AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

MINIREVIEW

The U.S. Culture Collection Network Responding to the Requirements of the Nagoya Protocol on Access and Benefit Sharing

Kevin McCluskey,[a] Katharine B. Barker,[b] Hazel A. Barton,[c] Kyria Boundy-Mills,[d] Daniel R. Brown,[e] Jonathan A. Coddington,[f] Kevin Cook,[g] Philippe Desmeth,[h] David Geiser ,[i] Jessie A. Glaeser,[j] Stephanie Greene,[k] Seogchan Kang,[l] Michael W. Lomas,[m] Ulrich Melcher,[n] Scott E. Miller,[o] David R. Nobles, Jr.,[p] Kristina J. Owens,[q] Jerome H. Reichman,[r] Manuela da Silva,[s] John Wertz,[t] Cale Whitworth,[u] David Smith[v]

Fungal Genetic Stock Center, Department of Plant Pathology, Kansas State University, Manhattan, Kansas, USA[a]; National Museum of Natural History, Smithsonian Institution, Washington, DC, USA[b]; Department of Biology, University of Akron, Akron, Ohio, USA[c]; Phaff Yeast Culture Collection, Food Science, University of California, Davis, Davis, California, USA[d]; Infectious Diseases and Pathology, College of Veterinary Medicine, University of Florida, Gainesville, Florida, USA[e]; Global Genome Initiative, National Museum of Natural History, Smithsonian Institution, Washington, DC, USA[f]; Bloomington Drosophila Stock Center, Department of Biology, Indiana University, Bloomington, Indiana, USA[g]; Belgian Science Policy Office, Brussels, Belgium[h]; The Fusarium Research Center, Penn State University, State College, Pennsylvania, USA[i]; U.S. Forest Service, Northern Research Station, Center for Forest Mycology Research, Madison, Wisconsin, USA[j]; USDA National Laboratory for Genetic Resources Preservation, Fort Collins, Colorado, USA[k]; Penn State University, State College, Pennsylvania, USA[l]; National Center for Marine Algae and Microbiota, East Boothbay Harbor, Maine, USA[m]; Oklahoma State University, Stillwater, Oklahoma, USA[n]; Smithsonian Institution, Washington, DC, USA[o]; UTEX Culture Collection of Algae, Austin, Texas, USA[p]; Eversole Associates, Bethesda, Maryland, USA[q]; Duke University School of Law, Durham, North Carolina, USA[r]; Fiocruz - Fundação Oswaldo Cruz, Rio de Janeiro, RJ, Brazil[s]; *E. coli* Stock Center, Yale University, New Haven, Connecticut, USA[t]; Bloomington Drosophila Stock Center, Department of Biology, Indiana University, Bloomington, Indiana, USA[u]; CABI, Surrey, United Kingdom[v]

ABSTRACT The U.S. Culture Collection Network held a meeting to share information about how culture collections are responding to the requirements of the recently enacted 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 (CBD). The meeting included representatives of many culture collections and other biological collections, the U.S. Department of State, U.S. Department of Agriculture, Secretariat of the CBD, interested scientific societies, and collection groups, including Scientific Collections International and the Global Genome Biodiversity Network. The participants learned about the policies of the United States and other countries regarding access to genetic resources, the definition of genetic resources, and the status of historical materials and genetic sequence information. Key topics included what constitutes access and how the CBD Access and Benefit-Sharing Clearing-House can help guide researchers through the process of obtaining Prior Informed Consent on Mutually Agreed Terms. U.S. scientists and their international collaborators are required to follow the regulations of other countries when working with microbes originally isolated outside the United States, and the local regulations required by the Nagoya Protocol vary by the country of origin of the genetic resource. Managers of diverse living collections in the United States described their holdings and their efforts to provide access to genetic resources. This meeting laid the foundation for cooperation in establishing a set of standard operating procedures for U.S. and international culture collections in response to the Nagoya Protocol.

Published 15 August 2017

Citation McCluskey K, Barker KB, Barton HA, Boundy-Mills K, Brown DR, Coddington JA, Cook K, Desmeth P, Geiser D, Glaeser JA, Greene S, Kang S, Lomas MW, Melcher U, Miller SE, Nobles DR, Jr., Owens KJ, Reichman JH, da Silva M, Wertz J, Whitworth C, Smith D. 2017. The U.S. Culture Collection Network responding to the requirements of the Nagoya Protocol on Access and Benefit Sharing. mBio 8:e00982-17. https://doi.org/10.1128/mBio.00982-17.

Editor Steven E. Lindow, University of California, Berkeley

Address correspondence to Kevin McCluskey, mccluskeyk@ksu.edu.

Contribution no. 17-345-J from the Kansas Agricultural Experiment Station.

