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Sam Halabi

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INTRODUCTION

Access to biological samples is crucial to the research and development process that leads to diagnostics, therapeutics, and vaccines to address new and reemerging infectious diseases.[1] Biological samples provide raw data about the pathogen, allow researchers to analyze the evolution of the pathogen, and to understand the mechanisms of replication and infection. Comprehensive understanding of human pathogens is the important first step toward developing effective treatments and vaccines. However, access to biological samples has become an increasingly substantial barrier to this essential step in the research and development process.[2]

Researchers at major institutions across the United States reported difficulty in obtaining any samples of the Ebola virus during the 2014-15 outbreak and even those that did obtain samples reported difficulties obtaining fresh samples thereafter to identify mutations in the virus as it

[*] Fulbright Canada Research Chair in Health Law, Policy, and Ethics at the University of Ottawa, Ontario; Associate Professor of Law at the University of Missouri–Columbia; Scholar at the O'Neill Institute for National and Global Health Law at Georgetown University. JD Harvard, MPhil Oxford (St. Antony's College), BA, BS, Kansas State University. The author thanks Jennifer Carter-Johnson, Yaniv Heled, Ana Santos Rutschman, Josh Sarnoff, Andrew Torrance, and Liza Vertinksky for helpful comments as well as Cynthia Ho, Jordan Paradise and the faculty and student organizers of the 2018 Wiet Life Sciences Symposium at Loyola University Chicago School of Law. The author also thanks the *Annals of Health Law and Life Sciences* editorial staff, including Jan Dervish, Jessica Fenton, Mary Hannosh, Loxley Keala, Bella Massini, John Meyer, Kara Simon, Jessica Sweeb, and Kaleigh Ward.

1. *See* Ivan Branković, Jelena Malogajski & Servaas A. Mooré, *Biobanking and translation of human genetics and genomics for infectious diseases,* 3 APPLIED & TRANSLATIONAL GENOMICS 30, 30-31 (2014) (discussing the role of "biobanks" in research and development related to infectious disease, including diagnosis and therapeutics); *see also* Anthony S. Fauci, *New and Reemerging Diseases: The Importance of Biomedical Research*, 4 EMERGING INFECTIOUS DISEASES 374, 374 (1998) (discussing the importance of investing in research on vaccines to prevent new and reemerging diseases).

2. Stacey Pereira, *Motivations and Barriers to Sharing Biological Samples: A Case Study*, 3 J. OF PERSONALIZED MED. 102, 102 (2013).

spread.[3] Researchers similarly encountered difficulties accessing adequate samples and disease data about the Zika virus, largely due to Brazilian law affecting material transfer.[4] As a result of Indonesia's 2006 refusal to share H5N1 virus samples with the World Health Organization's (WHO) Global Influenza Surveillance and Response System (GISRS) pending equitable access to benefits, including intellectual property rights, researchers at academic institutions and biomedical firms must now enter into material transfer agreements (MTAs) with the WHO in exchange for access to potentially pandemic strains of influenza.[5] Potential legal claims asserted by the Saudi government over the Middle East Respiratory Syndrome coronavirus (MERS-CoV) pervade ongoing research into antiviral and vaccine research against the virus.[6]

Access to biological samples, including human pathogens, is becoming more difficult while predictive analytics suggest that the next major infectious disease threat is likely to originate in the tropical zone where the above-mentioned countries lie, as well as many others (Fig. 1).[7] Joint ventures and collaborations between scientists in biodiverse but resource-scarce countries in Africa, Asia, and South America are growing in importance to the identification, sampling, biobanking, and research of potentially human pathogenic viruses. These collaborations are crucial to the detection, prevention, and response to infectious disease threats.

3. Julie Steenhuysen, *U.S. Ebola Researchers Plead for Ebola Virus Samples,* REUTERS (Nov. 5, 2014 6:05 AM), http://www.reuters.com/article/us-health-ebola-usa-research-exclusive-idUSKBN0IP1DZ20141105.

4. Associated Press, *Few Zika Samples are Being Shared by Brazil, Worrying International Researchers*, STATNEWS (last updated Feb. 4, 2016 12:19 PM), https://www.statnews.com/2016/02/03/zika-samples-brazil/.

5. David P. Fidler, *Influenza Virus Samples, International Law, and Global Health Diplomacy*, 14 EMERGING INFECTIOUS DISEASES 88, 88-89 (2008); *see also* Michelle Rourke, *On the Origin of Samples: Pathogen Provenance and the Rise of the Material Transfer Agreement*, 3 J. SCI. L. 1, 2 (2017).

6. Laurie Garrett, *Why a Saudi Virus is Spreading Alarm*, COUNCIL FOREIGN REL. (May 29, 2013), https://www.cfr.org/expert-brief/why-saudi-virus-spreading-alarm.

7. Kate E. Jones et al., *Global Trends in Emerging Infectious Diseases*, 451 NATURE 990, 993 (2008).

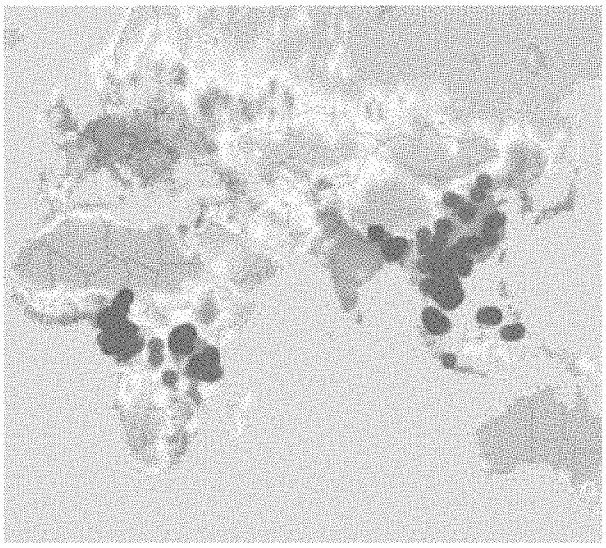

Fig. 1. **Global Distribution of Relative Risk of an Emerging Infectious Disease Event** as adapted from Jones, Patel, et. al., Global Trends in Emerging Infectious Diseases. Nature 451, 990-993. 21 February 2008.

Fig. 1 Legend
Green: No to low risk
Yellow: Medium risk
Red: High risk

A principal reason that access to biological samples has declined in these contexts is the ascendance of the MTA as the medium of transfer, especially between researchers (academic, commercial, non-profit) in different countries.[8] Surveys and interview-based studies of researchers have concluded that access to biological samples is increasingly hampered by negotiations over MTAs.[9] MTAs are instruments that define terms and provisions in connection with the transfer of materials for multiple purposes including safekeeping, storing (for instance, storage in gene banks), protecting intellectual property rights, prohibiting sharing with third or other downstream parties, and attributing credit in peer-reviewed journals.[10] MTAs are contracts protected by law. If one of their provisions is not followed, the contract is breached and the wronged party has the right to bring action against the other, including a suit for damages.

While MTAs originated when the distinction between upstream research conducted in noncommercial laboratories and academic institutions and

8. Tania Bubela, Jenilee Guebert & Amrita Mishra, *Use and Misuse of Material Transfer Agreements: Lessons in Proportionality from Research, Repositories, and Litigation*. 13 PLOS BIOLOGY (2015).

9. Victor Rodriguez, *Material Transfer Agreements: Open Science vs. Proprietary Claims*, 23 NATURE BIOTECHNOLOGY 489, 489 (2005).

