International Treaty Affects Microbiology Research

Many US microbiologists are not aware that treaties may affect their use of genetic resources, including microbes

by Kyria Boundy-Mills, David Smith, Kevin McCluskey, Stephanie Greene, and Cliff Duke

In 1993, the United Nations adopted the Convention on Biological Diversity (CBD)—a multilateral treaty, the goals of which include conservation of biodiversity, sustainable use of the components of biodiversity, and fair and equitable sharing of the benefits arising from the utilization of genetic resources (www.cbd.int). Recognizing that "biological diversity is a global asset of tremendous value to future generations," CBD establishes that countries have sovereignty over their biodiversity, and are entitled to benefits arising from its use. Because neither the CBD or the Bonn Guidelines included a mechanism to enable benefit sharing, a framework was needed to implement the goal of benefit sharing. This framework, the Nagoya Protocol, was adopted in 2010.

The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization (NP) was agreed to under the CBD to provide a transparent legal framework to implement access and benefit-sharing. The NP applies to both traditional knowledge and genetic resources, which includes microbes. It is important to understand that NP provides countries with guidelines; individual countries are enacting legislation to implement these guidelines.

The NP entered into force in October 2014 after ratification by 50 countries. NP aims to create transparency and legal certainty for both users

and providers of genetic resources by requiring all parties to establish national legislation for access to genetic resources, and by helping to ensure benefit-sharing after biological materials leave the country of origin. Such benefits can be monetary or nonmonetary. While transparency is a goal of the NP, it is an international treaty with a broad scope, negotiated over years with input from large numbers of people, institutions, and nations, and as such its coverage and implications impact life sciences researchers in every field. To assure compliance, those working in the microbial sciences should at least familiarize themselves with its general features.

Although the US did not ratify CBD, and by extension is not a party to the NP, US scientists must comply to the legislative, administrative, or policy measures enacted by countries that are parties to NP, when they use genetic resources that originate from those countries. NP has resulted in a growing network of regulations, agreements and contracts affecting both providers and users of genetic materials, with consequences for noncompliance.

Consequences for US scientists

It is important for US scientists to understand that they are subject to regulations involving the isolation, transport, or use of microbes that originate from NP signatory countries even if that use is within the US Failure to comply may result in consequences that impact US scientists and their international collaborators.

As of August 2017, 99 countries are parties to NP, and 34 of these have passed NP-related legislative, administrative, or policy measures, including China, India, Mexico, and the entire European Union. Consequences for noncompliance with these measures vary by country; for example:

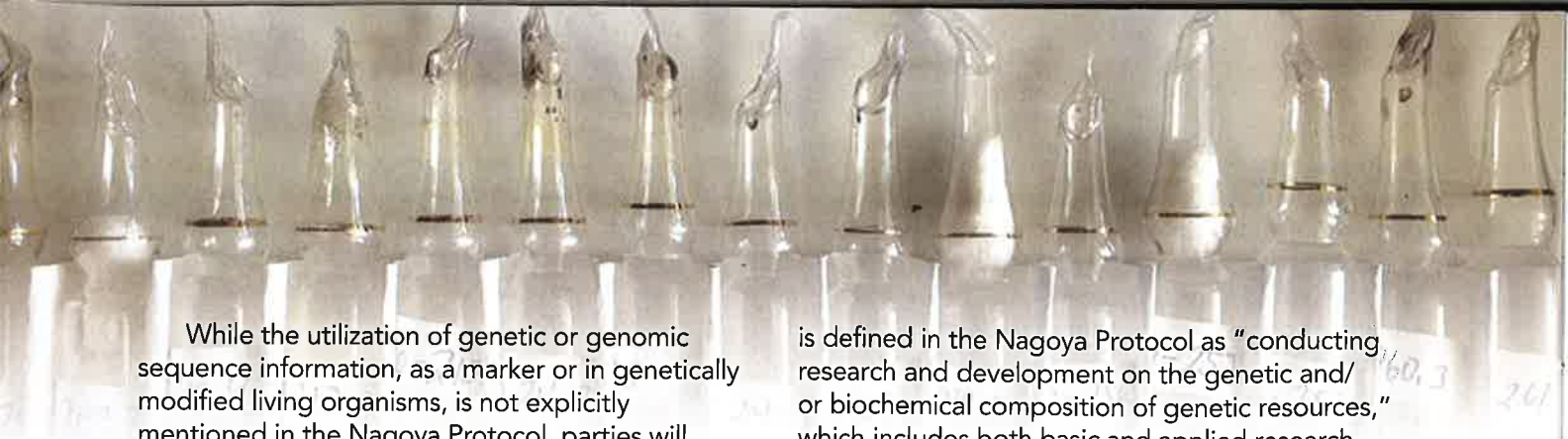
- Under South Africa Regulation 42(2), bioprospecting without a permit in South Africa can result in a fine of 5 to 10 million rand (US $700,000), or up to "three times the commercial value of the commercial activity in respect of which the offence was committed."
- China's Ministry of Environmental Protection issued a Notice on Enhancing the Access and Benefit-Sharing of Biological Genetic Resources in the Cooperation and Communication with Foreign Parties in October 2014. Government approval is required before bioprospecting in natural conservations, or removing resources.
- In August 2016, a law went into force related to genetic resources that are under French jurisdiction, including territories such as French Guiana. Researchers who conduct commercial R&D on French genetic resources without the required "track-and-trace" documentation are subject to a fine of up to 1 million Euros and up to one year in prison.
- Non-Brazilian researchers can collect biological material in Brazil only within a partnership with a Brazilian institution as the lead partner. Compliance measures in Brazil include seizure of samples and equipment, suspension of the sale of derived products, suspension of patents or licenses, fines, and/or closure of facilities, activities, or businesses.

