises?: The Dutch Central Bank's Supervision of Behavior and Culture*, 51 CORNELL INT'L L.J. 773 (2019) (both sources explaining and illustrating corporate social responsibility movement).

[120] *See* Conley & Williams, *Engage, Embed, and Embellish, supra* note 116, at 2–5.

[121] *See generally* Conley & Williams, *Global Banks as Global Regulators, supra* note 8 (providing analysis of adoption of Equator Principles).

[122] *See id.* at 558–62 (reviewing evidence for many of these motives in the banking context).

practice best are most qualified to set the standards.[123] But it is also possible that the outcome will be mere window dressing—weak and easily evaded standards that can nonetheless be sold to lawmakers and other relevant audiences.[124] Likewise, meaningful enforcement mechanisms can also be difficult to construct in the absence of governmental authority.[125] A central tenet of the corporate social responsibility movement, for example, is that investors and consumers, informed by adverse publicity and triple bottom line reporting, will become aware of noncompliance and penalize laggards. But the evidence for this "business case" for compliance is inconclusive; it is unclear whether either profits or share performance correlate with indicators of social responsibility.[126]

One can readily envision such a governance network arising with respect to CRISPR genome editing—indeed, the project may be witnessing its formative stages. Even in the absence of hard regulations, governmental authorities may play a role, perhaps by the promulgation of standards as ARRIGE has suggested.[127] The early evidence suggests that other key actors are likely to be scientists; NGOs; interested for-profit corporations and their principals; scientific gatekeepers including funders, journal editors, university officials, and voluntary scientific organizations; and organized voices speaking for affected communities and other public constituencies.[128]

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[123] *See* John M. Conley et al., *Scientific Social Responsibility: Lessons from the Corporate Social Responsibility Movement,* 15 AM. J. OF BIOETHICS 64, 65–66 (2015).

[124] *See* Conley & Williams, *Engage, Embed, and Embellish, supra* note 116, at 13–18 (providing evidence from the corporate social responsibility context).

[125] *See id.* at 20.

[126] *See* Conley & Williams, *Global Banks as Global Regulators, supra* note 8, at 560–61 (reviewing "the elusive 'business case'"); Conley & Williams, *Engage, Embed, and Embellish, supra* note 116, at 14, 21–23 (evaluating business case and presenting investor perspective).

[127] *See supra* notes 75–76 and accompanying text.

[128] For example, the National Institutes of Health (NIH) proposes to be a key actor. In April 2019, the NIH published its charter of NExTRAC (Novel and Exceptional Technology and Research Advisory Committee). It was created to review emerging biotechnologies such as gene editing and characterized as an updated RAC (Recombinant DNA Advisory Committee), which examined gene therapy research for thirty years. The agenda included updates from current

Depending on the actor, motivations to participate may include professionalism, ethics, principle, profit, self-promotion, and ideology; their respective contributions to the ultimate mix will strongly influence the quality of any standards that result. Scientific stakeholders may be best positioned to resolve thorny definitional questions such as distinguishing treatment and prevention from enhancement. Even in the absence of governmental sanctions, meaningful enforcement mechanisms could include access to funding and publication; academic hiring and promotion decisions; exclusion from important organizations; and, at the most basic human level, shame and obloquy versus honor and prestige. While these carrots and sticks can be significant, they fall short of the civil and criminal penalties that governments can exact.

There is growing evidence from the research to date that a range of gene editing stakeholders are already gravitating toward the new governance approach. The most significant piece of evidence is the World Health Organization's Expert Advisory Committee's recently issued draft report.[129] The report's lengthy definition of "good governance" is in fact a comprehensive definition of new governance:

> **Good governance** is not limited to formal regulation pursuant to legislation or judicial opinion. Governance is a system of norms as well as influence, and it includes forces to shape the direction and conditions of research and applications, such as well-crafted public and private funding priorities and conditions. Good governance also includes professional and industrial best practices, peer review and ethics assurance by publishers, and health care insurance coverage decisions for instance. Possible liability for harmful research or clinical care is an indirect source of governance, mediated by liability insurance.[130]

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technologies, questions in defining "emerging biotechnologies," and concerns about proper stakeholder engagement. *See* Carrie D. Wolinez, *Introducing the NExTRAC*, NAT'L INST. HEALTH (April 24, 2019), https://osp.od.nih.gov/2019/04/24/introducing-the-nextrac/ [https://perma.cc/Y3GB-RPWM]; *Novel and Exceptional Technology and Research Advisory Committee (NExTRAC) Agenda – December 5-6*, NAT'L INST. HEALTH, https://osp.od.nih.gov/wp-content/uploads/NExTRAC_Dec_2019_Agenda.pdf [https://perma.cc/G2AL-U9AF] (last visited Sept. 15, 2020).

[129] Expert Advisory Comm. on Developing Glob. Standards for Governance and Oversight of Hum. Genome Editing, *supra* note 79.

