Workshop Report

Genetic resources in the age of the Nagoya Protocol and gene/genome synthesis

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Report and analysis of an interdisciplinary workshop that took place on 18 November 2016.

Organised as a collaboration between the Engineering Life project (ERC 616510-ENLIFE) of the University of Edinburgh and OpenPlant (BBSRC and EPSRC BB/L014130/1) of the University of Cambridge.

Hosted by the Sainsbury Laboratory at the University of Cambridge.

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We would like to thank all the workshop participants for their contribution to the constructive and engaging discussions and for their contributions to the review process. Our deep gratitude to Dr Dmitriy Myelnikov for designing and producing this report to such a high quality.

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Executive Summary

This workshop was dedicated to exploring emerging questions and discussions around the practice of synthesising DNA in the context of global biological diversity use and regulation. From the scientific community, our participants included many synthetic biologists; thanks to their commitment to projects that explicitly depend on considerable quantities of synthesised DNA, synthetic biologists were already invested in these conversations and were well placed to inform us of practices currently undergoing change. As synthesised DNA is made and used widely throughout the biological sciences, much of what is reported here has significance well beyond synthetic biology.

In addition to scientists working with synthesised DNA, we brought in participants from across the range of institutions, organisations, and disciplines that have been engaged with the Convention on Biological Diversity (CBD) and discussions around access and benefit-sharing (ABS) for decades. Participants included representatives of natural history museums, international biological collections, bioinformatics institutes, and scholars from law, geography, history, and the social sciences.

Part one of our report summarises the presentations and discussion that took place at the workshop. Together, the presentations provide a snapshot of UK and European practices around genetic resources and ABS at a moment of rapidly changing technological capacities, regulatory frameworks, and global discourse. Discussion touched on many issues, from the challenges of valuing both monetary and non-monetary benefits to the appropriateness of bilateral approaches to ABS. For the authors of this report, the following three themes that emerged from the day are of particular interest:

Whose context?

A constant point of reflection throughout our discussion was the importance of the starting point for conversation, how this can dramatically change the focus and thus which issues seem most significant.

Conversation is framed in vastly different ways depending on whether one begins from the perspective of developing the sciences, or the question of what constitutes a biological resource or a proper mode for its valuation, or with a focus on the practices of synthesis, collecting, and of governance. Rather than attempt to reduce this multiplicity, or rank different perspectives according to principles, our report aims to capture these multiple perspectives, leaving each open for further exploration. Progress in discussion and deliberation will require a recognition of the times when parties do not agree, and explicit attention to the assumptions and values that are in tension at agonistic moments.

Thinking through history

A key feature informing our workshop was attention to the historical development of the uses of biological resources in science and its regulation. Such an approach allowed room for arguments both of continuity and of change, while also providing a structure for the workshop programme: Session 1 - Genetic resources before and after Nagoya; Session 2 - Synthesis; Session 3 - Continuity and change. These conversations were placed in a range of historical contexts, as different starting points incorporate different readings of history. Claims of novelty on behalf of synthetic biology thus had to be richly articulated. We would recommend that future workshops and discussions have a similar grasp on the historical motivations behind instruments such as the Nagoya Protocol (NP), and behind the development of communities such as synthetic biology and the development of scientific and institutional practices.

Attention to practice

Our workshop sought to add value to the international debate and discussion of these questions by gathering evidence as to scientific and institutional practices over time, drawing out details regarding what communities of practitioners used to do, what they do now, and what they are aiming to do in the future. These are desperately needed in order to better appreciate where dangers might lie and where attention should be directed. We cannot claim to have gathered comprehensive evidence of practices throughout the biological sciences, or of the ways in which they might change. But we did consistently encourage workshop participants to describe in detail what they do and the reasoning behind these practices, wherever possible. We hope such an emphasis demystifies aspects of sciences in the present, opening up paths for future research on their relations to industry and biological diversity.

In the second half of the report, authors Dr. Deborah Scott and Dr. Dominic Berry provide analysis of key themes of the workshop. The workshop occurred in late November 2016, a few weeks before the 2016 UN Biodiversity Convention in Cancun, Mexico. At the time of our workshop, we knew the Cancun negotiations would consider the questions of whether and how 'digital sequence information' of genetic resources fit with the established ABS practices and regulatory frameworks instituted in response to the CBD and the Nagoya Protocol. We did not anticipate that this issue would be so very prominent in the negotiations, resulting in the establishment of an Ad Hoc Technical Expert Group (AHTEG) and a two year process of information gathering and analysis leading up to the next round of negotiations for the CBD and NP. In section 2, we identify convergences and divergences between the Cancun negotiations and our Cambridge workshop, both the range of issues discussed and the priorities and values of participants. In section 3, we reflect on key themes and considerations for research and decision-making processes going forward.

Paths for future research

The following can serve as motivation for future research and investigation.