10. Bubela, Guebert & Mishra, *supra* note 8; *see also* ALAN B. BENNETT, WENDY D. STREITZ & RAFAEL A. GACEL, *Specific Issues with Material Transfer Agreements, in* INTELLECTUAL PROP. MGMT. IN HEALTH AND AGRIC. INNOVATION: A HANDBOOK OF BEST PRACTICES, 697-99 (A. Krattiger, et al. eds., 2007).

downstream applied research was sharper, they are now commonplace.[11] MTAs "may take a variety of forms, from letters accompanying a shipment of materials to detailed and formally negotiated contracts signed by both parties before a transfer of materials is made in or out of research units."[12] Outbound agreements often include asserted intellectual property rights to the material in question, whereas terms in inbound agreements may "impose research restrictions that infringe upon academic freedom or dissemination of research results, and may conflict with specific requirements of funding agreements."[13]

This article analyzes the substantial changes under way in the global system for infectious disease research demonstrated by the changing practices in negotiating MTAs. Instead of the open system of sharing bacterial and viral human pathogens that characterized the research system for much of the 20th Century, notions of "viral sovereignty," access contingent upon provisions like sharing research benefits, and acrimonious negotiations, are far more common.[14] The increasing barriers to the flow of research material and related data like genetic sequencing information are posing threats to public health responses and the potential use of such resources in diagnostic, therapeutic, and vaccine innovations.[15] This article assesses the extent of these barriers and proposes approaches that may address the global inequalities behind material transfer negotiation issues.

This article proceeds as follows: Part II provides a brief history of the human pathogen sharing system that existed prior to the movement for sovereignty over biological resources that commenced in the 1970s. That

11. *See Commission Staff Working Document Impact Assessment Accompanying the Document Proposal for a Regulation of the European Parliament and of the Council on Access to Genetic Resources and the Fair Sharing of Benefits Arising from their Utilization in the Union*, SWD (2012) 292 final (Apr. 10, 2012), https://eur-lex.europa.eu/legal-content/CS/ALL/?uri=CELEX:52012SC0292 ("Genetic resources, and sometimes also associated traditional knowledge, are of diverse importance across and within sectors, be it for commercial or non-commercial activities. Analytically, it is useful to distinguish between activities and players at the beginning of the genetic resources value chain ("upstream") and activities and players at its end ("downstream"). Those involved in "upstream" activities (collecting in the wild, description of collected material, storing in collections) face many common challenges in relation to access and benefit-sharing, the same goes for those involved in "downstream" activities (basic and applied research, product development and commercialization)."

12. Rodriguez, *supra* note 9, at 489.

13. Rodriguez, *supra* note 9, at 489.

14. J. Benjamin Hurlbut, *A Science That Knows No Country: Pandemic Preparedness, Global Risk, Sovereign Science*, BIG DATA & SOCIETY 1, 5-6 (2017); *see also* David P. Fidler, *Asia's Participation in Global Health Diplomacy and Global Health Governance*, 5 ASIAN J. WTO INT'L HEALTH L. POL'Y 269, 287 (2010).

15. Carolina dos S. Ribeiro et al., *How Ownership Rights Over Microorganisms Affect Infectious Disease Control and Innovation: A Root-Cause Analysis of Barriers to Data Sharing as Experienced by Key Stakeholders*, 13 PLOS ONE 1, 3 (2018).

system involved various means by which researchers, especially in Europe and North America, obtained pathogen samples from low- and middle-income countries as well as some *sui generis* systems like the WHO's system for influenza sample sharing and research.[16] Part III explains how the 1993 Convention on Biological Diversity, the 2010 Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization, and the 2011 WHO Pandemic Influenza Preparedness Framework shifted the system from one in which pathogens and other biological materials traveled essentially unregulated to one in which MTAs negotiated by governments and firms, but rarely researchers themselves, prevail. Part IV analyzes the disruptions the current regulatory system causes to the biomedical research system that leads to diagnostics, therapeutics, and vaccines. Part V provides a brief conclusion.

II. THE HISTORY OF HUMAN PATHOGEN SHARING

The free flow of biological resources, including pathogens, and the knowledge generated by those studying them, has resulted in some of the most important diagnostics, therapeutics, and vaccines that have saved billions of lives worldwide.[17] Since the 1950s, WHO's Global Influenza Surveillance and Response System (formerly Global Influenza Surveillance Network) has connected influenza samples from all over the world to reference laboratories, researchers, and vaccine manufacturers.[18] This connection has generated seasonal and pandemic flu vaccines that have saved hundreds of thousands of lives.[19] The transfer of Human Immunodeficiency Virus (HIV) mostly from west-central Africa has been crucial to the development of antiretroviral therapies that have drastically reduced its public health burden.[20] Similarly, the transfer of thousands of Ebola samples

16. *See generally Global Influenza Surveillance and Response System (GISRS)*, WORLD HEALTH ORG. (2015), http://www.who.int/csr/disease/OP_GISRS_FINAL.pdf [hereinafter *GISRS*].

17. Petra Klepac et al., *Towards the Endgame and Beyond: Complexities and Challenges for the Elimination of Infectious Diseases*, 368 PHIL. TRANSACTIONS ROYAL SOC'Y B: BIOLOGICAL SCI. 1, 1 (2013) ("Successful control measures have interrupted the local transmission of human infectious diseases such as measles, malaria and polio, and saved and improved billions of lives.").

18. *GISRS*, *supra* note 16.

19. *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/news/flu-vaccine-saved-lives.htm; *see also* Liz Szabo, *CDC: Vaccines Save Hundreds of Thousands of Lives*, USA TODAY (Apr. 24, 2014 1:00PM) https://www.usatoday.com/story/news/nation/2014/04/24/cdc-vaccine-benefits/8094789/.

20. *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, 2494 (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

out of Guinea, Liberia, and Sierra Leone during the 2014-15 outbreak led to the first rapid diagnostic for Ebola, several promising pharmaceutical candidates, and a vaccine that has demonstrated 100 percent protection against the virus.[21]

However, like most extractive and enterprising activities undertaken in low- and middle-income countries, the flow of biological resources including pathogens, results in benefits mostly enjoyed in wealthier countries.[22] Because life as a general matter (including seeds, plants for agriculture, and other biological resources) was viewed as the "common heritage" of humanity over most of the twentieth century, there were few barriers to researchers, firms, or foreign governments transferring biological resources out of poorer countries for purposes of research and development in wealthier countries.[23] Within the scientific community, this large-scale transfer occurred through what Patricia Garcia of the Universidad Peruana Cayetano Heredia calls three "semi-colonial" models: "postal", "parachute" and annexed sites.[24]

A. Postal Acquisition

The scientific process relies upon independent verification of results, sharing of data and other resources, and attributing contributions that advance human knowledge to scientific researchers. As a result, researchers often develop sharing and reciprocity norms that encourage scientists in low- and middle-income countries to share samples and related data with colleagues in wealthier countries with more advanced laboratory and technical capabilities.[25]

Under this model, researchers in wealthy countries request biological

(2010).

21. Ana Maria Henao-Restrepo, et al., *Efficacy and Effectiveness of an rVSV-vectored Vaccine Expressing Ebola Surface Glycoprotein: Interim Results from the Guinea Ring Vaccination Cluster-Randomised Trial*, 386 LANCET 857, 857 (2015).

22. *See generally* Ciara Staunton & Keymanthrj Moodley, *Data Mining and Biological Sample Exportation from South Africa: A New Wave of Bioexploitation Under the Guise of Clinical Care?,* 106 SOUTH AFRICAN MED. J. 136, 138 (2016) ("For decades there has been a unidirectional flow of samples out of Africa to various destinations in developed countries, with no benefit to local populations or local researchers.").

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

24. Patricia Garcia, Presentation for Salud Global, International Partnerships: View from the South. . . (last visited Oct. 11, 2018) (unpublished presentation, Universidad Peruana Cayetano Heredia).

25. *See generally* Kayvon Modjarrad et al., *Developing Global Norms for Sharing Data and Results during Public Health Emergencies*, 13 PLOS MED. 1, 2 (2016) (referencing the World Health Organization's consultation in Geneva, Switzerland in September 2015 to advance the developing of data sharing norms).

samples from colleagues in low- or middle-income countries, sometimes with the understanding that some other resource or knowledge will be shared.[26] Indeed, this is precisely how samples of the MERS-CoV virus were transferred to the Erasmus Medical Center in the Netherlands in 2012.[27] Ali Mohamed Zaki, an Egyptian physician working in Saudi Arabia, contacted scientists at Erasmus for technical help after he suspected that a novel virus caused the severe respiratory symptoms, renal failure, and death of a patient.[28] According to Zaki:

> [Erasmus] confirmed 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*.[29]

Dr. Zaki's experience is representative, and, but for the legal changes identified in this article, similar experiences would have continued, given that new technologies are making the transfer of biological materials across borders easier and more reliable.[30] There were millions of such transfers over the course of the 20th Century.[31] As discussed in Part III below, the transfer of MERS-CoV in this way occurred after the major changes in international law were implemented, and the result significantly delayed the response after MERS affected South Korea, as did the continued disputes between the Kingdom of Saudi Arabia and those that were developing diagnostics, therapeutics, and vaccines based on samples sent to Erasmus.[32]

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26. Garcia, *supra* note 24.

