DIGITAL SEQUENCE INFORMATION AND SCOPE OF THE NAGOYA PROTOCOL: BIOTECHNOLOGY & BIOLOGICAL SCIENCES RESEARCH COUNCIL (BBSRC), UK SUBMISSION TO THE CBD SECRETARIAT

BBSRC

1. BBSRC is one of seven UK research councils that work together as Research Councils UK (RCUK). We are funded by the UK government's Department for Business, Energy and Industrial Strategy (BEIS). We invest in bioscience research, training and infrastructure to generate new knowledge and foster positive social and economic impact for the UK and globally. In 2015-16, invested £473 million in world-class bioscience, people and research infrastructure. We currently support around 2,900 scientists and 2000 research students in universities and institutes across the UK.

Summary

2. As a public investor in biosciences research, BBSRC supports the Nagoya Protocol and the principles that underpin it. We agree that access and sharing of benefits arising from utilisation of genetic resources should be fair and equitable, as far as practicably possible, and enforced legally under the terms of the Protocol.

3. Digital sequence information (DSI) is routinely generated from, and/or utilised in, much, if not most of the research that BBSRC supports. BBSRC is not supportive of the inclusion of DSI within the scope of the Nagoya Protocol, since our own policies underpin *Open Research*, which includes the unrestricted public sharing of DSI arising from BBSRC-funded research. We also consider that inclusion of DSI may hamper realisation of the benefits that the Nagoya Protocol sets out achieve.

Open Research and Data Sharing

4. The principles of data sharing have been widely recognised for many years. The Organisation for Economic Cooperation & Development (OECD), has stated that:

   "Innovative scientific research has a crucial role in addressing global challenges - ranging from health care and climate change to renewable energy and natural resources management. The speed and depth of this research depends on fostering collaborative exchanges between different communities and ***assuring its widest dissemination****. The exchange of ideas, knowledge and data emerging from this research is fundamental for human progress.*

   "The rapid development in computing technology and the Internet have opened up new applications for the basic sources of research – the base material of research data – which has given a major impetus to scientific work in recent years. Databases are rapidly becoming an essential part of the infrastructure of the global science system."

5. As far back as 2004, a paper arising from the OECD, on "Promoting Access to Public Research Data for Scientific, Economic and Social Development" highlighted the following principles:
   - Publicly-funded research data are a public good, produced in the public interest

- Publicly-funded research data should be openly available to the maximum extent possible

The paper concludes that widespread data sharing will enable researchers, empower citizens and convey tremendous scientific, economic, and social benefits. BBSRC supports this view.

6. In common with many public research investors around the world, the UK Research Councils therefore champion openness in research, and making the outputs of publicly-funded research available freely for use. As mandated by BBSRC policy, data generated from the biosciences research that we support, including DSI, are made available publicly to encourage the greatest possible use and reuse.

7. The Research Councils are also signatory to the UK's Concordat on Open Research Data, which sets out to help ensure that the research data gathered and generated by members of the research community are made openly available for use by others wherever possible, in a manner consistent with relevant legal, ethical, disciplinary and regulatory frameworks and norms, and with due regard to the costs involved.

8. Putting DSI in scope of the Nagoya Protocol would hamper openness in research and also downstream innovation and social benefits, where any barrier is created to the re-use of data placed in the public domain. DSI routinely informs future scientific investigations in furtherance of collective human knowledge. For example, an independent report of 2016 commissioned by EMBL-EBI[1], confirmed the value and impact of EMBL-EBI's activities. This could serve as a proxy for the value and utility of open data in the life sciences generally, including reuse of research data arising from public research. It should also be noted that potential innovation and commercialisation benefits may be undetermined or unknown at the point of academic utilisation, particularly for the fundamental discovery research funded by BBSRC.

9. If DSI disappears from public databases, this may also hamper research seeking to specifically benefit biodiverse nations. One example of such research is the UK's Global Challenges Research Fund (GCRF), a 5-year £1.5Bn fund and a key component in the delivery of the UK Aid Strategy. GCRF aims to ensure that UK research takes a leading role in addressing the problems faced by developing countries through:
   - challenge-led disciplinary and interdisciplinary research
   - strengthening capacity for research and innovation within both the UK and developing countries
   - providing an agile response to emergencies where there is an urgent research need.

Challenges – scope

10. We consider that, at the very least, there should be an exemption for **academic utilisation** of DSI under the Nagoya Protocol. However, we note that (as with physical genetic resources), such an exemption could be impractical (for example within the framework of EU Regulation 511/2014, since legal compliance checkpoints exist at pre-commercial stages of research utilising genetic resources) or deter downstream innovation by placing greater burden on commercial users of the resource.