KEYWORDS biodiversity, biotechnology, environmental microbiology, genetic models, genome sequence

The U.S. Culture Collection Network (USCCN) is a U.S. National Science Foundation-funded Research Coordination Network that has provided opportunities for culture collection curators and other interested parties to interact since 2012. In recent years, biological collection staff have expressed concern over how to act in accordance with the 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 (CBD), which beginning in October 2014, placed new requirements on international collecting, research, and development based on biological organisms. While in the past, genetic resources were considered to be the shared heritage of humankind, the Nagoya Protocol requires every party (generally a country) to establish their own national legislation governing access to genetic resources with the goal of ensuring that benefits of genetic resource utilization are shared equitably with provider nations. The fact that the United States did not ratify the CBD and does not restrict access to genetic resources adds confusion to this issue. In an effort to assist U.S. living collection managers and through them, the research communities that they serve, the USCCN held a meeting in Arlington, VA, on 9 and 10 February 2017 (see Text S1 in the supplemental material) and invited culture collection managers, stakeholders, and policy makers to share their insight and information and to describe developing regulations affecting the use and sharing of living genetic resources. To ensure that timely information is publicly available, this meeting report will summarize existing legislation and describe how to find information on accessing genetic resources in accordance with relevant local regulations.

Living collections. Living collections have received, characterized, preserved, and distributed biological resources and information for basic and applied research for many years (1). These collections promote reproducibility in science and provide raw material for new areas of inquiry (2). Access to living resources has been foundational to research, health care, agriculture, and industry since the beginning of the modern era of biology. Public research resources have led to developments such as the green revolution, advanced health care, including antibiotics, drugs modulating immunity, and drugs modulating human metabolism, as well as drugs for diverse applications such as production of ingredients for food, feed, and fiber, industrial chemicals and processing agents, and even household products such as laundry detergent (3). Modern biotechnology based on PCR (4) or CRISPR (clustered regularly interspaced short palindromic repeat)-Cas (CRISPR-associated system) (5, 6) have their origins in material sourced from public living microbe collections.

Waves of discovery parallel the exploration of new sources, beginning with macrobiota and expanding to extreme terrestrial environments (7, 8) and marine environments in the modern era (9). The present frontier is the exploration of genome sequences using bioinformatic approaches coupled with manipulation of gene expression (10, 11). Many of these approaches depend on access to validated microorganisms from public culture collections (12, 13) many of which began as personal research collections or as the result of systematic collecting, mutagenesis, manipulation, or taxonomic description. Other collections are public repositories that focus on a target species or clades of organisms (14). Microbial and algal collections uniquely deal with genetic resources that may transcend geopolitical divisions because they are dispersed by wind (15, 16) or water currents (17). Most of these collections were established prior to and grew without anticipating the requirements of international treaties. While the collecting endeavors of the 1900s and before allowed the extraction and exploitation of once geographically limited resources and led to widespread distribution of valuable plant species (18), the ratification of the CBD in 1993 began a new era of sovereign rights to genetic resources. Just as countries are recognized to have sovereignty over

their mineral rights (19), the CBD assures that they also retain sovereignty over their biodiversity, even when it is utilized in another country.

THE CONVENTION ON BIOLOGICAL DIVERSITY

While the CBD outlined the principles for access and benefit sharing, specific procedures to achieve these worthy goals were not detailed in the original treaty. For almost 20 years, countries struggled to implement legislation and agreements that determine what types of materials are covered, what documentation and permits would be required prior to collecting, transporting, and using organisms, and what types of uses would be exempt from these restrictions. In light of these challenges, parties to the CBD agreed to negotiate an international regime of access and benefit sharing which culminated in the adoption of the Nagoya Protocol at the 10th meeting of the Conference of Parties to the CBD (COP) in Nagoya, Japan, in 2010 (20).

In October 2014, the Nagoya Protocol on Access and Benefit Sharing was ratified by the required number of countries and entered into force (21). The objective of the Nagoya Protocol is to assure that access to genetic resources is associated with conservation of biodiversity and fair and equitable benefit sharing; specifically, benefits are to be shared with the country providing access to its genetic resources. Although the United States has not signed or ratified the Protocol, participants at the February 2017 USCCN meeting heard that, just like our obligation to obey any national legislation when visiting a foreign country, U.S. researchers should comply with all "access and benefit sharing" (ABS) regulations enacted by the country from which they are collecting or otherwise utilizing genetic resources. Consequences of not following established regulations could include revocation of access to genetic resources, termination of grant support, or negative attention in scientific or public literature (22). Because they depend on national legislation in the provider country, consequences could fall on the local collaborator more heavily than on U.S. researchers. The benefits received by the country of origin can be monetary, in-kind (such as training), capacity building, or (for example) coauthorship on publications. The United States does not formally restrict access to genetic resources, although local entities (such as the U.S. National Park Service, state parks, or conservation areas) or landowners may restrict access or have specific requirements for the use of genetic resources collected from their sites. Regardless of collection history or original mission, U.S. living collections that contain organisms of international origin are impacted by the CBD and the Nagoya Protocol (23).

