UK Parliament POST

POSTNOTE

Number 630 September 2020

Digital Sequence Information

Evolving life sciences and agricultural research approaches may have a decreasing need to access physical resources in future, such as plant seeds or viral material. Information and genetic data may be all that is required for commercial exploitation of biological resources. This POSTnote summarises the challenge this creates for international discussions on the governance of genetic resources and the possible options for addressing these.

Overview heading

- Digital sequence information (DSI) refers to the digital biological data in various international negotiations around sharing benefits from the uses of genetic resources.
- A definition has yet to be agreed; it could be restricted to inherited genetic information, or cover all relevant digital biological data and even associated traditional knowledge.
- Millions of sequences are submitted annually to open access and public databases. Tracking their subsequent use would be challenging and could affect research.
- More countries may regulate DSI use domestically if negotiations fail to reach a resolution but, if flawed, an international approach could also hinder research.

Sharing the benefits of genetic resources

Use of natural biological resources is core to a range of economic activities, such as plant and animal breeding for agriculture. Before the 1980s, such resources were seen as the common heritage of humankind and available without restriction.[1] This led to issues of equity and fairness as developed countries had greater technological capacity to exploit biological resources than developing countries that are rich in such resources and associated traditional knowledge.[2,3] This included controversies over plant genetic resources.[4] Biodiverse developing countries argued it was unfair to pay for protected crop varieties (PN 517), which could not have been developed without the plant material originally collected in their territories and made available through seed banks and international repositories.[5]

Sovereignty over genetic resources

The 1992 Convention on Biological Diversity (CBD) established genetic resources are under national sovereignty. However, it is one part of international governance of genetic resources:

- The 2001 International Treaty for Plant Genetic Resources for Food and Agriculture (or 'Plant Treaty')[6,7,8] seeks to integrate aspects of intellectual property and national sovereignty for plant genetic resources (Box 1).[1,2,9,10]
- WHO Pandemic Influenza Preparedness Framework (Box 2).
- The UN Convention on the Law of the Sea (UNCLOS, Box 3).

Multilateral organisations with an interest in the governance of genetic resources include the CBD, the UN Food and Agriculture Organization (FAO), the World Intellectual Property Organization (WIPO, Box 4) and the World Trade Organization Council for Trade-Related Aspects of Intellectual Property (TRIPS). For instance, TRIPS requires member states to provide intellectual protection for plant varieties, either by patents or an effective stand-alone system, or a combination of both.[11]

A key governance consideration is how biological materials are accessed and the fair and equitable sharing of the benefits of their use. For example, it is anticipated that this will help deliver the UN Sustainable Development Goals of ending poverty and hunger (1 and 2) and protecting life on land (15).[12,13] The 2014 Nagoya Protocol to the CBD set out a detailed mechanism for access and benefit sharing (ABS) of "genetic material of actual or potential value" where genetic material is "of biological origin containing functional units of heredity".[14] Access is based on a system of bilateral contracts. There are examples of ABS contracts delivering benefits,[15,16] but few commercial agreements are known to have been concluded under the CBD (as they may be confidential),[17,18] and studies suggest the time taken to negotiate CBD ABS processes deter research.[19,20]

The Plant Treaty also defines genetic material as "any material of plant origin" containing functional units of heredity.[21] Unlike the CBD, it has a multilateral access and benefit sharing system

The Parliamentary Office of Science and Technology, Westminster, London SW1A 0AA
02072192840 **post@parliament.uk** **parliament.uk/post** **@POST_UK**

Box 1: Sharing crop plant genetic resources
The UN Food and Agriculture Organization (FAO) recognised national sovereign rights over plant genetic resources in 1991. The FAO Commission on Genetic Resources for Food and Agriculture oversees the International Treaty for Plant Genetic Resources for Food and Agriculture, as well as assessments of the state of genetic resources for food and agriculture.[22] The treaty addressed tensions over ownership of plant genetic resources in collections, such as gene banks of biological material from crop species and their wild relatives, and intellectual property rights over plant varieties.[23] It established a multilateral ABS system to "facilitate access to plant genetic resources for food and agriculture, and to share, in a fair and equitable way, the benefits arising from the utilization of these resources".[24] This applies to 64 specified crop species (other crops fall under the CBD). There are standardised terms and conditions for the exchange of 'materials'. The Commission has undertaken reviews of the issues raised by DSI since 2016,[25,26] and the Governing Body of the Treaty has sought evidence submissions on DSI.[27] However, the November 2019 negotiations on DSI, to revise the agreement for sharing material and expand the number of crops species covered, failed to reach consensus and will be re-visited in November 2021.[28]

that has generated research benefits for food security, with over 3.3 million samples distributed by 2017 (Box 1).[9] Payments of 1.1% of all sales may be applied to commercial crop varieties developed, depending on how intellectual property protection is provided. There are exemptions for sales below a set threshold and a voluntary payment system for plant breeders' rights (PN 517).[9] The sharing of the pooled financial benefits within the Plant Treaty framework has only occurred in 2018, despite Norway committing in perpetuity to pay 0.1% of seed sales.[29]

Since 2016, international negotiations on access and benefit sharing have begun to consider how to address the challenges that arise if research methods can substitute use of physical biological material with online genetic data.[21] The CBD have referred to this data as digital sequence information (DSI), and their approach will be influential in informing other frameworks.