↠ *Regulations in context – national and international*

International frameworks such as the Nagoya Protocol are always embedded in local and global contexts. At present, different states, and national scientific and bureaucratic institutions are developing systems that ensure compliance with the expectations of the NP. The form that such systems will take remains underdetermined and therefore flexible. Different understandings and valuations of digital sequence information (DSI) need to be seen within this broader context, and cannot be disentangled from earlier discussions and debates regarding material transfer, even if only as a matter of political pragmatism. Domestic action in response to decisions and procedures considered unjust is always a possibility. More work should be commissioned on the ways different countries are developing and collaborating in the creation of their processes for NP compliance.

↠ *'Innovation' is not a pipeline*

One of the strongest arguments made over the past few decades on behalf of synthetic biology is that it will revolutionise industrial production processes. Commercialisation has been a consistently emphasised feature from the outset. It is not the least bit surprising then that the

dependence of such scientists on DSI in order to complete proofs of industrial principle or develop new products has been viewed by some as the most recent incarnation of biopiracy. Many innovation strategists, economists, and some scientists espouse the view that industrialisation and innovation are organised in the form of a pipeline, with pure scientific research at one end leading to valuable new products at the other. Coming from history and social science, we argue that governance frameworks should recognise that the creation of novel products occurs in ways that are deeply non-linear, allowing negotiations to take a longer and broader perspective on ABS, one that promotes the creation of healthy and mutually beneficial relationships in the long term. We would urge greater transparency from those producing and commercialising novel products with regard to the role that DSI plays, and further research on this topic.

↠ *Following the infrastructure*

Throughout the workshop, participants were particularly interested in the kinds of resources already built for the accumulation of biological resources and the creation and dissemination of information about them. Also of particular interest were the new kinds of infrastructure, such as DNA foundries, being introduced. We would encourage further mapping exercises and deeper ethnographic and historical research into the production and design of infrastructure for the management and use of biological resources - everything from software and databases to storage facilities - so that the variety of ways in which scientific and commercial actors derive value from biological resources can become clearer, and so that recommendations for changes in future infrastructural components can be developed.

Contents

Introduction

This report records the 3rd in a series of experimental workshops organised by the Engineering Life project. More about that project, and the other workshops, can be found at the dedicated website: http://www.stis.ed.ac.uk/engineeringlife.

This workshop was organised with the aim of addressing ongoing discussions about the ways in which access and benefit-sharing (ABS) of genetic and biological resources - as defined by the Convention on Biological Diversity - is currently being developed. More specifically the workshop was designed to understand the relations between these emerging practices of ABS and those scientific and industrial practices that rely upon genetic digital sequence information (DSI) gathered from biological material, and which can be synthesised (in part or whole) into lengths of synthetic DNA.

The Engineering Life project was interested in these discussions and debates as part of its wide ranging research into biological engineering, with a more specific focus on synthetic biology. The capacity for DNA synthesis matters for the majority of biological scientists, but features particularly prominently in the working lives of synthetic biologists. One of the centres for synthetic biology which Engineering Life is currently exploring is that of the OpenPlant project, a synthetic biology project that is a joint initiative between the University of Cambridge, John Innes Centre and the Earlham Institute: https://www.openplant.org.

OpenPlant offers small sums of funding to cover short-term research projects and workshops, and encouraged that we apply to this fund so that we might co-organise a workshop addressing the topic of genetic resources in the age of the Nagoya Protocol and gene/genome synthesis. We were successful in that bid, and the workshop took place in November 2016. All the documentation relating to that workshop can be found in the Annex of this report.

Given that DSI was a central feature of attention in the December 2016 CBD and Nagoya Protocol negotiations, we felt that a record of our discussions in this workshop would be of use to negotiators and stakeholders going forward. We offer this document in that regard, so that it might help clarify certain points, and facilitate further debate and discussion.

The first section of the report is an account of the presentations and discussions that took place on the day of the workshop. In the second and third section, the authors Deborah Scott and Dominic Berry use their expertise to analyse this record in light of ongoing discussion of access and benefit-sharing and international biotechnology. We would like to reiterate that none of the participants in the workshop should be considered as committed to the arguments and views contained herein. Indeed, the aim of this workshop was not to create consensus on these topics, but to open up discussion and share divergent views. This report is offered in that spirit.

Lastly, Deborah and Dominic would like once again to record their thanks to all the workshop participants and the various funding councils that supported it (ERC, BBSRC, EPSRC).

Section 1

Cambridge workshop presentations and discussion

The workshop discussions took place under the Chatham House rule, https://www.chathamhouse.org/about/chatham-house-rule:

> *When a meeting, or part thereof, is held under the Chatham House Rule, participants are free to use the information received, but neither the identity nor the affiliation of the speaker(s), nor that of any other participant, may be revealed.*

Aside from the presentations, which reveal the name and institutional affiliation of the presenter, the rest of the discussion has been anonymised.

The workshop was split into four different sessions, details for which can be found in the Annex materials. In the following we provide a summary of each presentation (including small questions for clarification that were asked immediately after any given presentation) and the following discussions.