The Access and Benefit-Sharing Clearing-House. The Access and Benefit-Sharing Clearing-House (ABS Clearing-House [ABSCH]) (https://absch.cbd.int) hosted by the CBD Secretariat is a central repository designed to share ABS information relevant to implementation of the Nagoya Protocol. The ABSCH includes information regarding national requirements and procedures for access to genetic resources and associated traditional knowledge and the sharing of benefits arising from their use. The Nagoya Protocol requires that parties to the Protocol make available to the ABS Clearing-House information on legislative, administrative, or policy measures, national focal points, and competent national authorities responsible for providing information on how to access genetic resources and associated traditional knowledge, including how to obtain Prior Informed Consent (PIC) and establish Mutually Agreed Terms (MAT). Parties (countries) requiring PIC are required to issue a permit and register specific nonconfidential information from the permit on the ABS Clearing-House in order to constitute an Internationally Recognized Certificate of Compliance as proof that PIC, MAT, and all access requirements of the provider country have been properly met. The information gathered from a user constitutes a checkpoint to alert relevant authorities, in particular of the provider country, on how their genetic resources are being used. When fully implemented, these steps should be automatically managed by the clearinghouse mechanism (24).

NONLIVING OR ONCE-LIVING RESOURCES INCLUDING GENOME SEQUENCE INFORMATION

Because of the position of tissue, DNA, or other genetic resources as the foundation to provide whole-genome sequence information, representatives of the Global Genome Biodiversity Network (GGBN) described their efforts to promote fair access to genetic resources. They emphasized that new pathways to accessing genetic resources under the Nagoya Protocol are subject to decisions by parties to the Nagoya Protocol. The second Meeting of the Parties to the Nagoya Protocol (COP/MOP 2) was held very recently (December 2016), and some issues remain to be decided. One specific area currently being considered by the Parties to the Nagoya Protocol is the status of digital sequence information as it relates to the Nagoya Protocol. A compromise proposal was adopted by COP/MOP 2, which establishes a 2-year process to consider the potential implications of digital sequence information for the three objectives of the Convention on Biological Diversity, namely, biodiversity conservation, sustainable use of biodiversity, and the fair and equitable sharing of benefits arising from the use of genetic resources. The outcomes from this process will be considered at the third Meeting of the Parties in November 2018.

Because access to pathogen specimens is essential for detecting and responding to disease outbreaks, the Nagoya Protocol discusses disease outbreaks in Article 8 as requiring special consideration. COP/MOP also discussed the status of microbial pathogen specimens, and while no formal decisions have been made, the COP/MOP requested the Secretariat to conduct a study into criteria that could be used to identify what constitutes a specialized access and benefit-sharing agreement and the process for recognizing such an instrument. The ability to develop specialized ABS instruments (exemptions) will be important to the long-term success of the Nagoya Protocol. Examples of specialized instruments being discussed include the International Treaty on Plant Genetic Resources for Food and Agriculture and the Pandemic Influenza Preparedness Framework (25).

SPECIFIC LEGISLATION

National legislation in Brazil and the European Union (EU) has already been established, and representatives of each of these parties described their national legislation at the USCCN meeting. Because they are perceived as provider and end-user parties, respectively, their very different approaches to implementation of the Nagoya Protocol provide clear examples of how to obtain necessary authorization to access and utilize genetic resources.

(i) Brazil. Brazil implemented access and benefit-sharing legislation for genetic resources and associated traditional knowledge in 2001 through the Provisional Act 2186-16/2001. After almost 15 years of experience with this legal framework, law 13.123, which provides for access to genetic resources and associated traditional knowledge and on benefit sharing for the conservation and sustainable use of biodiversity, came into force on 17 November 2015. Importantly, Brazil has taken the position that access to all genetic resources from Brazil begins not when they were collected, exported, and deposited in collections but when the research and development activities (access) take place. Because this is contrary to the perspective that the date when a specimen was first isolated or characterized is the defining date for ABS, it deserves special notice. According to the new Brazilian definitions of access to genetic resources and research, the law reaches all activities conducted with Brazilian biodiversity. These activities include research related to molecular taxonomy, phylogeny, molecular ecology, and molecular epidemiology, as well as the use of information from genetic sequences published in public databases. Thus, Brazil considers that utilization of genome sequence for the purposes of research and development is the defining time, not when the organism was identified and characterized or when the genetic information was published. Additionally, the new law stipulates that all microorganisms collected from the national territory, territorial sea, exclusive economic zone, or continental platform is part of the Brazilian genetic resources. Moreover, the law

determines that foreign institutions can access Brazilian genetic resources only in partnership with a Brazilian institution and that, for all legal purposes, the Brazilian institution will be responsible for the activities of access to genetic resources. In this context, therefore, registration of access to Brazilian genetic resources is the responsibility of the collaborating Brazilian institution.

In general, the new law brings some improvements. Prior authorization procedures were replaced by electronic registration during the phase of research and technological development. This is followed by a notification process before the economic exploitation of a finished product derived from the access to genetic resources or associated traditional knowledge. Therefore, the benefit sharing occurs only when the marketing (sale) of these products take place. The registration and notification are conducted through the system developed by the Ministry of Environment National System for Genetic Heritage and Associated Traditional Knowledge Management (SisGen) by a representative of a Brazilian institution. Another novelty of the new law is in its establishment of the National Fund for Benefit Sharing (FNRB), which is linked to the Ministry of Environment. When a resource is commercialized, the user will have to deposit a defined amount of the net income acquired from the sale of the finished product. When the monetary resources deposited in FNRB arise from the economic exploitation of finished products that come from access to genetic resources obtained from *ex situ* collections, the collection will receive a defined portion of the financial resources.