27. Clare Dyer & Owen Dyer, *WHO to Probe Claims that Dutch Scientists Restricted Access to Novel Coronavirus*, 346 BMJ 1, 1 (2013).

28. 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.

29. *Id.*

30. Maryam Shabikhani et al., *The Procurement, Storage, and Quality Assurance of Frozen Blood and Tissue Biospecimens in Pathology, Biorepository, and Biobank Settings*, 47 CLINICAL BIOCHEMISTRY 258, 258-66 (2014).

31. Jimmie B. Vaught, et al., *Biospecimens and Biorepositories: From Afterthought to Science*, 21 CANCER EPIDEMIOL BIOMARKERS & PREVENTION 253, 253 (2012).

32. *See* Myoung-don Oh et al., *Middle East Respiratory Syndrome: What We Learned from the 2015 Outbreak in the Republic of Korea*, 33 S. KOR. J. INTERNAL MED. 233, 234 (2018) (stating that the MERS-CoV epidemic "lasted for two months" and resulted in the quarantine of over 16,000 individuals for 14 days).

B. Parachute Acquisition

Parachute acquisition refers to the collection of biological samples in a country by a foreign researcher who later returns to his or her home country to conduct research on the collected samples.[33] This form of collection can be extremely difficult to detect because using natural resources for their genetic components requires a minute quantity of genetic material.[34] For example, in the early 2000s, French researchers conducted interviews in Brazil and French Guiana to find out about local antimalarial remedies, including those derived from the indigenous *Quassia amara* shrub.[35] In 2005, that preliminary research was published.[36] Ten years later, a patent was granted for a new compound from the *Quassia amara* which had antimalarial properties.[37] Parachute acquisition is the kind of transfer now viewed broadly as "biopiracy" by low- and middle-income countries.[38] Its practice resulted in some of the measures that now encourage MTAs to govern the terms under which samples are transferred out of the host country's territory.[39]

Many low- and middle-income countries argue that there is a "unidirectional flow of samples" out of developing countries and into developed nations for both commercial and non-commercial research and development.[40] These countries argue that this flow has "impacted negatively on the development of local capacity, infrastructure and expertise" of the originating countries.[41] As a result, many countries now require foreign researchers to establish a collaboration with local researchers before obtaining local samples.[42]

C. Annexed Research Sites for the Collection of New Samples

The use of annexed research sites in the provider country is another method for obtaining local genetic resources.[43] This means that samples of genetic resources are collected locally, and that at least part of the research

33. Garcia, *supra* note 24, at 4.
34. Florian Rabitz, *Biopiracy after the Nagoya Protocol: Problem Structure, Regime Design and Implementation Challenges*, 9 BRAZ.POL. SCI. REV. 30, 38 (2015).
35. 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.
36. *Id.*
37. *Id.*
38. *Id.*
39. Daniel F. Robinson, *Locating Biopiracy: Geographically and Culturally Situated Knowledges*, 42 ENV'T & PLAN. 38, 47 (2010).
40. Staunton & Moodley, *supra* note 22, at 136.
41. Staunton & Moodley, *supra* note 22, at 136.
42. Staunton & Moodley, *supra* note 22, at 136-37.
43. Garcia, *supra* note 24, at 4.

on these genetic resources is conducted within the host country.[44] This can be done by foreign or local researchers. Annexed research sites that are funded, developed, and operated by foreign nationals without the participation of the originator country have the same effect as postal and parachute acquisitions of biological resources and related knowledge.[45]

On the other hand, annexed research may also 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.[46] 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.[47] Brazil, for example, requires foreign researchers to register with a local partner before commencing research activities.[48] These measures can help facilitate technology and information flow to poorer countries, but they also add a significant layer of bureaucracy and delay to the research process.

D. Global Influenza Pathogen Sharing

Over the many decades in which biological resources flowed from low- and middle-income countries for research and development in richer ones, there accompanied specific, international systems that addressed matters of particular concern to the international community. WHO's GISRS facilitates the collection and transfer of influenza samples from all over the world.[49] As a result of the Spanish influenza pandemic of 1918-19, which killed approximately three percent of the world's population and threatens to recur because of the virus's capacity to reassort,[50] WHO established GISRS after World War II.[51] The system "monitor[s] the evolution of influenza viruses and provides recommendations as to which candidate vaccine viruses should be included in seasonal and pandemic vaccines".[52] The system is structured around six WHO collaborating centers located in Australia, China, Japan, the

44. Garcia, *supra* note 24, at 4.
45. Garcia, *supra* note 24, at 4–5.
46. Garcia, *supra* note 24, at 17-18.
47. David Smith et al., *Explanation of the Nagoya Protocol on Access and Benefit Sharing and Its Implication for Microbiology*, 163 MICROBIOLOGY 289, 290 (2017).
48. *Id.* at 294.
49. *Self-Assessment of the Who Global Influenza Surveillance and Response System*, WORLD HEALTH ORG. 1, 6 (Oct. 2014), http://www.who.int/influenza/pip/virus_sharing/gisrs_self_assessment.pdf [hereinafter *Self-Assessment*].
50. SAM F. HALABI & JOHN MONOAHAN, FOOD AND DRUG REGULATION IN AN ERA OF GLOBALIZED MARKETS 64 (Sam F. Halabi ed. 2015).
51. *GISRS*, *supra* note 16.
52. *Self-Assessment*, *supra* note 49, at 6.

U.K. and the U.S., "four WHO essential resource laboratories, and 141 institutions recognized by WHO as national influenza centers (NICs) located in 111 countries."[53] NICs "collect clinical specimens for the detection of influenza viruses through national surveillance networks".[54] Until 2006, this system regularly collected influenza samples from around the world, distributed them to collaborating centers, and shared them with non-profit and for-profit actors to develop vaccines and antivirals.[55] In 2006 and 2007, Indonesia refused to share samples of H5N1, arguing the system took resources from poor countries to develop products that largely benefited populations in wealthy countries.[56] Its refusal threatened to up-end the global system of influenza surveillance and research that had existed for over 50 years.[57]

III. THE TRANSITION FROM UNENCUMBERED SHARING TO MATERIAL TRANSFER AGREEMENTS

Indonesia's position reflected the predictable course of a long-running dispute over distribution of wealth between wealthy and poorer countries. The latter countries regarded past and continuing exploitation by the former powers, or their corporate instrumentalities, as the basic reason for their poverty.[58] These sentiments justified some of the major redistributions, mostly in the form of nationalization, over the course of the 1950s, 1960s, and 1970s.[59]

A. The Path to Access and Benefit Sharing Material Transfer Agreements for Human Pathogens: The Convention on Biological Diversity and the Nagoya Protocol

In 1964, developing countries formed the United Nations Conference on Trade and Development (UNCTAD) in order to pursue trade-related development policies marginalized by what had become the trade negotiation forum for wealthy countries, the General Agreement on Tariffs and Trade

53. *Self-Assessment*, *supra* note 49, at 6, 16.

54. *Self-Assessment*, *supra* note 49, at 6.

55. *Operational Guidance on Sharing Seasonal Influenza viruses with WHO Collaborating Centers (CCs) under the Global Influenza Surveillance and Response System (GISRS)*, WORLD HEALTH ORG., 1, 4 (2007), http://www.who.int/influenza/gisrs_laboratory/national_influenza_centres/NIC_virus_sharing_guidance_20171103.pdf; Fidler, *supra* note 5, at 88.