Session 1
Genetic resources before and after Nagoya

Alan Paton
Royal Botanic Gardens, Kew

Paton spoke on collection management at Kew, and its compliance with and implementation of access and benefit-sharing (ABS) legislation. Kew's priorities are: to conduct research into plant and fungal diversity; to use the collections as a source of data-rich evidence for scientific research; and to disseminate their knowledge for broader society. Kew is a not for profit organisation. People often think of the gardens, but the preserved collections are the largest part, with around 7 million botanical specimens in the herbarium and 1.25 million fungi. Of the living specimens, there are around 50,000 species in the gardens and 35,000 in the seed bank. Laboratory based collections include a DNA tissue bank and digital collections. Most of Kew's collections have digital analogues; they are working to make these freely available via their website.

Kew staff and project partners collect about 25% of the material that comes into Kew, in the order of 26,000 accessions every year; the remainder are sent to Kew from other botanical institutions. For Kew collected material, Kew checks that, before going into the field, people have done their paperwork and have the necessary permits for collecting. The fieldwork is registered with its collection event, and Kew reviews the permissions and permits when the material comes back and does not touch the collection until the paperwork is matched up. The terms and conditions of the items must be known not only for the immediate research purposes they were collected for, but also for any later research that might be conducted on that material. They must ensure they have prior informed consent and know the terms of the supply agreement.

Kew has preferred conditions for material supply and donations. Their primary preference is to use the material for non-commercial research. This means using them for the common good in the areas of scientific research, education, and public display. They also want to be able to disseminate the materials so that other people can use them; their usual default is to send parts of the collection to other people and scientists who want to use the specimen, but with the major restriction that they do so under terms which prohibit commercialisation. To do commercial research on Kew's material will inevitably involve a re-negotiation and prior informed consent with the country they got the specimen from, even if the specimen was collected at a time prior to the Convention on Biological Diversity. All specimens are treated according to Nagoya Protocol provisions, regardless of whether they were collected pre-CBD or not. This is in part about building relationships and trust.

Challenges of implementation include unclear terms and conditions, particularly if the country being dealt with has no access laws or the ABS focal point is embryonic. Kew has many questions, such as whether visitors may consult the material, whether the material may be digitized, and whether results may be disseminated in publications or databases. The donor may be unsure, so Kew usually includes on the permissions forms what they will do with the material, to provide a record.

In collection management terms, not all collections are the same. Depending on whether the specimens will be kept as living, DNA, or herbarium material, they try to anticipate the associated risks. Some countries are happy for herbarium material to be collected but do not allow collection for DNA material, or may restrict sampling. A further restriction on what can be done with materials is the size of a collection and the pressure this places on Kew's resources. At present, they cannot track all of their herbarium collections, or all the

herbarium specimens coming in and out of Kew. Smaller collections, such as DNA and seed, are more important to track, as restrictions are more commonly placed on such material. Thus Kew has very good documentation of what happens over time to those collections.

The life of a specimen can be very varied. Samples can move between collections, duplicates may be made and sent to other herbaria, DNA extracted and the genetic information passed on to international databases (e.g. GenBank), seeds taken and cryopreserved elsewhere, and so on. There has been a rapid change over the past 18 months or so, as devices such as minIONs are becoming much more accessible and practical, is increased demand for DNA samples from Kew's collections. Particularly the movement of old archival collections into the DNA databases has increased greatly. In all this movement, some things are easy to track, and some things are difficult. Publications are initially easy to track, but what about the use of data down the line? Online databases pose similar challenges.

Paton ended with a number of observations. First, standard terms simplify things from a management perspective; they reduce costs and help make collection transparent. However, as access laws develop, the partner might be happy but the Ministry signing off on the access agreement might not like the standard terms. Second, in light of finite resources, Kew concentrates on tracking the material that seems to be of a higher risk. Third, the Nagoya Protocol's increased access laws are coming along just as more genetic data is being created from a whole variety of resources never used like this previously. And finally, Paton noted that of these many kinds of uses, some descriptive uses may later be turned into applied uses. Even if the value between the two is clear, what should be reported? Nobody is interested in every single use of biological material that might have a commercial use – after all, Kew's visitors alone would be huge amounts of paperwork. How shall we track material, and its future uses that are harder to track?

All specimens are treated according to Nagoya Protocol provisions, regardless of whether they were collected pre-CBD or not. This is in part abou tbuilding relationships and trust. There has been a rapid change over the past 18 months or so, as devices such as minIONs are becoming much more accessible and practical, is increased demand for DNA samples from Kew's collections. Particularly the movement of old archival collections into the DNA databases has increased greatly.

Chris Lyal

Natural History Museum, London

Lyal presented on the Nagoya Protocol and the work of the Natural History Museum (NHM). He began by noting that the NHM does many of the same kinds of activity as Kew, with large collections (around 80 million objects); while not possessing a botanical gardens, they do have living collections. They are currently in the process of finding out in detail the different types of holdings and reviewing workflows. Broadly speaking, Lyal described the Museum as having something of almost everything from around the world, and still acquiring more of something of almost everything from around the world.

