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The Nagoya Protocol and its implications for microbiology

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The Nagoya Protocol was drafted to ensure the fair and equitable sharing of benefits arising from the international use of genetic resources, but the lack of unified procedures and unclear definitions relating to microorganisms present considerable hurdles to microbiology research.

Field studies are critical for understanding the key ecosystem roles played by microorganisms to complement decades of laboratory-based research. They offer important insights into how complex microbial communities may respond to, and influence, climate change, in addition to agricultural and clinical implications, including disease outbreaks following host shifts. Studies addressing these crucial topics are only made possible through large collaborative networks that reflect a global scientific mission, the open exchange of data and the sharing of results with the general public.

But research without borders also has its drawbacks. Researchers in low- and middle-income countries (LMICs) remain underrecognized for their role in leading studies, and rarely, alongside their communities, reap the monetary and non-monetary benefits arising from discoveries based on genetic resources from their home countries[1]. Poorly planned and regulated field studies can also promote unsustainable and destructive research practices, including oversampling of rare taxa. Collectively, these issues called for, and continue to, a realignment in how biological resources are defined, collected and shared among international parties, along with ethical guidelines for researchers to pursue their questions through equitable and sustainable approaches.

In the past several decades there has been a steady recognition of these issues, and efforts are mounting to combat them. This included a call for the sharing of benefits arising from the use of genetic resources, introduced within the framework of the Convention on Biological Diversity (CBD) that was established in 1992. The CBD's three main objectives are the conservation of biodiversity, its sustainable use and the fair sharing of benefits arising from the use of genetic resources. The latter was subject to intense discussions among the CBD's parties, which resulted in the adoption of the Nagoya Protocol on Access and Benefit Sharing (ABS) in 2010 that came into effect in 2014 and has, to date, been ratified by 140 countries[2].

The Nagoya Protocol's laudable intent was to establish a framework ensuring that: (1) users of genetic resources share the benefits resulting from their use with the countries of origin (provider countries); (2) the rights of Indigenous people and traditional knowledge are respected; (3) both providers and users have legal clarity over the use of genetic resources; and (4) there is an incentive to use the funds generated through ABS for conservation efforts and facilitating biodiversity conservation by LMICs. At the time, provider countries expected financial revenues and non-financial benefits from ABS, and some scientists were hopeful that the Nagoya Protocol had the potential to enhance legal certainty and facilitate permit application processes[3]. Others, however, already voiced serious concerns that it was more likely to have the opposite effect, that is, overly complicated and bureaucratic procedures severely impeding both fundamental and applied research[4]. Unfortunately, while the CBD acknowledges the central importance of basic research to achieve its biodiversity goals, the Nagoya Protocol regulates fundamental and applied research equally and merely encourages the parties to "create conditions to promote and encourage research [...], including through simplified measures on access for non-commercial research purposes" (section 8a)[2].

This Comment highlights the challenges faced by microbiologists to remain compliant of the Nagoya Protocol given an uneven administrative landscape across signatory states, and the incompatibility of the protocol's core tenants with the biology of microorganisms.

Implications of the Nagoya Protocol

Given the binding nature of the Nagoya Protocol across its signatory countries, it is important to outline the reality of implementing its 36 articles. For researchers striving for direct access to genetic resources from a provider country, compliance is expected during project conceptualization and before obtaining samples for research. Upon clarifying national laws, procedures and point of contact, this critical step entails seeking and finalizing prior informed consent (PIC) and mutually agreed terms (MAT), as well as a material transfer agreement (MTA). Provider countries are then expected to issue a research permit. After publishing a record of it on the Access and Benefit-Sharing Clearing-House (ABSCH) website, an Internationally Recognized Certificate of Compliance (IRCC) is triggered. Countries vary substantially in their processing of requests, including timelines and success rates. And with an IRCC obtained, additional authorizations may be needed, including an export license, and access permits to specific sites. Both can be, and often are, issued by different local authorities, thereby complicating the administrative process. As an example, to collect and export biological samples from Argentina for molecular work, up to ten different documents are required from different local, regional and national authorities on timelines that can range from several weeks to years[5].