(ii) The European Union. The European Union is also a Party to the Nagoya Protocol and has developed blanket legislation that will apply to all EU member countries. The legislation, EU regulation no. 511/2014 on ABS compliance, recognizes the 12 October 2014 date of entry into force as being the relevant date after which access to genetic resources is subject to the provisions of the Nagoya Protocol. The legislation emphasizes that it is applicable to genetic resources from countries that have ratified the Nagoya Protocol, exercise sovereign rights, and have established ABS measures. Further, the regulation is applicable only when conducting research and development on the genetic and/or biochemical composition of genetic resources, including through the application of biotechnology. It does not apply to genetic resources that are already governed by specialized international instruments such as the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA), although the status of specialized instruments remains to be determined (see above).

Importantly, the focus of the EU regulations is on benefit sharing and leaves the control of access to genetic resources up to the individual member states. Some EU member states, such as the United Kingdom or Denmark, have decided not to limit access to sovereign genetic resources, and other than designating some restricted areas, do not require PIC and MAT. Countries such as France and Spain, however, are implementing regulatory control of access. Each European country will put in place implementation acts such as that in the United Kingdom where the Nagoya Protocol (Compliance) Regulations 2015 Statutory Instrument 2015 No. 821 was enacted in March 2015 (http://www.legislation.gov.uk/uksi/2015/821/pdfs/uksi_20150821_en.pdf). In the United Kingdom and across Europe, national authorities are supporting best practices through self-regulation tools to enable regulatory compliance. Various user communities have been invited to develop common approaches with the option for recognition by the EU Commission and Member States (Table 1).

Additionally, to enable due diligence, the European Commission will develop a list of biological collections with registered status. The Member States are responsible for considering inclusion and verification of these collections; however, the requirements and responsibilities of such a status have limited the number of culture collections engaging in this process. The advantage of accessing resources from a registered collection is that users of genetic resources will be considered as having exercised "due diligence" if they source their genetic resources from these registered collections.

TABLE 1 Sources of information and model documents

Resource[a]	Internet link(s)
U.S. Culture Collection Network	http://www.usccn.org
World Federation for Culture Collections	http://www.wfcc.info
Scientific Collections International	http://www.scicoll.org
Global Genome Biodiversity Network	http://www.ggbn.org/
Biotechnology Industry Organization (BIO), Guidelines for BIO Members Engaging in Bioprospecting, BIO Model MTA	https://www.bio.org/articles/bio-bioprospecting-guidelines
Consortium of European Taxonomic Facilities (CETAF), Code of Conduct and Best Practice for Access and Benefit Sharing	https://www.cbd.int/abs/submissions/icnp-3/EU-Taxonomic-practices.pdf
ABS-Management Tool, Best Practice Standard and Handbook for Implementing Genetic Resource Access and Benefit-sharing Activities	http://www.iisd.org/library/abs-management-tool-best-practice-standard-and-handbook-implementing-genetic-resource-access
Swiss Academy of Sciences, Access and Benefit Sharing Good Practice for Academic Research on Genetic Resources	http://www.iisd.org/pdf/2006/abs_swiss_abs_good_practice.pdf
Botanic Gardens Conservation International (BGCI), CBD manual for botanic gardens	https://www.bgci.org/policy/cbdmanual/
The Mediterranean Science Commission, CIESM Charter on ABS	http://www.ciesm.org/marine/charter/index.php
The ABS Capacity Development Initiative, The ABS Agreement, Key Elements and Commentary	https://chm.cbd.int/database/record/208696
Japan Bioindustry Association and METI, the Japanese Guidelines on Access to and Benefit Sharing of Genetic Resources	http://www.jba.or.jp/pc/en/library/pdf/2012_guideline_access_e.pdf
German Science Association, DFG guideline for CBD relevant research projects	http://www.dfg.de/formulare/1_021e/1_021e.pdf
Micro B3, ABS Model Agreement	http://biogov.uclouvain.be/staff/dedeurwaerdere/CH_Micro%20B3%20model%20agreement.pdf
International Union for Conservation of Nature (IUCN), An Explanatory Guide to the Nagoya Protocol on Access and Benefit-sharing	https://www.cbd.int/abs/side-events/icnp2/iucn-explanatory-guide-en.pdf
Microbial Resource Research Infrastructure (MIRRI) Best Practice Manual on Access and Benefit Sharing	http://www.mirri.org/fileadmin/mirri/media/Dokumente/MIRRI_ABS_Manual__web.pdf

[a]Organization and/or document(s).

The procedural requirements for the registration of collections of genetic resources (Article 5 of the EU ABS Regulation) are set out in the Implementing Regulation.

While not specifically linked to the registered collection approach, leaders in the EU culture collection community are developing a consortium of microbial collections in the EU. Building upon the success of their Global Biological Resource Center Network demonstration project (26), they have worked to develop the network of collections under the EU Framework 7 and call this network the Microbial Resources Research Infrastructure (MIRRI) (27). Taking advantage of existing codes such as MOSAICC (Micro-Organisms Sustainable use and Access regulation International Code of Conduct), they have developed an ABS policy that focuses on the operations of a typical microbial biological resource center (according to the Organisation for Economic Co-operation and Development [OECD] guidelines) (28). Their recommended best practices are translated into practice and supported by community-based interpretations tested with policy makers and regulators. The MIRRI ABS policy provides mechanisms of compliance from accession to supply, model documents such as material accession agreements (MAA) and material transfer agreements (MTA), and provides a decision tree to indicate when activities are in the scope of the protocol and the steps needed to be compliant. In addition to the MIRRI ABS Manual, many other best-practices guides are available (Table 1).