Like Kew, NHM carries out non-commercial collection-based research. Outputs include support for conservation activities such as the Global Taxonomy Initiative, which is cross-cutting and supports all of CBD implementation, as well as more academic papers. They use a range of techniques, including morphology, DNA sequencing, genomics, and biochemistry. They publish, and if a publication involves sequencing, they ensure that sequence is deposited in a database such as GenBank or EMBL.

Lyal explained that, when accessing and acquiring material, they not only consider the Nagoya Protocol, but the wider ABS regime which has been in existence since 1993. Within the ABS regime are more or

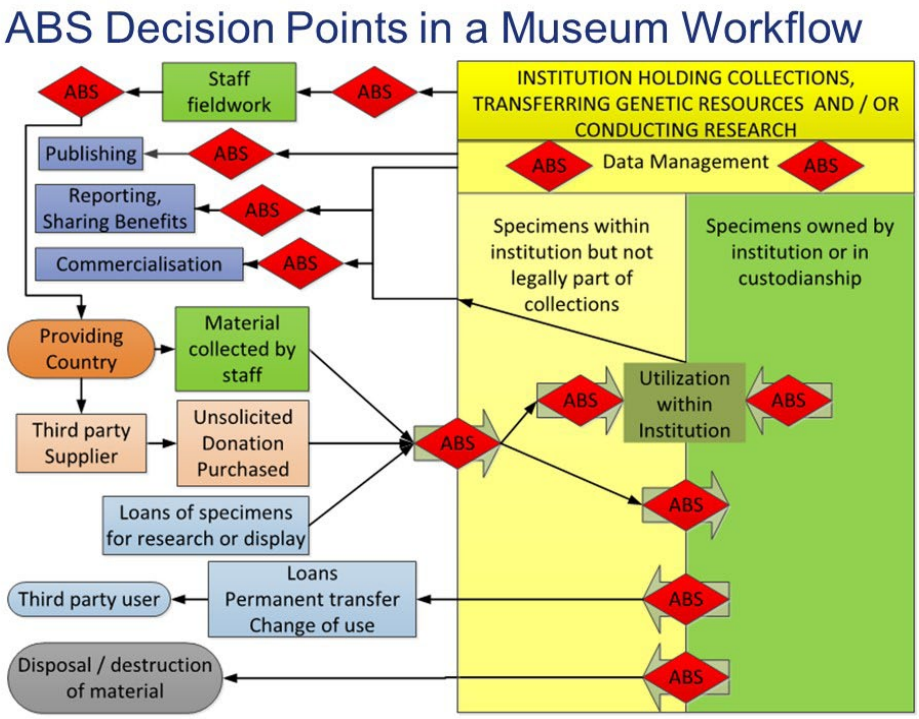

Fig. 1. Depiction of the Natural History Museum's ABS workflow with key decision points highlighted, courtesy of Chris Lyal

less nested the Nagoya Protocol, the EU regulations, and EU Member States' national compliance laws. On the provider side, the regime encompasses provider country regulations, which may be more than just ABS – they might include provisions for collecting in protected areas and private areas, regulations on particular species, etc., and include provisions independent of ABS. In many cases, benefit-sharing is a requirement independent of utilisation as described in the Nagoya Protocol. Collectors may enter into agreements to undertake capacity building, sharing information or deliver other benefits in order to access material, irrespective of subsequent utilisation. Agreements with the provider country are likely to be required and carry conditions that have to be honoured.

Considering the Natural History Museum's collections, many of the organisms may be examined for their morphology, but their DNA not examined. However, with increasing capacity to examine DNA, at some point in the future an increasing proportion of specimens may have their DNA examined. The DNA of specimens 100 years old are now routinely being examined, albeit not always with huge success, and Lyal predicts this will only become more common. Thus, members of staff need to know about ABS or any other conditions before undertaking activities such as molecular analysis or transfer to third parties – conditions agreed with the provider country may include many provisions. This poses quite a severe data management problem given the number of specimens in the collection, their disparate origins and the range of possible conditions.

The NHM collects or receives specimens, decides whether to study them, moves them into the main collection, and so on. Lyal showed a diagram of ABS decision points (*Fig. 1*) in a museum workflow, with each red diamond indicating a decision with ABS consequences. At these points, they need policy and procedural guidance. In order to start managing this flow and ensuring compliance, they make use of best practices and codes of conduct including the Consortium of European Taxonomic Facilities Code of Conduct and Best Practices (tinyurl.com/hmon7ff).

This has been submitted to the European Commission for recognition under the EU ABS Regulation. Other codes are also available; the NHM is developing with the Global Genome Biodiversity Network an extension to the 'Darwin Core' standards for biodiversity information, which will allow for the transfer of permit information, which can then be used across all public databases.

Lyal identified challenges related to reporting and the EU Regulation. One problem is mismatched systems for tracking and reporting. Under EU Regulation 511/2014 art. 7(1), NHM may be required to report to the UK Regulator on grant funded research that is within scope of the Regulation, but their grant funding information is held on an excel spreadsheet and their information on utilization is in a different and very complex database. Marrying those two is very challenging. There are also problems with understanding what the EU Regulation require and what ABS requires; there's a whole different language associated with ABS which staff can find quite challenging.