[1] EMBL-EBI is an intergovernmental organisation, based in the UK, that provides data services to scientists around the world

11. If DSI is placed within scope, the Protocol should, in fairness, also then ensure that provider nations with access laws consider access and utilisation frameworks that are **proportionate** and consider the wider benefits of Open Data, including the value to humanity in general of DSI being placed in the public domain without restrictions. This is even more important if, for example, academic access and utilisation of DSI were exempted. In that case, it would help ensure that provider countries' benefits sharing demands on subsequent commercial utilisation are not so unreasonable as to deter innovation R&D from taking place.

12. If it is determined that DSI is within scope for the Nagoya Protocol, this should **not** be applied retrospectively, for example to the date when the Protocol came into force for physical genetic resources. Instead, a future date should be agreed that allows sufficient time to consider all practical aspects of enforcement and compliance for DSI.

Challenges – synthetic biology and sequence homology

13. It is not clear how compliance with the Nagoya Protocol would be enforced where:
    a. identical genetic sequence is synthesised and assembled *de novo* by artificial means (artificial gene synthesis or 'DNA printing'), which is subsequently found in nature; or
    b. genetic sequences are synthesised, which, while not identical, lead to an identical protein sequence*;
    c. genetic sequence may occur naturally as the same across several species, and/or the same species across disparate geographical locations.

*DNA encodes amino acids, which are then assembled into proteins. The genetic code is made of four 'nucleotides' (abbreviated to A, T [which is 'U' in RNA], G, C); a given combination (i.e., sequence) of three of these four nucleotides codes for one amino acid. Each such combination is called a 'codon'. There are 64 possible combinations of three nucleotides (i.e., 64 codons) but there are only 20 different amino acids. The universal genetic code is therefore said to have *redundancy*, i.e., more than one codon can specify some amino acids[2]. Variations in DNA sequence can therefore sometimes still code for the same amino acid, leading to an identical protein sequence.

14. Scientists have also now achieved creation of synthetic nucleotides to extend the genetic code, which can function in 'semi-synthetic organisms' (SSOs), and have created synthetic 'xeno nucleic acids' ('XNA' molecules', to distinguish from DNA), to create the world's first artificial enzymes using synthetic biology. A genetic code of six rather than four DNA nucleotide bases will provide significant new opportunities for expanding genetic code functionality. This would be challenging where changes might be inserted into existing or known sequences to produce a gene product that is the same as that from the original genetic resource within scope of the Protocol.

15. Any variation introduced deliberately by artificial DNA synthesis that exploits natural or artificial genetic code redundancy would not be the same genetic code, in the strictest sense. Whether this constitutes utilisation under the Nagoya Protocol would be difficult to police and may need protracted examination by patent law experts. Regulation here

[2] For instance, the amino acid *Leucine* can be encoded by these codons: TTA, TTG, CTT, CTC, CTA, CTG

would likely be very difficult to formulate, and may risk future challenge even if formulated.

Diseases and emergencies

16. Application of rapid sequencing is invaluable in molecular epidemiology and phylogenetic outbreak tracing. Many genetic resources arising from agents of animal and plant diseases (including potential zoonoses that may threaten human health) will be in scope of the Nagoya Protocol. If DSI derived from such agents is also brought within scope, this may further hamper timely research in emergencies where plant or animal health is threatened. This is of concern particularly in relation to food production and other ecosystem services. Tracing the origin of a pathogen in an epidemic situation is likely to include sequencing and comparison with DSI in public databases, and, in turn, deposition of that pathogen's DSI into a public database for future reference.

17. In-field sequencing is also becoming increasingly important. This was used, for example, in the Zika and Ebola outbreaks; rapid sequencing would likely be deployed, similarly, in animal or plant health emergencies. In the longer term, pathogen DSI being available publicly without restrictions also supports public research on diseases and new treatments.

Consultation

18. We are grateful for this opportunity to comment on the issue of DSI. The Secretariat may wish to consider extending the current open consultation period to ensure that sufficient **factual, technical and scientific evidence** is gathered, particularly from biosciences researchers. Likewise, extending the open consultation period would give organisations supportive of extending scope of the Nagoya Protocol further opportunity to provide factual evidence for their positions, so that a fully informed and balanced approach may be determined.

19. We would also urge the Secretariat to engage directly with DSI experts and researchers from the academic and industrial sectors, to determine what consensus may be apparent on the potential inclusion of DSI within scope of the Nagoya Protocol, deepen understanding of the challenges, and also discover what practical solutions may be workable for the inclusion of DSI.

BBSRC
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