Today, nine years after the Nagoya Protocol entered into force, its track record is sobering (Fig. 1a). As of August 2023, the protocol's central administrative instrument, the ABSCH, lists National Focal Points as contact addresses for ABS applications for 136 out of the 140 Nagoya Protocol parties, but only about half of the parties (that is, 71) list a Competent National Authority (CNA) as required according to the protocol (note that some countries list multiple CNAs, so the total number is higher than 71). Additionally, only 20 countries provide ABS procedures on the ABSCH website (12 in English), thereby giving

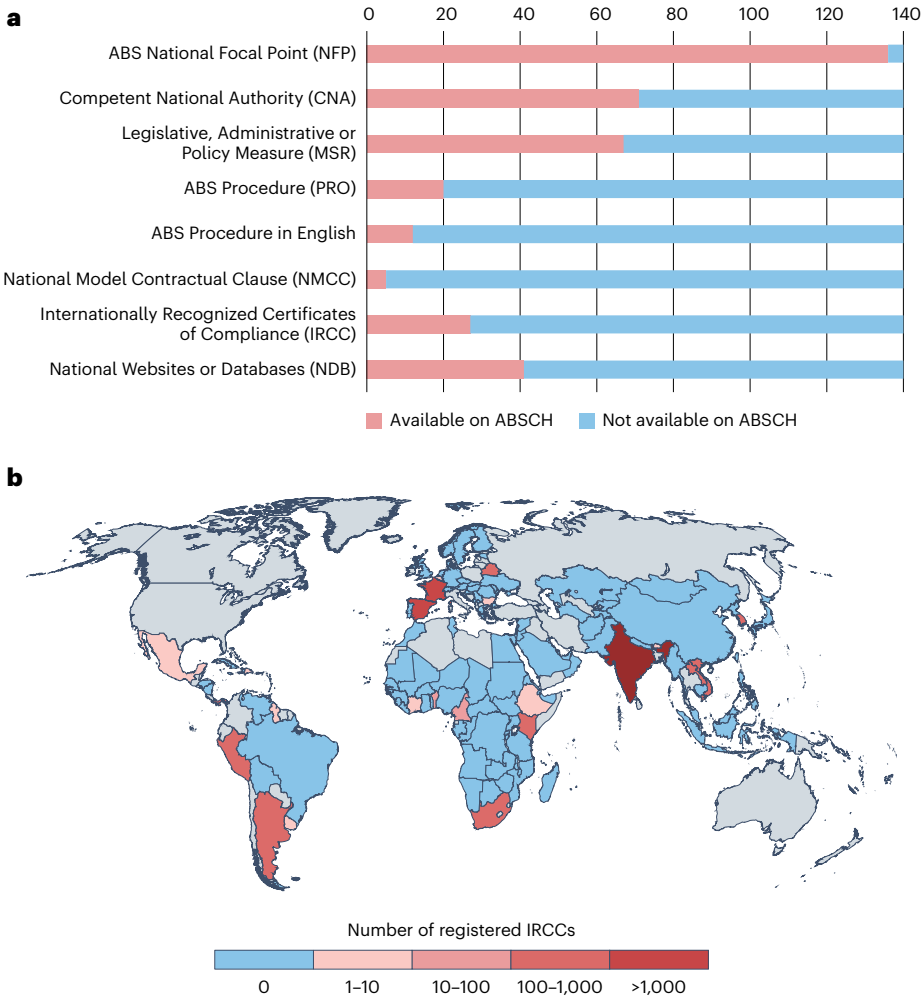

Fig. 1 | Implementation of the Nagoya Protocol in the participating countries. **a**, Number of countries (out of the 140 parties) for which the required or recommended information on responsible authorities and ABS measures is available (red) or not available (blue) on the official CBD website. **b**, Number of registered ABS permits (that is, IRCCs) per country as of August 2023. Grey, non-parties; blue, parties without any registered IRCCs; different shades of red, parties with registered IRCCs (see legend). Publ. note: Springer Nature is neutral about jurisdictional claims in maps.

an outline of the processes necessary to obtain Nagoya Protocol permits, and only 5 countries followed the protocol's recommendation to add model clauses for contractual agreements (Fig. 1a). Of the 4,932 officially registered permits (IRCCs) so far, more than 90% are from only 5 countries (India, France, Spain, Argentina and Kenya). Only 12 countries issued more than 20 permits, respectively, and more than 80% of the Nagoya Protocol parties (113 countries) did not register a single permit (Fig. 1b). The low number of permits is a testament to the often complex, lengthy and opaque application procedures that vary widely across countries and generate a substantial burden and legal insecurity for users of genetic resources[6]. On the providers' side, the expected monetary benefits from ABS regulations did not materialize[7], nor did ABS result in increased investment in conservation efforts. In conclusion, the Nagoya Protocol — although developed with the best of intentions — has not delivered on its promises. It has not resulted in substantial benefits to provider countries, and it has impeded fundamental and applied research in a number of countries that failed to implement streamlined procedures for obtaining genetic resource access permits[7]. In many LMICs, the latter is likely due to limited funds available to establish the necessary administrative infrastructure.