There are clear benefits of the Nagoya Protocol. It will hopefully give extra confidence to provider countries, which is very important. It has also raised awareness of what is going on, and has assisted NHM and others to help develop and then implement best practices.

Lyal ended by emphasising the importance of contract management. Contractual agreements should give clarity and certainty, and make use of standard clauses when possible because they simplify the whole process. Where there are gaps between user country and provider legislation, these must be managed and filled. Contract management plays a role in reassuring provider countries that the material collected can still be tracked, and that the collectors will be seen to be compliant. Lastly, thanks to the pipelines of information coming through, users can really start delivering non-monetary benefits far more effectively than possible in the past.

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Katie Beckett,
Regulatory Delivery, UK Department for Business, Energy and Industrial Strategy (BEIS)

Beckett's talk laid out the UK's implementation of its Nagoya Protocol obligations. In the UK, Regulatory Delivery is the competent national authority on ABS. The Department for Environment, Food and Rural Affairs (DEFRA) is the policy lead on ABS, and responsible for engaging in international discussions, for instance at the upcoming Convention on Biological Diversity (CBD) Conference of the Parties (COP), but also at a regional level with member states around the European Union. DEFRA is also where the national focal point on ABS resides. Regulatory Delivery is appointed by DEFRA to act as the implementing and enforcing body for ABS within the UK. The overall body works in a variety of regulatory areas, most with some kind of environmental component. Within Regulatory Delivery there is expertise in market based surveillance and also in supporting compliance among different stakeholders. They aim to address noncompliance when that occurs in a proportionate and pragmatic manner. Regulatory Delivery are based within the Department for Business, Energy and Industrial Strategy (BEIS)

The Nagoya Protocol entered into force in 2014. Given the level of awareness amongst UK users, Regulatory Delivery is still currently prioritising awareness raising. They do this through direct engagement with UK stakeholders across sectors, in a transparent and open way, not seeing it in their interest to enforce regulations that stakeholders may not yet be fully aware of. Stakeholders first need to know these regulations exist, then understand them, so that they can comply. Regulatory Delivery is there to support compliance

and to ensure businesses understand what their compliance obligations are. All of the events they attend to raise awareness serve a dual purpose, as it is through these events that they can better understand stakeholder practices, to inform their enforcement strategy. Coming to this workshop, for instance, helps them understand what is considered within scope, out of scope, and how they can work together with stakeholders to ensure their work continues in a way that is compliant.

Already at this stage, they can see successes. Companies are putting in place internal policies and training programmes, YouTube films and so on, all of which help to build awareness among staff. Beckett has felt in the past few months that companies do want to comply, and want to understand how to do that.

Challenges can be found at international and local levels. At the high level, she identified gaps in the information available at the ABS Clearing House. There is also the challenge of defining scope, both at the level of the EU Regulation as well as that of provider country legislation – this variation in scope can be a challenge when navigating compliance obligations. Turning to the more local challenges, awareness raising of staff, particularly in large organisations, can be difficult. And for smaller organisations, capacity to comply with these new procedures is a challenge. Last, Beckett noted the fear of misappropriation, of being accused of being a biopirate, is also a challenge that must be dealt with. They want to avoid people moving away from certain areas of research or from working with certain countries, for fear of being accused of such practices. It is important that we can ensure research and development of genetic resources continues, where both the provider of the resources and the user benefit from the outcomes of such research.

Elisa Morgera
University of Strathclyde
BENELEX project

Morgera leads the BENELEX project, which aims to better understand the meanings and aims of "fair and equitable" and "sharing" in relation to benefit-sharing, www.strath.ac.uk/research/strathclydecentreenvironmentallawgovernance/benelex.

This language is in the Nagoya Protocol, but not often discussed. Yet depending on our understanding of this fundamental premise, we may be able to look at the pragmatic aspects of ABS in a new light, or be more strategic about the practical challenges.

BENELEX addresses these key terms by looking into other areas of international law where the same terminology has come up, and trying to understand how these relate across very different regulatory or legal regimes. Does the adoption of these same words across different regulations expose an underlying rationality, and does understanding this rationality help us move beyond the more entrenched positions that exist on the more difficult aspects of the Nagoya Protocol (indeed those parts that couldn't be worked out in the Protocol)? Could this engender a different type of discussion?

"Sharing" is a key word in ABS. Looking at different treatises, there is a common idea that sharing is about agency. It is about more or less powerful state and non-state actors having a voice in a discussion about what should be seen as benefits and who the beneficiaries are. It is not about passively receiving 'benefits,' but participating in a dialogue among different partners. And this is not any kind of dialogue, but one that requires a concerted effort. Of course these can be very difficult discussions, as in most cases there will be a history that matters, and there may well be different kinds of understanding between stakeholders of what the interests are. Thus, in most cases of ABS, this discussion must be an iterative process. It is not a case of just signing consent forms, but rather something that is expected to go on over time, allowing a mutual understanding to evolve, and be responsive to the changing needs and capacities of the different partners.