(iii) Partner organizations and efforts. As a nongovernmental observer at the Meeting of the Parties to the Nagoya Protocol, Scientific Collections International provided a perspective on managing access to genetic information based on living and once-living collections. Similarly, the Ecological Society of America has engaged on this

TABLE 2 Holdings and distribution of participating genetic resources in the United States[a]

Collection name	Acronym	No. of strains					
		Total	From outside the USA	Accessioned after 1992	With public whole-genome sequence	Distributed within the USA	Distributed outside the USA
Fungal Genetics Stock Center	FGSC	26,000	568	1,800	600	21,551	9,504
The Mollicutes Collection	TMC	988	337	90	33	30	14
Bloomington Drosophila Stock Center	BDSC	59,915	7,929	58,060	214	109,792	107,603
Center for Forest Mycology Research Culture Collection	CFMR	13,241	2,200	7,730	30	10,327	2,633
Centre for Agriculture and Biosciences International	CABI	30,000	28,330	12,750	11	112	16,800
E. coli Genetic Stock Center	CGSC	10,000	0	6,927	8	43,741	42,438
Phaff Yeast Culture Collection	UCDFST	7,581	2,759	2,508	132	6,202[b]	1,285[b]
National Center for Marine Algae and Microbiota	NCMA	2,648	1,751[c]	1,803	20	711	457
UTEX Culture Collection of Algae	UTEX	3,026	1,300	1,030	10	18,265[b]	6,505[b]

[a]Data are since 1993 for collections participating in the 2017 USCCN meeting.
[b]Distribution data since 2006.
[c]Includes strains without geographic origin information or from international waters.

topic and will hold workshops later in 2017 and 2018 to share information on the Nagoya Protocol with leaders of scientific societies as a conduit to their membership. The American Phytopathological Society has been a leader in issues related to living microbe collections (29) and also provides administrative support to the USCCN.

The World Federation for Culture Collections (WFCC) has served as a venue for interaction among culture collections for nearly 70 years. As such, living microbe collections have the benefit of a history of codes of conduct to ensure fair and equitable access to genetic resources. Beginning with the MOSAICC code of conduct that was a response to the Bonn Guidelines on access to genetic resources and the fair and equitable sharing of benefits arising out of their utilization adopted under the framework of the CBD in 2002 (30), culture collections now have the benefit of the Transparent User-friendly System of Transfer for Science and Technology (TRUST), which is an updated code of conduct for sharing microbial resources. TRUST relies on a demonstrated chain of custody and requires collections to document where they received materials from and where they sent those materials. Among the presentations at the February 2017 meeting was a demonstration of how TRUST could facilitate microbial utilization in collaboration with CBD and the World Data Centre for Microorganisms (31).

U.S. COLLECTIONS AND THE NAGOYA PROTOCOL

Many U.S. collections hold materials that were isolated within the sovereign boundaries of another country (Table 2), and the status of individual strains may depend on yet-to-be enacted national legislation in the provider country. Many collections hold large numbers of isolates that were collected and deposited prior to the ratification of the CBD or the Nagoya Protocol. The Fungal Genetics Stock Center (FGSC), for example, holds more than 500 strains that were collected around the world prior to 1993 (Table 2). Other resources are isolated in common areas such as the open ocean, and they have unique legal status (32). Many U.S. research resource collections hold genetically characterized model organism strains with various histories such as strains that were isolated in the early classical genetic era, genetically crossed, mutagenized, and modified by various molecular genetic techniques (33–35).

Additional U.S. collections described at the February 2017 USCCN meeting included a freshwater alga collection (UTEX Culture Collection of Algae) (36), a cave microbe collection (University of Akron) (7), and a biodiversity collection of yeasts (Phaff Yeast Culture Collection, University of California, Davis) (37). These collections hold diverse resources used in genetic, biodiversity, and industrial biotechnology research. Of these collections, the FGSC is primarily a research resource repository serving a specific research community by holding and managing classical genetic and gene deletion mutant strains, in addition to nearly 5,000 wild-type strains isolated in nature around the world.

While classical and targeted genetic mutants are primarily research tools, their importance was recently reemphasized by the inability to recapitulate phenotypes seen in zebra fish gene suppression lines using mutant lines generated with molecular tools such as CRISPR-Cas (38).

Among the biodiversity collections described at the meeting, the collection of cave microbes held at the University of Akron has special provenance. Originally isolated in caves managed by the U.S. National Park Service, these strains will ultimately be distributed through the American Type Culture Collection as a special collection (http://www.cavescience.com/). Other collections represented at the meeting include the U.S. Department of Agriculture (USDA) Agriculture Research Service (ARS) Culture Collection (Peoria, IL), the USDA ARS security back-up collection (Fort Collins, CO), which holds more than 111,000 microbial isolates from 20 different U.S. culture collections, the Bloomington Drosophila Stock Center (Bloomington, IN), the USDA Forest Service's Center for Forest Mycology Research collection (Madison, WI), and The Mollicutes Collection of Cultures and Antisera (Gainesville, FL).