Box 2: Sharing pathogen material
The World Health Organization (WHO) has a Pandemic Influenza Preparedness (PIP) Framework for the sharing of pandemic influenza viruses within the Global Influenza Surveillance and Response System (GISRS), an international network of public health laboratories.[30] Commercial bodies may also access viral material,[31] after making a financial contribution to the running costs of the GISRS.[32] The PIP Framework relies on standardised agreements for the exchange of materials between provider countries and users, with the WHO as an intermediary.[33] It was created in 2011 following the refusal of Indonesia to share avian influenza virus samples from humans as they felt they were not afforded equitable access to resulting vaccines.[34,35] The PIP Framework is the only multilateral ABS instrument for a specific type of pathogen. All other pathogens (from animals or humans), such as coronaviruses or non-pandemic influenza, are regulated as "genetic resources" under the CBD and Nagoya Protocol.[36,37] Issues have continued over pathogen material collection outside the narrow scope of the PIP Framework, with events around Ebola virus vaccine development leading to accusations of unethical practices.[38,39] There are concerns the bilateral negotiation approach of the CBD and Nagoya Protocol hampers the exchange of pathogen samples,[40,41] with suggestions to expand the scope of the PIP Framework or to use it as the model for multilateral sharing of other pathogen samples.[40]

Box 3: UNCLOS areas beyond national jurisdiction
Discussions are ongoing under the UN Convention on the Law of the Sea to address governance gaps in relation to the use of marine biological resources in areas beyond national jurisdiction.[42] This includes governance of marine genetic resources in the high seas over which there are no sovereign rights (and hence do not fall under the CBD).[43] There are no 'providers' but there are benefits that could be realised from their use, and inequities could arise from the differences in technological capacity to use resources.[44-46] An example of a benefit from a deep sea resource include novel antimicrobial compounds from bacteria isolated from a deep sea sponge.[47] Options being considered include procedures for accessing or collecting the resources,[48] and the multilateral benefit sharing model proposed could see a share of the profit of commercialisation being paid into a financial benefit pool. There are concerns that the system may hinder academic and commercial research,[49] over whether regulation can extend to DSI,[50] and affect progress on other issues such as high seas marine protected areas.[51]

A shift to digital genetic resources

Studies suggest the rapid growth in digital genetic resources and advances in gene editing and synthetic biology will reduce the demand for physical genetic resources.[52,53,54] In the case of crop resources (Box 1), the physical germplasm of crops (usually seeds) and crop wild relatives are conserved in more than 575 gene banks worldwide, with a total of about 4.9 million samples maintained.[55] In the near future, it will be possible to obtain whole-genome sequences of all the samples in plant genebanks;[56] with extensive genome information already available for the most-produced crops worldwide.[57] By comparison, a complete genome sequence is already a standard requirement for describing a new bacterial species.[58]

Genomic techniques are increasingly providing data for a diverse range of crops,[52] which could shorten the process of selecting favourable genetic combinations and valued traits.[59] However, research linking the genetic variation in crops and relevant traits, such as drought resistance, is limited as they involve complex networks of genes.[60] As understanding of the genetic basis of desirable plant traits increases, these data could be mined to exploit the diversity in gene banks.[53] It could inform genome editing (PN 548), making precise changes in the segments of the genetic code linked to specific traits. Some traits involve large sections of DNA and changes still require

Box 4: The World Intellectual Property Organization
The World Intellectual Property Organization (WIPO), a UN Agency, has an Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore. Studies have suggested that the debates about whether genetic resources and traditional knowledge have been misappropriated (often referred to as 'biopiracy') are linked to concerns about intellectual property claims.[61] WIPO negotiations are ongoing for three instruments: a text for genetic resources, a text for traditional knowledge, and a text for traditional cultural expressions,[62] but they have stalled, with multiple versions of texts still under consideration.[63] WIPO has produced guidance on the interface between intellectual property, traditional knowledge and genetic resources.[64] There was also a landmark agreement in 2019 to share rooibos tea profits with indigenous people.[16] However, it remains unclear how traditional plant use, such as medicinal use,[65] can be easily decoupled from plant genome sequence information.[54,66]

conventional breeding with physical material.[67] As more genetic and biological data are digitised, synthetic biology approaches (PN 497) may allow such traits to be designed.[54,68,69] Synthetic biology could also allow use of plant DSI beyond agriculture,[70] or for DSI to be used to modify plants for non-food products;[71] such uses of crops falling outside the Plant Treaty.[53]

Defining what is meant by DSI

While the current definition of genetic material is confined to physical biological material,[21] some countries have proposed it should be changed to include DSI.[72] There is no internationally agreed definition of DSI; the term was initially intended to be a placeholder until a consensus could be reached on what was being discussed.[73,74] In 2018, the CBD COP14 requested a second Ad Hoc Technical Expert Group (AHTEG) on DSI,[75] to follow on from a previous DSI scoping study.[76] Three studies were commissioned: the concept, scope and current use of DSI;[77] DSI in public and private databases and DSI traceability;[78] and how domestic measures address benefit-sharing arising from commercial and non-commercial use of DSI.[79] These have been considered by the AHTEG.[80]

