Article

The Nagoya Protocol and the Legal Structure of Global Biogenomic Research

Michelle Rourke,[†] Sam Halabi,[††] Gian Luca Burci,[‡] & Rebecca Katz[‡‡]

[†] Dr. Michelle Rourke is a Commonwealth Scientific and Industrial Research Organisation (CSIRO) Synthetic Biology Future Science Fellow at Griffith University Law School in Brisbane, Australia. Her research focuses on the global regulation of access to genetic resources for the Australian synthetic biology community. Her Ph.D. examined how international access and benefit-sharing laws under the United Nations' Convention on Biological Diversity and its Nagoya Protocol impact access to physical virus samples and associated information, including genetic sequence data. Dr. Rourke is a member of the Global Virome Project's Ethical, Legal and Social Implications Working Group and a non-resident Affiliate of the Center for Global Health Science and Security at Georgetown University.

[††] Sam Halabi is the Manley O. Hudson Professor of Law at the University of Missouri, a Scholar at the O'Neill Institute for National and Global Health Law at Georgetown University, and the co-chair of the Ethical, Legal, and Social Implications Working Group of the Global Virome Project. He holds a J.D. from Harvard Law School, an M.Phil. from the University of Oxford (St. Antony's College) and a B.S., summa cum laude, from Kansas State University.

[‡] Gian Luca Burci is the co-chair of the Ethical, Legal and Social Issues Working Group of the Global Virome Project, an adjunct professor at the Graduate Institute Geneva and the former Legal Counsel of the World Health Organization. Professor Burci previously served as Legal Officer at the International Atomic Energy Agency in Vienna and in the United Nations Secretariat in New York.

[‡‡] Dr. Rebecca Katz is Professor and Director of the Center for Global Health Science and Security at Georgetown University. She earned her undergraduate degree from Swarthmore College, an M.P.H. from Yale University, and a Ph.D. from Princeton University.

"Rather than approaching access and benefit sharing as a problem to be overcome, it should be seen as an opportunity to work with partners in countries providing access to genetic resources, to increase the impact of the research being undertaken and, ultimately, to exercise the principles of equity and fairness." - Braulio Ferreira de Souza Dias[1]

I. INTRODUCTION

International research collaborations have been the engines of some of the most important advances in human health and nutrition over the last century. The Green Revolution, built on networks of scientists and resources drawn from the world's wealthiest and poorest countries, averted critical food shortages that faced the growing world population in the 1950s and 1960s.[2] The most promising vaccine candidates for devastating infectious diseases like Ebola and HIV have resulted from partnerships of financial resources, governments, and scientists from the Democratic Republic of Congo, Guinea, Liberia, Sierra Leone, South Africa, and Thailand. Orchestrated technology transfer and research capacity building in low- and middle-income countries have delivered advances in the ability of low-resource countries to manufacture medicines and vaccines. Scientists have worked together across borders as threats posed by infectious disease, malnutrition, and environmental degradation necessitate partnerships that match the technology and resources in wealthy countries with the knowledge and biodiversity abundant in many poorer ones.[3] These collaborations have rendered multiple positive effects—not only in the form of solutions to the problems initially considered, but also in the form of increased local capacity as laboratories are built, knowledge is shared, and technology is transferred.

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[1] Braulio Ferreira de Souza Dias, *Foreword* to RESEARCH AND DEVELOPMENT ON GENETIC RESOURCES: PUBLIC DOMAIN APPROACHES IN IMPLEMENTING THE NAGOYA PROTOCOL, at xviii (Evanson Chege Kamau et al. eds., 2015).

[2] Raj Patel, *The Long Green Revolution*, 40 J. PEASANT STUD. 1, 5-6 (2013).

[3] *See generally The Future of Food and Agriculture*, FOOD & AGRIC. ORG. UNITED NATIONS (2017), http://www.fao.org/3/a-i6583e.pdf (describing various areas of agriculture and collaborative approaches to food challenges).

There were, of course, negative effects as well. Not all of these research activities were collaborative, and many were exploitative. Researchers based in Europe and North America often transferred materials from low- and middle-income countries to laboratories in richer ones, sharing little of the resulting knowledge, technology, or products. It is this history that has made the environment for current life-sciences research collaborations so legally complex.

Indeed, much technological progress now occurs in a world of growing divisions between developing and developing countries.[4] Developments in international law over the last twenty-five years have worked to ensure that not only are the governments of the world's most biodiverse countries consulted about research activities, but also that the benefits from research flow to them and their populations. The promise of new breakthroughs in medicine and agriculture are therefore wedded to the international law of biodiversity, as well as imbued with ethical obligations to ensure that speculative research is not favored over using existing resources to meet the needs of humans living today, billions of whom live in poverty and deprivation. This Article endeavors to address that complex juxtaposition of scientific possibility and basic human needs.

As life sciences technologies have advanced, so too has the potential for these international collaborations to lead to breakthrough medicines, enhance food security, and protect ecological systems. The linchpin of this progress is the development of high throughput genetic sequencing technologies. Researchers are now able to generate and compare large stretches of DNA - 1 million bases or more - from different sources quickly and inexpensively. Such comparisons can yield massive amounts of information about the role of inheritance in susceptibility to infection and illness as well as responses to environmental influences. In addition, the ability to sequence genomes more quickly and inexpensively creates enormous potential for new diagnostics and therapies.[5] This is true not only for sequencing the human genome, but also for sequencing the genomes of simple and complex organisms that comprise the entire human environment.

This Article will first provide examples of where international collaborations have led to advances in medical and agricultural benefits for populations in both rich and poor countries. It will then describe how new life sciences research collaborations, primarily using genetic sequencing technology, may detect potential human pathogens, characterize microbial life, and catalogue the unique genetic information in all wildlife species. It will situate these biogenomic projects in the context of the international access and benefit sharing law, derived from several sources, but most importantly the 1993 Convention on Biological Diversity (CBD). Finally, this Article will analyze four of these new international collaborations to demonstrate that the common tensions that arise between

[4] *See, e.g.*, SAM HALABI, INTELLECTUAL PROPERTY AND THE NEW INTERNATIONAL ECONOMIC ORDER 43-45 (2018) [hereinafter Halabi, *Intellectual Property*].

[5] *See DNA Sequencing Fact Sheet*, NAT'L HUM. GENOME RES. INST. (Dec. 18, 2015), https://www.genome.gov/10001177/dna-sequencing-fact-sheet/.

generating scientific and other benefits through exploiting new research possibilities, and meeting the food and medical needs of the world's population today are often reconcilable.

Part I of this Article outlines the law and ethics of life sciences research partnerships as they unfolded over the course of the twentieth century. Part II analyzes how advances in genetic sequencing technology may accelerate the pace and impact of new life sciences research collaborations. Part II also examines the development of international law over the course of those technological advances, and how the law now requires or shapes partnerships to benefit all participants and to be mindful of constituencies who may or may not benefit. Part III examines four major collaborations, using these case studies to show how the international law of biodiversity is shaping their objectives and channeling their benefits and also addressing persistent ethical questions about the use and distribution of scarce resources. Part IV sets out the conclusions.

A. Agriculture and Nutrition

After World War II, virtually the entire globe, but especially the least developed regions of it, faced food shortages, growing populations, and regular famine.[6] In response, scientists from India, Mexico, the Philippines, and the United States, in partnership with major international organizations and foundations, created a global biological commons in plant genetic resources, implemented through a system of cross-country research experiments creating international nurseries, breeding hubs, and the free sharing of seeds and related genetic information.[7] The high-yield varieties of cereal grains resulting from these collaborations were accompanied by orchestrated technology transfers from wealthier countries to poorer ones. Farmers were able to adopt the new high yield varieties quickly, and food production was able to keep up with local population growth. Now known as the Green Revolution, the effort boosted average caloric intake in emerging regions as food prices declined, leading to better indicators of health and a longer life expectancy.[8]

The Green Revolution also created mechanisms to sustain the scientific collaborations that explained its success. Initially, a group of seventeen member countries, international organizations, and foundations comprised the Consultative Group for International Agricultural Research (CGIAR).[9] Seven new members were added in the 1970s that were primarily concerned with core breeding programs, including for livestock.[10] Then, five more members were

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[6] *See* William B. Dickinson Jr., *World Food Shortages*, *in* 2 EDITORIAL RESEARCH REPORTS 547 (1965), http://library.cqpress.com/cqresearcher/cqresrre1965072800.

[7] *See* Derek Byerlee & H.J. Dubin, *Crop Improvement in the CGIAR as a Global Success Story of Open Access and International Collaboration*, 4 INT'L J. COMMONS 452, 455-56 (2010).

[8] *See* R. E. Evenson & D. Gollin, *Assessing the Impact of the Green Revolution, 1960 to 2000*, 300 SCI. 758, 761 (2003).

[9] *See* Byerlee & Dubin, *supra* note 7, at 456.

[10] *See id.*

added in the 1980s with a strong focus on natural resources management and policy research.[11] Each member "relied on similar principles of networks and open sourcing," such as databases for natural resources management research, and "[b]y 2007, the CGIAR had grown to include 64 members," all with a continuing commitment to the research and development of genetic resources for food, especially for the world's poorest populations.[12] CGIAR research is carried out through international agricultural research centers (IARCs) located overwhelmingly in developing countries. The IARCs conduct research to improve and create new germplasm from which to develop seeds.[13]

It is estimated that "without the CGIAR and national program crop germplasm improvement efforts, food production in developing countries would have been almost 20% lower."[14] To compensate, another 20–25 million hectares of land under cultivation would have been necessary worldwide.[15] As Pingali notes, "[w]orld food and feed prices would have been 35–65% higher, and average caloric availability would have declined by 11–13%."[16] Overall, these efforts benefited virtually all consumers in the world, with disproportionate benefit being passed onto poor populations, who spend a greater share of their income on food.[17]

The benefits of the Green Revolution for local communities appear to significantly outweigh the costs. The Green Revolution had the effect of introducing or intensifying the use of fertilizer, insecticide, pesticide, and fungicide agents that have imposed a burden on local water and ecosystems.[18] Because large-scale farmers adopted Green Revolution more quickly, it had the effect of pressuring the market share and sustainability of smaller farms.[19] It also laid the groundwork for the increasing assertion of intellectual property claims over agricultural inputs, as seeds and pesticides available from the public domain decreased.[20] Yet its net effect has been profoundly positive. As researchers at Oregon State University concluded:

> The Green Revolution led to sizable increases in returns to land, and hence raised farmers' incomes. Moreover, with greater income to spend, new needs for farm inputs, and milling and marketing services, farm families led a general increase in

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[11] *See id.*; FRÉDÉRIC GAGNON-LEBRUN, INTERNATIONAL ENERGY TECHNOLOGY COLLABORATION AND CLIMATE CHANGE MITIGATION (2004).
[12] Byerlee & Dubin, *supra* note 7, at 457.
[13] *See* Evenson & Gollin, *supra* note 8, at 759.
[14] Prabhu Pingali, *Green Revolution: Impacts, Limits, and the Path Ahead*, 109 PROC. NAT'L ACAD. SCI. U.S. 12302, 12303 (2012).
[15] *Id.*
[16] *Id.*
[17] *Id.*
[18] Saidur Rahman, *Green Revolution in India: Environmental Degradation and Impact on Livestock*, 12 ASIAN J. WATER, ENV'T. AND POLLUTION 75 (2015).
[19] *See Green Revolution: Curse or Blessing?*, INT'L FOOD POL'Y RES. INST. 3 (2002), https://oregonstate.edu/instruct/css/330/three/Green.pdf [hereinafter IFPRI Report].
[20] Halabi, *Intellectual Property*, *supra* note 4, at 225 (noting the increase in wealthy states' intellectual property claims throughout 1980s and 1990s).

> demand for goods and services. This stimulated the rural nonfarm economy, which in turn grew and generated significant new income and employment of its own. Real per capita incomes almost doubled in Asia between 1970 and 1995, and poverty declined from nearly three out of every five Asians in 1975 to less than one in three by 1995.The absolute number of poor people fell from 1.15 billion in 1975 to 825 million in 1995 despite a 60 percent increase in population. In India, the percentage of the rural population living below the poverty line fluctuated between 50 and 65 percent before the mid-1960s but then declined steadily to about one-third of the rural population by 1993. Research studies show that much of this steady decline in poverty is attributable to agricultural growth and associated declines in food prices. The Green Revolution also contributed to better nutrition by raising incomes and reducing prices, which permitted people to consume more calories and a more diversified diet.[21]

B. Human Health and Medicine

The greatest non-military threats to human life (and some military ones) are posed by infectious diseases. Since 1981, HIV/AIDS has afflicted approximately 70 million, killing half of them.[22] Influenza killed 3% of the world's population in two years (1918-19) and continues to kill hundreds of thousands annually.[23] In the last 200 years, tuberculosis alone has killed over one billion people.[24] International scientific collaborations have resulted in medicines, vaccines, and preventative technologies that have drastically reduced the burdens imposed by these diseases.

1. *HIV/AIDS*

Scientists discovered the virus that caused AIDS in 1983, largely because of increasing reports of rare types of pneumonia, cancer, and other illnesses in specific populations like gay men, Haitians returning from the Democratic

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[21] IFPRI Report, *supra* note 19, at 3.

[22] Carlos del Rio, *The Global HIV Epidemic: What the Pathologist Needs to Know*, 34 SEMINARS DIAGNOSTIC PATHOLOGY 314-17 (July 2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5531065/pdf/nihms878509.pdf ("[B]y 1981 when the first case of AIDS were identified . . . HIV had been circulating in the US for a decade. Since then, more than 70 million people have been infected with HIV and about 35 million have died as a result. The World Health Organization (WHO) estimates that at the end of 2015, 36.7 million [34.0–39.8 million] people were living with HIV and an estimated 0.8% of adults aged 15 – 49 years are infected with HIV").

[23] *See* Richard Gunderman, *Ten Myths About the 1918 Flu Pandemic*, SMITHSONIAN MAG. (Jan. 12, 2018), https://www.smithsonianmag.com/history/ten-myths-about-1918-flu-pandemic-180967810/; Jennifer Latson, *What Made the Spanish Flu So Deadly?*, TIME (Mar. 11, 2015), http://time.com/3731745/spanish-flu-history.

[24] *See* Tom Paulson, *Epidemiology: A Mortal Foe,* 502 NATURE S2, S2 (2013).

Republic of Congo, and intravenous drug users.[25] By the end of 1986, "85 countries had reported 38,401 cases of AIDS to the World Health Organization."[26] By the early 1990s, the population of people living with HIV/AIDS exploded in sub-Saharan Africa, quickly comprising the large majority of the HIV/AIDS afflicted population worldwide.[27] By 2001, approximately twenty million people had died from AIDS, and another forty million people were infected and/or dying. Sub-Saharan Africa accounted for two-thirds of the people living with HIV/AIDS, despite holding a relatively small percentage of the global population.[28]

International scientific partnerships were crucial to the development of antiretroviral treatments that have drastically reduced mortality from the disease and have underpinned efforts to develop a vaccine.[29] The most promising candidate, RV144, resulted from international scientific collaborations stretching across the globe including major clinical trial sites in Thailand and South Africa.[30] A clinical trial of RV144 involved 26,658 participants in eastern Thailand.[31] Several factors have been noted as playing a critical role to the successful implementation of these trials. Namely, active inclusion of the local communities in the trial and performing trial activities within Thailand's existing healthcare system while also strengthening Thai healthcare infrastructure and capacity. Both the partial efficacy reported in the RV144 trial and the positive results of the subsequent immune correlates analysis suggest an effective HIV vaccine is within reach.[32]

The migration of HIV/AIDS research from richer to poorer countries, especially clinical trials, has resulted in large scale transfer of medical technology and knowledge to those countries. While there have been concerns

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[25] James W. Curran and Harold W. Jaffe, *AIDS: The Early Years and the CDC's Response*, 60 CENTER FOR DISEASE CONTROL & PREVENTION 64, 64-69 (2011); Robert C. Gallo & Luc Montagnier, *The Discovery of HIV as the Cause of AIDS*, 349 NEW ENG. J. MED. 2283, 2284 (2003).

[26] *History of HIV and AIDS Overview*, AVERT, https://www.avert.org/professionals/history-hiv-aids/overview#footnote35 (last updated Oct. 10, 2019).

[27] JONATHAN MANN AND DANIEL TARANTOLA, AIDS IN THE WORLD II: GLOBAL DIMENSIONS, SOCIAL ROOTS, AND RESPONSES 11 (1996).

[28] *The Global HIV/AIDS Epidemic*, KAISER FAM. FOUND. (Sept. 9, 2019), https://www.kff.org/global-health-policy/fact-sheet/the-global-hivaids-epidemic/.

[29] *See, e.g.*, *ADVANCE*, INT'L AIDS VACCINE INITIATIVE, https://www.iavi.org/our-work/clinical-epidemiology-research/advance (last visited Nov. 13, 2019).

[30] *See generally* Paul M. Sharp & Beatrice H. Hahn, *The Evolution of HIV-1 and the Origin of AIDS*, 365 PHIL. TRANSACTIONS ROYAL SOC'Y B: BIOLOGICAL SCI. 2487, 2499-90 (2010) (outlining the origins of HIV); *see also* Samuel Broder, *The Development of Antiretroviral Therapy and Its Impact on the HIV-1/AIDS Pandemic,* 85 ANTIVIRAL RES. 1, 1 (2010) (unpublished manuscript), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2815149/pdf/nihms153574.pdf (discussing the development of antiretroviral therapy).

[31] Tracey A. Day & James G. Kublin, *Lessons Learned from HIV Vaccine Clinical Efficacy Trials*, 11 CURRENT HIV RES. 1, 10 (2013) (unpublished manuscript), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4000156/pdf/nihms538919.pdf.

[32] *See* Ryan Lenora Brown & Lenny Bernstein, *Major HIV Vaccine Trial in South Africa Stokes Hope,* WASH. POST (Nov. 25, 2016), https://www.washingtonpost.com/national/health-science/major-hiv-vaccine-trial-in-south-africa-again-stokes-hope/2016/11/25/188cd56a-b0ff-11e6-be1c-8cec35b1ad25_story.html?utm_term=.2cbcabf5fb25.

raised about the standard of care adopted by researchers, the capacity-building efforts of training more medical workers, funding more laboratories, and educating more citizens have been well-documented.[33]

2. *Influenza*

Although there have been at least four influenza pandemics in the last century, the Spanish influenza pandemic of 1918-19 was by far the worst, killing approximately three percent of the world's population.[34] Influenza pandemics threaten to recur because of the virus's capacity to reassort.[35] Since the 1950s, WHO's Global Influenza Surveillance and Response System (formerly Global Influenza Surveillance Network) has served as one of the largest, continuously operating international life sciences research collaborations in the world, incorporating reference laboratories, researchers, and vaccine manufacturers.[36] This connection has generated seasonal and pandemic flu vaccines that have saved millions of lives.[37] The system "monitor[s] the evolution of influenza viruses and . . . provide[s] recommendations on which candidate vaccine viruses should be included in seasonal and pandemic vaccines."[38] The system is structured around six WHO collaborating centers located in Australia, China, Japan, the U.K. and the U.S., four WHO essential resource laboratories, and 142 institutions recognized by WHO as national influenza centers (NICs) located in 112 countries.[39] NICs collect clinical specimens for the detection of influenza viruses through national surveillance networks.[40] This system collects influenza samples from around the world, distributes them to collaborating centers, and shares them, pursuant to material transfer agreements, with non-profit and for-profit actors to develop vaccines and antivirals.[41]

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[33] *See, e.g.*, Lisa Judy Chin et al., *HIV/AIDS Research Conducted in the Developing World and Sponsored by the Developed World: Reporting of Research Ethics Committee Review in Two Countries*, 6 J. EMPIRICAL RES. HUM. RES. ETHICS 83 (2011); Amanda Silverio, *HIV Research in Africa: A Series of Paradoxes*, FALL-WINTER 2002 STAN. J. INT'L REL. (2002) (discussing the ethical issues facing HIV researchers).