56. Fidler, *supra* note 5, at 88.

57. Fidler, *supra* note 5, at 88.

58. DANIEL YERGIN & JOSEPH STANISLAW, THE COMMANDING HEIGHTS: THE BATTLE BETWEEN GOVERNMENT AND THE MARKETPLACE THAT IS REMAKING THE MODERN WORLD 88-90 (1998).

59. Guiliano Garavini, *Completing Decolonization: The 1973 'Oil Shock' and the Struggle for Economic Rights,* 33 INT'L HIST. REV. 473, 473-79 (2011).

(GATT).[60] 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 an equitable basis."[61] Shortly after its formation, UNCTAD began to focus on technology transfer as a crucial aspect of redistributing wealth.[62]

By the early 1970s, despite UNCTAD, nationalization, and the declaration that wealthy countries would help improve poorer countries, the relative position of developing countries compared to developed countries had barely narrowed, and for many, their absolute position had worsened.[63] As a result, developing countries became more aggressive in their calls for policies aimed at redistribution.[64] On April 19, 1972, Mexican President Luis Echeverria Alvarez urged the adoption of a Charter of Economic Rights and Duties of States aimed at exerting greater authority over natural resources.[65] At the time, those resources were thought to be mostly commodities like petroleum, rubber, and agricultural goods.[66] However, the general call for control over natural resources later expanded in the early 1990s to include human pathogens.[67]

In 1972, the U.N. also held the first of many global conferences on the Human Environment in Stockholm, Sweden.[68] In the decade after the 1972 conference, scientists and non-governmental organizations had elevated the issue of biodiversity as a pressing environmental issue.[69] The threats to the rainforests in the Amazon basin – logging, extraction, agriculture – illustrated the rapid loss of crucial biological resources, as well as the role that firms

60. John Toye, *UNCTAD at 50: A Short History*, UNCTAD 1, 3-4, 14 (2014), https://unctad.org/en/PublicationsLibrary/osg2014d1_en.pdf.

61. United Nations, *UNCTAD In Brief*, UNCTAD 1, 2 (2016), https://unctad.org/en/Docs/edmmisc17rev1_en.pdf.

62. United Nations, *Proceedings of the United Nations Conference on Trade and Development*, 227, U.N. DOC. TD 1, 97 (1968), http://unctad.org/en/Docs/td97vol1_en.pdf [hereinafter UNCTAD]; *see also* PETER DRAHOS, THE GLOBAL GOVERNANCE OF KNOWLEDGE: PATENT OFFICES AND THEIR CLIENTS 23 (2010).

63. 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. LAW. 295, 296 (1975).

64. *Id.*

65. *Id.*

66. UNCTAD, *supra* note 62, at 116-119.

67. Johnathon B. Tucker, *Biosecurity: Limiting Terrorist Access to Deadly Pathogens*, UNITED STATES INSTITUTE OF PEACE 27 (2003), https://www.usip.org/sites/default/files/pwks52.pdf.

68. *United Nations Conference on the Human Environment*, UNITED NATIONS, https://sustainabledevelopment.un.org/milestones/humanenvironment (last visited October 8, 2018).

69. 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.

played in that loss.[70] In 1987, the governing council of UNEP resolved to create a working group to explore the possibility of developing a legally binding treaty to protect biological resources.[71] In 1991, formal multilateral negotiations began on a Convention for Biological Diversity.[72]

Eventually these preparatory meetings culminated in the 1992 UN Conference on Environment and Development (or "Earth Summit"), held in June 1992 in Rio De Janeiro, the result of which included the Rio Declaration, the Convention on Biological Diversity (CBD), the U.N. Framework Convention on Climate Change, and the U.N. Convention to Combat Desertification.[73] The CBD traced a direct line to the 1962 United Nations General Assembly's 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".[74]

Article 15 of the CBD required "fair and equitable sharing of 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.[75] 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.[76] The Bonn Guidelines recommended the following provisions for contracts

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70. *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 and 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).

71. U.N. GAOR, 42ND SESS., 96TH PLEN. MTG.139, U.N. Doc. UNEP/GC.14/17 annex III (1987), http://www.un.org/en/ga/search/view_doc.asp?symbol=A/RES/42/184.

72. *History of the Convention*, CONVENTION ON BIOLOGICAL DIVERSITY, https://www.cbd.int/history/default.shtml (last visited Oct. 11, 2018).

73. *The Rio Conventions*, CONVENTION ON BIOLOGICAL DIVERSITY, https://www.cbd.int/rio/ (last visited Oct. 11, 2018); *see generally* Rep. of the U.N. Conference on Env't and Dev., Rio Declaration on Environment and Development, A/CONF.151/26, Vol. 1(1992) http://www.un.org/documents/ga/conf151/aconf15126-1annex1.htm.

74. U.N. GAOR, 17TH SESS., 1194TH PLEN. MTG. 15, U.N. Doc. A/5127 (1962), https://documents-dds-ny.un.org/doc/RESOLUTION/GEN/NR0/193/11/PDF/NR019311.pdf?OpenElement.

75. *Article 15. Access to Genetic Resources,* CONVENTION ON BIOLOGICAL DIVERSITY, https://www.cbd.int/convention/articles/default.shtml?a=cbd-15 (last visited Oct. 11, 2018); *see also generally* Thomas A. Kursar, *What Are the Implications of the Nagoya Protocol for Research on Biodiversity*? 61 BIOSCIENCE 256-57 (2011) (discussing the imperfect implementation of CBD in an attempt to improve biodiversity).

76. UNCTAD, *The Convention on Biodiversity and the Nagoya Protocol: Intellectual Property Implications*, UNCTAD 11 (2014), https://unctad.org/en/PublicationsLibrary/diaepcb2014d3_en.pdf.

between sovereign states and commercial 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;
>
> (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.[77]
>
> The CBD thus paved the way for the transfer of biological resources to take place through MTAs, often regulated by governments, rather than through informal sharing through scientific networks.

B. Bioprospecting after the Convention for Biological Diversity

In 1991, informed by the CBD negotiations, U.S. pharmaceutical firm Merck entered into an agreement with the government of Costa Rica.[78] Under that agreement, the National Biodiversity Institute ("INBio"), a non-profit scientific organization created by the government of Costa Rica, provided 10,000 samples of plants, animals, and soil to Merck.[79] Merck enjoyed the exclusive rights to study these samples for two years, and retained the patent rights on drugs developed using the samples.[80] In return, Merck agreed to pay INBio $1 million and to transfer $130,000 worth of laboratory equipment.[81] The agreement also specified royalties to be paid to the Costa Rican government's Ministry of Natural Resources.[82]

Another agreement pertaining to bioprospecting is the agreement executed between ICBG (International Cooperative Biodiversity Group, a U.S. governmental venture) and Bristol-Myers Squibb, Monsanto, and Glaxo

77. KATHARINA ROGALLA VON BIEBERSTEIN & KONSTANTIA KOUTOUKI, THE NAGOYA PROTOCOL: STATUS OF INDIGENOUS AND LOCAL COMMUNITIES 8 (2011)

78. Andrew W. Torrance, *Bioprospecting and the Convention on Biological Diversity*, HARVARD LAW SCHOOL, https://dash.harvard.edu/bitstream/handle/1/8965586/Torrance%2c_Andrew_00.html?sequence=2 (last visited on Oct. 16, 2018).

79. *Id.*

80. Michele Zebich-Knos, *Preserving Biodiversity in Costa Rica: The Case of the Merck-INBio Agreement* 6 J. ENV'T & DEV. 180, 183-184 (1997).

81. M.D. Coughlin Jr., *Using the Merck-INBio Agreement to Clarify the Convention on Biological Diversity*. 31 COLUM. J, TRANSNAT'L L. 337, 343 (1993).

82. *Id.*

Wellcome (a consortium of private companies) for the collection of Peruvian medicinal plants.[83] ICBG has executed contracts with different organizations for its bioprospecting activities.[84] The objective of the program is to benefit both Peruvian communities and the global scientific community by discovering and researching possibilities for new solutions to human health problems based on previously unexplored genetic resources.