A broad or narrow scope

The concept study reviewed the numerous terms applied to digitised genetic information, including: dematerialised genetic resources,[81] genetic information,[21] digital sequence data,[82] genetic resource sequence data,[83] genetic sequences,[84] and *in silico*.[85] There is no accepted definition of these terms, but they relate to digital information on the sequence order of subunits of molecules extracted from organisms (such as the order of the constituent subunits of DNA). Other commentators have suggested the term 'natural information'.[86] The concept study sets out four possible groupings that could be covered by DSI:

- Nucleotide sequence data (DNA and RNA);
- Nucleotide sequence and protein data;
- Nucleotide sequence, protein and metabolite data (the entirety of the molecules produced in cells[87]);
- Nucleotide sequence, protein, metabolite and other associated data, such as traditional knowledge.

In their consideration of the study, AHTEG recommended excluding other associated data in the final grouping. However, DSI could range from inherited genetic material, to broader factors that regulate the activity of genes (PN 451), or all cell molecular data.[80] The study suggested that if the traceability of DSI use is a concern, the narrowest group of nucleotide sequence data (NSD) would be pragmatic as does the study on databases (see below). The DSI term also does not distinguish between data and information. Raw sequence data has to be analysed to provide information;[76] for instance, special search tools can be used to compare it against reference sequences in databases to determine sequence relationships.[88] However, below a certain length sequence uniqueness can't be determined, and evolutionary relationships leads to long stretches of identical DNA being present in related organisms.[77]

Open access nucleotide sequence data

The International Nucleotide Sequence Database Collaboration (INSDC) incorporates GenBank in the United States,[89] the European Nucleotide Archive,[90] and the DNA Data Bank of Japan.[91,92] The participants maintain a unified database of sequence data (Box 5), with all three mirroring each other on a daily basis. The INSDC provides the internationally recognised system of accession numbers for the data submitted. Without an accession number, nucleotide sequence data results cannot be published in scientific journals. The CBD study estimated there are 10 to 15 million INSDC users across every country in the world. The greatest volume of users are in the US (23%) and China (15%) but these countries also contribute the most data to the INSDC (the UK has 3.5% of users).[78]

The country of origin tag became required metadata in 2011 for sequence data and 16% of sequences have a country tag, and over half the country-tagged sequences come from (were sourced from, not just sequenced in) four countries (US, China, Canada and Japan). Metadata can also include information on the collection holding the genetic resource, such as a botanic garden.[78] INSDC data are freely available, and are regularly downloaded into private company databases. Companies also submit nucleotide sequence data to the INSDC that appear as part of patent applications to obtain an accession number, even if the sequence already has an existing accession number. The country of origin information is not associated with these patent applications. These data are also submitted to commercial databases that collect patent disclosed NSD data. Other regulatory tracing challenges the study highlighted included:

- At least 24% of INSDC sequence entries are human genetic resources or those from 'model organisms' used as laboratory strains, which do not fall under the CBD.
- Any additional requirements could introduce friction into the flow of data between INSDC and research databases (Box 6). The volume of sequence data being generated is already on the scale of 'big data' (PN 468).[9]
- Difficulty of sequence traceability once outside of the INSDC.

Domestic Measures on DSI

Implementation of national measures, including compliance measures (Box 6), determines how ABS is realised.[93] The study on domestic measures categorises countries into those advocating international measures to impose benefit-sharing obligations on DSI use, others that view it as falling outside the scope of the CBD, and those seeking to promote unrestricted access to DSI.[79] Sixteen countries have now introduced national measures to regulate DSI and a further 18 are preparing to do so. The existing ABS bilateral contract system is the main tool used to regulate conditions of use of DSI as well as the resulting benefit-sharing obligations:

Box 5: International Nucleotide Sequence Database

The INSDC arose from harmonisation of standards, formats and protocols for the collection of nucleotide sequence data and metadata in the 1980s.[94] It is underpinned by agreements that require sequences to be freely available to maximise benefits to society.[95,96] Its policies require unrestricted access to all data in databases and that it will not attach statements to records that restrict access, limit the use of the information in these records or prohibit certain types of publications based on these records (the exception being data from consenting human donors).[97] With millions of sequences submitted each year, it provides a core part of the life sciences research infrastructure and costs an estimated $50 million each year to maintain. The databases link to more than 1,600 other databases divided into 15 subcategories,[98] which either allow data collection on a specialised topic in one place or provide bioinformatic tools to analyse data.[78]

Box 6: ABS compliance in the UK and EU

The more than 120 signatory countries to the 2014 Nagoya Protocol are obligated to establish ABS compliance and monitoring measures. There are now 174 ABS national focal points (Defra in the UK).[36] The EU Regulation (EU) No 511/2014 on Nagoya Protocol compliance measures requires users of physical genetic resources to apply a 'due diligence' approach consisting of three elements: information gathering, risk assessment, and risk mitigation.[99] Following ABS best practice can reduce the compliance burden, such as that produced by the Consortium of European Taxonomic Facilities recognised under the EU Regulation. This requires natural history museums, botanic gardens and other relevant institutes to set up an ABS management system.[100] However, best practice guidance for other sectors is lacking and concerns have been raised about the impacts of the ABS regulations on non-profit and commercial research.[101] The BEIS Office for Product Safety and Standards is responsible for enforcement of ABS regulations, which have been placed in UK legislation.[102] It provides advice and support to UK organisations engaged in commercial and non-commercial R&D relevant to ABS and a range of sanctions are available to them to ensure compliance.[103] Other countries have yet to fully implement measures,[79,104] and access concerns have been raised about the resulting national and regional legislative patchwork.