[34] SAM F. HALABI & JOHN MONAHAN, *Regulatory Capacity in Low- and Middle-Income Countries, in* FOOD AND DRUG REGULATION IN AN ERA OF GLOBALIZED MARKETS 64 (Sam F. Halabi ed., 2015); Antoine Flahaut & Patrick Zylberman, *Influenza Pandemics: Past, Present, and Future Challenges*, 32 PUB. HEALTH REV. 319, 324-25 (2010).

[35] Halabi and Monahan, *supra* note 34, at 64-65.

[36] PIP Advisory Group, Global Influenza Surveillance and Response System, Self-Assessment of the WHO Global Influenza Surveillance and Response System, WHO 1, 6 (2014), http://www.who.int/influenza/pip/virus_sharing/gisrs_self_assessment.pdf [hereinafter *Self-Assessment*].

[37] *CDC Study: Flu Vaccine Saved 40,000 Lives During 9 Year Period,* CTRS. FOR DISEASE CONTROL & PREVENTION (Mar. 30, 2015), https://www.cdc.gov/flu/spotlights/2014-2015/flu-vaccine-saved-lives.htm; *see also* Liz Szabo, *CDC: Vaccines Save Hundreds of Thousands of Lives*, USA TODAY (Apr. 24, 2014), https://www.usatoday.com/story/news/nation/2014/04/24/cdc-vaccine-benefits/8094789/.

[38] *Self-Assessment*, *supra* note 36.

[39] *CDC's World Health Organization (WHO) Collaborating Center for Surveillance, Epidemiology and Control of Influenza*, CDC (Nov. 24, 2015), https://www.cdc.gov/flu/weekly/who-collaboration.htm.

[40] *Global Influenza Surveillance and Response System (GISRS)*, WHO (2015), https://www.who.int/csr/disease/OP_GISRS_FINAL.pdf.

[41] *Operational Guidance on Sharing Seasonal Influenza viruses with WHO Collaborating Centers (CCs) under the Global Influenza Surveillance and Response System (GISRS)*, WHO (2017) at 1, 4, http://www.who.int/influenza/gisrs_laboratory/national_influenza_centres/NIC_virus_sharing_guidance_20171103.pdf.

As with other international research collaborations, this sharing system is accompanied by technology transfer agreements between the World Health Organization, European and U.S. governments, and facilities in Brazil, Egypt, India, Indonesia, Kazakhstan, Thailand, and Vietnam.[42] There are now 13 influenza vaccine manufacturers in low-income countries and 4 in upper middle-income countries with a capacity to produce 450 million doses.[43]

"[S]everal manufacturers, including some in developing countries, are establishing adjuvant production and the use of these dose-sparing technologies is anticipated to become more common within the next several years, doubling their current pandemic capacity."[44] India's pharmaceutical industry is now not only producing influenza vaccines, but undertaking independent research and development. By volume, India's drug industry is the world's fourth largest, producing approximately 20% of active pharmaceutical ingredients.[45] Traditionally, Indian firms spent little revenue on research and development and most drug discovery research was supported by publicly funded research institutes. In 2006, more than 175 firms had established research and development centers and approximately 15 firms engaged in discovery research, spending around 10% of revenue on research and development.[46] "The industry's total annual R&D investment is estimated at around US$170 million, which is miniscule compared to that of 'big pharma', though this expenditure 'buys' more R&D in India than in North America or Europe due to lower labour costs . . ."[47] India, for example, is developing a vaccine against dengue, a mosquito-borne disease that uniquely affects populations in poorer countries.[48]

3. *Tuberculosis*

Tuberculosis (TB) is one of the world's deadliest diseases, with a particularly profound impact on low- and middle-income countries. "More than 95 percent of TB deaths occur in low- and middle-income countries, and just seven countries account for 64 percent of that total (in ranked order): India, Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa."[49] TB can

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[42] Martin Friede, *Snapshot of Current Influenza Vaccine Manufacturing Capacity Worldwide and Summary of WHO-HHS Activities to Promote Technology Transfer*, WHO (2011), http://www.who.int/phi/Session1B_Current_Manufacturing_Capacity_Worldwide_Friede.pdf.
[43] Kenneth A. McLean et al, *The 2015 Global Production Capacity of Seasonal and Pandemic Influenza Vaccine*, 34 VACCINE 5412 (2016).
[44] *Id.*
[45] Hans Löfgren, *The Global Biopharma Industry and the Rise of Indian Drug Multinationals: Implications for Australian Generics Policy*, AUSTL. & N.Z. HEALTH POL'Y 4 (2007).
[46] *Id.* at 5.
[47] *Id.*
[48] Sathyamangalam Swaminathan & Navin Khanna, *Dengue Vaccine Development: Global and Indian scenarios*, 84 INTL. J. INFECTIOUS DISEASES S80, S83-84 (2019).
[49] Carol Dukes Hamilton, *Outsmarting TB Using Research and Collaboration*, R&E SEARCH FOR EVIDENCE (Dec. 11, 2017), https://researchforevidence.fhi360.org/outsmarting-tb-using-research-collaboration.

quickly develop a resistance to treatments, even multiple-drug resistance.[50] Because resistance arises locally and contextually, the fight against TB requires both international collaborations and dedicated resources to local variants.[51]

Broadly, this dynamic in the disease, and the research required to address it, have caused researchers in Europe and North America to build research infrastructure in affected countries, while those countries target their more limited resources on projects within national borders.[52] The Division of AIDS (DAIDS), the National Institute of Allergy and Infectious Diseases (NIAID) within the U.S., and the National Institutes of Health (NIH), have funded infrastructure for routine technical and scientific input into several research networks across the world.[53] This infrastructure is adapted at the local level for research into diagnostics, specific drug regimens for treating drug-susceptible pulmonary TB; and preparation for recruitment into a high-profile, global study of a new drug and shorter treatment regimen to treat multidrug-resistant TB.[54]

Bibliometric studies confirm the growing research and development capacity in low- and middle-income countries through these partnerships. Of published TB-related research papers, U.S.-based scientists produced the most publications of any one country, with 18.4% of all references.[55] Among the top five publishing countries, three were high-burden TB developing countries: India, China, and South Africa. Average year-on-year increases in publications was 13.1% for the top five countries, nearly double that of the increase among all countries.[56]

Coordinating efforts by the World Health Organization and regional bodies identify where international versus local resources may be most effectively used.[57] Rationalized research and innovation is one of the three pillars of the World Health Organization's End TB Strategy, and the WHO has developed the Global Action Framework for TB Research to foster high-quality TB research for the period 2016 to 2025 at global and national levels.[58]

The net benefit to local research and disease treatment capacity has been significant. TB technology transfer programs have re-purposed buildings,

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[50] *Global Tuberculosis Report 2017*, WHO (2017), https://www.who.int/tb/publications/global_report/gtbr2017_main_text.pdf.
[51] *Two Arizona Leaders in Scientific Collaboration Partner to Advance Global TB Research*, CRITICAL PATH INSTITUTE (May 1, 2017), https://c-path.org/two-arizona-leaders-in-scientific-collaboration-partner-to-advance-global-tb-research/.
[52] James S. Molton et al, *International Tuberculosis Research Collaborations Within Asia*, 10 BMC RES NOTES 1, 4 (2017).
[53] Hamilton, *supra* note 49.
[54] *Id.*
[55] Vaidehi Nafade et al., *A Bibliometric Analysis of Tuberculosis Research, 2007-2016*, 13 PLOS ONE 1, 3 (2018).
[56] *Id.*
[57] WHO, Ministerial Declaration of 17 November 2017, WHO Doc. WHO/HTM/TB/2017.11 (2017), https://www.who.int/tb/features_archive/Moscow_Declaration_to_End_TB_final_ENGLISH.pdf?ua=1
[58] Molton, *supra* note 52, at 5.

provided significant support for laboratory development, and supported travel for local health workers to be trained in Europe and North America as training programs are developed in country.[59] Investment in TB research pays off disproportionately given the costs in worker mortality and morbidity to say nothing of the toll it takes on children in developing countries. The World Health Organization argues that "investing in TB research today will offer significant cost savings to health systems in the long run. The Copenhagen Consensus has identified spending on TB as a 'best buy,' based on the calculation that reducing deaths from TB would be worth US$43 for every dollar spent."[60]

II. SEQUENCING THE WORLD: THE NEXT GENERATION OF INTERNATIONAL RESEARCH COLLABORATIONS FOR HUMAN HEALTH AND NUTRITION

The aforementioned research efforts in human health, agriculture, and medicine required massive investments of capital, labor, and technology and frequently responded to malnutrition and public health crises or emergencies rather than investing in detection and prevention of food insecurity and disease. Recent international collaborations aim to address the imbalance between response and prevention, seeking to anticipate and address future challenges to human health and security rather than responding to those that now exist. It may be possible to meet these objectives through developments in genetic sequencing technologies, which not only allow the production of genetic sequence data at lower cost to low- and middle-income countries, but also leverage new high-throughput sequencing technologies (broadly referred to as next generation sequencing).[61] Together with so-called "big data" analytics, scientists undertaking these efforts argue that mapping genomes of viruses, bacteria, and other microbiological organisms will help humans prepare for the next pandemic of a heretofore unknown viral pathogen, reveal mechanisms in the microbiome that might facilitate the development of novel biotechnologies like new medicines, and create more varieties of high-yielding, pest-resistant seeds that reduce the environmental cost and increase the sustainability of agriculture.[62]

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[59] Abraham Sunday Alabi et al, *Enhanced Laboratory Capacity Development: A Boost for Effective Tuberculosis Control in Resource-limited Settings*, 56 INT'L J. INFECTIOUS DISEASES 81, 81-84 (2017).

[60] *Global investments in Tuberculosis research and development: past, present and future,* WHO (2017) at 14, https://apps.who.int/iris/bitstream/handle/10665/259412/9789241513326-eng.pdf;jsessionid=85D5DE6DEDAF623F73B40D2769631B64?sequence=1.

[61] Sam Behjati & Patrick S. Tarpey, *What is Next Generation Sequencing?,* 98 ARCHIVES DISEASE CHILDHOOD EDUC. PRAC.EDITION 236, 236 (2013).

[62] *Id.*; *see generally* Purna C. Kashyap, et al., *Microbiome at the Frontier of Personalized Medicine*, 92 MAYO CLINIC PROC. 1855 (2017) (predicting more precise targeting of pathogens through next generation sequencing and large-scale biogenomic projects); Rajeev K. Varshney et al., *Harvesting the Promising Fruits of Genomics: Applying Genome Sequencing Technologies to Crop Breeding*, 12 PLOS BIOLOGY 1 (2014) (predicting that advances in next generation sequencing will lead to more precise identification of beneficial traits in breeding crops).

A. The Proliferation of Genetic Sequencing Technologies and Collaborative Partnerships

These possibilities exist largely because of the plummeting cost of genetic sequencing and analysis technologies. The first human genome took US$2.7 billion and almost 15 years to complete.[63] Now, genome sequencing and analysis cost around US$1,400.[64] The sequencing can be done in a few days, and analysis in a few weeks.[65] The decline in cost is often compared to Moore's Law in the semi-conductor sector. According to Moore's hypothesis, unit cost per circuit component falls as the number of components in an integrated circuit increase.[66] The (largely accurate) prediction is that as integrated circuits increase in complexity, they decrease in cost. With respect to genetic sequencing, the trend is even more dramatic [See Figure 1].

[63] Meg Tirrell, *Unlocking my Genome: Was it Worth it?*, CNBC (Dec. 10, 2015), https://www.cnbc.com/2015/12/10/unlocking-my-genome-was-it-worth-it.html.
[64] *Id.*
[65] *Id.*
[66] Chris A. Mack, *Fifty Years of Moore's Law,* 24 IEEE TRANSACTIONS SEMICONDUCTOR MANUFACTURING 202, 202 (2011).

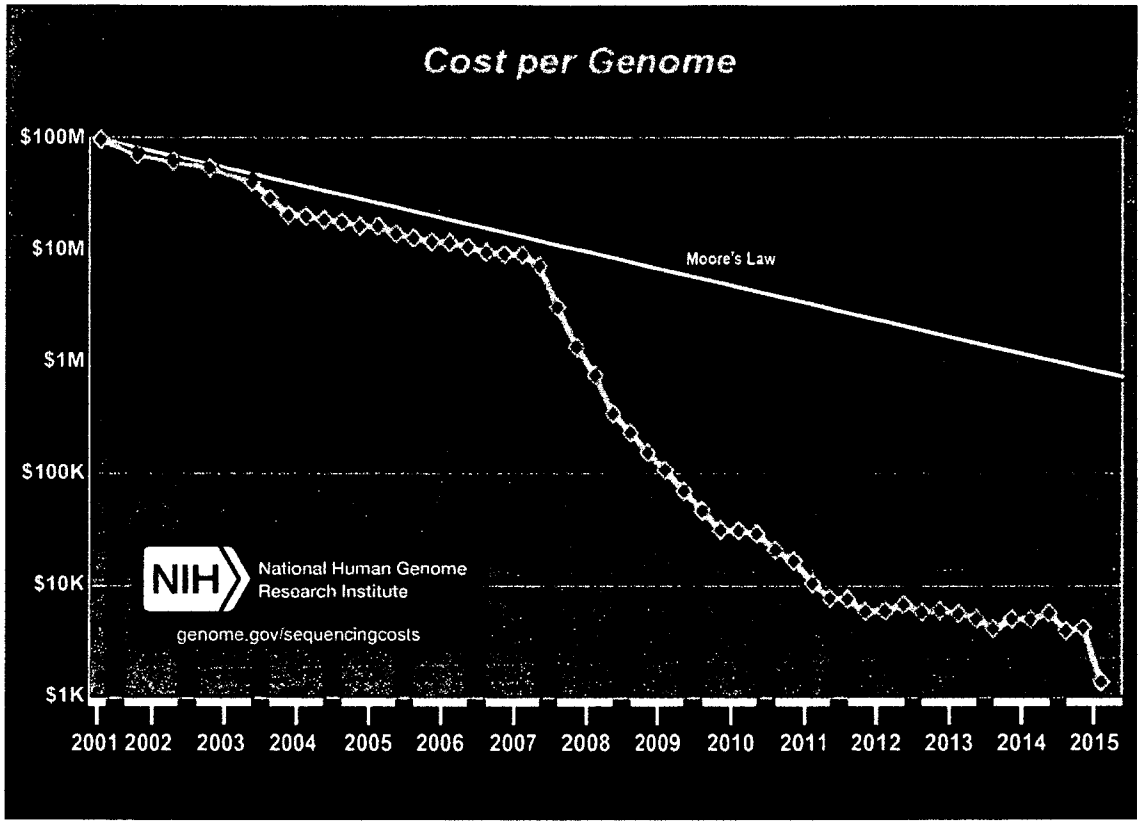

Figure 1[67]

While the availability of sequencing technologies and associated laboratory capacity remain concentrated in wealthier countries, there is already significant progress toward establishment and maintenance of that capacity in low- and middle-income countries. According to a 2015 analysis, 20 of the world's 603 international laboratories offering genetic testing were in middle-income and none were in low-income countries.[68] An analysis by Mohamed Helmy, Mohamed Awad, and Kareem Mosa showed that in the majority of developing countries outside of Africa there are at least 1-10 genetic sequencing projects underway and in many low- and middle-income countries, there are entire centers devoted to such research.[69]

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[67] *The Cost of Sequencing a Human Genome*, NAT'L HUMAN GENOME RES. INST., https://www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost (last updated Oct. 24, 2019).

[68] Fasil Tekola-Ayele & Charles N. Rotimi, *Translational Genomics in Low and Middle Income Countries: Opportunities and Challenges,* 18 PUB. HEALTH GENOMICS 242, 243 (2016).

[69] Mohamed Hemly et al., *Limited Resources of Genome Sequencing in Developing Countries: Challenges and Solutions,* 9 APPLIED & TRANSLATIONAL GENOMICS 15, 17 (2016).

These projects and centers are rarely stand-alone investments made by governments. Rather, they have emerged through joint-ventures, public-private partnerships, and international development programs. For example, the African Center of Excellence for Genomics of Infectious Diseases (ACEGID) at Redeemer's University (Nigeria) was established with the support of the World Bank and the U.S. National Institutes of Health to serve several institutions in the surrounding region, including Senegal, Nigeria, and Sierra Leone.[70] The Genome Science Program at the Los Alamos National Laboratory, USA and research institutions in several developing countries including Jordan, Uganda, and Gabon is similarly aimed at developing genomic research capacity in low- and middle-income countries, which typically contribute tailored levels of funding, equipment, and training.[71]

This benefit has materialized in a relatively short period of time. ACEGID-established laboratories and researchers performed the first diagnosis of Ebola virus disease in Nigeria and Sierra Leone and were able to track its origin and evolution in West Africa.[72] ACEGID scientists partnered with physicians from the Irrua Specialist Teaching Hospital in Nigeria to sequence and quickly contain a recent outbreak of Lassa fever.[73] The Genome Science Program generates a positive "impact [on] almost all areas of the life sciences and presents opportunities for technology and economic development."[74]

Indeed, many of the current large-scale biogenomic efforts began with government-to-government cooperation on scientific research relevant to human health and nutrition. The Global Virome Project (see Part III A), which aims to identify unknown future viral threats through the development of a comprehensive ecologic and genetic database of virtually all naturally-occurring viruses, originated with the PREDICT project based at the University of California-Davis, which established genetic sequencing partnerships with scientists in 31 countries.[75] The EU project Micro B3 (Marine Microbial Biodiversity, Bioinformatics, Biotechnology) (see Part III C) "develops innovative bioinformatic approaches and a legal framework to make large-scale data on marine viral, bacterial, archaeal and protist genomes and metagenomes accessible for marine ecosystems biology and to define new targets for biotechnological applications."[76] Micro B3 builds upon a highly interdisciplinary consortium of 32 academic and industrial partners comprising

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[70] Onikepe A Folarin, Anise N. Happi & Christian T. Happi, *Empowering African Genomics for Infectious Disease Control,* 7 GENOME BIOLOGY 515, 515 (2014).
[71] Helen H. Cui, et al., *Building International Genomics Collaboration for Global Health Security*, 3 FRONTIERS PUB. HEALTH 1, 1-8 (2012).
[72] Stephen K. Gire, et al., *Genomic Surveillance Elucidates Ebola Virus Origin and Transmission During the 2014 Outbreak*, 345 SCI. 1369, 1369 (2014).
[73] B. David Zarley, *How a Nigerian Genome Team Contained a Lassa Fever Outbreak With International Partners*, QUARTZ AFRICA (Mar. 27, 2019), https://qz.com/africa/1580888/lassa-fever-outbreak-contained-by-nigerian-genome-team/.
[74] Cui, *supra* note 71, at 3.
[75] *About PREDICT*, UC DAVIS VET. MED., https://ohi.vetmed.ucdavis.edu/programs-projects/predict-project/about (last visited Nov. 13, 2019).
[76] *The Micro B3 Project*, MICRO 3, https://www.microb3.eu (last visited Nov. 13, 2019) [hereinafter The Micro B3 Project homepage].

world-leading experts in bioinformatics, computer science, biology, ecology, oceanography, bioprospecting and biotechnology. Yet these biogenomic projects, and the partnerships that undergird them, are emerging in a distinctly new legal and ethical milieu than did the Green Revolution or biomedical research over most of the twentieth century.