What materials are involved?

This varies, country to country. The Nagoya Protocol applies to all genetic resources: microbes, plants, animals, and parts such as flowers and seeds. NP also applies to traditional knowledge associated with use of these genetic materials. Public microbial culture collections in other countries have worked with relevant government officials to establish procedures for deposit and distribution of microbes that comply with their country's NP guidelines. Because the US is not a party to CBD, US microbe collections, which may contain microbes from outside the US, have had less guidance regarding NP, but are now establishing procedures.

Whether NP applies to a specific microbe strain depends on the country of origin and the date it was isolated. NP legislation may apply to a microbe if the country of origin has claimed sovereign rights to its biodiversity through passing NP legislation. Article 8 of NP advises countries to allow special considerations to promote exchange of genetic resources for food and agriculture, noncommercial research, and present or imminent emergencies such as human, animal, or plant health.

Because the US is not a signatory to the NP, isolation, export, study, or commercial development of microbes originally isolated in the US is not affected. However, microbes used in the US as standards may be under ABS regimes, especially if they were collected from countries party to NP.



While the utilization of genetic or genomic sequence information, as a marker or in genetically modified living organisms, is not explicitly mentioned in the Nagoya Protocol, parties will consider how digital sequence information is relevant to the objectives of the CBD and NP. An ad hoc technical expert group will meet at the CBD Secretariat in February 2018 to discuss the use of digital sequence information under the NP. Ultimately, any regulations on the use of sequence information or genetic resources will be according to national legislation in each provider country.

What dates are pertinent?

Again, this varies country to country. NP legislation of many (but not all) countries applies to organisms originating from that country after the NP legislation went into effect. Organisms isolated prior to NP legislation are exempt in many countries. It is therefore important to preserve "heirloom" microbes isolated by past generations of microbiologists, such as those preserved in public culture collections.

While most countries consider the year an organism was originally "accessed" as the year it was isolated, Brazil considers "access" to include utilization. In other words, Brazilian legislation applies to use of any Brazilian microbes since the legislation was passed, regardless of the year the microbe was isolated from Brazil. US microbiologists are advised to educate themselves on Brazilian legislation when using any microbes from Brazil for either basic or applied research.

What activities are affected?

Users of genetic resources, including microbes, have responsibilities to follow NP and other regulations of the countries in which they work. Users are also bound by the requirements of any microbes' country of origin, even when they are used in the US Under these regulations, "utilization" of genetic resources is defined in the Nagoya Protocol as "conducting research and development on the genetic and/or biochemical composition of genetic resources," which includes both basic and applied research.

Culture collections in NP signatory countries are responsible for informing users who access the material of the provider country requirements. Culture collection activities that are generally exempt include confirmation of identity of the materials received by the collection, preservation, and storage. In contrast, research done to add value may be considered as utilization and trigger benefit-sharing for some countries.

Implementation of the NP has resulted in different actions and regulations in the ratifying countries. In the European Union (EU), an EU-wide regulation came into effect in 2014, but the member countries have chosen to apply it in different ways. The EU Regulation is triggered by utilization only when access to the genetic resource was after the date the provider country introduced regulation to implement the Nagoya Protocol. Most European countries currently do not restrict access and use of their genetic resources, with the exception of France and Spain (others may follow).