- Prior informed consent procedures are undertaken to provide information about the anticipated research project.[105]
- The provider country granting consent, and the user applying, then negotiate Mutually Agreed Terms to govern monetary and non-monetary benefit-sharing.
- These can include Material Transfer Agreements on the transfer of research material between institutions or individuals, or they can be separate documents.[106]

In conjunction with access to physical genetic resources, some jurisdictions attach conditions to sequencing-related research to indirectly address DSI use. Others have introduced separate measures on DSI use; for instance, legislation in Brazil and India defines information about the components of genetic resources as subject to ABS separately from physical material.[54] However, such bilateral approaches will not bind third parties who obtain the DSI from databases. The study suggests countries may amend contractual clauses to prevent publication of DSI, conflicting with external researchers' publication obligations and affecting researchers within those countries. Countries can promote unrestricted use of DSI by choosing to not apply measures, such as the US, Japan and Canada. For example, a project is being funded to sequence and place the genetic codes of all 60,000 species known to inhabit Britain on the INSDC.[107]

Addressing the DSI challenge

The CBD negotiations reflect developed countries resisting further implementation of benefit sharing (including to DSI), while developing countries seek more rules and binding agreements.[29,108] Stronger compliance and enforcement mechanisms may ensure benefits are shared, but if they deter research, there will be fewer benefits to be shared.[9] In 2013, patent activity involving biodiversity focused on only about 4% of species,[61] and most research using genetic resources does not yield commercial products.[65] It often relies on many resources and modification of the products over years,[109] creating difficulties in determining the contribution of individual resources,[77,54] and non-monetary benefits, such as scientific capacity building, are more likely outcomes. Organisations representing users of genetic resources have expressed concerns about the effects of including DSI under the CBD framework in response to consultations including UK organisations.[60,83,110-124] These include impacts on biodiversity and conservation research that uses nucleotide sequences to identify species.[125,116,126]

Informational governance

It remains unclear whether DSI is a genetic resource, the utilisation of a genetic resource or its application.[54] There have also been difficulties reconciling the boundaries of intellectual property rights with ABS (Box 6),[127,54] with offices created in Peru and India to dispute patents involving their genetic resources.[128] Commentators suggest that DSI is an informational governance challenge created by the disembodiment of property and knowledge,[54,129,130] which has previously occurred in other sectors.[131] In response to restrictions, evidence from the economics of information suggests that users will opt to use DSI from similar genes that are freely available on the INSDC.[132,86,130]The Plant Treaty Global Information System may include digital object identifiers for all genetic resources in the multilateral system to ensure traceability,[60,133] but the INSDC is a far larger resource. While the INSDC sequence data provide a non-monetary benefit for research globally, inequalities occur in data access and use.[134]

The current CBD model of users negotiating bilateral contracts with provider countries may continue,[135] but with more countries implementing DSI benefit sharing regulation. Researchers and their institutions would remain responsible and liable for ABS compliance,[136] including for DSI. The Global Initiative on Sharing All Influenza Data (GISAID) offers an alternative approach to DSI for research that allows access to and use of data, while owners retain information rights.[29,137] However, the responsible research and innovation dialogue around use of countries' genetic resources and potential impacts on their environment and society remains limited.[138]

A Global Multilateral Benefit Sharing Mechanism

Another option is for signatories to the existing multilateral organisations to agree upon a new governance mechanism for DSI. The CBD, along with WIPO and FAO, may be best placed to collaboratively address the governance gap.[54] It has been suggested the CBD could shift from a bilateral approach to a 'Global Multilateral Benefit Sharing Mechanism'.[139] There are implementation options of varying complexity, but all include open access to DSI.[135] One set of commentators have suggested a multilateral fund could be combined with 'bounded openness over natural information' approach, with royalties paid upon commercialisation to the fund and the percentage negotiated based on scientific advice with the money held by the fund.[140] Commentators have also highlighted other options:

- An existing international institution claims governance over DSI; those that govern by judgement (such as the WTO's Dispute Settlement Mechanism) or by majority opinion may be best situated to address the issues.[54]
- Negotiating an entirely new regime, or convention.[135,54] This would be a lengthy process and creating a new multilateral biodiversity fund in addition to existing ones, such as the Global Environment Facility,[128] may be contentious.

POST is an office of both Houses of Parliament, charged with providing independent and balanced analysis of policy issues that have a basis in science and technology. POST is grateful to all contributors and reviewers. For further information on this subject, please contact the co-author, Dr Jonathan Wentworth.