Beginning with the seventh meeting of the Conference of the Parties to the CBD in 2004, groups of developing countries, including the Group of Like-Minded Megadiverse Countries, pressed for a treaty to regulate material transfer terms.[85]

C. Indonesia and the Origins of Viral Sovereignty

In 2006, Indonesia withheld H5N1 avian flu samples from WHO GISRS, compromising efforts to monitor and produce vaccines in response to the avian flu outbreak that threatened to become easily transmissible from birds to humans and then between humans.[86] Indonesia asserted that its decision was a response to an Australian company's patent on a vaccine derived from a virus sample that Indonesia provided to WHO.[87] More importantly for purposes of human pathogen sharing, Indonesia argued that the H5N1 virus samples it had collected in its territory constituted the same kinds of natural resources as petroleum or rubber would previously have been considered, as well as a form of biodiversity protected under Articles 15 and 16 of the CBD.[88] Indonesia agreed to resume sharing under an interim agreement that granted it access to antivirals and vaccines, and promised to develop a broader international agreement on influenza pathogen access and benefit sharing.[89] Indonesia's actions introduced the previously unknown concept of "viral sovereignty" to the scientific sharing process.[90] "Viral sovereignty" refers to situations in which countries assert that viruses located and isolated from within their territories are their sovereign property.[91]

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83. 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 & CONSERVATION 176, 182 (2015).

84. *Id.*

85. Convention on Biological Diversity, *Report of the Seventh Meeting of the Ad Hoc Open-Ended Working Group on Access and Benefit-Sharing*, UNEP (2009), https://www.cbd.int/doc/meetings/abs/abswg-07/official/abswg-07-08-en.doc.

86. David Fidler, *supra* note 5, at 88.

87. David Fidler, *supra* note 5, at 88.

88. David Fidler, *supra* note 5, at 90.

89. David Fidler, *supra* note 5, at 89.

90. Shahar Hameiri, *Avian Influenza, 'Viral Sovereignty', and the Politics of Health Security in Indonesia,* 27 PAC. REV. 333, 347 (2014).

91. *Id.* at 345.

Spurred by Indonesia's actions and the response it generated within the WHO, countries negotiated the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization (Nagoya Protocol), a treaty that established the regulatory framework for MTAs.[92] The treaty required a government's "prior informed consent" over its sovereign human pathogens and "mutually agreed terms" for the return of benefits, should those pathogens be shared.[93] The Nagoya Protocol regulates commercial, non-profit, university-driven, and all other forms of microbiological research that lead to drugs, medical therapies, vaccines and other products derived from genetic resources in member states (the majority are developing countries) and, given the limited reach of current international instruments, fundamentally changes the nature and process of international scientific research.[94]

D. Lawyers Substitute for Scientists in the Global Infectious Disease Research System

The structure of graduate training all over the world for scientists includes little if any coursework or experiential curriculum aimed at negotiating research inputs.[95] Graduate education and training emphasizes academic coursework in the early years of a master or doctoral level program followed by active research.[96] While there are no surveys of written curricular components, survey-based research involving scientists shows that most researchers do not know how their biological samples are obtained, do not know how to use an MTA, and rarely participate in negotiations when they do occur.[97]

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92. Elisa Morgera, et al., *Relationship with International Agreements and Instruments, in* UNRAVELING THE NAGOYA PROTOCOL, 85, 103-04 (2015).

93. 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, U.N. Doc. UNEP/CBD/COP/DEC/X/1 to the Convention on Biological Diversity, (Oct. 29, 2010) UNEP/CBD/COP/DEC/X/1 of 29 U.N.T.S. A-30619 [hereinafter Nagoya Protocol].

94. Convention of Biological Diversity, Fact-Finding and Scoping Study on Digital Sequence Information on Genetic Resources in the Context of the Convention on Biological Diversity and the Nagoya Protocol, U.N. Doc. CBD/DSI/AHTEG/2018/1/3 (2018), https://www.cbd.int/doc/c/e95a/4ddd/4baea2ec772be28edcd10358/dsi-ahteg-2018-01-03-en.pdf.

95. *See e.g.*, *Microbiology & Immunology M.S. & Ph.D. Courses,* UNIVERSITY OF MICHIGAN, https://medicine.umich.edu/dept/microbiology-immunology/education/courses/ms-phd-courses (last visited Oct. 16, 2018) [hereinafter MICHIGAN]*; see also Biological & Biomedical Sciences Course Guide*, YALE UNIVERSITY, https://medicine.yale.edu/bbs/training/Courses%202018_270029_284_1737_v4.pdf (last visited Oct. 16, 2018) [hereinafter YALE] (demonstrating that doctorate program coursework may not include education or training on negotiating research inputs).

96. MICHIGAN, *supra* note 95; YALE, *supra* note 95.

97. Gurdial singh Nijar et al., *The Implementation of the Nagoya ABS Protocol for the Research Sector: Experience and Challenges*, 17 INT'L ENVTL AGREEMENTS: POL., L. & ECON.

As a result, lawyers and public officials have become a more significant barrier for access, research, sharing, and publication. Before the Convention on Biological Diversity, and the changes it facilitated, when scientists received shipments of biological materials, undertook field work in foreign countries, or worked in partnership with institutions abroad, they encountered few obstacles to the normal scientific process.[98] To be certain, customs and import laws regulate biological samples as they move across borders, but for the most part, those laws have rarely been assessed as erecting a significant barrier to infectious disease research.[99]

Lawyers by the nature of *their* training are more likely to view their clients' interests through criteria more familiar to them – trying to ensure monetary benefits flow to their clients (research universities and firms), maximizing their ability to control the use of samples including control over transfer and notification of new inventions, and scrutinizing material transfer agreement terms. While these are important factors to consider, there are additional interests in the overall infectious disease research process that scientists are better able to identify and communicate. The participation of scientists in the transfer process is therefore essential for the preservation of both institutional interests and the integrity of the research process. Whether through adaptations in graduate training or better forums for scientists to participate in the negotiation process, better integration of their viewpoints is important to reducing the barriers erected through MTAs.

IV. MATERIAL TRANSFER AGREEMENTS AND THE NEW SYSTEM OF PATHOGEN SHARING

A. The Barriers Material Transfer Agreements Pose

The effect of these movements in international law – toward greater assertion of sovereign proprietary rights over biological resources – and the

607, 617 (2016); *see also* Claire Lajaunie & Calvin Wai-Loon Ho, *Pathogens Collections, Biobanks and Related-Data in a One Health Legal and Ethical Perspective*, 145 PARASITOLOGY 688, 691 (2017).

98. *See e.g.*, *Guide to Shipping Biological Materials*, DARTMOUTH COLLEGE, http://www.dartmouth.edu/~ehs/biological/biosafety_docs/shipping_guide.pdf (last visited Oct. 16, 2018); *see also International Regulations for Packing and Shipping of Microorganisms*, EUROPEAN BIOLOGICAL RESOURCE CENTRES NETWORK (last revised Dec. 2010), https://www.dsmz.de/fileadmin/Bereiche/Microbiology/Dateien/Kultivierungshinweise/EBRCN_information_resource_on_transport_update_Dec_2010.pdf (demonstrating the guidelines that infectious disease research scientist must abide by when shipping biological materials intranationally and internationally).