Relevance of the Nagoya Protocol for microbiology

When drafted, the protocol accounted for concepts of biodiversity that remain largely incompatible with the biology of microorganisms. The incongruence is threefold. First, legislation was drafted and enacted while microbial communities were poorly characterized across most environments, including regions heralded as biodiversity hotspots for plants and animals (for example, rainforests). Countries hosting speciose floras and faunas may not necessarily be as diverse in their microorganisms, as indicated by comparisons of soil microbial communities in temperate and subtropical regions[8]. However, our understanding of microbial biogeography is still at an early stage, which is why recent efforts to map the distribution of taxa across terrestrial and aquatic environments are so critical. Unfortunately, these global

BOX 1

Moving forward

Considering the limited success of the Nagoya Protocol and the challenges associated with the complexity and diversity of ABS regulations within and across Nagoya Protocol parties, there is a need to implement changes that ensure ABS while encouraging basic research. Here, we provide suggestions for measures that could be discussed at the upcoming 2023 United Nations Climate Change Conference (COP 28).

- Ensure that all Nagoya Protocol parties implement streamlined, transparent and clear procedures (including information on maximum decision times for permit applications) to comply with ABS regulations and provide information thereof on the ABSCH website (see Articles 13 and 14 of the protocol).
- In line with Article 8 of the protocol, encourage fundamental research by: (1) re-defining the "Utilization of genetic resources" (Article 2) to explicitly exclude basic research with the purpose of taxonomy, phylogenetics and biodiversity monitoring (and potentially other uses with non-commercial purpose) from ABS regulations, as has already been done in the European Union[15]; (2) incentivizing the establishment of simplified procedures for permit application processes for all areas of fundamental (that is, non-commercial) research; (3) creating a fast-track permit application procedure for already established international collaborations between researchers from provider and user countries.
- Encourage all Nagoya Protocol parties to quickly implement exceptions from the Nagoya Protocol for researchers of provider countries to allow genetic resources to be sent abroad for commercially provided analytical services (for example, high-throughput sequencing, proteomics and metabolomics). In parallel, funds raised through ABS could be used to expand research infrastructure in LMICs in addition to the current and stated aims for conservation, thereby mitigating the reliance of provider states on international commercial services.
- Based on the current deliberations on DSI, the CBD should explore the possibility of revising the Nagoya Protocol from a bilateral to a multilateral ABS framework. In this context, an international biodiversity fund could be envisioned that is financed by contributions from users of genetic resources and distributes funds among provider countries according to the use of these resources. These funds should be specifically used to promote conservations efforts and the protection of biodiversity.
- In future discussions about regulatory frameworks with possible impacts on open science, an increased participation and engagement of scientists from both high-income countries and LMICs in the discussions and the decision-making process is necessary to adequately consider the negative consequences for fundamental and applied research.

surveys remain constrained by policies aiming to protect communities of bacteria, archaea and fungi that are yet to be defined, counterproductive to the mission of the CBD. Second, the establishment of PIC and MAT between providers and users generally requires taxonomic classification of the genetic resource at the time of collection or export. While this can already be challenging for megadiverse groups of animals or plants, it is effectively impossible for microorganisms before detailed laboratory work and sequencing. Obtaining permits for environmental samples or host-associated microbial communities can therefore be particularly challenging[9]. Furthermore, if high-throughput sequencing facilities are not available, taxonomic identification can even be the reason for local researchers in LMICs to send samples to collaborators or sequencing companies abroad. While some countries have recognized this issue and enacted special exemptions from the Nagoya Protocol for this particular scenario (for example, Brazil[9]), others have not. Third, the concept of local endemism — the confinement of a species to a single geographical location — rarely applies to microorganisms. Most microbial taxa are widespread and capable of dispersing across vast distances and in short time periods[8]. The high genetic relatedness of certain microbial species across continental sampling sites further negates the case for local endemism, diversity hotspots and extinction threats, three foundational concepts behind the Nagoya Protocol.