Endnotes

1. Rabitz, F. (2017). The Global Governance of Genetic Resources: Institutional Change and Structural Constraints. Routledge.
2. Frison, C. (2018). Redesigning the Global Seed Commons: Law and Policy for Agrobiodiversity and Food Security. CRC Press.
3. Oberthür, S, and Rosendal, G. (2014). Global Governance of Genetic Resources: Access and Benefit Sharing after the Nagoya Protocol. Routledge & CRC Press.
4. Aoki, K. (2008). Seed Wars: Controversies and Cases on Plant Genetic Resources and Intellectual Property. Carolina Academic Press.
5. Louka, E. (2006). International Environmental Law: Fairness, Effectiveness, and World Order. Cambridge University Press.
6. CBD History of the Convention
7. Malbon, J. *et al.* (2014). The WTO Agreement on Trade-Related Aspects of Intellectual Property Rights. Edward Elgar Publishing.
8. Food and Agriculture Organization of the United Nations, International Treaty on Plant Genetic Resources for Food and Agriculture.
9. Rabitz, F. (2017). Access without benefit-sharing: Design, effectiveness and reform of the FAO Seed Treaty. *Int. J. Commons*, Vol 11, 621–640.
10. Halewood, M. (2013). What kind of goods are plant genetic resources for food and agriculture? Towards the identification and development of a new global commons. *Int. J. Commons*, Vol 7, 278–312.
11. Helfer, L. (2005). Intellectual Property Rights in Plant Varieties: International Legal Regimes and Policy Options for National Governments.
12. UNDP. (2018). ABS is Genetic Resources for Sustainable Development.
13. UNDP-GEF. Global ABS – Access & Benefit Sharing.
14. CBD. The Nagoya Protocol on Access and Benefit-sharing.
15. Laird, S. A. *et al.* (2008). Access and benefit-sharing in practice: trends in partnerships across sectors. Secretariat of the Convention on Biological Diversity.
16. Nordling, L. (2019). Rooibos tea profits will be shared with Indigenous communities in landmark agreement. *Nature*, Vol 575, 19–20.
17. 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*, Vol 6, 11.
18. Laird, S, Virnig, A, Wynberg, R. (2018). Access and Benefit-Sharing Agreements: resources and background materials. Voices for Biojustice.
19. Divakaran Prathapan, K *et al.* (2018). When the cure kills—CBD limits biodiversity research. *Science*, 360, 6396, 1405-1406.
20. Rourke, M. (2018). Access and benefit-sharing in practice: non-commercial research scientists face legal obstacles to accessing genetic resources. *POLICY Anal.*, Vol 13, 20.
21. Lawson, C. *et al.* (2019). The future of information under the CBD, Nagoya Protocol, Plant Treaty, and PIP Framework. *J. World Intellect. Prop.*, Vol 22, 103–119.
22. FAO (2019). The state of the world's biodiversity for food and agriculture.
23. Food and Agriculture Organization of the United Nations, International Treaty on Plant Genetic Resources for Food and Agriculture.
24. Food and Agriculture Organization of the United Nations, International Treaty on Plant Genetic Resources for Food and Agriculture
25. Heinemann, J. A. *et al.* (2018). Exploratory fact-finding scoping study on "digital sequence information" on genetic resources for food and agriculture. Background Study 68.
26. Welch *et al.* (2017). Potential Implications of New Synthetic Biology.
27. International Treaty on Plant Genetic Resources for Food and Agriculture (2019). Submissions on digital sequence information (DSI). Food and Agriculture Organization of the United Nations.
28. International Treaty on Plant Genetic Resources for Food and Agriculture (2019). Global biodiversity conference concludes past midnight. FAO.
29. Lawson, C. *et al.* (2020). Information as the latest site of conflict in the ongoing contests about access to and sharing the benefits from exploiting genetic resources. *Queen Mary J. Intellect. Prop.*, Vol 10, 7–33.
30. WHO, Pandemic Influenza Preparedness (PIP) Framework.
31. WHO, PIP Partnership Contribution.
32. WHO, Virus Sharing, *WHO*.
33. WHO, Standard Material Transfer Agreements 2 (SMTA2).
34. Prip, C, Rosendal, K. (2015). Access to genetic resources and benefit-sharing from their use (ABS) – state of implementation and research gaps. FNI Report 5/2015.
35. Morgera, E, Buck, M, and Tsioumani, E. (2012). The 2010 Nagoya Protocol on Access and Benefit-sharing in Perspective: Implications for International Law and Implementation Challenges. Brill Nijhoff.
36. Lajaunie, C. *et al.* (2020). Nagoya Protocol and Infectious Diseases: Hindrance or Opportunity? *Front. Public Health*, Vol 8,
37. WHO (2017). Review of the Pandemic Influenza Preparedness Framework
38. Schopper, D. *et al.* (2017). Research Ethics Governance in Times of Ebola. *Public Health Ethics*, Vol 10, 49–61.
39. WHO. (2016). Implementation of the International Health Regulations (2005) - Report of the Review Committee on the Role of the International Health Regulations (2005) in the Ebola Outbreak and Response.
40. Laird, S. *et al.* (2020). Rethink the expansion of access and benefit sharing. *Science*, Vol 367, 1200–1202.
41. GISAID - WHO Report on the Public Health Implications of Nagoya Protocol, 13 May 2019.
42. Blasiak, R. *et al.* (2018). Corporate control and global governance of marine genetic resources. *Sci. Adv.*, Vol 4, eaar5237.
43. Rabone, M. *et al.* (2019). Access to Marine Genetic Resources (MGR): Raising Awareness of Best-Practice Through a New Agreement for Biodiversity Beyond National Jurisdiction (BBNJ). *Front. Mar. Sci.*, Vol 6,
44. IUCN (2013). IUCN Information Papers for the Intersessional Workshop on Marine Genetic Resources.
45. iied Briefing. (2019). Marine genetic resources in areas beyond national jurisdiction: a 'common heritage of mankind'.
46. Morgera, E. (2018). Fair and equitable benefit-sharing in a new international instrument on marine biodiversity: A principled approach towards partnership building? 5, 2018-2019.
47. Xu, D. *et al.* (2018). Bioprospecting Deep-Sea Actinobacteria for Novel Anti-infective Natural Products. *Front. Microbiol.*, Vol 9,
48. UNCLOS. (2020). Textual proposals submitted by delegations by 20 February 2020, for consideration at the fourth session of the Intergovernmental conference on an international legally binding instrument under the United Nations Convention on the Law of the Sea on the conservation and sustainable use of marine biological diversity of areas beyond national jurisdiction (the Conference), in response to the invitation by the President of the Conference in her Note of 18 November 2019 (A/CONF.232/2020/3).
49. Heffernan, O. (2020). Why a landmark treaty to stop ocean biopiracy could stymie research. *Nature*, Vol 580, 20–22.