99. Olive Sturtevant, *The ABCs of Importing and Exporting Products, Samples and Biologics across International Borders*, CELL THERAPY SOC'Y (Apr. 27, 2014), https://c.ymcdn.com/sites/www.celltherapysociety.org/resource/resmgr/2014_AnnualMtgPresentations/QO4_O.Sturtevant.pdf.

practicalities of transferring biological samples across borders has been profound. The Nagoya Protocol established a complex framework for regulating scientists' (including botanical gardens, universities, libraries, and certainly for-profit firms) ability to conduct research in low- and middle-income countries.[100] Under the Nagoya Protocol, a researcher would ideally contact the country's national focal point (NFP), an administrative body suggested by the treaty, to commence access-and-benefit sharing negotiations.[101] The NFP, in turn, would identify the correct "competent national authority" to discuss prior informed consent and mutually agreed terms for benefit sharing.[102] While this seems straightforward, the competent national authority may be a ministry of health, ministry of environment, ministry of indigenous issues, ministry of interior, or some other department.[103] In Brazil, for example, up to nine ministries may have jurisdiction over the pathogen at issue.[104]

In some countries, the competent national authority will issue permits generally known as "internationally recognized certificates of compliance," which "serve as evidence that the genetic resource which it covers has been accessed in accordance with prior informed consent and mutually agreed terms as required by the domestic legislation or regulatory requirements of the Party providing prior informed consent".[105] The terms of the agreement outline how the samples are to be used and stored, whether the samples may be kept after the term of the initial permission, whether they should be returned to the provider or destroyed, and whether the samples or any part thereof may be transferred to third parties and under which conditions.[106]

Benefit-sharing terms cover topics such as how the research results will be disseminated, how related data will be managed, how intellectual property rights (including monetary terms for royalties and licenses) will be developed, and how the provider country ought to be acknowledged in research publications.[107]

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100. Myrna E. Watanabe, *The Nagoya Protocol on Access and Benefit Sharing: International Treaty Poses Challenges for Biological Collections*, 65 BIOSCIENCE 543, 544 (2015).

101. Thomas Greiber et al., *An Explanatory Guide to the Nagoya Protocol on Access and Benefit-sharing*, 83 INT'L UNION FOR CONSERVATION NATURE ENVTL. POL'Y L. PAPER 1, 144-47 (2012).

102. *Id.*

103. *See generally Id.* (stating that state agencies are competent national authority).

104. Manuela da Silva & Maria Jose Amstalden M. Sampaio, *National Implementation of Access & Benefit-Sharing for Non-Commercial Academic Research* (July 30, 2013), https://naturwissenschaften.ch/uuid/6f9ebac2-9382-52ca-bd68-fa63ae772fce?r=20180809175703_1527108611_5edd3f22-4d57-552c-b2e1-8a74dc0c62ee.

105. NAGOYA PROTOCOL, *supra* note 93, at 13.

106. Greiber, *supra* note 101, at 181.

107. Amrita Mishra & Tania Bubela, *Legal Agreements and the Governance of Research Commons: Lessons from Materials Sharing in Mouse Genomics*, 18 OMICS 254, 256 (2014).

Research staff usually lacks both the knowledge and legal authority to enter into contracts like MTAs on behalf of their institutions.[108] Instead, at most leading research-intensive institutions including universities and firms, MTAs are drafted and negotiated by legal counsel located within technology transfer offices (TTOs) or research services offices.[109] These offices manage research partnerships, sponsored research, as well as commercialization activities such as patenting, technology licensing, and creating new companies.[110] As described above, the result is a protracted negotiation process that often lacks significant scientific input.

The volume of these agreements is large and increasing. For example, "one large pharmaceutical company indicated that it had six administrators dealing with more than 1,000 MTAs in 2000, and many of these agreements required lengthy negotiation."[111] Material transfers between private- and public-sector institutions are typically the most complex kinds of negotiations and are much more prone to failure.[112] The ascent of MTAs has created a feedback effect.[113] When a provider declares that it owns the results of research using its material, or even requires its permission to conduct certain kinds of research, it may become difficult or impossible to complete follow-up research, because an entirely new MTA is required for the new, secondary material or data created.[114]

The relatively scant evidence suggests that the increasing prevalence of MTAs is restricting research efforts.[115] In 2004, eighteen percent of academic requests for genetic materials were denied, while industry requests were similarly denied thirty-three percent of the time.[116] Most problems arise from MTAs and associated delays.[117] For example, researchers hoping to develop "combination microbicides" – the combining of different biological agents that act at different points in the infection process – must overcome challenges in "obtaining sufficient information about the properties of needed materials."[118] Genetic resources are not typically sources of much market

108. Bubela, Guebert, & Mishra, *supra* note 8, at 1.
109. Mishra & Bubela, *supra* note 107, at 256.
110. Mishra & Bubela, *supra* note 107, at 256.
111. BENNETT, STREITZ & GACEL, *supra* note 10, at 699.
112. BENNETT, STREITZ & GACEL, *supra* note 10, at 703.
113. Mishra & Bubela, *supra* note 107, at 256.
114. BENNET, STREITZ & GACEL, *supra* note 10, at 699.
115. Mishra & Bubela, *supra* note 107, at 256.
116. John P. Walsh, Wesley M. Cohen & Charlene Cho, *When Excludability Matters: Material versus Intellectual Property in Academic Biomedical Researc*h, 36 RES. POL'Y 1184, 1191 (2007).
117. Zhen Lei, Rakhi Juneja & Brian D. Wright, *Patent versus Patenting: Impediments of Intellectual Property Protection for Biological Research*, 27 NATURE BIOTECHNOLOGY 36, 38-39 (2009).
118. JEROME H. REICHMAN, PAUL F. UHLIR & TOM DEDEURWAERDERE, GOVERNING DIGITALLY INTEGRATED GENETIC RESOURCES, DATA, AND LITERATURE: GLOBAL

value, but instead, in market terms, are just "precompetitive inputs" that require combination with "large quantities of [other] genetic materials" to result in biomedical breakthroughs.[119] With MTAs, researchers encounter high transaction costs, substantial delays, and even refusals to negotiate for access or use, thus burdening the scientific research process.[120]

B. Burdening the Research and Development Process: Pandemic Influenza, MERS-CoV and Zika

While Indonesia's withholding of H5N1 samples generated greater systems for benefit sharing both in the short-term and through the 2011 WHO's Pandemic Influenza Preparedness Framework, it presented a major threat to global public health.[121] As David Fidler, a global expert on the law of infectious diseases, noted, "[w]ithout access to Indonesia's influenza strains, global surveillance was jeopardized, as was the refinement of diagnostic reagents and the development of intervention strategies, which depend on the information surveillance provides."[122] At that point in time, H5N1 exhibited a sixty percent fatality rate among those infected, and its potential to spread more easily between humans was unknown.[123]

In the context of MERS-CoV, some argue that the dispute between the Erasmus Medical Center and the Saudi government caused substantial delays in researchers' access to viral samples.[124] According to the Saudi Ministry of Health, Erasmus had obtained the virus illegally and the conditions it imposed on other researchers delayed development of treatments and vaccines.[125] Negotiations between the U.S. and Saudi governments for virus samples involved elaborate demands for research in Saudi territory, participation by Saudi scientists, and other technological requirements.[126]

Similar difficulties emerged after clusters of microcephaly and other neurological disorders in newborns were associated with the Zika virus in Brazil in 2015.[127] Even before cases became known in the United States,

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INTELLECTUAL PROPERTY STRATEGIES FOR A REDESIGNED MICROBIAL RESEARCH COMMONS 73 (2016).

119. *Id.* at 33, 80, 110.

120. K. S. Jayaraman, *Entomologist Stifled by Indian Bureaucracy*, 452 NATURE 7 (2008) (discussing a case where entomologist studying the Western Ghat in India were forced to abort their project by local authorities due to biopiracy fears).

121. Fidler, *supra* note 5, at 88.

122. Fidler, *supra* note 5, at 88.

123. J. S. Malik Peiris, Menno D. de Jong & Yi Guan, *Avian Influenza Virus (H5N1): A Threat to Human Health*, 20 CLINICAL MICROBIOLOGY REVIEWS 243, 252 (2007).

124. Garrett, *supra* note 6.

125. Garrett, *supra* note 6, at 2. (stating that they must "contractually agree not to develop products or share the sample without the permission of Erasmus and the Fouchier laboratory").