B. Accessing Genetic Resources: Historical Models

Unlike past international collaborations, every step of the scientific process now faces a significantly changed ethical and legal landscape. Where previous collaborations were accomplished through informal transfer of the required genetic resources (e.g. a researcher has a colleague in host country send biological samples to labs in Europe or North America, annexed research sites, or "parachute" acquisition), scientific teams must now navigate laws and regulations passed pursuant to the Convention on Biological Diversity and its implementing Nagoya Protocol, which requires that parties obtain the prior informed consent of providing countries before commencing research on their genetic resources and that benefits associated with that research be shared according to mutually agreed terms.[77] This regulatory mechanism is known as access and benefit-sharing (ABS). The following discussion provides in greater detail how research was formerly conducted, and the changes ushered in by the Convention on Biological Diversity and the Nagoya Protocol.

1. Transfer of Samples between Collaborators

The scientific method requires verification of other scientists' research results, access to inputs like reagents (in the biological sciences), and sharing of results for replication and future research.[78] This necessitates a level of openness and sharing of research materials used to conduct original experiments. Scientific norms encourage researchers to share samples and laboratory reagents with each other for the purposes of verification and furthering the scientific endeavor as a whole.[79] Therefore, scientists will often informally share their biological samples with other scientists. Informal transfer is also common in citizen science projects where members of the public collect samples in their own country and send those samples to scientific researchers in other countries.

Under this model, as it prevailed over the course of the twentieth century, researchers, largely based in wealthy countries, received biological samples from colleagues in low- or middle-income countries, sometimes with the understanding that some other resource or knowledge would be shared in

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[77] The FAO's International Treaty on Plant Genetic Resources for Food and Agriculture also influences these partnerships where they cover one of the 35 food crops or 29 forages listed in Annex 1 of the treaty. Similarly, enhanced biosecurity regulations also influence the transfer of biological material.
[78] NATIONAL ACADEMY OF SCIENCES ET AL., 1 RESPONSIBLE SCIENCE: ENSURING THE INTEGRITY OF THE RESEARCH PROCESS 36 (1992).
[79] *Id.*

return.[80] Indeed, this is how samples of the Middle East Respiratory Syndrome coronavirus (MERS-CoV) were transferred to the Erasmus Medical Center in the Netherlands.[81] Ali Mohamed Zaki, an Egyptian physician working in Saudi Arabia, contacted scientists at Erasmus for technical help after he suspected a novel virus caused the severe respiratory symptoms, renal failure, and death of a patient.[82] According to Zaki:

> [Erasmus] confirm[ed] my initial findings and asked me to send them a small portion of patient zero's sample because they wanted to do some more testing and they were running out of RNA. I didn't have any mechanism to ship a live virus sample while maintaining the cold chain during transit. So, I filtered the sputum sample and mixed the filtrate with Vero cells, packaged the tightly capped tube in appropriate biohazard containers and shipped it with a private carrier at room temperature as a diagnostic sample. It worked. They received it in the Netherlands and managed to recover the live virus, the first genetic analysis of this novel virus published in *New England Journal of Medicine*.[83]

These sorts of informal sharing practices were common over the course of the 1960s, 1970s, and 1980s and, given many researchers lack knowledge about changes in national and international law, almost certainly continue to some extent today.

As a result of new norms introduced by the Convention on Biological Diversity and the Nagoya Protocol discussed below, transfers of samples are now unlikely to occur between the parties without the conclusion of Material Transfer Agreements (MTAs). MTAs are usually standardized forms, outlining what the user party can and cannot do with the transferred materials (and may include limitations on commercial use or applying for intellectual property rights), which party, if any, has ownership rights over the materials, and whether or not those rights are transferrable.[84] The transfer of genetic resources between colleagues is likely to remain an important source of samples for scientific research, although domestic regulations implementing the CBD and Nagoya Protocol have led to these transfers becoming increasingly formalized.

2. *Parachute Acquisition of Host Country Samples*

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[80] Clare Dyer & Owen Dyer, *WHO to Probe Claims that Dutch Scientists Restricted Access to Novel Coronavirus*, 346 BMJ 1 (2013); Sam Halabi, *Viral Sovereignty, Intellectual Property, and the Changing Global System for Sharing Pathogens for Infectious Disease Research*, 28(1) ANNALS OF HEALTH L. 101, 106-07 (2019).

[81] Dyer, *supra* note 80, at 1.

[82] Islam Hussein, *The Story of the First MERS Patient*, NATURE MIDDLE EAST (June 2, 2014), https://www.natureasia.com/en/nmiddleeast/article/10.1038/nmiddleeast.2014.134.

[83] *Id.*

[84] Philip Mirowski, *Livin' with the MTA*, 46 MINERA 317, 318 (2008).

Parachute acquisition, often referred to simply as "field work," is the collection of genetic resources in the host nation by a foreign researcher who later returns to his or her home country to conduct research on the collected samples. Given that the use of natural resources for their genetic components requires a minute quantity of genetic material, such collection activities can be extremely difficult to detect.[85] Parachute acquisition is often discovered to have occurred in cases of egregious misappropriation of a host nation's genetic resources and where there is a great deal of money involved. For example, in the early 2000s, French researchers conducted interviews in French Guiana as part of their investigation into antimalarial compounds, including those derived from the *Quassia amara* tree.[86] Their research was published in 2005.[87] In 2015, the researchers obtained a patent on a compound derived from the *Quassia amara* that had antimalarial properties.[88] While apparently undetected for many such transfers, these kinds of issues become significant at the time of downstream product commercialization, and many countries now require that the origin of genetic resources be disclosed in patent applications.

As with informal transfer, parachute acquisition is now widely viewed as "biopiracy."[89] The "unidirectional flow of samples" out of low- and middle-income countries and into wealthy nations for both commercial and non-commercial research and development has "impacted negatively [] the development of local capacity, infrastructure and expertise."[90] Parachute acquisition without first obtaining prior informed consent from the host government is no longer generally accepted as a method for collecting biological samples, even if those samples are being used for non-commercial purposes. This exploitative practice precipitated some of the formalizing measures, such as requiring MTAs, which now govern the terms under which samples are transferred out of the host country's jurisdiction.[91]

3. *Annexed Research Sites for the Collection of New Samples*

Although less used than informal transfer and parachute acquisition, annexed research sites in the provider country provide another method for obtaining local genetic resources.[92] This method means that samples of genetic

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[85] Florian Rabitz, *Biopiracy After the Nagoya Protocol: Problem Structure, Regime Design and Implementation Challenges,* 9 BRAZ. POL. SCI. REV. 30, 38-39 (2015).
[86] Janna Rose, *Biopiracy: When Indigenous Knowledge is Patented for Profit*, THE CONVERSATION (Mar. 7, 2016), http://theconversation.com/biopiracy-when-indigenous-knowledge-is-patented-for-profit-55589.
[87] *Id.*
[88] *Id.*
[89] *Id.*
[90] C. Staunton & K. Moodley, *Data Mining and Biological Sample Exploration from South Africa: A New Wave of Bioexploitation Under the Guise of Clinical Care?*, 106 S. AFR. MED. J. 136 (2016).
[91] Daniel F. Robinson, *Locating Biopiracy: Geographically and Culturally Situated Knowledges*, 42 ENV'T & PLAN. 38, 47 (2010).
[92] *See, e.g.*, *Material Transfer Agreement on Plant Genetic Resources for Food and Agriculture "National Programme on Plant Genetic Resources and Agro-biodiversity Conservation and*

resources are collected locally, and that at least part of the research on these genetic resources is conducted within the host country. This collection and research can be done by foreign or local researchers. Providing that there is no transboundary movement of genetic resources, this practice may technically exist outside of the remit of the CBD and Nagoya Protocol detailed *infra*. At their best, annexed research sites encourage the active participation of partners within the provider country to foster international collaboration, conduct training, share expertise, engage in technology transfer, and help build scientific capacity in the host nation.[93] Some countries have implemented laws that require foreign scientists to engage with the local scientific community even if they do not intend to transfer any biological resources outside of the host country. Brazil, for example, requires foreign researchers to register with a local partner before commencing research activities.[94] At their least helpful, annexed sites may be established, funded, and staffed entirely by foreign research entities, contributing little to local research capacity, and perhaps sharing little in terms of the benefits that result from research.

C. The Changing International Legal Landscape for Accessing Genetic Resources

The models for obtaining genetic resources enumerated *supra* flourished when the prevailing paradigm in scientific research was openness and sharing, and the resources under study—seeds, plants for agriculture, and other biological resources—were viewed as the "common heritage" of humanity.[95] While this paradigm facilitated research generally, it did not necessarily do so equitably or ethically. Eventually, the dynamics of these kinds of biological research collaborations—in which the benefits of the research flowed to and largely stayed in European and North American countries where advanced technology for analysis and products were located—became intertwined with larger international legal movements. In 1964, the U.N. General Assembly established the United Nations Conference on Trade and Development (UNCTAD) to pursue trade-related development policies that would be more favorable to developing countries.[96] UNCTAD existed to "maximize the trade, investment and development opportunities of developing countries and assist them in their efforts to integrate into the world economy on

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Utilization" of the Czech Republic, Czech Gene Bank, CRI, WORLD INTELL. PROP. ORG., https://www.wipo.int/tk/en/databases/contracts/texts/crgenebank.html (last visited Nov. 13, 2019).

[93] U.N. Conference on Trade & Dev., Facilitating Transfer of Technology to Developing Countries: A Survey of Home-Country Measures, at 1, U.N. Doc. UNCTAD/ITE/IPC/2004/5 (2004).

[94] David Smith et al., *Explanation of the Nagoya Protocol on Access and Benefit Sharing and Its Implication for Microbiology,* 163 MICROBIOLOGY 289, 294-95 (2017).

[95] *See e.g.,* INT'L UNION FOR CONSERVATION OF NATURE, ACCESSING BIODIVERSITY AND SHARING THE BENEFITS: LESSONS FROM IMPLEMENTING THE CONVENTION OF BIOLOGICAL DIVERSITY 1 (Santiago Carrizosa et al., eds., 2004).

[96] JOHN TOYE, UNCTAD AT 50: A SHORT HISTORY 3-4, 14 (2014).

an equitable basis."[97] Shortly after its formation, UNCTAD began to focus on technology transfer as a crucial priority for development.[98]

Control over natural resources was also prioritized.[99] On April 19, 1972, Mexican President Luis Echeverría Álvarez urged the adoption of a Charter of Economic Rights and Duties of States aimed at exerting greater authority over natural resources.[100] At the time, those resources were thought to be mostly commodities like petroleum, rubber, and agricultural goods.[101] However, the general call for control over natural resources later expanded in the late 1980s to include genetic and microbiological resources.[102]

In 1972, the United Nations also held the first of many global conferences on the Human Environment in Stockholm, Sweden.[103] In the decade after the 1972 conference, scientists and non-governmental organizations identified biodiversity as a pressing environmental question.[104] The threats to the rainforests in the Amazon basin—logging, extraction, agriculture—illustrated the rapid loss of crucial biological resources.[105] In 1987, the Governing Council of the United Nations Environmental Programme (UNEP) created a working group to develop a legally binding treaty to protect biological resources.[106] In 1991, formal multilateral negotiations began on a Convention for Biological Diversity.[107]

Eventually these preparations led to the 1992 U.N. Conference on Environment and Development (or "Earth Summit"), held in June 1992 in Rio De Janeiro, the outcome of which included the Convention on Biological Diversity (CBD).[108] The CBD descended not only from environmental conferences but also from the 1962 United Nations General Assembly's

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[97] U.N. Conference on Trade and Dev., *UNCTAD in Brief*, U.N. Doc. UNCTAD/EDM/17/REV.1 (2016).
[98] U.N. Conference on Trade and Dev., 2d Sess., at 353-55, U.N. Doc. TD/97 (1968).
[99] Charles N. Brower & John B. Tepe Jr., *The Charter of Economic Rights and Duties of States: A Reflection or Rejection of International Law?*, 9 INT'L. LAWYER 295, 296 (1975).
[100] *Id.*
[101] U.N. Conference on Trade & Dev. Secretariat, *Trade and Development Report*, at 32, U.N. Doc. UNCTAD/TDR/2/Rev.1 (1982).
[102] Jonathon B. Tucker, *Biosecurity: Limiting Terrorist Access to Deadly Pathogens*, U.S. INST. OF PEACE 27 (2003), https://www.usip.org/sites/default/files/pwks52.pdf.
[103] *United Nations Conference on the Human Environment*, U.N. SUSTAINABLE DEV., https://sustainabledevelopment.un.org/milestones/humanenvironment (last visited Nov. 13, 2019).
[104] Daniel H. Janzen, *The Future of Tropical Ecology*, 17 ANN. REV. ECOLOGY & SYSTEMATICS 305, 305-306 (1986); *see generally* José Luiz de Andrade Franco, *The Concept of Biodiversity and the History of Conservation Biology*, 32 HISTORÍA 21, 21-25 (2013) (explaining the history of the rise of biodiversity as a scientific concern).
[105] *See generally* Michael J. Heckenberger et al., *The Legacy of Cultural Landscapes in the Brazilian Amazon: Implications for Biodiversity*, 362 PHIL. TRANSACTIONS ROYAL SOC'Y B: BIOLOGICAL SCI. 197, 197-208 (2007); *see also* Christopher Uhl & Ima Celia Guimaraes Vieira, *Ecological Impacts of Selective Logging in the Brazilian Amazon: A Case Study from the Paragominas Region of the State of Peru*, 21 BIOTROPICA 98, 98-106 (1989).
[106] U.N. GAOR, 42d Sess., 96th plen. mtg. at 139, U.N. Doc. UNEP/GC.14/17 annex III (1987).
[107] *History of the Convention*, CONVENTION ON BIOLOGICAL DIVERSITY, https://www.cbd.int/history/.
[108] *Id.*; *see generally* U.N. Conference on Env't & Dev., *Rio Declaration on Environment and Development*, U.N. Doc. A/CONF.151/26, Vol. 1 (1992).

Declaration on Permanent Sovereignty over Natural Resources, which asserted that it was the inalienable right of each state to handle natural resources as they saw fit and that any profits resulting from the use of these resources should be shared "between investors and the recipient state."[109]

The CBD established that developing countries should not only control access to genetic resources, but also benefit from any commercial value generated from their utilization.[110] The CBD adopted as one of its objectives the promotion of conservation and sustainable use of biological diversity, while seeking "fair and equitable" sharing of benefit derived.[111] The CBD's goal of "access and benefit sharing" includes both plant genetic resources as well as the relevant technology associated with their development.[112] It also codified the protection of indigenous peoples and the traditional knowledge they had developed especially for medical and agricultural applications, including a principle of compensation when firms or others commercialized that knowledge.[113] The CBD created a legal zone in which biodiverse countries could set terms for exploitation and the protection of their citizens to share in the benefits of any commercialization of their resources.[114] More than 39 nations have created Access and Benefit Sharing (ABS) regimes via their domestic laws, with particular activity from biodiverse states like Brazil, China, Costa Rica, and South Africa.[115]

1. *Article 15 of the CBD Established Sovereign Rights over Genetic Resources and Their Exploitation*

Article 1 of the CBD requires the "fair and equitable sharing of the benefits arising out of the utilization of genetic resources," a phrase that gave rise to a great deal of uncertainty, even as it shaped national "bioprospecting" laws.[116] The CBD reaffirmed "the sovereign rights of States over their natural resources" and recognized that "the authority to determine access to genetic resources rests with the national governments and is subject to national legislation."[117] "Genetic resources" are defined as "genetic material of actual or

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[109] G.A. Res. 1803 (XVII), at 15 (Dec. 14, 1962).

[110] Convention on Biological Diversity, June 5, 1992, 1760 U.N.T.S. 79 [hereinafter CBD]. There are 198 States party to the CBD. The United States is not a party.

[111] CBD, *supra* note 110, art. 1.

[112] Jonathan Carr, *Agreements that Divide: TRIPS vs. CBD and Proposals for Mandatory Disclosure of Source and Origin of Genetic Resources in Patent Applications*, 18 J. TRANSNAT'L L. AND POLICY 131, 133 (2008).

[113] CBD, *supra* note 110, art. 8.

[114] Michiel Korthals & Bram De Jonge, *Two Different Ethical Notions of Benefit Sharing of Genetic Resources and Their Implications for Global Development*, 28 NEW GENETICS AND SOC'Y 87, 88 (2009).

[115] Nicolas Pauchard, *Access and Benefit Sharing under the Convention on Biological Diversity and Its Protocol: What Can Some Numbers Tell Us about the Effectiveness of the Regulatory Regime?*, 6 RESOURCES 1,11 (2017).

[116] CBD, *supra* note 110, art. 1; Thomas A. Kursar, *What Are the Implications of the Nagoya Protocol for Research on Biodiversity?*, 61 BIOSCIENCE 256, 256-57 (2011) (discussing the imperfect implementation of CBD in an attempt to improve biodiversity).

[117] CBD, *supra* note 110, art. 15(1).

potential value" and "genetic material" means "any material of plant, animal, microbial or other origin containing functional units of heredity."[118] The treaty's governing body, the Conference of the Parties (COP), has excluded human genetic resources from the scope of the CBD, but the definition of "genetic resources" still captures most, if not all, non-human genetic resources of interest to scientists in the biology-based disciplines.

In accordance with the CBD, the "countries of origin" of genetic resources[119] must "facilitate access to genetic resources for environmentally sound uses."[120] The "country of origin of genetic resources" is defined as "the country which possesses those genetic resources in *in-situ* conditions," that is, "conditions where genetic resources exist within ecosystems and natural habitats."[121] Accessing genetic resources within other countries' jurisdictions "shall be subject to prior informed consent" of the provider[122] and "shall be on mutually agreed terms."[123] The ultimate objective of these provisions was to enable biodiverse countries to secure a share in the "benefits arising from the commercial and other utilization of genetic resources."[124] In short, this was a grand bargain of access to genetic resources in exchange for sharing the benefits derived from utilizing those genetic resources. Access to genetic resources and the sharing of the associated benefits has been termed "access and benefit-sharing" (ABS) within the regulatory framework of the CBD. The CBD is a "framework convention" setting the broad parameters for agreement between and within the Contracting Parties then implementing their own legislation, administration, and policies to give effect to their CBD commitments.