50. Yu, C. (2020). Implications of the UNCLOS Marine Scientific Research Regime for the Current Negotiations on Access and Benefit Sharing of Marine Genetic Resources in Areas Beyond National Jurisdiction. *Ocean Dev. Int. Law*, Vol 51, 2–18.
51. Nature Editorial (2018). Protect the high seas from harm. *Nature*, Vol 553, 127–128.
52. Aubry, S. (2019). The Future of Digital Sequence Information for Plant Genetic Resources for Food and Agriculture. *Front. Plant Sci.*, Vol 10,
53. Welch *et al*. (2017). Potential Implications of New Synthetic Biology.
54. Smyth, S. J. *et al.* (2020) Implications of biological information digitization: Access and benefit sharing of plant genetic resources. *J. World Intellect. Prop.*, Vol 23, 3-4, 267-287
55. FAO (2019). The state of the world's biodiversity for food and agriculture.
56. Wambugu, P. W. *et al.* (2018). Role of genomics in promoting the utilization of plant genetic resources in genebanks. *Brief. Funct. Genomics*, Vol 17, 198–206.
57. Scheben, A. *et al.* (2018). Bottlenecks for genome-edited crops on the road from lab to farm. *Genome Biol.*, Vol 19, 178.
58. Chun, J. *et al.* (2018). Proposed minimal standards for the use of genome data for the taxonomy of prokaryotes. *Int. J. Syst. Evol. Microbiol.*, Vol 68, 461–466.
59. Halewood, M. *et al.* (2018). Using Genomic Sequence Information to Increase Conservation and Sustainable Use of Crop Diversity and Benefit-Sharing. *Biopreservation Biobanking*, Vol 16, 368–376.
60. CGIAR. (2018). Potential implications of the use of digital sequence information on genetic resources for the three objectives of the Convention on Biological Diversity.
61. Oldham, P. *et al.* (2013). Biological Diversity in the Patent System. *PLOS ONE*, Vol 8, e78737.
62. WIPO. (2019). Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore, Fortieth Session.
63. Intellectual Property Watch. (2018). WIPO Members Agree On Revision Of Draft Treaty On Protection of TK, Folklore.
64. World Intellectual Property Organization. (2020). Intellectual Property and Genetic Resources, Traditional Knowledge and Traditional Cultural Expressions.
65. Wynberg, R. and Laird, S. (2009). Bioprospecting, Access and Benefit Sharing: Revisiting the 'Grand Bargain'. in *Indigenous Peoples, Consent and Benefit Sharing: Lessons from the San-Hoodia Case*. (eds. Wynberg, R. et al.) 69–86. Springer Netherlands.
66. Phillips, P. *et al.* (2018). Access and Benefit-Sharing in the Age of Digital Biology. in *Genetic Resources, Justice and Reconciliation: Canada and Global Access and Benefit Sharing*. (ed. Oguamanam, C.) 181–195. Cambridge University Press.
67. Friedrichs, S. *et al.* (2019). Meeting report of the OECD conference on "Genome Editing: Applications in Agriculture—Implications for Health, Environment and Regulation". *Transgenic Res.*, Vol 28, 419–463.
68. Royal Society, Synthetic biology – there are no widely accepted definitions, but the Royal Society describes it as involving 'the design and construction of novel artificial biological pathways, organisms and devices or the redesign of existing natural biological systems'.
69. Bagley, M. A. *et al.* (2014). The Nagoya Protocol and Synthetic Biology Research: A Look at the Potential Impacts. Social Science Research Network.