One way in which the above is commonly described across different levels of international law is 'laying the grounds for partnership', be that in terms of a public

private partnership, or in the sense that we find in the Rio Declaration on the Environment and Development as a 'heightened form of cooperation' among countries (i.e. building of a global partnership for sustainable development). To some extent these notions move us away from a logic of exchange, which may characterize ABS in practice.

Morgera then turned to the idea of 'fair and equitable'. Again, treaties do not go into very much detail about this. We will all have different views on what is fair and equitable, and these are conversations that need to be had in concrete situations. There is not yet any agreed way to measure when an ABS project has been completed in a way that is fair and equitable under the terms of the Nagoya Protocol. This is a challenge, and much of the discussion at the international level is about what conduct counts as fair and equitable. International law (particularly international human rights law) does give us some indication – both on the procedural side (particularly with regard to what it means to have agency and give someone a voice), and also the more substantive aspect, to understand how sharing on terms of mutual understanding can lead to human well-being.

This may also help us move away from the 'monetary and non-monetary' false dichotomy, and allows us to look at how certain parameters of fairness and equity can be addressed in the choice of specific benefits in light of international human rights law. It might, for instance, be worth considering whether the human right to science can be a reference point for ABS. This is not a new, fanciful right; it has existed for as long as human rights law has existed. What a human right to science might mean is admittedly not entirely clear, but an international process is ongoing to try and clarify what the obligations of states are regarding those conducting science. There are four legs that have been identified (A/HRC/20/26) and these speak very directly to the aims of the Nagoya Protocol. First, accessing/sharing in the benefits of science, which to Morgera captures very nicely the fair and equitable aims of

Sharing is not about passively receiving 'benefits,' but participating in a dialogue among different partners.

Nagoya. Second, the right for all to contribute to science, which Nagoya affirms through the benefits we find for others to become active partners in scientific research. Third, there is an obligation to protect against the negative impacts of scientific research. This is not particularly well spelt out in the Nagoya Protocol, which assumes that biotechnology will be positive, so the right to science provides a parameter to keep in mind when discussing fair and equitable sharing under the Nagoya Protocol to protect against negative impacts. Fourth, the obligation to ensure that the priorities of scientific research focus on key issues for the most vulnerable. This concept is present in the Nagoya Protocol, finding a reference to priority needs amongst the list of shared benefits, but it is buried and left to wide interpretation. If we take the human right to science as our guide, we recognise that priority needs are not just one type of benefits, but in fact are a key discussion to be had. In other words, not any benefit among those listed under the Nagoya Protocol would do to ensure fairness and equity, and the four dimensions of the human rights to science provide a set of considerations that can guide the dialogue among partners.

To conclude, Morgera identified concrete ways in which these indications can become reality. She pointed to how international organisations connect databases, facilitate interoperability amongst existing resources, try to understand how actors work with each other (or fail to), and try to provide procedures for monitoring existing ABS efforts, with a view to contributing, in an interconnected way, to questions of sharing of information, capacity building and technology transfer, as well as providing international oversight and support. A concerted and iterative dialogue on fairness and equity, on the basis of international human rights standards, can lead to very concrete solutions on the basis of broader legal notions that are not very

prominent in current ABS discussions (more information and references at E. Morgera, "Fair and Equitable Benefit-sharing at the Crossroads of the Human Right to Science and International Biodiversity Law," *Laws* 4 (2015):803–831, open access at www.mdpi.com/2075-471X/4/4/803).

Discussion from session 1

↠ *Shared benefits or access to advancements?*

One attendee highlighted that some people have argued that the Nagoya Protocol has effectively established a bureaucratic exercise that might ultimately limit access to benefits, because companies will simply find workarounds. According to this argument, we are already seeing companies spending hundreds of millions of dollars to effectively, albeit perhaps not intentionally, evade rules on access to materials. This person agreed that it is a powerful argument that countries should have access to science and products enabled by initial access to their materials, but they proposed that perhaps a better way to regulate would be to address what benefits are, rather than concentrate on modes of enablement.

A respondent recognised but did not agree with the argument that the objectives of the Nagoya Protocol are not best served by its creation, and that instead of creating incentives for partnership it has created disincentives for scientists or others to engage. They saw a need to look at the balance of interests at the state level. There is an interest for access to occur, there is an interest for science to go ahead, but there are other interests as well; it is not the case that we think science should go ahead at all costs. They argued for not just access, but access on terms that work for all parties. On the scientific side, this respondent saw relevant questions as including what direction research should take and who would see benefits. The Nagoya Protocol is not about imposing burdens, but rather about starting discussions; one of its key features in comparison to other international agreements is that it opens up a dialogue, where stakeholders are asked about what they are doing, what standards they are developing. Bringing these examples to the international level is very important for agreement on fairness.

It might, for instance, be worth considering whether the human right to science can be a reference point for ABS.

In response, a concern was raised that, the more wide-ranging agreements on ABS became, the more "stasis" might be introduced as projects become entangled in multiple requirements. This attendee referenced the problem in intellectual property of patent thickets. Thus, however socially admirable engagement and collaboration may be, from a pragmatic perspective it will lead to additional layers of complexity. An immediate response to this argument was that, however many agreements may apply, they should each be aware of the broader picture and what comes next in chains of decisions. Shortcuts won't help, and exceptions will produce more problems.