126. Garrett, *supra* note 6, at 5.

127. Rafael A. Larocca et al., *Vaccine Protection against Zika Virus from Brazil*, 536 NATURE 474, 474 (2016).

Paulo Gadelha, President of Fiocruz, a major Brazilian research institution, said he could not send samples abroad due to a new Brazilian law that protects national genetic resources.[128] Researchers at the CDC relied on Zika viruses taken from earlier outbreaks in French Polynesia to work on Zika diagnostics, and other researchers attempted to sequence Zika's genetic code using virus samples from Puerto Rico.[129] In the U.K., researchers used samples drawn from Micronesia, the site of an outbreak in 2007.[130] The French relied on samples from Polynesia and Martinique.[131] In Spain, scientists used a Ugandan strain of Zika supplied by the United States.[132] Even scientists in Portugal, a country that shares extensive cooperative ties to Brazil, had to work with a U.S. sample from the 1980s.[133] The result was, again, delays in the development of diagnostics, therapeutics and vaccine candidates for the vector-borne illness.[134]

C. Solutions to Material Transfer Agreement Problems

The pace of low- and middle-income countries' demands to share the benefits of biomedical research resulting from the use of human pathogens taken from their territory has exceeded the development of legal mechanisms to balance equity and science.[135] While MTAs formed under the Nagoya Protocol and other access-and-benefit sharing laws ensure benefits flow to low- and middle-income countries, they also restrict and impede research and development.[136] Whatever their merit in ensuring that benefits are equitably shared, research capacity in low- and middle-income countries is increased, and biodiversity is protected, MTAs represent problems for the global biomedical research process that must be solved.[137] Some of these solutions now exist on a small scale, as they were developed to address experiences in individual countries, especially the United States.[138] These solutions may be expanded either within the national jurisdiction of individual countries, or

128. Roberta Jansen, *A Polêmica do Envio de Amostras Brasileiras de Zika Vírus ao Exterior*, BBC BRAZIL (Feb. 8, 2016), www.bbc.com/portuguese/noticias/2016/02/160208_zika_polemica_cientistas_rj.

129. Maria Cheng, Raphael Satter, & Joshua Goodman, *AP Newsbreak: Few Zika Samples Being Shared by Brazil*, ASSOCIATED PRESS (Feb. 3, 2016), https://apnews.com/2db2a3581d2a42a08f5b031419cb09ed.

130. *Id.*

131. *Id.*

132. *Id.*

133. *Id.*

134. *Id.* (noting that it is also infectious through sexual contact).

135. SVEND REMOE, MATERIAL TRANSFER AGREEMENTS: A MULTIPURPOSE TOOL FOR INTERNATIONAL COOPERATION (2014).

136. *Id.* at 10.

137. *Id.* at 9.

138. *Id.*

established and operated at a global scale, especially for research areas of particular concern to global population health.[139]

1. Repositories and Biobanks

Generally "biobank," "biorepository," "biospecimen resource," and "biological resource center" all refer to the facilities and related processes that govern the collection, processing, and storage of biological specimens, often for specific classes of diseases like cancer, HIV/AIDS, and malaria.[140] Databases and bio-repositories not only provide common research resources, but are also made possible because those contributing to them and drawing from them agree to do so through MTAs that prohibit further negotiation.[141] These common pool resources are available to all users on terms that encourage "efficiency, equitable use, and sustainability, and that are managed by groups of varying sizes and interests."[142] Much of these repositories' development was sparked by trends towards commercialization of research outputs from public institutions in the U.S., which led to the assertion of intellectual property rights over research reagents.[143]

There is variation in how repositories accept deposits from researchers, though the determining factors usually include quality, novelty, and potential interest from the research community.[144] Other repositories may be structured such that they only accept deposits of reagents from a specific project or strain.[145] Finally, some repositories may not accept deposits and will only distribute those materials generated by associated projects or facilities.[146] By acknowledging the original source repository, other researchers are directed to that repository, which enhances visibility and profile, two important factors in repository sustainability models.[147]

Repositories have the benefit of handling distribution, including negotiations surrounding the manner in which materials are distributed.[148] Perhaps most importantly,

> [E]stablished large-scale resource generation projects, repositories, and

139. *Id.*
140. Vaught, Henderson & Compton, *supra* note 31, at 1; *see also* Akin Abayomi et al., *Challenges of Biobanking in South Africa to Facilitate Indigenous Research in an Environment Burdened with Human Immunodeficiency Virus, Tuberculosis, and Emerging Noncommunicable Diseases*, 11 BIOPRESERVATION & BIOBANKING 347, 349 (2013).
141. Mishra & Bubela, *supra* note 107, at 255.
142. Mishra & Bubela, *supra* note 107, at 254.
143. Mishra & Bubela, *supra* note 107, at 254-56.
144. Mishra & Bubela, *supra* note 107, at 265.
145. Mishra & Bubela, *supra* note 107, at 265.
146. Mishra & Bubela, *supra* note 107, at265.
147. Mishra & Bubela, *supra* note 107, at 269.
148. Mishra & Bubela, *supra* note 107, at 265.

> databases have the opportunity to develop governance mechanisms, including standardized and simplified MTAs, that implement the data and materials sharing policies of key funding agencies, concurrently building capacity in research management with partner or recipient institutions.[149]

One disincentive for deposits from the research community, however, is the fact that researchers often bear the cost of the deposit.[150] Funding agencies could incentivize deposits, therefore, by requiring specific line items in budgets representing the cost of deposits in repositories, which would be reimbursed using public funds.[151]

For example, the Malaria Research and Reference Reagent Resource Center facilitates malaria research by improving availability of parasite, vector, and human reagents and standardized assays.[152] Under this regime, otherwise known as the "MR4" regime, researchers have access to a centralized resource that provides parasites, proteins, reagents, and mosquitos for reference standards or to generate new renewable reagents.[153] Over 600 labs worldwide have deposited or withdrawn from the repository for purposes of malaria research.[154] The National Institutes of Health (NIH) runs a similar program for HIV/AIDS through its AIDS Reagent Program.[155] An MR4 model could be expanded to other diseases, and international agreements formed that shift the costs of participating from researchers to governments.

2. Standardized Material Transfer Agreements for Routine Research and Emergencies

MTAs always posed problems domestically and internationally.[156] In the U.S., solutions in both the routine and emergency contexts included standard MTAs, essentially boilerplate documents that specified the rights of the transferor and the transferee.[157] In the early 1990s, NIH developed the Uniform Biological MTA (UMBTA), and more recently developed the Standard Letter Agreement (SLA) for relatively simple transfers.[158]

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149. Mishra & Bubela, *supra* note 107, at 268.
150. Mishra & Bubela, *supra* note 107, at 269.
151. Mishra & Bubela, *supra* note 107, at 269.
152. Malaria Research and Reference Reagent Resource Center, *History of the MR4*, BEI RESOURCES, https://www.beiresources.org/About/MR4.aspx (last visited on Nov. 8, 2018).
153. *Id.*
154. *Id.*
155. *NIH AIDS Reagent Program: The Source of Critical HIV Research Materials*, AIDS REAGENT, https://www.aidsreagent.org/ (last updated Aug. 17, 2018).
156. Bubela, Guebert, & Mishra, *supra* note 8, at 5.
157. Bubela, Guebert, & Mishra, *supra* note 8, at 2.
158. Uniform Biological Material Transfer Agreement: Discussion of Public Received; Publication of Final Format of the Agreement, 60 Fed. Reg. 12,771 (Mar. 8, 1995).

Internationally, the instrument developed to facilitate access to influenza samples from the GISRS includes two types of standard MTAs: SMTA-1 (which covers exchanges between laboratories in the GISRS system) and SMTA-2. SMTA-2 governs the obligations of research institutions and firms outside the World Health Organization GISRS when using samples drawn from the system.[159] Since these MTAs are standardized, they help to reduce transaction costs that are normally associated with exchange and transfer, especially through limiting the involvement of lawyers and governments.[160] They help protect national or sovereign rights by stipulating to the specific use of the material, limiting or prohibiting commercial use, and restricting possible illegitimate or unacceptable claims on intellectual property.[161] SMTAs may require recipients to make all non-confidential information from the research available, and make the material available to others to facilitate conservation/storage. Further distribution of the material must be conducted under a new SMTA.[162]

During the Zika public health emergency, the U.S. government developed a specific "emergency use simple letter agreement," (EUSLA) under which Zika samples could be shared for "any legitimate purpose," broadening the typical language used for material transfers.[163] This EUSLA was adopted at the international level through the Global Health Security Initiative with the WHO as an advisor to the project.[164] The EUSLA facilitated approximately 160 agreements to transfer Zika resource materials between academic, government and industry researchers.[165]

3. Specialized International Instruments

While more complex and lengthier, MTA problems may also be addressed through specialized international instruments, a mechanism envisioned in Article 4 of the Nagoya Protocol.[166] The resolution to Indonesia's complaints

159. WORLD HEALTH ORG., PANDEMIC INFLUENZA PREPAREDNESS FRAMEWORK FOR THE SHARING OF INFLUENZA VIRUSES AND ACCESS TO VACCINES AND OTHER BENEFITS 14 (2011).