70. Srinivasan, P. *et al.* (2020). Biosynthesis of medicinal tropane alkaloids in yeast. *Nature*, 1–6.
71. Capell, T. *et al.* (2020). Potential Applications of Plant Biotechnology against SARS-CoV-2. *Trends Plant Sci.*, Vol 25, 635–643.
72. CBD. (2020). Zero draft of the post-2020 global biodiversity framework.
73. Ad hoc Intergovernmental technical working group on aquatic genetic resources for food and agriculture. (2018). Draft exploratory fact-finding scoping study on "digital sequence information" on genetic resources for food and agriculture.
74. CBD. (2019). 2017-2018 inter-sessional period.
75. CBD. (2018). Digital sequence information on genetic resources.
76. Laird, S. A. *et al.* (2018). 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.
77. Houssen, W, Sara, R, and Jaspars, M. (2020). Digital Sequence Information on Genetic Resources: Concept, Scope and Current Use.
78. Rohden, F *et al*. (2020). Combined study on Digital Sequence Information (DSI) in public and private databases and traceability.
79. Bagley, M, et al. (2020). Fact-finding Study on How Domestic Measures Address Benefit-sharing Arising from Commercial and Non-commercial Use of Digital Sequence Information on Genetic Resources and Address the Use of Digital Sequence Information on Genetic Resources for Research and Development.
80. CBD. (2020). Report of the Ad Hoc Technical Expert Group on Digital Sequence Information on Genetic Resources.
81. Global Network for the right to Food and Nutrition. (2018). The Dematerialization of Plant Genetic Resources.
82. Ambler, J. *et al.* (2020). Including Digital Sequence Data in the Nagoya Protocol Can Promote Data Sharing. *Trends Biotechnol.*
83. International Chamber of Commerce, Knowledge Solutions Department. (2019). Digital sequence information and benefit sharing, ICC submission to the CBD.
84. WHO, Pandemic Influenza Preparedness (PIP) Framework.
85. UN General Assembly. (2019). Revised draft text of an agreement under the United Nations Convention on the Law of the Sea on the conservation and sustainable use of marine biological diversity of areas beyond national jurisdiction.
86. Vogel, J. (2018). Not Just A Matter Of Matter: 'The Way Forward' For The UNCBD, NP And Half-Earth. *Intellectual Property Watch*.
87. Roessner, U. and Bowne, J. (2018). What is metabolomics all about? *BioTechniques*, Vol 46, 363–365.
88. Lobo, I. (2008). Basic Local Alignment Search Tool (BLAST). Nature Education 1(1):215.
89. GenBank, Overview.
90. EMBL-EBI, European Nucleotide Archive.
91. DDBJ, About DDBJ Center.
92. INSDC, International Nucleotide Sequence Database Collaboration,.
93. Sirakaya, A. (2019). Balanced Options for Access and Benefit-Sharing: Stakeholder Insights on Provider Country Legislation. *Front. Plant Sci.*, Vol 10,
94. Stevens, H. (2018). Globalizing Genomics: The Origins of the International Nucleotide Sequence Database Collaboration. *J. Hist. Biol.*, Vol 51, 657–691.
95. Maxson Jones, K. *et al.* (2018). The Bermuda Triangle: The Pragmatics, Policies, and Principles for Data Sharing in the History of the Human Genome Project. *J. Hist. Biol.*, Vol 51, 693–805.
96. Kaye, J. *et al.* (2009). Data Sharing in Genomics – Re-shaping Scientific Practice. *Nat. Rev. Genet.*, Vol 10, 331–335.