↠ *Potential vs. actual benefits?*

One attendee was concerned that discussion of "benefits" usually conflate different processes. At the point of the collection of materials and even international distribution of materials, for instance, we can't speak of actual benefits but rather potential scientific benefits. Perhaps this should be regarded as a separate issue from the benefits that eventually go on to be accrued from those materials. They wondered if it would help to functionally distinguish these steps.

One response was that it is often simply not possible to distinguish clear-cut points in a research process - 'this is where I do access, this is where I do research, this is where research becomes R&D'. So asking when it is only research, or even 'pre-research', this is very difficult. Even the access itself can be a considered a scientific activity. So whereas at the regulatory level it might be thought helpful to distinguish these activities, in practice this could actually be a challenge. This respondent wanted to emphasise that negotiations are a long standing process in which parties keep

each other informed of what is happening, and require a dialogue with providers as to where they see benefits – having access to technologies, sending PhD students along, etc. – might be seen as significant scientific benefits.

↠ *Modalities and goals of non-monetary benefit-sharing*

An attendee noted that understanding non-monetary benefit-sharing is not simple. It is often difficult for practitioners dealing with such benefits to know what they are doing, what it costs, or how those benefits can be shared effectively. Much of benefit-sharing is the returning of specimens to locations in donor countries (hopefully to somewhere they will be looked at again), sending scientific papers based on those materials (and there is always a strong risk that these end up in filing cabinets and are never looked at again), and sending lists of specimens (when we might not be sure if these specimens fit into scientific work underway at their end). They noted that their organization is interested in using non-monetary benefits to improve the ability of donor countries to conserve and use sustainably their biodiversity, in line with the ambitions of the CBD. This is of course something that would be done in partnership, that there would be no room for simply saying to donor countries 'this is how you do it'!

Another participant noted it would be helpful to have ways to report on non-monetary benefits over time, as this is quite difficult. They gave an example of a person in a donor country being trained by the user organisation - how can this person's career be tracked? They added that this also relies on agreement among multiple actors as to the desired non-monetary benefits. The partner institution may want certain things, the ministry responsible for ABS may want other things; if there has not been a conversation between them, this can take time and work can occur effectively at cross purposes. For example, a partner institution might say 'yes that's fine, we've been sharing these for years and are happy to get publications', but the Ministry may say 'oh no, our genetic heritage belongs to us' – and if the restrictions can't be implemented, the collection will be returned. The attendee noted that such incidents make long term relationships difficult, and can close down research collaborations.

↠ *Drivers of the Nagoya Protocol*

An attendee noted that large pharmaceutical companies have been mining biodiverse regions for new molecules and new enzymes for a century (a practice this person referred to as biopiracy), and asked whether a sense of the injustice of current practices and potential future income and industry building was the major driver for Nagoya.

A respondent identified that for Nagoya, as opposed to ABS more generally, the major driver was compliance. The Nagoya Protocol gives confidence to provider and user countries (bearing in mind that at given times any country can be a user or a provider) that there is oversight of the utilisation taking place. They urged the room to keep ABS and the Nagoya Protocol apart, because the Nagoya Protocol is only one instrument, while ABS is rather larger. In regard to the larger 'green gold' question, as they put it, they agreed there is a strong and valid perception of injustice.

↠ *Valuing monetary benefits: expectations and trends*

Another attendee asked how much of the discussion and debate on benefits is primarily based around expected monetary benefits. Are these negotiations being based on a presumed massive industrial growth over the next century predicated on access to living systems?

One respondent had been at a recent meeting on compliance where it was shared that the average financial benefit accrued from an ABS agreement was in the region of $12,000, which they considered to not be much. Whether this is an appropriate financial benefit or not was not something they wanted to comment on. Another attendee noted that some provider countries are very explicit about the expected financial benefit. They gave the example of Brazil, which expects 1% of the

profit accrued by the final products derived from their biological materials.

↠ *Distance from original genetic material*

An attendee raised the example of the company Ginkgo Bioworks, which they described as having bought up 2/3rds of the world's DNA synthesis capacity, through an order with Twist and Gen9 (the two main DNA synthesis companies) for 600 million base pairs. Ginkgo's approach when they want to look at a metabolic pathway is to take 100 genes or so, synthesise all of them, and then modify them. They make use of computer evolutionary techniques to create optimised pathways, which is where the value is going to lie, using existing biodiversity as an inspiration. But they have broken the direct link between the materials; they have also broken the direct link between what they are creating and what they started from. So, in their case, even if they are using the information from the original material, what they end up with is not that anymore. So, they asked, are we setting up a bureaucracy which is no longer fit for purpose?