[130] *Id.*

Similarly, its list of "tools for governance" enumerates all the possible mechanisms for shaping behavior that new governance theorists have envisioned:

Tools for Governance:

- Law: Declarations, Treaties, Conventions, Legislation, Regulation
- Judicial rulings
- Ministerial decrees
- Conditions on research funding
- Moratoria
- Accreditation, registration, licensing
- Professional self-regulation
- Research ethics guidelines
- Collaboration with publishers and conference organizers
- Education and training of researchers and clinician-scientists
- Interest groups and public influencers[131]

A second recent example comes from the 2020 Genome Writers Guild Conference. A representative from the U.S. National Institute of Standards and Technology ("NIST") emphasized the government's interest in a new governance approach to gene editing.[132] As its name suggests, NIST, which is part of the U.S. Department of Commerce, works with the academic and private sectors "[t]o promote U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life."[133] Importantly, it is not a regulatory agency.

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[131] *Id.*

[132] *See* Genome Writers Guild, *supra* note 90 (broadcasting the address of Samantha Maragh titled "A Consortium Approach to Foster Confidence in Gene Editing" beginning at 24:17).

[133] *NIST Mission, Vision, Core Competencies, and Core Values*, NAT'L INST. STANDARDS & TECH. (Jan. 26, 2017), https://www.nist.gov/about-nist/our-organization/mission-vision-values [https://perma.cc/5HKG-GER9].

Samantha Maragh, the Leader of NIST's Genome Editing Program,[134] speaking on a panel with the odd title of "EU Regulatory Landscape – genome engineering and supporting the public trust,"[135] gave a presentation entitled "A Consortium approach to foster confidence in genome editing technology."[136] The consortium that NIST is sponsoring is a public-private collaboration, currently including thirty-seven organizations from government (most prominently, the USFDA), industry, academic science, and the non-profit sector. Its purpose, Maragh said, "meant to be enabling, not limiting"—specifically, its goal should be the advancement of gene editing technology.[137] One might question whether "foster[ing] confidence" is anything more than a public relations objective or whether confidence, as opposed to safety, is an appropriate concern for a standard-setting body, as well as the absence of public voices from the consortium. But there is no doubt that Maragh was describing a new governance network not fundamentally different from the Equator Principles signatories.

One reason that a new governance approach is being endorsed for gene editing research is that it can be much easier to implement than more traditional regulatory approaches, especially at the international level. As the speed with which the Equator Principles were adopted illustrates,[138] professional and other private stakeholders can move quickly, and on a global scale. In every other category, however, the promise of a new governance approach to gene editing research is equivocal. If done well, it can certainly promote public trust, work consistently across international boundaries, and result in meaningful enforcement. Because scientists would be critical stakeholders, the categories are interrelated: success in one depends on corresponding success in

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[134] Genome Writers Guild, *supra* note 132.

[135] In the first place, it is unclear what it means to "support" public trust unless the trust is already there. In any event, none of the six speakers said anything about public trust.

[136] Genome Writers Guild, *supra* note 132, at 24:17.

[137] *Id*. at 35:42.

[138] *See* Conley & Williams, *Global Banks as Global Regulators, supra* note 8, at 545 (reviewing initial adoption, revision, and rapidly growing acceptance over seven years).

the others. Thus, scientists can retain their autonomy and create public trust only by promoting strong standards and submitting to rigorous enforcement. The Equator Principles experience is again relevant here. It is unclear whether they really have reduced the adverse social and environmental impacts of large-scale projects.[139] There is widespread agreement that the participating banks have done a reasonably diligent job of monitoring their borrowers, but equally widespread concern that the adoption of the Principles may have driven some project sponsors to seek out non-participating lenders in Russia, China, and elsewhere.[140] But despite this mixed evidence, new governance is the only approach with realistic potential to promote each of the objectives identified in Table 1 in the short to medium term.

Table 1: Evaluating Approaches to Governance

Priorities	International Treaty	National Laws	Professional Self-Governance	New Governance
Scientific Control	–	–	+	+/–
Regulatory Teeth	+	+	–	+/–
International Harmonization	+	–	–	+/–
Public Trust	+	+/–	–	+/–
Ease of Implementation	–	–	+/–	+

Summary of the different approaches to governance and the ability of each to promote the enumerated priorities.

VII. CONCLUSION

As the embryo experiments in China illustrate, the early implementation of human genome editing has had a "ready-fire-aim" quality. Scientific self-regulation has not been able to anticipate events well enough to secure widespread

[139] *See id.* at 562–64 (reviewing inconclusive evidence).
[140] *See id.* at 566–67.

international allegiance to common standards and has thus been relegated to clean-up responses in the wake of scandal. Regulation by international law is a long and contested process at best; the complexities of human genome editing only lengthen the odds against such a solution. Negotiating and implementing consistent nation-by-nation regulations is not much easier. This may be a situation where a hybrid new governance approach, despite its inevitable shortcomings, will be far preferable to the chaos of no meaningful governance at all. Early evidence suggests that the scientific community and its various constituencies are heading in this direction, with constant attention to public engagement along the way. Given the potential costs of doing nothing, these are developments that the Authors encourage despite their shortcomings.