160. Uniform Biological Material Transfer Agreement, *supra* note 158, at 12,771; WORLD HEALTH ORG., *supra* note 159.

161. *See generally* WORLD HEALTH ORG., *supra* note 159.

162. *See generally* WORLD HEALTH ORG., *supra* note 159.

163. Maria Julia Marinissen, Michael R. Mowatt, & Kevin Brand, Remarks at the 2018 FLC Nat'l Meeting, 2018 FLC Interagency Partnership Award: Zika Virus Specimen and Material Sharing, (Apr. 25, 2018), (available at https://docs.google.com/viewer?url=https%3A%2F%2Fmeeting.federallabs.org%2Fwp-content%2Fuploads%2F2018%2F04%2FFLC-Award-Panel-180425-HHS-FINAL-180423.pptx.).

164. *Id.* at 9.

165. *Id.* at 13.

166. Nagoya Protocol, *supra* note 93, at 5.

about the GISRS was the 2011 Pandemic Influenza Preparedness Framework (PIP).[167] The PIP was explicitly committed to "increas[ing] the access of developing countries to vaccines and other pandemic related supplies."[168] Under the Framework, major pharmaceutical manufacturers retain their ability to access samples shared through GISRS, however firms using the system must contribute towards half the cost of its maintenance (approximately $30 million annually).[169]

Firms must promise to share either intellectual property, products developed through use of the system, or other medical countermeasures critical to pandemic response:

> For manufacturers of vaccines and/or antivirals, the recipient shall commit to at least two of the following options:
>
> A1. Donate at least 10% of real time pandemic vaccine production to WHO.
>
> A2. Reserve at least 10% of real time pandemic vaccine production at affordable prices to WHO.
>
> A3. Donate at least X treatment courses of needed antiviral medicine for the pandemic to WHO.
>
> A4. Reserve at least X treatment courses of needed antiviral medicine for the pandemic at affordable prices.
>
> A5. Grant to manufacturers in developing countries licenses on mutually agreed terms that should be fair and reasonable including in respect of affordable royalties, taking into account development levels in the country of end use of the products, on technology, know-how, products and processes for which it holds IPR for the production of (i) influenza vaccines, (ii) adjuvants, (iii) antivirals and/or (iv) diagnostics.
>
> A6. Grant royalty-free licenses to manufacturers in developing countries or grant to WHO royalty-free, non-exclusive licenses on intellectual property rights, which can be sublicensed, for the production of pandemic influenza vaccines, adjuvants, antivirals products and diagnostics needed in a pandemic. WHO may sublicense these licenses to manufacturers in

167. David P. Fidler & Lawrence O. Gostin, *The WHO Pandemic Influenza Preparedness Framework: A Milestone in Global Governance for Health*, 306 JAMA 200, 201 (2011).

168. SAM F. HALABI, INTELLECTUAL PROPERTY AND THE NEW INTERNATIONAL ECONOMIC ORDER OLIGOPOLY, REGULATION, AND WEALTH REDISTRIBUTION IN THE GLOBAL KNOWLEDGE ECONOMY 164 (2018) [hereinafter HALABI]; WORLD HEALTH ORG., *supra* note 159.

169. HALABI, *supra* note 168; Lawrence O. Gostin et. al., *Virus Sharing, Genetic Sequencing, and Global Health Security*, 345 SCI. 1295, 1296 (2014); *see also* Fidler & Gostin, *supra* note 167, at 201.

> developing countries on appropriate terms and conditions and in accordance with sound public health principles.[170]

Although the framework is specific to pandemic influenza, the outbreak of Ebola in West Africa and more general calls for equitable sharing of benefits using genetic resources from developing countries have made it a preliminary model for redistributing wealth from richer countries to poorer ones.[171] The U.N.'s review panel that convened in the wake of the Ebola crisis explicitly called for the agreement to be extended to "other novel pathogens", making it legally binding, and achieving an appropriate balance between obligations and benefits, in accordance with the principles of the 2010 Nagoya Protocol to the CBD.[172] The PIP framework took four years to materialize, but because its MTA terms have been negotiated, it may represent a plausible solution to at least discreet classes of human pathogen sharing and any resulting benefits, including intellectual property.[173]

4. Training and Education of Scientific Investigators

There is little about the education and training of infectious disease researchers, virologists, and microbiologists to help them adjust to a role involving negotiation and advocacy in the material transfer process.[174] Some scientists join university or commercial TTOs, and others reach administrative roles where they are able to share their expertise both directly and through organizations like the Association of University Technology Managers, but generally the structure of scientific education has not kept pace with the changes in the management of biological research inputs.[175]

Given that researchers must be active voices in the material transfer process, this aspect of modern research must change. International research collaborations in the field of infectious disease increasingly require researchers to be more extensively knowledgeable about regulations covering the sampling of biological resources, terms of MTAs, and formal agreements establishing research partnerships.[176] As most analysts of the problem have

170. WORLD HEALTH ORG., *supra* note 159, at 34.

171. HALABI, *supra* note 169; WORLD HEALTH ORG., *supra* note 159, at 34.

172. Rep. of the High-level Panel on the Global Response to Health Crises, *Protecting Humanity from Future Health Crises,* at 18, U.N. Doc. A/70/723 (Feb. 9, 2016); HALABI, *supra* note 169, at 165.

173. Suerie Moon et. al, *Will Ebola Change the Game? Ten Essential Reforms Before the Next Pandemic. The Report of the Harvard-LSHTM Independent Panel on the Global Response to Ebola*, 386 LANCET 2204, 2214 (2015).

174. *Id.* at 2204; *see also* Uniform Biological Transfer Agreement, *supra* note 158, at 12771; *see also* MICHIGAN, *supra* note 95; *see also* YALE, *supra* note 95.

175. Moon, *supra* note173, at 2214; *see also* MICHIGAN, *supra* note 95; *see also* YALE, *supra* note 95.

176. Moon, *supra* note 173, at 2214; *see also* Uniform Biological Transfer Agreement,

concluded, knowledge of "prior informed consent," "mutually agreed terms" and "access and benefit sharing" must be integrated with the education and research process, as researchers must now collaborate more with lawyers to ensure that access to human pathogen samples continues as expeditiously as possible.[177]

CONCLUSION

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.[178] However, the perception that genetic resources are in the public domain persists in the biological sciences, and many researchers are still unaware of the legal requirements surrounding the collection and use of environmental genetic resources for research purposes.[179]

MTAs were born from an interest to protect proprietary information.[180] Appropriately constructed, MTAs can define the legal terms of transfer and storage between the parties, while also accounting for intellectual property rights concerns.[181] They are, however, ultimately a new barrier to research, especially for infectious diseases.[182] This article argued that current mechanisms that have developed on a small scale – repositories, standardized MTAs, specialized international instruments, and curricular changes in scientific education and training – may help lower these barriers to breakthroughs in diagnostics, therapeutics, and vaccines.

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supra note 158, at 12771, *see also* Kate Davis et. al, *An Access and Benefit-Sharing Awareness Survey for Botanic Gardens:*
Are They Prepared for the Nagoya Protocol? 98 SOUTH AFRICAN J. OF BOTANY 148, 156 (2015).

177. Davis, *supra* note 176.

178. Bubela, Guebert, & Mishra, *supra* note 8, at 1; *see also* Lajaunie & Ho, *supra* note 97, at 691.

179. Lajaunie & Ho, *supra* note 97, at 690 – 91.

180. Bubela, Guebert, & Mishra, *supra* note 8, at 1.

181. Bubela, Guebert, & Mishra, *supra* note 8, at 7.

182. Bubela, Guebert, & Mishra, *supra* note 8, at 1.