Before 2010, CBD Article 15 had been largely guided by the non-binding Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of Their Utilization.[125] The Bonn Guidelines recommended the following provisions for contracts between sovereign states and research entities:

> (a) Regulating the use of resources in order to take into account ethical concerns of the particular Parties and stakeholders, in particular indigenous and local communities concerned;
> (b) Making provision to ensure the continued customary use of genetic resources and related knowledge;

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[118] *Id.* art. 2.
[119] *Id.* art. 15(3).
[120] *Id.* art. 15(2).
[121] *Id.* art. 2.
[122] *Id.* art. 15(5).
[123] *Id.* art. 15(4).
[124] *Id.* arts. 1, 15(7).
[125] U.N. Conference on Trade & Dev., The Convention on Biological Diversity and the Nagoya Protocol: Intellectual Property Implications, 11, U.N. Doc. UNCTAD/DIAE/PCB/2014/3 (2016).

> (c) Provision for the use of intellectual property rights include joint research, obligation to implement rights on inventions obtained and to provide licenses by common consent;
> (d) The possibility of joint ownership of intellectual property rights according to the degree of contribution.[126]

2. *The Nagoya Protocol Clarified Conditions for Researchers' Access to Genetic Resources and the Sharing of Benefits Arising from their Study and Development*

The 2010 Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization (Nagoya Protocol) aimed to encompass the broader universe of drugs, medical therapies, agrochemical products, vaccines and other products derived from genetic resources not clearly governed by the CBD.[127] The Nagoya Protocol, formed to give specific content to Article 15 of the CBD, regulates access to genetic resources in party states and establishes mechanisms for fair and equitable sharing of benefits arising out of the utilization of genetic resources.[128] It is committed to the equitable sharing of research collaborations and ensuing benefits.[129]

Countries adopting legislation or regulation pursuant to the treaty ensure that access to any genetic resources within the territory of that country is conditioned on prior informed consent not only of the country of origin but also "[i]n accordance with domestic law," and the consent of indigenous and local communities.[130] Moreover, once access to genetic resources results in a commercially viable product:

> benefits arising from the utilization of genetic resources as well as subsequent applications and commercialization shall be shared in a fair and equitable way with the Party providing such resources that is the country of origin of such resources or a Party that has acquired the genetic resources in accordance with the Convention.[131]

The precise nature of benefit-sharing, both monetary and non-monetary, is left to the states themselves to negotiate with those who generate commercialized products. As discussed in Halabi's *Intellectual Property*:

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[126] Konstantia Koutouki & Katharina Rogalla von Bieberstein, *The Nagoya Protocol: Sustainable Access and Benefits-Sharing for Indigenous and Local Communities*, 13 VT. J. ENVTL. L. 513, 522-23 (2011).
[127] Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity, Oct. 29, 2010, UNEP/CBD/COP/DEC/X/1 [hereinafter Nagoya Protocol].
[128] Kursar, *supra* note 116, at 256-57.
[129] Evanson Chege Kamau et al., *The Nagoya Protocol on Access to Genetic Resources and Benefit Sharing: What Is New and What Are the Implications for Provider and User Countries and the Scientific Community?* 6 L., ENV'T & DEV. J. 246, 249 (2010) [hereinafter Kamau, *What Is New*].
[130] Nagoya Protocol, *supra* note 127, art. 7.
[131] *Id.* art. 5.

> The economic purpose of the Nagoya Protocol was explicit. The CBD as it was initially formed lacked a legal framework for cross-border application of its rules. User country governments were not obligated to address complaints or assist others. After six years of negotiations, the Nagoya Protocol brought "greater legal certainty and transparency" regarding the exchange of genetic resources while "reaffirm[ing] and clarif[ying] the [CBD's] broad economic scope." It further addressed issues concerning scientific research, also neglected by the CBD and created new enforcement provisions for user and provider nations to implement within their respective national legal systems.[132]

Before the Nagoya Protocol, the non-binding Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of Their Utilization, a set of voluntary guidelines issued subsequent to the Convention on Biological Diversity but before Nagoya, guided implementation of CBD Article 15.[133] The Nagoya Protocol entered into force on October 12, 2014, and has 116 Parties.[134] The Nagoya Protocol defines "[u]tilization of genetic resources" as "research and development on the genetic and/or biochemical composition of genetic resources, including through the application of biotechnology."[135] The term "research and development" (R&D) is not further defined so the term should be understood to embody its ordinary meaning.[136] Any use of the genetic resources, including the generation and analysis of genetic sequence data could therefore qualify as "utilization of genetic resources" within the remit of the CBD and Nagoya Protocol.

Benefits provided in exchange for accessing and utilizing genetic resources can be monetary, which could include an up-front payment for an access permit or the payment of royalties on any resulting commercialized products.[137] Such monetary benefits may be the appropriate form of benefit-sharing when the users are conducting research and development with commercial intent. Non-monetary benefits may be better suited when the research is non-commercial (academic research), and can include the sharing of relevant research results, sharing of technology and knowledge, collaboration with local scientists or education and training.[138] The essence of ABS under the CBD and Nagoya

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[132] Halabi, *Intellectual Property*, *supra* note 4, at 176.
[133] Conference of the Parties to the Convention on Biological Diversity, *Sharing of the Benefits Arising out of their Utilization,* SECRETARIAT OF THE CONVENTION ON BIOL. DIVERSITY (2002).
[134] *Parties to the Nagoya Protocol,* CONV. ON BIOL. DIVERSITY, https://www.cbd.int/abs/nagoya-protocol/signatories/ (last visited Nov. 13, 2019).
[135] Nagoya Protocol, *supra* note 127, art. 2.
[136] Evanson Chege Kamau & Gerd Winter, *Research and Development under the Convention on Biological Diversity and the Nagoya Protocol, in* 1 RESEARCH AND DEVELOPMENT ON GENETIC RESOURCES: PUBLIC DOMAIN APPROACHES IN IMPLEMENTING THE NAGOYA PROTOCOL 31-32 (Evanson Chege Kamau et al. eds., 2017).
[137] Nagoya Protocol, *supra* note 127, Annex.
[138] *Id.*

Protocol is that the party accessing genetic resources reach prior informed consent and mutually agreed terms with the providing party and the benefits shared reflect their particular circumstances.

To reiterate, those conducting research with non-commercial intent are still expected to abide by the host nation's ABS rules. However, Parties have been encouraged to implement "simplified measures on access for non-commercial research purposes."[139] The Nagoya Protocol recognizes that in some cases, what started out as non-commercial research will lead to the development of a marketable product or process and requires Parties to the Nagoya Protocol to take "into account the need to address a change of intent."[140] This may require the user to renegotiate benefit-sharing obligations with the provider to better reflect that new utilization. When such a provision is included in the original mutually agreed terms, this is referred to as a "come-back clause."[141]

The effect of the CBD and the Nagoya Protocol is that there are a variety of domestic rules and regulations for accessing genetic resources all around the world. Some countries are operating under the ABS regime outlined in the CBD, others have agreed to comply with both the CBD and the Nagoya Protocol, and others still are yet to implement domestic ABS laws despite being Party to one or both of these instruments. There are definitional ambiguities and unclear provisions in both the CBD and Nagoya Protocol, but as a minimum, users can expect that they will have to seek the prior informed consent (PIC) of the providing authority and establish mutually agreed terms (MAT) before accessing or utilizing the provider's genetic resources. It is essential that parties wishing to collect or utilize genetic resources originating in other countries consult the National Focal Point (NFP), i.e. the regulatory authority charged with referring biological research efforts to the appropriate agency (Competent National Authority, or CNA) of the originating country to ensure researchers are fully aware of and compliant with domestic laws.[142]

The Nagoya Protocol requires its Parties to put in place measures ensuring that users within their jurisdiction have accessed genetic resources (and any traditional knowledge of Indigenous Peoples and local communities that is associated with genetic resources) in compliance with the provider nation's ABS rules.[143] Non-compliance can result in more than just reputational damage to the researchers involved. In some jurisdictions, non-compliance will attract penalties under civil law (e.g., fines) and even prosecution under criminal law.[144]

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[139] *Id.* art. 8(a).
[140] *Id.*
[141] Kamau, *What Is New*, *supra* note 129, at 256.
[142] Caroline von Kries et al., *Micro B3 Model Agreement on Access to Marine Microorganisms and Benefit Sharing: Text and Commentary, in* RESEARCH AND DEVELOPMENT ON GENETIC RESOURCES: PUBLIC DOMAIN APPROACHES IN IMPLEMENTING THE NAGOYA PROTOCOL 335-36 (Evanson Chege Kamau et al. eds., 2017) [hereinafter Annotated Model Agreement].
[143] Nagoya Protocol, *supra* note 127, arts. 15(1), 16(1).
[144] K. Divakaran Prathapan et al., *When the Cure Kills – CBD Limits Biodiversity Research*, 360 SCI. 1405, 1406 (2018).

The laws of China, France (French Guiana), India, and South Africa provide good examples of how enforcement operates. Under Chinese law adopting the Nagoya Protocol, "genetic resources should be restricted to use in China, and the research should include the participation of a Chinese party."[145] China encourages the parties to engage in cooperative research projects to register the intellectual property of the inventions that emerge from that research in China.

A recent study notes that:

> China's Ministry of Environmental Protection led a number of other government ministries in issuing a Notice on Enhancing the Access and Benefit-Sharing of Biological Genetic Resources in the Cooperation and Communication with Foreign Parties in October 2014. This Notice requires government approval for foreign parties (1) bio-prospecting in natural conservations and (2) to remove certain of those resources deemed highly valuable from China. Plans are underway to issue a more detailed regulation on acquiring and utilizing genetic resources in the near future.[146]

Similarly, in the context of India, the same study notes that:

> India imposes access requirements on "biological resources" for research and commercial purposes on entities that are not incorporated in India. Authorisations from the National Biodiversity Authority may be required (i) to obtain biological resources from India, (ii) to apply for a patent on results of R&D on the resources, or (iii) to transfer the biological resource as well as the results of the research. The National Biodiversity Authority may oppose the grant of IP rights linked to Indian biological resources or associated traditional knowledge. Indian law grants the authority the power to do so around the globe. [147]

Like India and China, South Africa maintains a system of notifications and permits that distinguish between the discovery and commercialization of indigenous biological resources. Foreign companies and other persons may apply for a permit to bio-prospect, but must do so jointly with South African entities. The aforementioned study notes that "[w]ith the recent amendments of May 2015, bio-prospecting and bio-trading without a permit can be fined by up

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[145] *Global Enforcement of the Nagoya Protocol in Life Sciences Industries*, COVINGTON & BURLING LLP 2 (2016), https://www.cov.com/-/media/files/corporate/publications/2016/12/global_enforcement_of_the_nagoya_protocol_in_life_sciences_industries.pdf [hereinafter Covington Report].

[146] *Id.* at 2.

[147] *Id.* at 2-3.

to five or even ten million rand (around US$700,000), or a fine 'equal to three times the commercial value of the activity in respect of which the offence was committed, whichever, is the greater. (Regulation 42(2))'".[148]

In August 2016, a new French law entered into force, creating the French Agency for Biodiversity.[149] The law ratified the Nagoya Protocol and established a system for authorizing access to genetic resources under the jurisdiction of France.[150] In the case of France, the above study notes that:

> The law states that financial benefit-sharing is calculated on the global turnover realized from the product derived from the genetic resource, capped at 5 percent. The access permit may be refused if the proposed benefit-sharing by the applicant "manifestly" does not correspond to its financial capacity. The new access legislation replaces the region-specific rules that already existed for the Amazonian Forest National Park in French Guyana.[151]

a. Obtaining Prior Informed Consent and Agreeing to Terms under the Nagoya Protocol

The first step to ensure compliance usually entails contacting the NFP to obtain information and approaching the Competent National Authority (CNA) – which may be a Ministry of Environment, Ministry of Health, Ministry of Science and Technology, or other ministry of the provider country – to obtain PIC and establish MAT prior to obtaining any new materials. In some cases, CNAs will issue permits or Internationally Recognized Certificates of Compliance (IRCCs) which "serve as evidence that the genetic resource which it covers has been accessed in accordance with [PIC and MAT] as required by the domestic [ABS] legislation or regulatory requirements of the Party providing [PIC]."[152] The terms of the agreement normally outline how the samples are to be used and stored, whether the samples can be retained beyond the duration of the initial project, whether they should be returned to the provider or destroyed, and whether the samples or any subsamples (derived from the original samples) can be transferred to third parties and under what conditions.[153] Terms may also cover how to deal with changes of intent (from non-commercial research to commercial product development) and any intellectual property considerations. Benefit-sharing terms will need to cover items such as how the research results

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[148] *Id.*

[149] *Reclaiming biodiversity, nature and landscapes*, GOUVERNEMENT.FR, (Aug. 22, 2016) https://www.gouvernement.fr/en/reclaiming-biodiversity-nature-and-landscapes.

[150] Covington Report, *supra* note 145, at 3.

[151] *Id.*

[152] Nagoya Protocol, *supra* note 125, art. 17(3).

[153] *See, e.g.*, Global Genome Biodiversity Network, *Guidance: Best Practice for Access and Benefit-Sharing*, GGBN (June 2015) at 3-4, 6-7, https://absch.cbd.int/api/v2013/documents/A68FE827-FF28-39B4-34C3-1AC435B0500A/attachments/GGBN%20Guidance%20_Best_Practice_June_2015-Final.pdf.

will be disseminated, how related data will be managed, and how the provider country ought to be acknowledged in research publications.

For one-off collecting activities and short-term projects, obtaining permits or IRCCs for each individual sample may be achievable. However, this may not be efficient for long-term collaborations or "big science" projects. The Global Genome Biodiversity Network, a global consortium of organizations supporting the collection, maintenance and sharing of research-quality genomic specimens, has established best practice guidelines for ABS for the collection of biological materials, stating that "[i]n cases where an institution conducts long-term or repeated project[s] in certain Providing Countries, it might be beneficial to develop framework agreements between the National Competent Authorities of the involved countries."[154] Part III will analyze four large-scale international biogenomic research collaborations, providing case studies on how they have addressed ABS when obtaining multiple samples for both commercial research and development as well as for purely non-commercial (academic) purposes in multiple jurisdictions.

National jurisdiction includes the land and air column within the defined territorial borders of a country, as well as its territorial waters and the exclusive economic zone.[155] In accordance with the CBD and Nagoya Protocol, countries have the authority to exploit and regulate their genetic resources by implementing domestic ABS legislative, administrative and policy measures.[156] Some countries are party to the CBD alone; others are party to the CBD and Nagoya Protocol. Some countries have decided to implement relatively strict regimes for accessing genetic resources within their territories, and others still are yet to put any access controls in place.[157] All of this complicates the conduct of scientific research that uses genetic resources from around the globe.

b. Micro-organisms as "genetic resources" under the CBD and Nagoya Protocol

Some have argued that the unique properties of micro-organisms make them inappropriate targets for regulation under the CBD and Nagoya Protocol's ABS regime.[158] The third objective of the CBD is the same as the objective of the Nagoya Protocol: "the fair and equitable sharing of the benefits arising out

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[154] *Best Practice for Access and Benefit-Sharing,* GLOBAL GENOME BIODIVERSITY NETWORK 4 n.3 (Apr. 8, 2017), http://www.ggbn.org/docs/ABS_Guidance/GGBN%20Guidance%20_Best_Practice_June_2015-Final.pdf.

[155] United Nations Convention on the Law of the Sea art. 2, Dec. 10, 1982, 1833 U.N.T.S. 397.

[156] CBD, *supra* note 110, arts. 3, 15(1).

[157] *See* Santiago Carrizosa, *Diversity of Policies in Place and in Progress, in* ACCESSING BIODIVERSITY AND SHARING THE BENEFITS: LESSONS FROM IMPLEMENTING THE CONVENTION ON BIOLOGICAL DIVERSITY 9, 43-50 (Santiago Carrizosa et al. eds., 2004).

[158] *See, e.g.*, Jörg Overmann & Amber Hartman Scholz, *Microbiological Research Under the Nagoya Protocol: Facts and Fiction,* 25 SCI. & SOC'Y 85, 85 (2017).

of [or 'from'] the utilization of genetic resources,"[159] indicating that these instruments are not just about biodiversity conservation but also include issues of equity and sustainable development. Whether or not they are suitable targets for *in situ* conservation, micro-organisms and viruses plausibly fit the definition of "genetic resources" under the CBD and Nagoya Protocol, and countries have asserted their authority to regulate the ABS of micro-organisms in their domestic laws.[160] Still others have yet to take a position on the scope of the CBD and the Nagoya Protocol with respect to micro-organisms. Acknowledging the complexity of the various legal positions taken with respect to the matter, this Article assumes for purposes of analyzing the legal and ethical questions at issue that micro-organisms are within the scope of the CBD and the Nagoya Protocol.

c. Specialized International Instruments under the Nagoya Protocol

The Nagoya Protocol makes allowances for specialized instruments that regulate ABS for specific genetic resources. The CBD and Nagoya Protocol do not apply to specific subsets of genetic resources "[w]here a specialized international access and benefit-sharing instrument applies that is consistent with, and does not run counter to the objectives of the [CBD and Nagoya Protocol]."[161] While not formally acknowledged as such, the World Health Organization's *Pandemic Influenza Preparedness Framework* (PIP Framework) bears many of the markers of such a specialized international instrument. Adopted by the World Health Assembly in 2011 to regulate access to pandemic influenza viruses through the WHO's Global Influenza Surveillance and Response System (GISRS), the PIP Framework, through MTAs, regulates access to influenza genetic resources and specifies the sharing of associated benefits like pandemic influenza vaccines and antiviral medications.[162] The PIP Framework does not include research and development activities that are conducted outside of the GISRS, so any utilization of pandemic influenza viruses outside of the PIP Framework is likely to be covered by the domestic laws that countries have implemented to meet their obligations under the CBD and Nagoya Protocol.[163] Similarly, the PIP Framework does not apply to seasonal influenza viruses.

The U.N. Food and Agriculture Organization's International Treaty on Plant Genetic Resources for Food and Agriculture, 2001 may serve as a specialized international instrument for the crops and forages covered by the text

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[159] CBD, *supra* note 110, art. 1 ; Nagoya Protocol, *supra* note 127, art. 1.

[160] *See generally* Michelle Rourke, *Viruses for Sale: All Viruses are Subject to Access and Benefit-Sharing Obligations Under the Convention on Biological Diversity*, 39 EUR. INTELL. PROP. REV. 79 (2017) (explaining how the CBD and Nagoya Protocol have allowed States to assert sovereignty in regulating genetic material).

[161] Nagoya Protocol, *supra* note 127, art. 4(4).

[162] WHO, PANDEMIC INFLUENZA PREPAREDNESS: SHARING OF INFLUENZA VIRUSES AND ACCESS TO VACCINES AND OTHER BENEFITS (2011) [hereinafter PIP Framework].