EXISTING PRACTICES

To allow comparison and establish precedent, participants at the February 2017 meeting shared their accession and distribution practices. It was clear that this was an area where each collection's practices reflected the historical role of each collection as well as the types of material in the collection (Table 2). Historical biodiversity collections and research resource collections often have very simple accession and transfer requirements, while formal government collections often have more-formal MTA agreements (39). The terminology for accession and distribution contracts was very different for different types of collections. The fact that most living collections can distribute materials while keeping the original distinguishes them from other types of collections. Efforts to develop best practices for sharing invertebrate biological control organisms acknowledge that living microbial genetic resources for biocontrol have unique issues relating to the Nagoya Protocol (40).

MICROBIAL GENETIC RESOURCES AND A MICROBIAL COMMONS

The dinner talk provided history on the development of the Nagoya Protocol beginning with the Bonn Declaration (41) and continuing through the current protocol. The talk emphasized the context of the CGIAR (Consultative Group for International Agricultural Research) system and their participation in the multilateral system of access and benefit sharing developed as part of the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA) (42). In this context, the potential advantages of a "Microbial Commons" with predefined multilateral access and benefit-sharing guidelines were presented. This approach is considered in paragraphs 12 and 16 of the EU regulation no. 511/2014 which also recognizes that the ITPGRFA (43) and the Pandemic Influenza Preparedness Framework (44) are consistent with the Nagoya Protocol. The flexibility in the Nagoya Protocol, including Articles 4 and 20, enable the recognition of the practices of the microbial sector, such as the TRUST code of conduct or the Pandemic Influenza Preparedness Framework (25). Article 19 on model contractual clauses recognizes the advantage of having standardized contracts such as those developed by microbial collections for deposit and distribution of material, the Material Accession (or Deposit) Agreement and the Material Transfer Agreement, respectively. This is an area of intense discussion and negotiation, as national legislation develops in countries around the world (45).

SUMMARY

Although the United States did not ratify the CBD and is not a signatory to the Nagoya Protocol, this international agreement does affect U.S. scientists. The Nagoya Protocol provides countries with a framework to implement one of the three objectives of the CBD, namely, the fair and equitable sharing of benefits arising out of the utilization of genetic resources. The Nagoya Protocol sets out core obligations for its

contracting parties to take measures in relation to access to genetic resources, benefit sharing, and compliance, which may impact the requirements for collecting, transporting, and using microbes of international origin. The specific terms vary by country of origin, including what organisms are covered, what uses are restricted, and what agreements and permits must be obtained. Information on ABS procedures and requirements continue to emerge as the parties enact national regulations. Curators and customers of U.S. biological collections are encouraged to refer to the Access and Benefit-Sharing Clearing-House website for updated information on emerging legislation and regulations that apply to the use of living biological diversity.

SUPPLEMENTAL MATERIAL

Supplemental material for this article may be found at https://doi.org/10.1128/mBio.00982-17.

TEXT S1, DOCX file, 0.1 MB.

ACKNOWLEDGMENT

The USCCN is supported by grant DBI-1534564 from the U.S. National Science Foundation.