97. Karsch-Mizrachi, I. *et al.* (2018). The international nucleotide sequence database collaboration. *Nucleic Acids Res.*, Vol 46, D48–D51.
98. Rigden, D. J. *et al.* (2020). The 27th annual Nucleic Acids Research database issue and molecular biology database collection. *Nucleic Acids Res.*, Vol 48, D1–D8.
99. Bioresources for Oliviculture. (2019). Guidelines on the legal and ethical management of the germplasm databanks – second release.
100. Consortium of European Taxonomic Facilities. (2018). Code of Conduct and Best Practice for Access and Benefit-Sharing.
101. Milieu Law and Practice (2020). Analysis of implications of compliance with the EU ABS Regulation for research organisations and private sector companies.
102. The Nagoya Protocol (Compliance) Regulations 2015
103. GOV.UK, Regulations: The Nagoya Protocol on access and benefit sharing (ABS).
104. CBD. (2019). Report on the Global Capacity-building Workshop on Monitoring the Utilization of Genetic Resources under the Nagoya Protocol.
105. CBD, Frequently Asked Questions on Access and Benefit Sharing.
106. ABSCH, Access and Benefit-Sharing Clearing-House.
107. Sanger Institute, Ambitious project to map genomes of all life on British Isles funded by Wellcome.
108. Hammond, E. (2017). Gene sequences and biopiracy: Protecting benefit-sharing as synthetic biology changes access to genetic resources. Third World Network, Briefing Paper 93.
109. Newman, D, and Cragg, J (2020). Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. *Journal of Natural Products,* 83, 3, 770–803.
110. CBD. (2018). Synthesis of views and information on the potential implications of the use of digital sequence information on genetic resources for the three objectives of the Convention and the objective of the Nagoya Protocol.
111. BBSRC. (2017). Digital sequence information and scope of the Nagoya Protocol: biotechnology & biological sciences research council (BBSRC), UK submission to the CBD secretariat
112. The Chartered Institute of Patent Attorneys, 2019, Digital Sequence Information on Genetic Resources: Submission of views.
113. Bastow, R, *et al.* (2019). Open Access to Digital Sequence Information Benefits the Three Objectives of the Convention on Biological Diversity.
114. Scott, D and Berry, D. (2017). Workshop Report: Genetic resources in the age of the Nagoya Protocol and gene/genome synthesis.
115. ESA. (2017). ESA submission on The Use of Digital Sequence Information and the benefits thereof for the three objectives of the Convention on Biological Diversity.
116. The Global Genome Biodiversity Network. (2017). GGBN Submission.
117. International Federation of Pharmaceutical Manufacturers & Associations. (2017). IFPMA views on the potential implications of the use of Digital Sequence Information (DSI) on the objectives of the Nagoya Protocol (NP).
118. LGC-Group. (2017). Nagoya Protocol-LGC comments.
119. NHM, RBGK, RBGE. (2017). Potential implications of the use of digital sequence information on genetic resources for the three objectives of the Convention and for the Nagoya Protocol.
120. Royal Society Biology. (2017). Response from the Royal Society of Biology to the UK Government Department for Environment, Food & Rural Affairs (Defra) request for views and relevant information on potential implications of the use of Digital Sequence Information (DSI) on genetic resources for the three objectives of the Convention on Biological Diversity (CBD) and for the objective of the Nagoya Protocol on Access and Benefit Sharing (ABS).
121. Society for Applied Microbiology. (2017). Society for Applied Microbiology Position on Digital Sequence Information and the Nagoya Protocol.
122. UK Bioindustry Association. (2017). The UK BioIndustry Association (BIA)'s response to the CBD Secretariat's consultation on the impact of Digital Sequence Information (DSI) regulation in the Nagoya Protocol.
123. Wellcome Trust and Wellcome Trust Sanger Institute, 2017, The use of digital sequence information on genetic resources CBD Submission
124. Welcome Sanger Institute, 2019, Digital sequence information on genetic resources CBD Submission.
125. Davis, K. *et al.* (2017). Introduction to Access and Benefit-Sharing and the Nagoya Protocol: What DNA Barcoding Researchers Need to Know. Pensoft Publishers.
126. Earth BioGenome Project.
127. Kim, T. (2011). Expanding the Arsenal against Biopiracy: Application of the Concession Agreement Framework to Prevent Misappropriation of Biodiversity. Science and Technology Law Review, 14, 1
128. Callahan, M. *et al.* (2017). A Critical Guide to Intellectual Property. *Intellect. Prop.*, 292.
129. Muller, M. (2015). Genetic Resources as Natural Information : Implications for the Convention on Biological Diversity and Nagoya Protocol. Routledge.
130. Vogel, J. H. *et al.* (2011) The economics of information, studiously ignored in the Nagoya Protocol on access to genetic resources and benefit sharing. Law, Environment and Development Journal, 7, 1, 52.
131. Hargreaves, I. (2011). Digital Opportunity: A review of Intellectual Property and Growth.
132. Vogel, J. (2018). Ending Unauthorised Access To Genetic Resources (aka Biopiracy): Bounded Openness. *Intellectual Property Watch*.
133. Halewood, M. *et al.* (2018). Plant genetic resources for food and agriculture: opportunities and challenges emerging from the science and information technology revolution. *New Phytol.*, Vol 217, 1407–1419.
134. Rohden, F *et al.* (2020). Combined study on Digital Sequence Information (DSI) in public and private databases and traceability. .
135. ABS Capacity Development Initiative, the South African National Department of Environment, Forestry and Fisheries, and the Norwegian Government. (2019). First Global Dialogue on Digital Sequence Information.
136. Kumar, D. M. (2018). The Nagoya Protocol: Legal Protections for Genetic Resources and Ramifications for Aquatic Science. *Limnol. Oceanogr. Bull.*, Vol 27, 31–35.
137. GISAID - Terms of Use.
138. Laird, S and Wynberg, R. (2016). Locating Responsible Research and Innovation Within Access and Benefit Sharing Spaces of the Convention on Biological Diversity: the Challenge of Emerging Technologies, *Nanoethics*, 10, 189–200.
139. Sánchez, M, 2016, Transcript of New Approaches to Access and Benefit Sharing: The Case for Bounded Openness and Natural Information, side event at CBD Conference of the Parties XIII.
140. Vogel, J. (2018). The Global Multilateral Benefit-Sharing Mechanism: Where Will Be the Bretton Woods Of The 21st Century? *Intellectual Property Watch*.
141. Global Environment Facility.