[163] WHO Secretariat, *Implementation of the Nagoya Protocol and Pathogen Sharing: Public Health Implications*, WHO (2017), https://www.who.int/influenza/pip/2016-review/NagoyaStudyAdvanceCopy_full.pdf?ua=.1.

of the treaty. The collection and use of genetic resources from the high seas are governed by the U.N. Convention on the Law of the Sea (UNCLOS) and are currently being negotiated, while access to resources from Antarctica is governed by the Antarctic Treaty where sovereignty claims are currently in abeyance.[164]

d. Genetic Sequence Data under the CBD and Nagoya Protocol

The term "genetic resources" under the CBD and Nagoya Protocol refers to the physical materials but may also be broad enough to include genetic sequence data derived from the physical resources themselves. Indeed, some countries have chosen to interpret the term "genetic resources" to include data and information associated with the physical resource.[165] There is concern, particularly in the PIP Framework forum at WHO, that not including data within the definition of "genetic resources" may provide users with the opportunity to circumvent ABS. However, making genetic sequence data subject to benefit-sharing obligations conflicts with the open access ideals of scientific research, where data is published in public databases for other researchers to access and utilize. Many international organizations and research bodies have taken positions with respect to whether "digital sequence information" and underlying genetic resources are coterminous with respect to the CBD and Nagoya Protocol. In Part III, we examine how four international research collaborations have addressed this legal complexity.

e. ABS as an Opportunity for Better Collaborations

While informal transfers of biological samples still occur, such practices are likely to decrease in frequency as researchers become aware of their obligations under the CBD, Nagoya Protocol, and various domestic laws, and as the transfer of genetic resources is further formalized. While many have viewed ABS regulations as a barrier to research, and there is no doubt that it adds yet another layer of bureaucracy at the research planning stage, it may also be framed as an opportunity to include scientists in provider nations.[166] This is particularly important in developing countries that may not have the capacity to initiate their own large-scale research projects, as the examples in Part I illustrate. Cooperative research between industrialized nations and (often developing) biodiverse countries can provide training opportunities and facilitate technology transfer, giving developing countries the capacity to conduct future research of their own and further the scientific endeavor as a whole.[167] Furthermore, partners in biodiverse nations have a great deal to contribute to collaborative ventures, including specialized local knowledge, novel perspectives and ideas, and assistance with navigating their country's domestic ABS regulations. Collaborations with partners in nations that contribute genetic resources to the

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[164] *See* CHARLES LAWSON, REGULATING GENETIC RESOURCES: ACCESS AND BENEFIT SHARING IN INTERNATIONAL LAW 26, 93 (2012).
[165] *See* ARTI K. RAI & MARGO A. BAGLEY, THE NAGOYA PROTOCOL AND SYNTHETIC BIOLOGY RESEARCH: A LOOK AT THE POTENTIAL IMPACTS 6 (Synthetic Biology Project ed., 2013).
[166] *Id.* at 24.
[167] *Id.* at 25.

project presents a win-win scenario for large-scale scientific projects. There are already many examples of successful collaborations with substantial benefits being shared, although these are predominantly non-monetary benefits in the form of laboratory equipment and supplies, training, and so on.[168]

For large-scale biological research collaborations that intend to collect and utilize genetic resources from multiple countries, obtaining PIC and negotiating MAT can be a hugely burdensome process, even when the project does not have commercial intent. In one description of a large-scale genetic sequencing project still in the planning phases,[169] *The Economist* reported:

> It is also an effort in danger of running into the Nagoya [P]rotocol. Permission will have to be sought from every government whose territory is sampled. That will be a bureaucratic nightmare. Indeed, John Kress of the Smithsonian, another of the [Project's] founders, says many previous sequencing ventures have foundered on the rock of such permission.[170]

The complexities of obtaining access from every government providing genetic resources to large-scale biology projects is compounded when what started out as non-commercial research is translated into a marketable end product, in which case, there may be a requirement to renegotiate MAT.

The default mode of ABS as prescribed by the CBD and the Nagoya Protocol is a bilateral agreement between the provider nation and the user of the genetic resource. In the context of large-scale international research collaborations, this would necessitate approaching every participant's NFP and CNA to apply for permits and/or negotiate benefit-sharing terms. The Nagoya Protocol does consider other ABS modalities, including multilateral benefit-sharing arrangements which are particularly useful in situations with multiple provider and user parties. In such situations, it may be more efficient to devise a set of ABS conditions that are broadly compliant with both the CBD and Nagoya Protocol that can be used as standard terms and conditions for collaborative activities.

f. The Effect of the CBD and Nagoya on Historical Models of Accessing Genetic Resources

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[168] Perhaps the most celebrated was the agreement between the National Biodiversity Institute of Costa Rica (INBio) and the United States pharmaceutical company Merck. *See* Hanne Svarstad, *National sovereignty and genetic resources, in* BIODIPLOMACY: GENETIC RESOURCES AND INTERNATIONAL RELATIONS 53-54 (Vicente Sánchez & Calestous Juma eds., 1994).

[169] This is a description of the Earth BioGenome Project which is covered in detail in the third case-study, *infra*, Section III.D.3.

[170] *Sequencing the World: How to Map the DNA of All Known Plants and Animal Species on Earth*, THE ECONOMIST (Jan. 23, 2018), https://www.economist.com/science-and-technology/2018/01/23/sequencing-the-world.

As the above analyses illustrate, past models of cross-border access of genetic resources are anachronistic as a practical matter, and, in many cases, illegal. For example, if a researcher requests that colleagues in another country transfer genetic resources across international borders without obtaining the PIC of the provider nation's CNA, that transfer may amount to a circumvention or even contravention of the provider country's domestic ABS laws.[171] In such circumstances, it is likely the responsibility of the individual and/or organization sending the samples to ensure that they have complied with their home country's access laws. This does not necessarily protect the user of informally transferred samples from any legal liability, as parties to the Nagoya Protocol are directed to implement measures to ensure "that genetic resources utilized within its jurisdiction have been accessed in accordance with ... the domestic [ABS] legislation or regulatory requirements of the other Party."[172] The enforcement mechanisms, however, remain opaque and uncertain although reputational risk remains important and can end a project effectively cancelling the social license to operate. It is now imperative to formally establish the provenance of those samples, demonstrate that PIC was obtained by an authorized provider and outline the MAT for the use of those samples. Increasingly these kinds of transfers will need to be accompanied by the Nagoya Protocol's Internationally Recognized Certificates of Compliance that certify PIC and establish lawful provenance.[173] The collection (or sampling) of new genetic materials, specimens or samples from the environment (i.e. *in situ* genetic resources not accessed through type collections or *ex situ* repositories) may be subject to domestic ABS regulations, especially if those materials are to be used outside of the originating country. These rules apply as much to research scientists with non-commercial intent as they do to commercial entities such as pharmaceutical or cosmetic companies looking to create a marketable product or process from genetic resources.

Access and benefit-sharing regulations have changed the way that some research scientists from museums, biobanks, universities and government research institutes collect and share samples. However, the perception that genetic resources are in the public domain persists (according to the ideal of open access) in the biological sciences and many researchers are still unaware of the legal requirements surrounding the collection and use of genetic resources for research purposes.[174] As such, unofficial methods for obtaining specimens for use in scientific research continue.[175] These practices are, however, disappearing,

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[171] It is worth noting here that because the CBD and Nagoya Protocol accept state sovereignty over genetic resources, the ABS administrative and policy measures can apply to the transfer of genetic resources across domestic borders as well as international borders. Users of genetic resources should be aware that some countries have implemented sub-national ABS measures.

[172] Nagoya Protocol, *supra* note 127, art.15(1).

[173] *Id.* art.17.

[174] Swen C. Renner et al., *Import and Export of Biological Samples from Tropical Countries – Considerations and Guidelines for Research Teams,* 12 ORGANISMS, DIVERSITY & EVOLUTION 81, 82 (2012).

[175] *See* Claire Lajaunie & Calvin Wai-Loon Ho, *Pathogens Collections, Biobanks and Related-Data in a One Health Legal and Ethical Perspective,* 145 PARASITOLOGY 688, 689 (2018) ("For these reasons, most pathogens have been shared without written documentation on appropriate management and use, or without having obtained formal approval from national authorities.").

and users of genetic resources need to ensure that their research activities comply with the relevant access laws of the provider countries.

3. *The Ethics of Large Biogenomic Projects*

Separately from the changing law governing international scientific research collaborations in the life sciences, some lawyers, scientists, and human rights advocates argue that there are important ethical considerations that may weigh against large investments in large-scale biogenomic mapping projects not oriented toward specific objectives for human health and welfare. These critics argue that given the vulnerability of many poor populations in low- and middle-income countries to infectious disease, malnutrition, and lack of access to healthcare, costly investments in research should be re-directed to disease surveillance, food security, and universal health coverage. In one recent opinion, Professors Edward Holmes, Andrew Rambaut, and Kristian Andersen criticized the Global Virome Project (see Part III A) as an imprudent investment given how vulnerable populations may be most effectively protected against the next pandemic. They argue that genomic surveys of animal viruses, while optimal for advancing a general understanding of viral evolutions, are unlikely to predict the next outbreak strain.[176] They write "influenza viruses [for example] have circulated in horses since the 1950s and in dogs since the early 2000s . . . [t]hese viruses have not emerged in human populations, and perhaps never will — for unknown reasons."[177] Viruses evolve at a rate that may render substantial investment too difficult to scale.[178]

Andersen, Holmes, and Rambaut instead advocate more intensive monitoring of at-risk populations through detailed screening of people who are exhibiting symptoms that cannot easily be diagnosed, using advanced technologies to map "the human 'infectome'."[179] They argue that pandemics may be prevented by training local clinicians and health-oriented NGOs, to spot spillover events. Once an emerging outbreak virus had been identified, it would be analyzed quickly to establish what type it is and the mechanisms driving its transfer amongst species of hosts. Relevant data would be passed to key stakeholders, from researchers and health workers on the ground to international agencies such as the WHO, so long as the data can be shared without intruding on patient privacy concerns and other ethical issues.[180]

Similarly, Keith Robison, a researcher with Warp Drive Bio, argued that the Earth BioGenome Project would not lead to useful discoveries without

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[176] Edward C. Holmes, Andrew Rambaut & Kristian G. Andersen, *Pandemics: Spend on Surveillance, Not Prediction,* 558 NATURE 180, 180 (2018) ("Broad genomic surveys of animal viruses will almost certainly advance our understanding of virus diversity and evolution. In our view, they will be of little practical value when it comes to understanding and mitigating the emergence of disease.").
[177] *Id.* at 181.
[178] *Id.*
[179] *Id.* at 182.
[180] *Id.*

defined objectives.[181] Better investments might be made, Robison argues, in specific insights for classes of new pharmaceuticals, interpretive technologies (rather than just sequencing), or scaling the project to specific species in order to maximize geographic variation.[182] This may be especially true given the state of sequencing technologies that would be used.

Large-scale biological projects that are not designed to test specific hypotheses are often derided as fishing expeditions. These criticisms make sense at first impression – it would seem that a dollar spent on basic research is a dollar not spent on a specific, more actionable intervention that might improve human welfare. Yet these projects make it clear that they bring with them technology investments in places and institutions that need them, do so with both abstract and practical objectives in mind, and have already accounted for scaling their activities so that they do not represent chaotic, random sequencing of all life. If designed properly, these fishing expeditions will not only catch some fish, they can also equip others with the ability to continue fishing on their own.

While there remain loopholes through which some unethical or legally suspect research may be undertaken, it is unlikely that large-scale international projects will be tempted to exploit these loopholes anymore, or otherwise find ways to avoid benefit-sharing obligations when collecting and utilizing the genetic resources of other nations. Today, the risk is such that the project could be shut down owing to the Nagoya Protocol's compliance mechanisms or simply to public outcry:

> Most rational researchers and industry will inevitably be seeking to avoid the public relations issues of having a project identified as non-compliant under the [ABS Clearing House Mechanism] and then run the risk of having their research called "biopiracy."[183]

III. GLOBAL BIOGENOMIC PROJECTS: CAPACITY BUILDING AND BENEFIT SHARING

The law and ethics of these emerging scientific research endeavors are complex and intertwine overlapping currents in international environmental law, public health preparedness, food security, and heated discussions about global wealth disparities. In this Part, we analyze four large biogenomic studies (there are dozens of smaller ones, many of which do not implicate the legal and ethical questions presented here) in order to understand whether these projects aim to comply with national and international access and benefit sharing law and contribute meaningfully to the building of research, public health, and agricultural capacity in the countries in which they operate or whether, as critics allege, they are largely oriented toward abstract research objectives unlikely to

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[181] Keith Robison, *Earth BioGenome Project: Ill-Conceived Megaproject Du Jour*, OMICS!OMICS! (Feb. 28, 2017), http://omicsomics.blogspot.com/2017/02/earth-biogenome-project-ill-conceived.html.
[182] *Id.*
[183] DANIEL F. ROBINSON, BIODIVERSITY, ACCESS AND BENEFIT-SHARING: GLOBAL CASE STUDIES 15 (2015).

translate into scientifically valuable outcomes or improvements in low- and middle-income countries. Each will provide some insights as to how to approach ABS rules and regulations depending on the size and overarching intent of the project. These case studies will detail the aims of the projects, the types of genetic resources that the projects seek to obtain and how they go about doing so. Each of the case studies will conclude by examining the capacity-building and ABS lessons and implications for future large-scale collaborative biological projects.

These projects are at different stages of implementation and address in different ways and at different levels of accomplishment the challenge of reconciling access to biological resources, the generation of scientific results and the equitable management of the benefits arising from their utilization. As the analyses demonstrate, these projects emphasize the importance of discovery and characterization of biological organisms as pathways both to scientific progress and collaboration within and between scientific communities and towards future research, development, and innovation.

A. The Global Virome Project

1. Project Description and Aims

The "Global Virome Project" (GVP) was launched at a meeting in Bellagio, Italy, in 2016 and is currently at a stage of institutional development and planning.[184] The GVP is led by a group of scientists and researchers coming from governmental and scientific institutions as well as non-governmental organizations and academia. The leadership of the initiative comes from the USA with the support of scientists and public authorities in other key countries such as China, Brazil, and Thailand.

The rationale of the GVP starts from the widely accepted consideration that the world is chronically unprepared for outbreaks of emerging and re-emerging diseases, particularly those with pandemic potential, and that most of the high-risk pathogens that have caused outbreaks in the recent past – predominantly viruses – are of animal origin.[185] The risk of zoonotic spillover is largely a function of human encroachment into wildlife habitats, in particular by increasing contacts with species that have proven to be reservoirs of viruses such as bats, primates, and rodents.[186] The transboundary consequences of such spillovers are then magnified by growing population density and high levels of mobility across countries. That this applies to countries at all levels of

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[184] *Bellagio Initiative on the Global Virome Project*, GLOBAL VIROME PROJECT (2016), https://static1.squarespace.com/static/581a4a856b8f5bc98311fb03/t/582120e4ff7c5080cc611fd6/1478566120350/GVP+Bellagio+Initiative.pdf (last visited Nov. 13, 2019).

[185] *See* Laurel Hamers, *Global Virome Project is Hunting for More than 1 Million Unknown Viruses*, SCI. NEWS (Feb. 22, 2018), https://www.sciencenews.org/article/global-virome-project-unknown-virus-outbreak.

[186] *See* Robin McKie, *Scientists Aim to Stop the Devastation of Zika-like Pandemics*, THE GUARDIAN (June 24, 2018), https://www.theguardian.com/science/2018/jun/24/global-pandemic-prevented-map-animal-virus-ebola-sars-zika.

development and social mobility is proven by the quick spread of the 2014-2016 Ebola outbreak across Guinea, Liberia, and Sierra Leone, and further on to other African countries such as Nigeria.[187] The predictable intensification and acceleration of international outbreaks of zoonotic diseases in the future point to the inadequacy of the current reactive approach to prevention and control, whereby states and international organizations such as WHO rush to identify pathogens only after the start of an outbreak.[188] This approach inevitably causes delays in characterizing the pathogens, managing risk and clinical interventions, and laying the ground for the development of medical countermeasures such as diagnostics, vaccines, and antivirals. It should be added that public health responses generally target one pathogen at a time, thus ignoring possible similarities among viruses belonging to the same family for the purposes of developing more generally effective countermeasures.

Available data and statistical models have suggested an alternative approach that is currently being developed through the GVP, building on a concurrent multi-team project on emerging pandemic threats led by the University of California-Davis.[189] It is reported that "[a]round 263 viruses from 25 viral families are known to infect humans;" an extrapolation based on historical patterns leads to the predictable presence of more than 1.6 million viruses in mammalian and bird hosts alone, of which between 631,000 and 827,000 may have zoonotic potential.[190] In other words, more than 99% of animal viruses remain undiscovered, many of them with the potential of becoming the source of future zoonotic outbreaks.

The GVP aims at reversing the reactive approach described above through the establishment of a "global atlas of zoonotic viruses."[191] In synthesis, the GVP constitutes a 10-year global scientific initiative to proactively identify a high proportion of animal viruses in a number of particularly relevant hosts (bats, rodents, primates, and aquatic birds) in countries rich with those species and characterize those with spillover potential. By both scaling up sampling and sequencing technology (in particular in developing countries) as well as establishing a global network of scientists from various disciplines, the GVP's ultimate objective is to build an unprecedented database of viruses in their ecological context. As in the case studies reviewed in the previous section, the ultimate product of GVP would be an open-access database of genetic sequences beside biobanks containing actual samples. The aforementioned PREDICT project has offered a proof of concept by achieving the identification of about

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[187] *See* Bryan Walsh, *The World is Not Ready for the Next Pandemic*, TIME (May 4, 2017), http://time.com/4766624/next-global-security/.
[188] *See id.*
[189] PREDICT is implemented by a consortium of institutions led by the School of Veterinary Medicine of the University of California at Davis. *See Global Virome Project*, UC DAVIS VET. MED., https://ohi.vetmed.ucdavis.edu/programs-projects/global-virome-project (last visited Nov. 13, 2019).
[190] Dennis Carroll et al., *The Global Virome Project*, 359 SCI. 872, 872 (2018).
[191] Dennis Carroll et al., *Building a Global Atlas of Zoonotic Viruses*, 96 BULL. WHO 292, 292 (2018).

1,000 new viruses since its inception in 2009.[192] The GVP aims to scale up those achievements, focusing on large-scale sampling and viral discovery rather than on capacity building and epidemiological analysis, which is instead the focus of PREDICT.

2. Capacity Building, Access, and Benefit Sharing

The goal of the GVP is to enhance current international surveillance programs by sampling the aforementioned animal species, sequencing viral families, and creating an atlas for researchers to understand how those viruses may spill over to human hosts. This would facilitate targeted surveillance and prevention, as well as inform necessary behavioral changes to increase protection of human populations. It would also shorten the time gap between outbreak detection and identification of the virus. The primary legacy of the GVP in scientific terms would be both sample biobanks and databases of sequence information as well as metadata. Available information could be processed through a "big data" approach to identify patterns and similarities among viruses and facilitate predictions about their zoonotic potentials.[193] Furthermore, the second main legacy would be increased laboratory, sampling, and surveillance capacity in participating developing countries (since most of the targeted animal species live in tropical and equatorial regions). The PREDICT project alone trained approximately 5,000 individuals in 30 countries in disease detection and increased the sequencing capacity of over 60 labs to undertake a range of research tasks.[194]

As represented in recent publications, there are two benefits to the project. The first is that the availability of samples and sequences of pathogens causing outbreaks will save precious time and resources and enable the quicker production of diagnostics and medicines. The second benefit is that the sequencing and characterization of a high number of viruses belonging to the same family could facilitate the development of broad-spectrum vaccines that could be effective against a number of viruses sharing similar genetic characteristics. The GVP could play a complementary role to public-private partnerships that support riskier investments in the development of new medicines or vaccines by providing access to the necessary samples or

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[192] *See* Donald G. McNeil, Jr., *Scientists Were Hunting for the Next Ebola. Now the U.S. has Cut Off Their Funding*, N.Y. TIMES (Oct. 25, 2019), https://www.nytimes.com/2019/10/25/health/predict-usaid-viruses.html.