REFERENCES

1. Smith D, Fritze D, Thompson F, Stackebrandt E. 2013. Public Service Collections and Biological Resource Centers of Microorganisms, p 267–304. *In* Rosenberg E, DeLong EF, Stackebrandt E, Lory S, Thompson F (ed), The prokaryotes: prokaryotic biology and symbiotic associations, 4th ed. Springer-Verlag, Berlin, Germany.
2. McCluskey K, Boundy-Mills K, Dye G, Ehmke E, Gunnell GF, Kiaris H, Polihronakis Richmond MP, Yoder AD, Zeigler DR, Zehr S, Grotewold E. 2017. The challenges faced by living stock collections in the USA. eLife 6:e24611. https://doi.org/10.7554/eLife.24611.
3. Dugan FM, Jr, Wiest A, McCluskey K. 2011. Public germplasm collections and revolutions in biotechnology. J Biosci 36:205–209. https://doi.org/10.1007/s12038-011-9060-y.
4. Mullis K, Faloona F, Scharf S, Saiki R, Horn G, Erlich H. 1986. Specific enzymatic amplification of DNA in vitro: the polymerase chain reaction. Cold Spring Harb Symp Quant Biol 51:263–273. https://doi.org/10.1101/SQB.1986.051.01.032.
5. Ishino Y, Shinagawa H, Makino K, Amemura M, Nakata A. 1987. Nucleotide sequence of the iap gene, responsible for alkaline phosphatase isozyme conversion in Escherichia coli, and identification of the gene product. J Bacteriol 169:5429–5433. https://doi.org/10.1128/jb.169.12.5429-5433.1987.
6. Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna JA, Charpentier E. 2012. A programmable dual-RNA–guided DNA endonuclease in adaptive bacterial immunity. Science 337:816–821. https://doi.org/10.1126/science.1225829.
7. Pawlowski AC, Wang W, Koteva K, Barton HA, McArthur AG, Wright GD. 2016. A diverse intrinsic antibiotic resistome from a cave bacterium. Nat Commun 7:13803. https://doi.org/10.1038/ncomms13803.
8. Ferrer M, Golyshina O, Beloqui A, Golyshin PN. 2007. Mining enzymes from extreme environments. Curr Opin Microbiol 10:207–214. https://doi.org/10.1016/j.mib.2007.05.004.
9. Newman DJ, Cragg GM. 2016. Drugs and drug candidates from marine sources: an assessment of the current "state of play". Planta Medica 82:775–789. https://doi.org/10.1055/s-0042-101353.
10. Fischer J, Schroeckh V, Brakhage AA. 2016. Awakening of fungal secondary metabolite gene clusters, p 253–273. *In* Schmoll M, Dattenbock C (ed), Gene expression systems in fungi: advancements and applications. Springer, Cham, Switzerland. https://doi.org/10.1007/978-3-319-27951-0_11.
11. Müller R, Wink J. 2014. Future potential for anti-infectives from bacteria–how to exploit biodiversity and genomic potential. Int J Med Microbiol 304:3–13. https://doi.org/10.1016/j.ijmm.2013.09.004.
12. Stromberg PM, Dedeurwaerdere T, Pascual U. 2013. The heterogeneity of public ex situ collections of microorganisms: empirical evidence about conservation practices, industry spillovers and public goods. Environ Sci Policy 33:19–27. https://doi.org/10.1016/j.envsci.2013.04.003.
13. Stackebrandt E, Smith D, Casaregola S, Varese GC, Verkleij G, Lima N, Bridge P. 2014. Deposit of microbial strains in public service collections as part of the publication process to underpin good practice in science. SpringerPlus 3:208. https://doi.org/10.1186/2193-1801-3-208.
14. McCluskey K. 2017. A review of living collections with special emphasis on sustainability and its impact on research across multiple disciplines. Biopreserv Biobank 15:20–30. https://doi.org/10.1089/bio.2016.0066.
15. Smith DJ, Timonen HJ, Jaffe DA, Griffin DW, Birmele MN, Perry KD, Ward PD, Roberts MS. 2013. Intercontinental dispersal of bacteria and archaea by transpacific winds. Appl Environ Microbiol 79:1134–1139. https://doi.org/10.1128/AEM.03029-12.
16. Nielsen KB, Kjøller R, Bruun HH, Schnoor TK, Rosendahl S. 2016. Colonization of new land by arbuscular mycorrhizal fungi. Fungal Ecol 20:22–29. https://doi.org/10.1016/j.funeco.2015.10.004.
17. Flombaum P, Gallegos JL, Gordillo RA, Rincón J, Zabala LL, Jiao N, Karl DM, Li WK, Lomas MW, Veneziano D, Vera CS, Vrugt JA, Martiny AC. 2013. Present and future global distributions of the marine cyanobacteria Prochlorococcus and Synechococcus. Proc Natl Acad Sci U S A 110:9824–9829. https://doi.org/10.1073/pnas.1307701110.
18. Shear CL. 1933. Exploring and collecting expeditions. Science 78:580. https://doi.org/10.1126/science.78.2034.580.
19. Schrijver N. 2008. Sovereignty over natural resources: balancing rights and duties, vol 4. Cambridge Studies in International and Comparative Law. Cambridge University Press, Cambridge, United Kingdom.
20. Herkenrath P, Harrison J. 2011. The 10th meeting of the Conference of the Parties to the Convention on Biological Diversity—a breakthrough for biodiversity? Oryx 45:1–2. https://doi.org/10.1017/S0030605310001663.
21. Smith D, da Silva M, Jackson J, Lyal C. 2017. An explanation of the Nagoya Protocol and Access and Benefit Sharing, and its implication for microbiology. Microbiology 163:289–296. https://doi.org/10.1099/mic.0.000425.
22. Bourdy G, Aubertin C, Julian V, Deharo E. 2017. Quassia "biopiracy" case and the Nagoya Protocol: a researcher's perspective. J Ethnopharmacol 206:290–297. https://doi.org/10.1016/j.jep.2017.05.030.
23. Desmeth P. 2017. The Nagoya Protocol applied to microbial genetic resources, p 205–217. *In* Kurtboke I (ed), Microbial resources: from functional existence in nature to applications Academic Press, London, United Kingdom.
24. Pauchard N. 2017. 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? Resources 6:11. https://doi.org/10.3390/resources6010011.
25. Cressey D. 2017. Treaty to stop biopiracy threatens to delay flu vaccines. Nature 542:148. https://doi.org/10.1038/542148a.
26. Fritze D, Martin D, Smith D. 2012. Final report on the GBRCN Demonstration Project. GBRCN Secretariat, Braunschweig, Germany.
27. Schüngel M, Stackebrandt E, Bizet C, Smith D. 2013. MIRRI-The Microbial Resource Research Infrastructure: managing resources for the bio-economy. EMBnet J 19:5–8. https://doi.org/10.14806/ej.19.1.706.