Beyond the general problems with applying the Nagoya Protocol regulations to microbiology, a growing reason for concern is the potential hurdle the protocol can present to the rapid exchange of samples and data necessary to adequately respond to emerging infectious diseases[10]. The recent COVID-19 pandemic has dramatically illustrated how important the rapid international exchange of samples and the public release of sequence data was for the timely development of diagnostic tests and vaccines[11]. This exchange, however, happened on a voluntary basis, with provider countries renouncing their right to negotiate ABS terms on viral samples in favour of a rapid international effort to combat the disease[11]. By contrast, the sharing of seasonal influenza virus samples has previously suffered from delays caused by conflicts with national legislations on ABS, in turn resulting in delays in vaccine development[10]. Thus, there is an urgent need to reconcile the restrictions imposed by the Nagoya Protocol on the exchange of genetic resources with the necessity to respond rapidly through internationally coordinated research efforts to future disease outbreaks.

Despite the shortcomings of the Nagoya Protocol, the CBD parties are currently exploring options to implement ABS regulations on the use of digital sequence information (DSI). This is because developments in synthetic biology increasingly allow for using sequence information for commercial purposes without the need to collect new physical samples. Such a shortcoming was recognized by the Nagoya Protocol parties early on, triggering a heated discussion on the inclusion of DSI in the Nagoya Protocol framework. However, given the current life sciences' heavy reliance on the principles of open data and open science, and particularly the open exchange of DSI in global databases, the prospect of an extension of the protocol's bilateral ABS rules to DSI sparked resistance and fear of a bureaucratic nightmare in most of the scientific community[12]. Scientists, scientific organizations, funding agencies and governments responded by publishing statements and papers on the importance of open data and the negative

impacts that a bilateral approach on DSI access would have for the life sciences, and specifically for biodiversity research and conservation efforts[13]. Fortunately, at the most recent Convention of the Parties to the Convention on Biological Diversity (COP15) in Montreal in 2022, the CBD parties agreed in Decision 15/9 to abandon a bilateral approach on DSI in favour of exploring a multilateral framework[14]. Although the details still need to be developed, Decision 15/9 explicitly acknowledges the importance of open access to DSI for the life sciences[14], so the final agreement will hopefully present a solution that provides true benefits to the provider countries while not impeding access to DSI for users[13]. If successful, such a scenario would then provide the opportunity to rethink the Nagoya Protocol's bilateral framework for the access of physical samples in favour of a more efficient and sustainable solution. Decision 15/9 explicitly mentions the "potential to voluntarily extend the multilateral mechanism to genetic resources or biological diversity" among the "Issues for further consideration", opening the door for simplifying ABS regulations in the future[14].

Potential barriers and paths forward

While the Nagoya Protocol aims to ensure fair and equitable sharing of benefits, it does not distinguish between commercial and non-commercial utilization of genetic resources. As a result, one unintended consequence is a growing hesitation to initiate scientific collaborations between high-income countries and biodiverse LMICs[1]. Such hesitancy may culminate in more isolated scientific communities that function and develop in parallel, rather than collaboratively through the exchange of ideas, training and resources. The risk of further alienating and sidelining researchers in LMICs is substantial, which may result in skewed and unrepresentative research fields. We acknowledge the core concerns addressed by the Nagoya Protocol, and we emphasize that users of genetic resources have an ethical — in addition to the legal — responsibility to share the benefits arising from the use of these resources with the provider countries. However, we also point out that signatory countries should be expected to develop functioning bureaucracies to navigate their regulations in a clear and straightforward manner. In Box 1, we provide a list of suggested measures that could be discussed by the Nagoya Protocol parties to reduce the bureaucratic burden of the protocol and to encourage research in both provider and user countries.

Nine years following the implementation of the Nagoya Protocol, reaching the CBD's goals seems farther away than ever, with biodiversity research racing to catalogue the organisms we are currently destroying and to understand their functions in natural ecosystems. Additionally, during the COVID-19 pandemic, the world came to realize the necessity for the rapid exchange of research samples and data in the event of an imminent global emergency. The coupled crises of climate change and biodiversity loss unfold on a different timeline, but already have increasingly dramatic impacts on human life and well-being. Given that microbes are major players whose activities can exacerbate global change but may also provide powerful novel solutions to problems arising due to anthropogenic activities, we must ask whether we can afford to delay fundamental research on the identity, distribution and activities of microorganisms by an increasing bureaucratic burden of access regulations. Considering the dramatic speed of biodiversity loss, many organisms may not be here for much longer to be described and studied, unless policymakers and regulatory institutions across countries work together to facilitate and support, rather than to constrain, fundamental science in a fair and equitable international effort.

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Competing interests

The authors declare no competing interests.