[193] *See* Carroll et al., *The Global Virome Project*, *supra* note 190, at 872 ("We estimate, from analysis of recent viral discovery data, that ~1.67 million yet-to-be-discovered viral species from key zoonotic viral families exist in mammal and bird hosts—the most important reservoirs for viral zoonoses. By analyzing all known viral-host relationships, the history of viral zoonoses, and patterns of viral emergence, we can reasonably expect that between 631,000 and 827,000 of these unknown viruses have zoonotic potential. We have no readily available technological countermeasures to these as-yet-undiscovered viruses. Furthermore, the rate of zoonotic viral spillover into people is accelerating, mirroring the expansion of our global footprint and travel networks, leading to a nonlinear rise in pandemic risk and an exponential growth in their economic impacts.") (internal citations removed).

[194] *See* McNeil, Jr., *supra* note 192.

sequences, including potentially the recently established Coalition for Epidemic Preparedness Innovations (CEPI).[195]

3. Implications for Large-Scale Biological Projects

Indeed, the structure of the GVP as articulated in a number of presentations and publications is oriented not only toward facilitating access and benefit sharing, but also toward building capacity tailored to each participant country's particular circumstances. The planned structure of the GVP is a decentralized/federal one where activities are managed independently at the national level while a central hub will provide coordinating and normative functions, in particular through the adoption of agreed protocols on operating procedures and technical requirements.[196]

From a political perspective, the GVP may attract the attention of key governments and move beyond a purely scientific project, for example by becoming an intergovernmental program not dissimilar from the WHO's systems for pandemic influenza preparedness. To the extent that the international access component of the GVP falls under the Nagoya Protocol, participating entities will have to comply with the multiple legal requirements of the Protocol, (e.g. in terms of prior informed consent and mutually agreed terms for access and benefit-sharing).

From the beginning, the GVP has committed to compliance with the Nagoya Protocol, declaring that:

> The GVP's field operations are designed to contribute to host countries' systems and capacities, providing benefits including, but not limited to, promoting research collaboration; sharing of data and research results; and building in-country research capacity. Further, the Global Virome Project will work in partnership with governments where they determine that a specialized international instrument (Article 4.4 of the Nagoya Protocol) or special considerations (Article 8 of the Nagoya Protocol) may best guide the implementation of the CBD's and the Nagoya Protocol's access and benefit sharing principles.[197]

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[195] *See* Eri Togami et al., *The Global Virome Project*, BULL. WHO 4-5 (2018), https://www.who.int/bulletin/online_first/BLT.17.205005.pdf ("The recently launched Coalition for Epidemic Preparedness Innovations [CEPI] represents a critical step to address known viral threats, such as the Middle East respiratory syndrome coronavirus, Lassa fever and Nipah virus, for which vaccine or countermeasure development is challenging. The Virome project aims to complement the coalitions' innovations by characterizing the size, structure and composition of the pool of unknown viruses related to the viral targets on which the coalition is focused.") (internal citations removed).

[196] *See* Carroll et al., *Building a Global Atlas of Zoonotic Viruses*, *supra* note 191, at 292 ("The Global Virome Project will operate as a federation of national and regional projects led by in-country researchers, who are in turn connected to a global hub that provides standardized protocols and monitors progress.").

[197] ELSI Working Group, GVP Statement on Compliance with the Nagoya Protocol (on file with author).

The GVP's leadership is currently considering options with regard to both biobanks to store samples and, more importantly, databases to store and regulate access to sequences and metadata. A number of such data repositories are already in operation, such as GISAID[198] in Germany and GenBank[199] in the USA; they could either provide possible models to manage new national or multilateral databases, or even to host GVP-origin genetic sequences.
Economists at the EcoHealthAlliance have estimated that:

> Having a baseline of identified viral sequences would lead to earlier detection and quicker response times, lowering both epidemic frequency and impact. These improvements would not have an immediate impact, but benefits would accumulate throughout and beyond the lifespan of the GVP. For our calculations, we assume that these benefits collectively lead to an average of 10% in savings from damages in all events in the next 30 years ($290-480 billion). As such, a $1.2 billion Global Virome Project would return over $200 dollars in savings for each dollar invested. As the EcoHealth Alliance notes:
>
> > Even if the GVP only reduces the likelihood and impact of EIDs by 10%, this project would generate large returns on investment . . . [t]he premature loss of lives and economic shocks account for the largest proportion of economic damages from EID events. A $120 million annual budget for a 10-year Global Virome Project is an investment that could produce exceptionally high returns.[200]

Much of this benefit will occur through the catalysation of "technological advances in risk assessment, diagnostics and countermeasures" in developing countries.[201]

B. Earth Microbiome Project (EMP)

1. Project Description and Aims:

The Earth Microbiome Project (EMP) was launched in August 2010 and is an ongoing effort to genetically sequence "the uncultured microbial diversity of this planet."[202] The term "microbiome" refers to all microorganisms (bacteria, archaea and single-celled eukaryotes) that inhabit a particular environment or larger organism. The EMP aims to characterize the "bacterial, archaeal, and

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[198] *Home Page*, GISAID, https://www.gisaid.org/ (last visited Nov. 13, 2019).
[199] *GenBank Overview*, NCBI, https://www.ncbi.nlm.nih.gov/genbank (last visited Nov. 13, 2019).
[200] ECOHEALTHALLIANCE PREDICT MODELING & ANALYTICS TEAM, GLOBAL COSTS OF EMERGING INFECTIOUS DISEASES: AN ECONOMIC CASE FOR THE GLOBAL VIROME PROJECT 2 (2018), http://livescience.ecohealthalliance.org/predict/reports/2018-04-16-edi-economic-case-for-the-GVP.pdf.
[201] Togami et al., *supra* note 195, at 5.
[202] Jack A. Gilbert et al., *The Earth Microbiome Project: Successes and Aspirations*, 12 BMC BIOLOGY 1, 1 (2014).

eukaryotic microbial diversity" that comprise the Earth's entire microbiome.[203] By way of explanation, the microbiome of different species of trees will exhibit high levels of variability, even if they grow side by side in the same forest. The microbiome of a lake will vary with temperature and weather events, meaning that different species of microbes will thrive as the environmental conditions change. Therefore, even with hundreds of thousands of samples the data generated by the EMP will only represent a minute proportion of the Earth's actual microbiome.

The EMP has already resulted in a database of genetic sequences that is incremental and comparable. More sequences can be added to the database over time so that researchers have access to as much of the known genetic sequence data from around the world as possible. Until the advent of high-throughput genetic sequencing technologies, a lot of microbial species were not "discoverable" by scientists because most microorganisms are not readily culturable. That is, they cannot be grown or amplified in the laboratory for further study. Looking for the genetic material contained in environmental samples ensures that researchers are capturing genetic sequences from all microbes, not just those that can be cultured. So far, the majority of the sequences that have been generated by the EMP are of ribosomal ribonucleic acid (rRNA) molecules. Ribosomes are present in all cells and are sufficient markers of genetic variability across species, so rRNA is often used in taxonomic studies to construct phylogenies, a type of evolutionary family tree that groups organisms based on genetic relatedness.[204]

The EMP was founded and led by microbial ecologist Jack Gilbert of Argonne National Laboratory, microbiologist Rob Knight of the University of California, San Diego, and biologist Janet Jansson of Pacific Northwest National Laboratory. The Project initially relied on crowdsourcing to obtain samples. They put out the call to microbial ecologists from around the world to send in environmental samples to be analyzed by the laboratories of the three EMP cofounders in the United States.[205] In a 2011 blog post requesting sample contributions, one of the EMP Steering Committee members, Jonathan Eisen of the University of California, stated that "[e]xamples of things that could be useful include soil samples from a transect along the equator, filtered water from all lakes in Minnesota, deep sea sediment cores, filtered air from giant dust storms, microbial mats from hypersaline ponds, and so on."[206]

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[203] Luke R. Thompson et al., *A Communal Catalogue Reveals Earth's Multiscale Microbial Diversity*, 551 NATURE 457, 458 (2017).

[204] *Id.* There is, of course, an ongoing controversy about the appropriate and suitable taxonomic frameworks; *see, e.g.*, Charles Lawson, *Taxonomic Conceptions of Algae, Animals, Fungi and Plants in Granting Intellectual Property Privileges*, 19 GRIFFITH L. REV. 472 (2010).

[205] Luke R. Thompson, *Wrangling the Microbiomes of Earth*, NATURE MICROBIOLOGY COMMUNITY (Nov. 1, 2017), https://naturemicrobiologycommunity.nature.com/users/69805-luke-thompson/posts/22169-wrangling-the-microbiomes-of-earth; *Laboratories*, EARTH MICROBIOME PROJECT, http://www.earthmicrobiome.org/people/laboratories (last visited Nov. 13, 2019).

[206] Jonathan A. Eisen, *Wanted: Sample Collections for the Earth Microbiome Project (EMP); Help Make an Open Field Guide to the Microbes*, PHYLOGENOMICS: THE TREE OF LIFE BLOG (Apr. 27, 2011), https://phylogenomics.blogspot.com/2011/04/wanted-sample-collections-for-earth.html.

In the first phases of the EMP, the environmental samples were sent to one of the EMP wet labs which extracted the nucleic acids and generated the genetic sequence data. The genetic sequence data was published on the EMP's online database and is openly accessible for anyone to explore.[207] This meant that researchers from around the world could have their existing samples genetically sequenced for just the price of shipping them to the EMP labs in the United States. Researchers were then free to analyze the genetic sequence data of not only the samples they provided, but the samples of all other contributors.

In the current phases of the EMP, researchers can contribute data directly to the database if they follow the EMP's standardized protocols for sample and metadata collection, DNA extraction, and genetic sequencing. Creating standardized procedures ensures the integrity of the data despite being contributed by disparate laboratories. It can reduce bias and may allow for more accurate comparisons with the rest of the EMP data.[208] Some of the data analysis is being conducted by members of the EMP working group, but the EMP also encourages researchers from around the world to interrogate the EMP genetic sequence database, conduct their own analytics and publish the findings. The only stipulation is that the EMP be acknowledged in the Methods and Acknowledgements sections of the publication and that the original EMP paper be cited.[209] This communal approach to data generation and analysis has already led to around 60 peer reviewed studies in academic journals.[210] Because the EMP is building its database from constituent scientific projects that are testing their own individual hypotheses, the EMP has managed to avoid derision as a "fishing expedition", a common insult directed at large scale projects that collect samples and data without a clearly defined plan for their use.

The results of the EMP have been promising, and the database of microbial genetic sequences continues to expand. In their 2017 meta-analysis of 97 independent studies that contributed to and used EMP data,[211] the EMP team reported that more than 2.2 billion microbial genetic sequences had been generated from 27,751 environmental samples.[212] This included the "a total of 307,572 unique sequences", that is, genetic sequences that were not previously known to science.[213] As expected, this represents only a minute fraction of the Earth's actual microbiome, but it is a good starting point. The main contribution of this large-scale project appears to be the promulgation of standardized research methods that have been accepted and used by those contributing

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[207] *See Data and Code,* EARTH MICROBIOME PROJECT, http://www.earthmicrobiome.org/data-and-code/ (last visited Nov. 13, 2019).
[208] Jack A. Gilbert & Folker Meyer, *Modeling the Earth Microbiome*, 7 MICROBE 64, 68 (2012).
[209] *Home Page*, EARTH MICROBIOME PROJECT, http://www.earthmicrobiome.org/ [hereinafter Earth Microbiome Home Page] (last visited Nov. 13, 2019).
[210] *See Publications,* EARTH MICROBIOME PROJECT, http://www.earthmicrobiome.org/publications/ (last visited Nov. 13, 2019).
[211] *See* Luke R. Thompson et al., *supra* note 202, at 458 (Supplementary Table 1).
[212] *Id.* at 458 (sequence reads were between "90-151 base pairs.").
[213] *Id.* at 459.

samples and data to the EMP and are likely to be used as communal standards for a while to come.

2. Capacity Building, Access and Benefit Sharing

Looking for diverse species of microorganisms within diverse environmental samples including soil, water, feces, sponges and corals, meant that the EMP team needed a broad (but not necessarily systematic) sampling strategy. In the initial phases of the project, "[t]he EMP solicited the global scientific community for environmental samples and associated metadata spanning diverse environments and capturing spatial, temporal, and/or physicochemical covariation."[214] There were some doubts as to how successful the crowdsourcing strategy would be as it was assumed that researchers would be reluctant to hand over their samples for testing.[215] While there is usually little financial value in the samples for the research teams that collected them, their value is wrapped up in the physical (and sometimes bureaucratic) efforts that it took to obtain the samples in the first place and the ongoing costs of storage.

The crowdsourcing of samples "from researchers around the world" was deemed "a success" as early as 2014,[216] and by May 2018, the EMP was no longer accepting sample contributions from scientists as they had reportedly reached processing capacity.[217] According to one report, "[m]ore than 500 researchers sent in samples, from 43 countries across the world. The team soon had thousands of samples–all neatly packed into about 25 freezers across the three founders' laboratories".[218] It could be argued that the generosity of donors to the EMP demonstrates that the Mertonian norm of communality is still alive and well in the sciences, despite the constant pressures to commercialize academic outputs. [219]

Crowdsourcing samples allowed the EMP to amass specimens from 43 different countries, representing all seven continents.[220] The EMP was founded in 2010, the same year that the Nagoya Protocol was adopted by the Conference

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[214] *Id.* at 458.
[215] Gilbert et al., *supra* note 202, at 1.
[216] *Id.*
[217] Earth Microbiome Home Page, *supra* note 209. ("The Earth Microbiome Project is a systematic attempt to characterize global microbial taxonomic and functional diversity for the benefit of the planet and humankind.").
[218] Katarina Zimmer, *Researchers Catalog Earth's Microbiome,* THE SCIENTIST (Feb. 1, 2018), https://www.the-scientist.com/notebook/researchers-catalog-earths-microbiome-30120.
[219] Note that Merton originally used the term "communism" not "communality" which has been used here. Since the publication of Merton's famous essay in 1942, the word "communism" has come to take on additional significance and meaning that was not in keeping with the way Merton used the term. The other three scientific norms that Merton identifies as "the ethos of science" are universalism, disinterestedness and organized skepticism. *See* ROBERT K. MERTON, *The Normative Structure of Science*, in THE SOCIOLOGY OF SCIENCE: THEORETICAL AND EMPIRICAL INVESTIGATIONS 268-278 (Robert K. Merton & Norman W. Storer eds., 1973).
[220] Luke R. Thompson et al., *supra* note 203, at 458 (2017).

of the Parties to the CBD.[221] This means that there could be up to 43 different sets of ABS regulations that may apply to the samples that were being sent to the EMP laboratories in the United States. In the 2010 report from the first EMP meeting on sample selection and acquisition, the authors note that:

> The bottlenecks for this project will likely not be sequencing, but rather identifying projects that can provide samples, determining whether the samples adhere to strict requirements for associated metadata that support integration efforts, and the infrastructure, protocol and legal implications of such an endeavor.[222]

And the same report goes on to note that:

> Obtaining samples from outside of the US would be the most significant problem, licenses and permits would be required, and the countries from which samples were sent would need to agree to sequencing and downstream analysis to prevent litigation. Rick Stevens [of Argonne National Laboratory] suggested that the EMP could potentially ship a sequencer into the country and this would prevent shipping costs and permits for the physical samples or DNA. Rob Knight suggested that one possible solution would be to have visitors come and extract samples at an EMP affiliated Laboratory.[223]

The report therefore indicates that the organizers of the EMP were aware that there were indeed legal considerations for the transnational movement of samples. However, it is not clear if the awareness extended only to biosafety and import/export controls, or whether it included ABS and the associated requirements of obtaining PIC and establishing MAT before utilizing other nations' sovereign genetic resources. The authors of the report state the requirement for "licenses and permits," although this could be for import/export controls (such as international agreed sanitary laws), not necessarily access permits. However, one thing that does seem to suggest an awareness of ABS is the suggestion to "ship a sequencer" into the host country as a cost-effective alternative to paying for "shipping costs" of samples "and permits."[224] This would constitute a form of an annexed research site (described in Part II). It should be noted, however, that many countries may now wish to regulate access to the genetic sequence data in the same way that they regulate access to the samples themselves.

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[221] *Id.* at 457.
[222] Jack A Gilbert et al., *The Earth Microbiome Project: Meeting Report of the 1st EMP Meeting on Sample Selection and Acquisition*, 3 STANDARDS IN GENOMIC SCI. 249, 250 (2010).
[223] *Id.* at 252.
[224] *Id.*

3. Implications for Large-Scale Biological Projects:

The crowdsourcing approach used by EMP is relevant because it circumvents the need to collect samples anew. The coordinating researchers may have been working on the assumption that either these historical samples are not within the remit of the CBD and considered common heritage,[225] that they are the lawful property of the scientists (or their institutions) that collected them, or that all of the regulatory hurdles have been cleared at the original point of access.

The report from the first "EMP meeting on sample selection and acquisition" held in October 2010 indicated that the discussion was premised on the fact that individual scientists or research teams (teams of scientists that work together, usually with a principal investigator or lab head, are often referred to in the scientific community as "labs") owned the samples in their possession. The biggest and "possibly insurmountable" problem discussed was actually the "ego" of scientists not wanting to share their samples or data or to be beaten to publication by other researchers with access to their samples or data.[226] The report indicated that the meeting participants were aware of the potential for commercial outcomes.[227] Furthermore, there seemed to be some hesitance about receiving samples from outside the U.S.,[228] but the reasons for this are unclear in the report. In terms of the samples sourced from other researchers, there may be an assumption that the samples were initially collected in compliance with ABS regulations. This leaves compliance up to the contributors of samples to the larger EMP. However, this does not necessarily indemnify the EMP-affiliated laboratories that are utilizing the shipped samples to generate sequence data from ABS obligations unless they can be sure that as third-party users, they are not subject to any viral use clauses stemming from the original ABS contract.