Brazil, on the other hand, triggers benefit-sharing when a product is placed on the market. Microbes that may have been isolated decades ago from Brazil are impacted when used for commercial purposes. Brazilian legislation declares that any use of Brazilian microbes (including in the US) must now be in collaboration with a Brazilian scientist, and defines in detail what benefits they expect for use of their genetic resources.

Different national regulatory bodies and institutions and culture collections are trying to put into place clear and user-friendly guidelines and procedures—not always an easy task. The uncertainties that may arise in the scientific community because of the myriad issues and use cases covered by the NP make it essential that those whose research and livelihoods may be affected can find the information and resources they need.

Getting the Word Out

Kyria Boundy-Mills is a Professional Research Microbiologist in Food Science and Technology at the University of California, Davis. Dr. Boundy-Mills has been the curator of the Phaff Yeast Culture Collection since 2001. She maintains the collection, distributes strains to researchers, and performs research that builds and/or taps the collection. She and David Smith received the 2017 ASM USFCC/J. Roger Porter Award, which recognizes efforts by scientists who sustain major resources used by the scientific community.

ASM: When did you become aware of the NP's potential impact on microbiologists?

KBM: As the Nagoya Protocol was being negotiated in 2010, I was in the middle of a 5-year NIH-funded international collaboration with researchers from Indonesia. My postdoc, Irnayuli Sitepu, attended the planning meeting in Montreal just before joining my lab and brought knowledge of the emerging issues to our group. Our team members on both sides kept on top of the NP discussions to make sure our project policies and procedures were in line with the emerging developments.

ASM: How did you become informed about the issue?

KBM: In 2015, I co-organized a session on culture collections at a yeast meeting in Italy. The presenters, mostly curators of culture collections, co-authored an article on emerging opportunities and issues facing culture collections. I thought it would be a light fluffy piece, highlighting interesting products and services. Surprisingly, a large proportion of the article [Boundy-Mills KL, Glantschnig E, Roberts IN, Yurkov A, Casarégola S, Daniel H-M, Groenewald M, Turchetti B (2016) Yeast culture collections in the 21st century: New opportunities and challenges. Yeast 33 (7):243-260. doi:10.1002/yea.3171] was about the impact of the Nagoya Protocol. That's when I realized that my knowledge of this issue was seriously lacking. I worked with colleagues in the US Culture Collection Network to plan a workshop on the Nagoya Protocol in February 2017, aimed at US culture collection curators, to explore the impact of NP on US culture collections and US microbiologists. Findings of this meeting were recently published in *mBio*. This article summarizes and further explores issues related to the impact of NP on research by US microbiologists.

ASM: What inspired you to take action to inform others?

KBM: The Nagoya Protocol has become a top issue of discussion at international microbiology meetings I have attended, but has hardly been mentioned in US meetings. In discussions with other US microbiologists over the last few years, most either hadn't heard of CBD or the Nagoya Protocol, or assumed that since the US did not ratify CBD, the policies did not affect them. I then learned of the serious consequences to both US microbiologists and their international collaborators if they fail to follow NP legislation. I felt compelled to share information that will help protect my friends and colleagues.

ASM: How can people learn more/keep informed?

KBM: A few key resources are the Convention on Biological Diversity website, which covers the CBD and its protocols, including:

- The CBD and NP website (www.cbd.int/convention/).
- The Access Benefit-Sharing Clearing House (www.absch.cbd.int), a platform for exchanging information on emerging access and benefit-sharing legislation by country.
- The US Culture Collection Network website (www.usccn.org).
- The US State Department website with resources for US scientists (www.state.gov/e/oes/ecw/access/index.htm).
- Results of a US Culture Collection Network workshop on the Nagoya Protocol, recently published in *mBio*: Kevin 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, D., Owens, KJ., Reichman, JH., da Silva, M., Wertz, J., Whitworth, C., Smith, D. 2017. The US Culture Collection Network Responding to the Requirements of the Nagoya Protocol on Access and Benefit-Sharing. *mBio* 8(4) e00982-17. doi:10.1128/mBio.00982-17.
- A more global discussion of the impact of NP on microbiology: David Smith, Chris Lyal, Manuela da Silva, Julien Jackson (2017) Explanation of the Nagoya Protocol on Access and Benefit-sharing and its implication for microbiology. Microbiology 163: 289-296. doi:10.1099/mic.0.000425. www.mic.microbiologyresearch.org/content/journal/micro/10.1099/mic.0.000425.