28. Organisation for Economic Co-operation and Development. 2007. OECD best practice guidelines for biological resource centres. Organisation for Economic Co-operation and Development, Paris, France.
29. Kang S, Blair JE, Geiser DM, Khang CH, Park SY, Gahegan M, O'Donnell K, Luster DG, Kim SH, Ivors KL, Lee YH, Lee YW, Grünwald NJ, Martin FM, Coffey MD, Veeraraghavan N, Makalowska I. 2006. Plant pathogen culture collections: it takes a village to preserve these resources vital to the advancement of agricultural security and plant pathology. Phytopathology 96:920–925. https://doi.org/10.1094/PHYTO-96-0920.
30. Secretariat of the Convention on Biological Diversity. 2002. Bonn guidelines on access to genetic resources and fair and equitable sharing of the benefits arising out of their utilization. Secretariat of the Convention on Biological Diversity, Montreal, Quebec, Canada.
31. Wu L, Sun Q, Desmeth P, Sugawara H, Xu Z, McCluskey K, Smith D, Alexander V, Lima N, Ohkuma M, Robert V, Zhou Y, Li J, Fan G, Ingsriswang S, Ozerskaya S, Ma J. 2016. World Data Centre for Microorganisms: an information infrastructure to explore and utilize preserved microbial strains worldwide. Nucleic Acids Res 45(D1):D611–D618. https://doi.org/10.1093/nar/gkw903.
32. Leary D, Vierros M, Hamon G, Arico S, Monagle C. 2009. Marine genetic resources: a review of scientific and commercial interest. Mar Policy 33:183–194. https://doi.org/10.1016/j.marpol.2008.05.010.
33. Kleiner GR, Wibberg D, Winkler A, Kalinowski J, Wertz JE, Friehs K. 2016. Complete draft genome sequence of Escherichia coli JF733. Genome Announc 4:e00298-16. https://doi.org/10.1128/genomeA.00298-16.
34. Colot HV, Park G, Turner GE, Ringelberg C, Crew CM, Litvinkova L, Weiss RL, Borkovich KA, Dunlap JC. 2006. A high-throughput gene knockout procedure for Neurospora reveals functions for multiple transcription factors. Proc Natl Acad Sci U S A 103:10352–10357. https://doi.org/10.1073/pnas.0601456103.
35. Gallaher SD, Fitz-Gibbon ST, Glaesener AG, Pellegrini M, Merchant SS. 2015. Chlamydomonas genome resource for laboratory strains reveals a mosaic of sequence variation, identifies true strain histories, and enables strain-specific studies. Plant Cell 27:2335–2352. https://doi.org/10.1105/tpc.15.00508.
36. Brand JJ, Andersen RA, Nobles DR. 2013. Maintenance of microalgae in culture collections, p 80–89. *In* Richmond A, Hu Q (ed), Handbook of microalgal culture: applied phycology and biotechnology, 2nd ed. Wiley Interscience, Hoboken, NJ.
37. Boundy-Mills KL, Glantschnig E, Roberts IN, Yurkov A, Casaregola S, Daniel HM, Groenewald M, Turchetti B. 2016. Yeast culture collections in the twenty-first century: new opportunities and challenges. Yeast 33:243–260. https://doi.org/10.1002/yea.3171.
38. Ledford H. 2017. CRISPR studies muddy results of older gene research. Nature News. Nature Publishing Group, London, United Kingdom.
39. McCluskey K, Parsons JP, Quach K, Duke CS. 2017. An evaluation of the status of living collections for plant, environmental, and microbial research. J Biosci 42:321–331. https://doi.org/10.1007/s12038-017-9685-6.
40. Mason PG, Cock MJW, Barratt BIP, Klapwijk JN, van Lenteren JC, Brodeur J, Hoelmer KA, Heimpel GE. 2017. Best practices for the use and exchange of invertebrate biological control genetic resources relevant for food and agriculture. BioControl 2017:1–6. https://doi.org/10.1007/s10526-017-9810-3.
41. Tully S. 2003. The Bonn guidelines on access to genetic resources and benefit sharing. Rev Eur Comp Int Environ Law 12:84–98. https://doi.org/10.1111/1467-9388.00346.
42. Reichman JH, Uhlir PF, Dedeurwaerdere T. 2016. Governing digitally integrated genetic resources, data, and literature: global intellectual property strategies for a redesigned microbial research commons. Cambridge University Press, New York, NY.
43. Halewood M, Andrieux E, Crisson L, Rwihaniza Gapusi J, Wasswa Mulumba J, Kouablan Koffi E, Yangzome Dorji T, Raj Bhatta M, Balma D. 2013. Implementing 'mutually supportive' access and benefit sharing mechanisms under the Plant Treaty, Convention on Biological Diversity, and Nagoya Protocol. Law Environ Dev J 9:68–96.
44. Wilke M. 2013. The World Health Organization's Pandemic Influenza Preparedness Framework as a public health resources pool, p 315–342. *In* Chege Kamau E, Winter G (ed), Common pools of genetic resources: equity and innovation in international biodiversity law. Routledge Research in International Environmental Law. Routledge, New York, NY.
45. Overmann J, Scholz AH. 2017. Microbiological research under the Nagoya Protocol: facts and fiction. Trends Microbiol 25:85–88. https://doi.org/10.1016/j.tim.2016.11.001.