There is an awareness expressed by the EMP meeting attendees that there may be a requirement to obtain a permit when receiving samples from outside the U.S., but it is not clear if that permit is related to any ABS obligations. It could be referring to import/export permits as opposed to access permits. Indeed, there is no sense that there is an awareness of any rights to the samples other than those that are attributed (by the meeting attendees) to the scientists that collected and are storing them. This points to lack of awareness of the principles of resource sovereignty and ABS contained in the CBD and Nagoya Protocol. This is understandable given the timing of the project. The initial meetings (and this sample acquisition meeting) were held in 2010, before the Nagoya Protocol was adopted. There was (and still is) limited awareness of these issues and how

[225] This may indeed be the case if the crowd-sourced samples were collected prior to the entry into force of the CBD on December 29, 1993.
[226] Gilbert et al., *supra* note 222, at 252-3.
[227] *Id.* at 250.
[228] Noting here that the U.S. is not party to the CBD, and thus cannot be a party to the Nagoya Protocol.

sovereign authority over genetic resources might impact sampling practices or the use of those genetic resources.[229]

A team of Brazilian researchers detailed the benefits of locally-led microbiome projects as strengthening conservation efforts, building infrastructure to protect national genetic heritage, training new scientists and researchers, increasing the use of beneficial organisms, suppressing pathogenic microorganisms in plants and humans and building the technological base of the country.[230]

C. Micro B3 (Biodiversity, Bioinformatics and Biotechnology)

1. Project Description and Aims:

The Marine Microbial Biodiversity, Bioinformatics, and Biotechnology project, shortened to the Micro B3 project, was a European venture that operated from January 1, 2012 until December 31, 2015.[231] The Micro B3 project was not itself a bioprospecting project. Rather, it was an interdisciplinary effort to reduce technical and legal barriers for smaller marine bioprospecting projects and to standardize and integrate marine microbiological datasets for maximum utility for both non-commercial scientists and commercial researchers. The advent of high-throughput sequencing technologies has resulted in vast amounts of data, and the Micro B3 project was largely a response to the fact that "the processing and analysis of the data mostly outcompetes the bioinformatic capacities of many researcher groups and institutes in the marine field."[232] Thus, the Micro B3 project would facilitate the characterization of "marine viral, bacterial, archaeal and protists genomes and metagenomes"[233] "by providing access to, and by integrating genomic, oceanographic and Earth observation databases into, one Micro B3 Information System (MB3-IS), based on global standards for sampling and data processing."[234]

The Micro B3 project was, at its core, about building bioinformatics capacity in Europe, but one of its key features was Ocean Sampling Day (OSD).[235] Held on June 21, 2014 and repeated in 2015, the OSD was "a simultaneous global mega-sequencing campaign aiming to generate the largest standardized

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[229] For a discussion on the limited awareness of ABS in botanic gardens even after the introduction of the Nagoya Protocol, *see* Kate Davis et al., *An Access and Benefit-Sharing Awareness Survey for Botanic Gardens: Are They Prepared for the Nagoya Protocol?*, 98 S. AFR. J. BOTANY 148 (2015).
[230] Victor S. Pylro et al., *A Step Forward to Empower Global Microbiome Research Through Local Leadership*, 24 TRENDS IN MICROBIOLOGY 767-70 (2016).
[231] The Micro B3 Project homepage, *supra* note 76.
[232] *Id.*
[233] *Id.*
[234] *Micro B3*, MICROBIAL BIODIVERSITY, BIOINFORMATICS, BIOTECHNOLOGY 4 (2012), https://www.microb3.eu/sites/default/files/media_material/printed_material/MICROB3_Brochure_Lowres_25_01_2013.pdf [hereinafter Micro B3 brochure].
[235] Sarah J. Bourlat et al, *Genomics in Marine Monitoring: New Opportunities for Assessing Marine Health Status*, 74 MARINE POLLUTION BULL. 19, 25 (2013).

microbial data set in a single day."[236] The water sampling was conducted by contributors at 191 sites around the world using Micro B3 standardized procedures,[237] and the microbial samples were sent to a laboratory in Germany for DNA analysis. This was essentially a proof of concept for the Micro B3 Information System (through which the data was processed) and a test of the best practices protocols that had been developed by the project.[238] The 2014 OSD resulted in the collection and characterization of "155 16S/18S rRNA amplicon data sets, 150 metagenomes, and a rich set of environmental metadata," providing "the largest standardized data set on marine microbes taken on a single day"[239] and "more than 80 peer-reviewed publications."[240]

2. Capacity Building, Access and Benefit Sharing

The Micro B3 project was attuned to the commercial potential of marine microbial resources, stating that they provide "excellent opportunities for bioprospecting for novel enzymes of industrial interest and for metabolic products."[241] Thus, from the outset, the project focused on issues of ABS and the creation of model ABS agreements that would suit both non-commercial (public) and commercial (private) stakeholders. The MicroB3 project description notes:

> Since Micro B3 is likely to bring about the discovery of new biotechnological applications for marine microbial data, there are complex issues of intellectual property involved, particularly given that much of the data gathered originates in exclusive economic zones or areas of ocean completely beyond any national jurisdiction.[242]

The Micro B3 project therefore makes for a useful case study into the sorts of ABS policies that can be applied to microbial sample collection, data generation and information sharing.

The Micro B3 project was headed by Dr. Frank Oliver Glöckner, Head of Microbial Genomics and Bioinformatics Research Group at the Max Planck Institute and Professor of Bioinformatics at Jacobs University, Germany.[243] It

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[236] Anna Kopf et al., *The Ocean Sampling Day Consortium*, 4 GIGASCIENCE 1, 2 (2015).
[237] *Ocean Sampling Day*, MICRO B3 (2015), https://www.microb3.eu/osd.html.
[238] Micro B3 brochure, *supra* note 234, at 3.
[239] Kopf, *supra* note 236, at 1.
[240] *Report from the Micro B3 Final Conference 2-5 November 2015*, MARINE BIOTECH ERA-NET (Nov. 17, 2015), http://www.marinebiotech.eu/news-and-events/era-news/report-micro-b3-final-conference-2-5-november-2015.
[241] *Background*, MICRO B3, https://www.microb3.eu/about.html (last visited Nov. 13, 2019) (emphasis omitted).
[242] Micro B3 brochure, *supra* note 234, at 3; *see also* Rüdiger Wolfrum & Nele Matz, *The Interplay of the United Nations Convention on the Law of the Sea and the Convention on Biological Diversity*, 4 MAX PLANCK Y.B. OF U.N. L. 445, 462 (2000) https://www.mpil.de/files/pdf2/mpunyb_wolfrum_matz_4.pdf (The "exclusive economic zones" of nation states are within the remit of the CBD).
[243] Micro B3 brochure, *supra* note 234, at 2.

built on preexisting European projects and collaborations and worked alongside the European Marine Biological Resource Centre and the European Life Sciences Infrastructure for Biological Information.[244] The Micro B3 project was funded by the European Union's (EU) Seventh Framework Programme (7FP), a research and innovation funding scheme that ran from 2007-2013.[245] The Micro B3 was arranged as an "interdisciplinary consortium of 32 academic and industrial partners"[246] based in Europe, and the project team included specialists in bioinformatics, data modelling, intellectual property and experts from biotech companies. [247]

As part of the standardized protocols developed by the Micro B3 project and used in the Ocean Sampling Day, the Micro B3 team developed policies for ABS, material transfer, and data transfer agreements. The acknowledgement that marine microbial bioprospecting could ultimately result in marketable products meant that appropriate attribution of intellectual property and compliance with the Nagoya Protocol were key considerations from the outset of the Micro B3 project.[248] The project was divided into nine 'Work Packages,' one of which was Work Package 8: "Intellectual Property (IP) Management for Marine Bioprospecting."[249] The aims of the IP Work Package were outlined on the projects website:

> (a) efficient dissemination of materials, software, data and published results to a wide range of science communities and other users / stakeholders (b) appropriate IP protection and management (including patent, copyright and trade secrecy issues) (c) measures for compliance with the provisions of the Nagoya Protocol on access and benefit sharing with a view to involve resource states in the R&D activities and contribute to the protection and preservation of the marine biodiversity.[250]

The Micro B3 project differentiates between "pre-competitive utilization/research" of marine microbial genetic resources, and use or research for "competitive research and for hybrid situations", recognizing that the Micro B3 project will have the potential to generate both.[251] The pre-competitive research is that which is conducted for furthering science generally, the results of which will be in the public domain. The latter refers to any proprietary

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[244] *Id.*
[245] *Understanding the Seventh Framework Programme*, EUR. COMMISSION., https://ec.europa.eu/research/fp7/index_en.cfm?pg=understanding (last updated Aug. 25, 2015).
[246] The Micro B3 Project homepage, *supra* note 76.
[247] Micro B3 brochure, *supra* note 234.
[248] *Id.* at 3.
[249] *Work Packages,* MICRO B3, https://www.microb3.eu/work-packages.html (last visited Nov. 13, 2019).
[250] *Intellectual Property (IP) Management for Marine Bioprospecting*, MICRO B3, https://www.microb3.eu/work-packages/wp8.html (last visited Nov. 13, 2019) [hereinafter WP8 Webpage].
[251] *Id.*

research and development which will be eligible for protection under the standard suite of intellectual property protections.

The project uses data gleaned from microbial genetic resources collected in both the sovereign oceanic areas belonging to coastal countries as well as areas beyond national jurisdiction (ABNJ) on the high seas.[252] For those samples collected on the high seas, the United Nations' *Convention on the Law of the Seas* (UNCLOS, 1982) applies.[253] This treaty treats the "natural resources" on the high seas as a global commons, in part regulated by the International Seabed Authority. The commentary to the Micro B3 model agreement explains:

> [T]he access to and the utilization of genetic resources taken from the ABNJ is free (Articles 87, 256 UNCLOS), but limited by the respect of the conditions laid down by UNCLOS, and by the respect of the interests of other States and of the right under the convention with respect to activities in the Area (Article 87). No access agreement needs to be, nor can be, concluded.[254]

The majority of the sampling activity associated with the Micro B3 project and the Ocean Sampling Days occurred "within internal waters, the territorial sea, and the exclusive economic zone of coastal states" and in these cases, the CBD's provisions on accessing genetic resources applied.[255] The Micro B3 project therefore adopted an approach "based on the Nagoya Protocol" which entered into force in October, 2014, while the project was running and aimed "to produce model [ABS] contracts and good practice standards specifically tailored to the marine field."[256] The final model agreement is available online;[257] so, too, is an insightful discussion detailing the objectives of, and the conflicts between, the regulatory frameworks that the model agreement is based upon.[258] The model agreement not only serves as the recommended contract for Micro B3 partners, but the authors of the agreement have noted that it "can also be used for other projects, such as those on genetic resources other than marine microorganisms", and would probably require only "minor changes in the text" of the template.[259]

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[252] Micro B3 Brochure, *supra* note 234, at 3.
[253] For a discussion on the jurisdiction of UNCLOS and its application to living and non-living "natural resources," see Lawson, *supra* note 164, at 93.
[254] Annotated Model Agreement, *supra* note 142, at 335.
[255] *Id.* at 330.
[256] Micro B3 Brochure, *supra* note 234, at 3.
[257] Caroline von Kries et al., *Micro B3 Model Agreement on Access to Marine Microorganisms and Benefit-Sharing* (Dec. 17, 2013), https://www.microb3.eu/sites/default/files/pdf/MICRO_B3_ABS_model_agreement_17122013%20explanatory%20notes.pdf [hereinafter Kries et al., Model Agreement 2013].
[258] WP8 Webpage, *supra* note 250.
[259] Annotated Model Agreement, *supra* note 142, at 331.

The model agreement is between the original user of the genetic resources, the 'Recipient', and the Provider State.[260] It is designed to apply to the utilization of genetic resources and to cover all potential research outcomes, including public domain research, commercial research and development, and situations where the genetic resources are initially used for non-commercial research purposes but are later used in the production of a commercial product.[261] The latter is deemed a "hybrid" situation and is covered by a "change of intent clause" where the Provider maintains the right to renegotiate benefit sharing under MAT if the intended utilization of the genetic resource in question changes.[262] It is worth noting here that this clause "does not give the Provider a one-sided right to withdraw its consent, but rather enables it to renegotiate the contract."[263]

Another article of note in the Micro B3 model agreement is the inclusion of a viral license clause, which states that third parties receive the resources under the same terms as the original Recipient.[264] The agreement explains the viral license clause further:

> This clause guarantees that all the obligations of the initial agreement will be imposed on subsequent use of the materials and the produced data when transferred. When the viral license clause is used, the scientist/scientific institution is allowed to transfer the material to third parties if they sign a new contract in which they commit themselves to respect the conditions of the initial ABS agreement ... At each transfer however, according to the Nagoya Protocol, consent is required from the competent national authority in the provider country[.][265]

3. Implications for Large-Scale Biological Projects:

The Micro B3 project created various tools and standardized agreements that can be modified and tailored for use with other projects. The "absence of an overarching legal framework for access and benefit sharing in the marine environment" was seen as one of the major obstacles "limiting the usability of the ever increasing datasets for marine biodiversity research and biotechnological applications."[266] Therefore, creating a workable ABS policy was one of the primary objectives of the Micro B3 project from the outset, setting

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[260] The text of the Micro B3 model agreement, as well as an extensive commentary on all of its articles is provided in Model Agreement 2013, *supra* note 257. Much of the discussion here is based on that commentary.

[261] Annotated Model Agreement, *supra* note 142, at 331.

[262] *Id.* at 345.

[263] *Id.*

[264] Model Agreement 2013, *supra* note 257, at 4; *see* Model Agreement, *supra* note 142, at 345.

[265] Model Agreement 2013, *supra* note 257, at 4. *See* Model Agreement, *supra* note 142, at 345.

[266] *Final Report Summary - MICRO B3 (Marine Microbial Biodiversity, Bioinformatics and Biotechnology)*, CORDIS, https://cordis.europa.eu/project/rcn/101555/reporting/en?rcn=174440 (last updated June 29, 2016).

it apart from other large scale research projects where the primary objective was the collection and analysis of research data.

Since the Nagoya Protocol did not enter into effect until October 12, 2014, the Micro B3 project got a head start on determining how its provisions were likely to affect large-scale scientific activities, creating "[a]n innovative legal framework and model contracts for the protection and sustainable use of marine genetic resources."[267] The resultant model agreement complies with the requirements of the Nagoya Protocol, recording the granting of PIC[268] and establishing MAT.[269] It provides both the Recipient and the Provider of the marine microbial genetic resources sourced from the Provider's sovereign territory with legal certainty about the permissible uses and the terms of benefit sharing before those samples are even collected. For the purposes of the Micro B3 project, the model agreement "was hardly used, because the [participating] coastal States, most of which were European, either did not operate an ABS regime or did not apply it because the samples were taken by their own research teams."[270] The attention paid to ABS and the associated issues of IP protections, along with the outputs generated by the IP Work Package of the Micro B3 project, offer significant insight as to how ABS can and should be approached by other large-scale scientific endeavors to ensure compliance with ABS regulations and legal clarity for all stakeholders.

With respect to PIC under Nagoya, the creators of the Micro B3 model agreement noted that:

> "Whether a Provider State has established an ABS regime or not can only be determined by examining its domestic legislation and practices. According to upcoming rules of User States, a due diligence obligation applies in such cases. This means that the researcher has to take due care to find out the domestic procedure of the Provider State, if any exists. He/she is not required to carry out an in-depth legal analysis. Rather, it is sufficient diligence if he/she seeks advice at the national focal point on ABS of the Provider State."[271]

This statement reinforces the fact that informal transfers of genetic resources, even for non-commercial research purposes, are no longer appropriate. Researchers must now exercise due diligence in meeting ABS obligations.[272]

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[267] *Background*, MICRO B3, https://www.microb3.eu/about.html (last visited Nov. 13, 2019).
[268] *See* Annotated Model Agreement, *supra* note 142, at 346.
[269] *See id.* at 331("The aim of the Model Agreement is thus to serve as model contractual clauses for mutually agreed terms according to Article 19 of the Nagoya Protocol.").
[270] EVANSON CHEGE KAMAU & GERD WINTER, *Unbound R&D and bound benefit sharing, in* RESEARCH AND DEVELOPMENT ON GENETIC RESOURCES: PUBLIC DOMAIN APPROACHES IN IMPLEMENTING THE NAGOYA PROTOCOL 19 (Evanson Chege Kamau, Gerd Winter & Peter-Tobias Stoll eds., 2017).
[271] Annotated Model Agreement, *supra* note 142, at 330-331.
[272] *See* Sivaramjani Thambisetty, *Due Diligence and ABS Compliance Under EUR 511/2014* 3 (London Sch. of Econ., Law Policy Briefing Paper No. 33, 2019).

Even if there is no domestic ABS legislation or regulations in the country from which researchers wish to obtain samples, it is still worth approaching the provider nation to determine whether they wish to exercise any form of sovereign rights (legislative, administrative or policy measures) over the genetic resources of interest, for no other reason than to ensure that there are no unexpected legal challenges at a later date, including reputational risk from claims of "biopiracy." If the NFP (or CNA) of the provider nation chooses to waive its sovereign right to participate in ABS negotiations for the genetic resources of interest, it is worth getting this decision in writing so as to demonstrate later that sufficient steps were taken to establish whether ABS obligations existed at the time of access.

One major implication of the Micro B3 project's analysis of ABS requirements and the development of its Nagoya Protocol-compliant model agreement is the indirect recognition that any data gleaned from the physical samples of microbial genetic resources belongs to the same jurisdiction from which the physical samples originated. Indeed, it has been noted that "the Micro B3 Agreement is a good example of how benefit sharing obligations can travel with the digital resource separately from the physical sample."[273] The model agreement details the terms of use not only for the "accessed genetic resource" but also for "associated genetic knowledge," which is defined as "any experimental or observational data, information and other findings on the composition, life conditions and functions of the accessed genetic resources."[274] The model agreement contains clauses that ensure that the ABS "obligations of the initial ABS agreement . . . will be imposed on any third party receiving the material and/or the knowledge associated with the [genetic resource]."[275] This application of viral clauses to the original sample and to the data, information, and knowledge that are associated with that sample are something that should be considered when initiating a bioprospecting project, whether or not there is commercial intent.

The Micro B3 project recognizes that the adoption of "appropriate" ABS rules can actually "promote R&D activities . . . and generate funding for biodiversity conservation."[276] There are undoubtedly major administrative hurdles that accompany these sorts of activities; ABS regulations are but one source of such hurdles. The Micro B3 project's model agreement provides a workable starting point for those wishing to access microbial genetic resources for research and development, and it clarifies how some of the more ambiguous ABS provisions of the CBD and Nagoya Protocol might be settled. The key point is that ABS, as it is outlined in these international instruments, is a compromise between the provider and recipient parties. The Micro B3 project's model agreement establishes a practical compromise that ensures the efficient production and promulgation of public-domain scientific information while

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[273] Fran Humphries, *Banking on a Patent Solution for Sharing Antarctica's* Ex Situ *Genetic Resources*, *in* BIODIVERSITY, GENETIC RESOURCES AND INTELLECTUAL PROPERTY 62 (Charles Lawson & Kamalesh Adhikari eds., 2018).

[274] Kries et al., Model Agreement 2013, *supra* note 257, at 8.

[275] Annotated Model Agreement, *supra* note 142, at 347.

[276] WP8 webpage, *supra* note 250.

guaranteeing that a portion of the benefits from subsequent commercial applications will be shared with the resource provider. According to Pooja Bhatia and Archana Chugh, under Micro B3, "agreements in line with the national laws shall be more effective. The marine bioprospecting contracts can be a significant tool for the development of a successful access and benefit sharing mechanism that will safeguard the interests of the indigenous communities as well as monitor the use of marine bioresources in an environment friendly and sustainable manner."[277]

D. Earth BioGenome Project (EBP)

1. Project Description and Aims:

The idea of the Earth BioGenome Project (EBP) evolved out of a meeting at the Smithsonian Institute in November 2015,[278] and the Project was announced on February 23, 2017.[279] The ambitious aim of the EBP is to genetically sequence the Earth's known eukaryotic species (approximately 1.5 million plant, animal and fungal species) over ten years.[280] The plan is to fully annotate (describe) the genetic sequence data and make it available for use by the scientific community and industry, forming the building blocks of further research, development and innovation.

In January 2018, a partnership between the EBP and the Earth Bank of Codes was announced at the World Economic Forum in Davos, Switzerland.[281] The Earth Bank of Codes will store the genetic sequence data, encoding information about its origin and terms of use. The collaboration between the EBP and the Earth Bank of Codes is part of the World Economic Forum's "Fourth Industrial Revolution for the Earth" initiative and is being sold as an investment opportunity to leverage funding from public-private partnerships.[282] The endeavor is expected to cost around US$4.7 billion, an outlay that the EBP sees as something of a bargain given the ability of the US$3 billion Human Genome Project to contribute "nearly $1 trillion" to the US economy in the first ten years after its completion.[283]

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[277] Pooja Bhatia & Archana Chugh, *Role of Marine Bioprospecting Contracts in Developing Access and Benefit Sharing Mechanism for Marine Traditional Knowledge Holders in the Pharmaceutical Industry,* 3 GLOBAL ECOLOGY AND PRESERVATION 176, 187 (2015).

[278] *Sequencing the World, supra* note 170.

[279] Elizabeth Pennisi, *Biologists Propose to Sequence the DNA of All Life on Earth*, SCI. MAG. (Feb. 24, 2017), http://www.sciencemag.org/news/2017/02/biologists-propose-sequence-dna-all-life-earth.

[280] *Roadmap: Project Plan*, EARTH BIOGENOME PROJECT, https://www.earthbiogenome.org/roadmap (last visited Nov. 13, 2019).

[281] Lisa Howard, *Earth BioGenome Project Aims to Sequence DNA From All Complex Life,* U.C. DAVIS (Apr. 23, 2018), https://www.ucdavis.edu/news/earth-biogenome-project-aims-sequence-dna-all-complex-life.

[282] Fon Mathuros, *New Partnership Aims to Sequence Genomes of All Life on Earth, Unlock Nature's Value, Tackle Bio-Piracy and Habitat Loss*, WORLD ECON. F. (Jan. 23, 2018), https://www.weforum.org/press/2018/01/new-partnership-aims-to-sequence-genomes-of-all-life-on-earth-unlock-nature-s-value-tackle-bio-piracy-and-habitat-loss.

[283] Howard, *supra* note 281.

Chaired by Professor Harris Lewin of U.C. Davis and co-chaired by John Kress of the Smithsonian Institution and Gene Robinson of University of Illinois,[284] the leadership team of the EBP comprises interdisciplinary experts from the United States, United Kingdom, China, Germany, Korea, Australia, Chile, Canada, Norway, Spain, Denmark, and Brazil.[285] The Project is currently in its infancy but is expected to consist of a "global network of communities" that will contribute specimens and data to the EBP.[286] Sample collection, data generation, and analysis will begin in the eight countries of the Amazon basin,[287] which hosts 20-25 percent of the world's land-based biodiversity.[288] This will form something of a pilot project for the global rollout of the EBP in later years. The EBP has partnered with various scientific institutes that will conduct the sequencing, including BGI (formerly known as the "Beijing Genomics Institute") in China, the Wellcome Trust's Sanger Institute in the United Kingdom, and Rockefeller University's Genomic Resource Center in the U.S.[289] The sequence data generated from this first phase of the EBP in the Amazon will be stored in the Amazon Bank of Codes, itself a test platform to be trialed before the worldwide expansion of the EBP and the creation of the larger Earth Bank of Codes.

The EBP has also partnered with the Global Genome Biodiversity Network (GGBN), "the world's major resource of tissues and DNA from voucher specimens," and will also be working to coordinate the collation of data from other projects, "including the Vertebrate Genomes Project, the Global Invertebrate Genome Alliance, the 10,000 Plant Genomes Project, the 5000 Insect Genomes Project, and others."[290] That is, not all the genomic sequence data will be generated by the EBP itself, but there is a view to store as much data as possible in the Earth Bank of Codes. This is key to the EBP because the Bank of Codes is supposed to form a "global public good digital platform" that makes the genetic resource genomic data visible and usable by third parties, but where the "fair and equitable sharing of benefits is embedded in the design" of the platform:[291]

> It would support national governments and states in Amazon-basin countries to implement the Nagoya Protocol .... Importantly, the platform would represent a broad-based

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[284] *Leadership*, EARTH BIOGENOME PROJECT, https://www.earthbiogenome.org/ebp-leadership (last visited Nov. 13, 2019).
[285] *Participating Institutions*, EARTH BIOGENOME PROJECT, https://www.earthbiogenome.org/participating-institutions (last visited Nov. 13, 2019).
[286] Howard, *supra* note 281.
[287] World Economic Forum, *Juan Carlos Castilla-Rubio: Unlocking the Value of The Amazon*, YOUTUBE (Apr. 26, 2018), https://www.youtube.com/watch?v=QCQr9-3XFKk&feature=youtu.be (presentation given to the World Economic Forum in Davos, January 2018) [hereinafter Castilla-Rubio Youtube talk].
[288] EARTH BANK OF CODES, https://www.earthbankofcodes.org (last visited Nov. 13, 2019).
[289] *Sequencing the World*, *supra* note 170.
[290] Howard, *supra* note 281; *see* Pennisi, *supra* note 279.
[291] Castilla-Rubio Youtube talk, *supra* note 287.

> partnership between the Amazonian nations' biodiversity regulatory authorities and multistakeholder coalitions. By unlocking significant economic value from the Amazon basin, an inclusive bio-based economy is feasible for the first time in history.[292]

2. *Capacity Building and Access and Benefit Sharing*

One of the objectives of the collaboration is to create an "inclusive bio-economy"[293] that will support environmental conservation in many of the world's most biodiverse regions and address issues of biopiracy by distributing a portion of the benefits from the use of genetic sequence data back to the nations of origin. In this sense, the EBP and Earth Bank of Codes collaboration is not only supportive of the CBD and Nagoya Protocol—it also intends to use new computing technologies to influence how ABS is conducted into the future.[294]

Some of the physical samples for the EBP will be obtained from member institutes of the GGBN "which is compiling lists and images of specimens at museums and other biorepositories around the world."[295] This means that samples will be used in accordance with the GGBN standards and policies. "The [GGBN] standard requires that genetic samples provided for research by GGBN member institutions (i.e., nonhuman biological repositories) be associated with permitting and other legal information associated with access and benefit sharing."[296] The Smithsonian Institute will also be a valuable source for eukaryotic samples that can be genetically sequenced. These institutions, however, only house a small subset of the world's eukaryotic species and so the EBP will need to branch out and collect samples from nature. The samples would be obtained from participating partners and, interestingly, the Project "also plans to capitalize on the 'citizen scientist' movement to collect specimens."[297]

The EBP does plan to make ABS policy documents and agreements available online, although at the time of writing these "were currently under development."[298] It is clear from the Project's promotional materials that ABS issues lie at the very core of the EBP mission. The leadership team has stated that participants from around the world will have to comply with domestic ABS laws:

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[292] *Harnessing the Fourth Industrial Revolution for Life on Land*, WORLD ECON. F. 18 (2018), http://www3.weforum.org/docs/WEF_Harnessing_4IR_Life_on_Land.pdf.
[293] *Id.* at 15-16.
[294] *Id.* at 16.
[295] Pennisi, *supra* note 279.
[296] Harris A. Lewin et al., *Earth BioGenome Project*, 115 PROC. NAT'L ACAD. SCI. U.S. 4325, 4331 (2018).
[297] Howard, *supra* note 281; *see* Lewin et al., *supra* note 296, at 4329.
[298] *Cooperation Agreement Between FAPESP and the Earth Biogenome Project*, SAO PAULO RES. FOUND. (July 19, 2019), http://www.fapesp.br/en/13011.

> The EBP will adhere to the principles of the Nagoya Protocol by *(i)* requiring participants to comply with regulations on biodiversity use at the national level and *(ii)* using the established tools and resources on access and benefit sharing. Specifically, the EBP aims to provide fair, equitable, open, and rapid access to and sharing of the benefits of the eukaryotic genomes of planet Earth.[299]

Access to the territory to collect samples from participating countries is, however, still seen as a political challenge for the EBP to overcome,[300] and the leadership team acknowledges that the project could be delayed by interruptions to the sample-acquisition pipeline.[301] While there is substantial discussion about the regulation of data accessed from the Bank of Codes and how the benefits of the use of genetic sequence data will be distributed, there is much less discussion about whether the EBP intends to engage in benefit-sharing negotiations for access to the physical samples in order to generate the sequence data. This could be seen as the initial upstream use of the physical genetic resources by the EBP and its associates. There is little doubt that "[t]he EBP will comply with access and benefit sharing laws through partnerships with organizations, such as the Amazon Third Way Initiative and the Amazon Bank of Code."[302] It is just the case that it is not yet clear precisely how this will be achieved.

Downstream benefit-sharing by third-party users of the genetic sequence data is integrated into the design of the EBP and its Bank of Codes. The founder of the Amazon Bank of Codes, Juan Carlos Castilla-Rubio,[303] describes the database as "an open library of the Amazon's biological data (particularly DNA sequences)" which will "also track who does what with those data, and automatically distribute part of any commercial value that results from such activities to the country of origin."[304] This will be achieved using Blockchain, the technology that "underpins" cryptocurrencies like Bitcoin.[305]

With the introduction of Bitcoin in 2009, Blockchain technology and Bitcoin were essentially synonymous until the separation of Blockchain, or distributed ledger technology—distributed databases that maintain continuously growing lists of ordered records.[306] Today, this technology is becoming ubiquitous and is "used for all kinds of interorganizational cooperation."[307] Blockchain can be defined as a:

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[299] Lewin et al., *supra* note 296, at 4331.
[300] Ben Schiller, *How A Bank Of All The World's Genetic Codes Hopes To Save Nature*, FAST COMPANY (Feb. 28, 2018), https://www.fastcompany.com/40534363/how-a-bank-of-all-the-worlds-genetic-codes-hopes-to-save-nature.
[301] *See* Lewin et al., *supra* note 296, at 4329-30.
[302] Lewin et al., *supra* note 296, at 4333.
[303] Mathuros, *supra* note 282.
[304] *Sequencing the World*, *supra* note 170.
[305] *Id.*
[306] Vinay Gupta, *A Brief History of Blockchain*, HARV. BUS. REV. (Feb. 28, 2017), https://hbr.org/2017/02/a-brief-history-of-blockchain.
[307] *Id.*

> Distributed electronic ledger that uses cryptographic software algorithms to record and confirm immutable transactions and/or assets with reliability and anonymity. It has no central authority and allows for automated contracts that relate to those assets and transactions (smart contracts).[308]

Juan Carlos Castilla-Rubio from the World Economic Forum's Global Future Council on the Environment and Natural Resource Security[309] recognized the potential for this technology in creating a "bio-economy":

> By registering biological and biomimetic intellectual property (IP) assets on blockchain, this code bank will record the provenance, rights and obligations associated with nature's assets to track their provenance and use. When value is created from accessing these assets, smart contracts would facilitate the fair sharing of benefits to the custodians of nature and for its protection.[310]

Thus, the use of genetic sequence data by third parties that access that data from the (Amazon or Earth) Bank of Codes is tracked, providing a mechanism for originating nations to obtain benefits if the use of their data results in a market product or process. Indeed, the Bank of Codes system "can be employed to create 'smart contracts' that monitor and execute themselves."[311] In order for such a system to work, one assumes there would need to be a matrix of contracts: one set of legal agreements between the originator countries and the Bank of Codes, another between the Bank of Codes and individual third-party users (probably terms of use agreed to upon registering as a user of the Bank of Codes), and then the "smart contracts" that would represent a legal agreement between the third-party user and the country of origin, mediated by the Bank of Codes. The EBP has already engaged with governments, regulators, local communities, corporate organizations, and scientists to establish the attribution and benefit-sharing principles inherent in this system.[312] Clearly it is more complicated than a standard bilateral ABS agreement, but the transaction costs absorbed by the establishment of the Bank of Codes would reduce the barrier to entry for potential (academic and commercial) users, giving them legal clarity about the terms of use and negating the need for them to enter into protracted bilateral ABS negotiations themselves. Reducing such barriers could go a long way to finally making ABS a financially viable mechanism to capture benefits for the providers of genetic resources.

3. *Implications for Large-Scale Biological Projects*

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[308] *Harnessing the Fourth Industrial Revolution for Life on Land*, *supra* note 292, at 16.
[309] Mathuros, *supra* note 282.
[310] *Harnessing the Fourth Industrial Revolution for Life on Land*, *supra* note 292, at 16.
[311] *Sequencing the World*, *supra* note 170.
[312] Castilla-Rubio Youtube talk, *supra* note 287.

Like the Micro B3 project, the EBP is noteworthy for its embrace of the ABS objectives of the CBD and Nagoya Protocol. Where the EBP differs is in its collaboration with the Amazon Bank of Codes, which not only respects ABS requirements but also intends to track the use of resources and automatically executes benefit-sharing agreements. This is something the collaboration hopes to take to the Conference of the Parties to the CBD in 2020, with a view to "help redraw several components of the CBD itself."[313] The EBP will not only comply with ABS regulations, it could potentially shape the way ABS is conducted in the future.[314] A report published in the Proceedings of the National Academy of Sciences concludes that "the economic impact of the EBP is likely to be very large and globally distributed."[315]

Past biological research projects often treated ABS regulations as an afterthought, an obstacle that has to be overcome in order to conduct the important work of the project. The EBP is significant, as it has ABS at the very core of what it wants to achieve: "A goal of the EBP is to globalize its activities through novel partnerships that build scientific capacity in developing countries, including the capacity to utilize, not just create, a legacy resource."[316]

The implementation of technology may make some of the aspirational goals of the CBD and Nagoya Protocol more practical. The World Economic Forum rightly noted that the "[h]uman capacity to capture, store and process data has been transformed to a degree impossible to conceive at the time of the Rio Summit."[317] While the operational details are still unclear, technologies like Blockchain hold real potential to transform the ABS landscape, making what has been a very flawed concept more workable. In particular, it has the potential to deal with some of the issues surrounding the use of the intangible aspects of genetic resources that includes data, information, and traditional knowledge. Regulating the transboundary movement of physical biological samples has proven exceptionally difficult and inefficient, and there are additional problems associated with the movement and use of data and information. Without a radical redesign of the default bilateral transactional ABS model that has thus far proven ineffective as a wealth redistribution device and as an environmental conservation mechanism, the international community may have to rely on technological solutions to the ABS problem.

One of the main ABS problems that the Bank of Codes could solve is determining what is considered non-commercial versus commercial utilization of genetic resources. Quite often it is unfeasible to determine whether the use of a genetic resource (or in this case, its sequence data) will result in a commercial product. By tracing the inputs to research and development (or at the very least, monitoring the users who are likely to create commercial outputs), there is a

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[313] *Harnessing the Fourth Industrial Revolution for Life on Land, supra* note 292, at 16.

[314] There is great potential for these technologies to assist with ABS, but they are unlikely to resolve some of the more conceptual or political issues of ABS.

[315] Lewin et al., *supra* note 296, at 4332.

[316] *Id.* at 4329.

[317] *Harnessing the Fourth Industrial Revolution for Life on Land, supra* note 292, at 11.

greater likelihood of detecting when monetary benefits are generated and ought to be distributed to provider nations. The World Intellectual Property Organization (WIPO) has been considering mandatory disclosure of the country of origin on patent applications that could also address this problem since the early 2000s.[318] The country of origin disclosure on patent applications would have the added benefit of capturing the use of physical genetic resources and any sequence data that happened to be accessed outside the proposed Bank of Codes. However, the advantage offered by technological solutions like the Bank of Codes is that the system does not rely on the honesty of patent applicants at the downstream end of the innovation process. Rather, users are registered at the upstream stages where there are not yet as many vested interests in maximizing far-off profits.

This is not to say that regulatory technologies hold all of the answers. There are still major problems associated with ABS that cannot be fixed by Blockchain and similar ledger technologies. The Blockchain approach does not yet track the use of physical samples of genetic resources. There are undoubtedly ways to integrate this Bank of Codes approach to include physical biobanks, however, the Bank of Codes is still just a concept: it has not yet been created or tested. There are many ways to share data outside of the Bank of Codes system; digital sequence information which is represented as just a string of characters ('A', 'G', 'C' and 'T's), can easily be emailed to people who have not registered with the Bank of Codes. There is also the issue of convergent and divergent evolution: many genes have similar structures across different species, so if there is a sequence of interest in the Bank of Codes, there is very likely a similar one available elsewhere (published on the openly accessible GenBank database, for instance) that is not associated with terms of use.

The objective of fair and equitable benefit sharing within the CBD and Nagoya Protocol were a response to the exploitative research and development practices of technologically advanced countries utilizing the genetic resources of biodiverse low- and middle-income countries. As a result, large-scale biogenomic projects are, to a large extent, starting to incorporate these equity imperatives in the design of their projects. This is not to say that the problems that the CBD and Nagoya Protocol sought to address have been resolved, that the mechanism of choice - access and benefit sharing - has been entirely successful, nor that the power imbalances that were once pervasive in international scientific collaborations have disappeared completely. However, it does demonstrate that these large-scale international projects and the scientists at their helm recognize the requirement and inherent value of sharing the benefits of scientific research and development with countries of origin and helping to build capacity for future scientific efforts in those nations.

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[318] *See generally Key Questions on Patent Disclosure Requirements for Genetic Resources and Traditional Knowledge*, WORLD INTELL. PROP. ORG. (2017), https://www.wipo.int/edocs/pubdocs/en/wipo_pub_1047.pdf (explaining history of WIPO consideration of whether and how to require disclosure of TK in patent applications).

IV. CONCLUSION

International research collaborations in the life sciences have unlocked critical innovations toward the benefit of human health and welfare. The rapid proliferation of genetic sequencing technologies, big-data analytics, and awareness of the wealth located in the earth's biodiversity are opening significant, global opportunities for these innovations to be realized ever more quickly with even greater impact on humanity. Contemporaneously with these movements in technology, national and international law have moved to ensure that past disparities in the exploitation of natural resources are not repeated and that the basic human needs of the earth's population are fairly addressed.

These are all issues for which the fixes may also be technological, but there are also the more vexing justice issues of ABS that have been in question for decades. For instance, who decides what is "fair and equitable" when it comes to attribution and benefit-sharing? How do users ensure that indigenous peoples and local communities are receiving a fair share of the benefits when ABS is negotiated with the governments of States Parties and not the indigenous communities themselves? How is the share of benefits attributed if there are multiple jurisdictions in which a gene of interest naturally occurs? These are questions of value that regulatory technologies cannot address. They will require good old-fashioned diplomacy and slow-going compromise through international forums. Twenty-five years after the introduction of the CBD, we are still grappling with many of the same issues of equity and justice that the CBD was an attempt to address.

This Article has endeavored to analyze how international law is shaping these currents and how notions of fairness have emerged to shape where investments in research should be ethically made. The analysis of global biogenomic enterprises herein has focused on how genetic resources are collected and studied, and how projects may proceed through the changing legal landscape of ABS. The early evidence is that these projects not only integrate the transfer of knowledge and technology as an inherent objective, but also have made explicit plans for the sharing of benefits arising from the utilization of genetic resources.