↠ *Institutional practices and temporal scope of ABS*

One attendee wanted to know how some UK institutions had made the decisions that all of their materials would be treated as though covered by the CBD, even if collected prior to 1992. A respondent said this decision went back to the early 90s. Institutions at that time wanted to create a best practice which, particularly in the absence of an access law, would lay out clearly what these organisations would and would not do. They wanted a level of consistency not only to make lives easier but also to boost trust with partner countries. It was felt that if those conditions weren't applied to all the collections, it would build in distrust, by keeping open the possibility of workarounds. It was considered a question of best science practice.

↠ *The complications and possibilities of genetic information and ABS*

An attendee noted that, while a lot of sequence information is given freely in international databases, it might be argued that this can be used for commercial purposes. This seemed to raise the chance that institutions who think they are complying with ABS expectations are not actually able to fully comply. At present many institutions are only in a position to police the physical and not the conceptual.

Another attendee responded to the question of reconstructing DNA. In order to do this, they pointed out, you need a great deal of information. For example, in order to complete a BLAST (Basic Local Alignment Search Tool) search, you need all the sequences, otherwise every sequence that you add to it changes the coefficient of the alignment. So each sequence matters for BLAST results, and each different set of sequences can get you to different ways of reconstructing the organism. Thus, each of the millions of sequences in BLAST are contributors. How then do you apportion the benefit? And surely everyone who has contributed to that alignment could be entitled to a benefit?

This was responded to with the comment that it often becomes even more complicated because, for instance, when a company like Ginkgo obtains the sequences, they then recombine them, essentially doing design on existing natural sequences. So in this case if you wanted to make some kind of fixed royalty arrangement, you would effectively end up with 100% of the product being consumed by the financial expectation of the agreement.

Building on this discussion, another attendee returned to the question of the difference between ABS on the one hand and the Nagoya Protocol as a tool to manage ABS. They pointed to examples of scientists conducting ABS without knowing they were, before 1992. The CBD and Nagoya Protocol have provided an opportunity for scientists to do a better job of organising their scientific work, and recording the ABS they are doing. Likewise, structuring sequence information as part of benefit-sharing would ensure that some principles of ABS are included and that the Nagoya Protocol is being abided. This is all the more important in those situa-

tions where so many people contribute sequences that it is not clear who is responsible. From a legal perspective we might also then have grounds for excluding someone from gaining a right to a shared benefit as their contribution was so small. The purpose, they went on to say, must surely not be to create a costly administrative system.

↠ *Approaches to ABS beyond bilateral?*

An attendee asked whether there were international discussions about pooling benefits across countries. One response was that there is the option of a multilateral approach within the Nagoya Protocol, but that this was a very sensitive issue because the Protocol is based on a bilateral system. They pointed to the International Treaty for Plant Genetic Resource's (ITPGRFA) multilateral mechanism for benefit-sharing, but said to their knowledge it had not succeeded in bringing any substantial benefits back into the system, and had a limited scope of only about 60 plant species. They saw the World Health Organization's Pandemic Influenza Preparedness (PIP) framework as working a bit better, but noted it is narrow in scope as well.

The initial questioner then wondered whether an easier approach might be a kind of royalty that would apply to any biological product that came from natural systems that would go into a national pool, which could be devoted to protecting biodiversity, or supporting biotechnology and development in provider countries. Wouldn't it have less administrative oversight? One response was that this might be more administratively simple, but would effectively create a new tax. Perhaps such a tax could be set at a level that could be usable, but would it not then be simpler for countries to set up a tax system that uses this money for whatever they want?

Another attendee joined in on this point and emphasised the importance of distinguishing between two aspects of benefit-sharing that are often conflated: the accruing of benefits and the sharing of benefits. In the context of the ITPGRFA, the accruing of benefits has been difficult; the expectation that a percentage would come from commercialisation has not materialised into actual money going into the system. And yet the system is working in its sharing of benefits; there have been cycles of projects where people (mostly researchers but also some farmers) have received capacity building training and funds to carry out research and work for the benefit of conservation and sustainable use. Thus far it has relied on voluntary contributions from certain governments, which is clearly not ideal, but it has been viable. The discussion there has evolved to considering an upfront payment rather than linking to future possible commercialization.

They then turned to the WHO PIP system, which requires upfront payment. They noted the PIP is unique, because there was a pre-existing monopoly on the resource, access is controlled, and tracking is easier. Still, the attendee found it may be helpful for our purposes. For one, the WHO asks industries using their labs and materials to pay an upfront fee, but they also reach out to others through questionnaires to find out if they would be willing to pay the annual fee and contribute to the system. It's an example of engaging in dialogue with different providers, and perhaps with different kinds of users, to find out what they are interested in receiving and giving. It shows that these kinds of pooling can be made to work, and can be made attractive. The attendee noted that in any system there will be loopholes and people trying to exploit those loopholes. But the fact that such problems exist also mean you can use them for inspiration. In this case, how to make participating fully an attractive option. If you just tell someone, 'you are too far removed from the work, so you have lost your right to benefit,' they may just refuse to participate ever again with the system. Instead, we may want to focus on how the system being created can add value to a variety of stakeholders. At the ITPGRFA and the WHO, they are using international cooperation to explore how to provide incentives, whether to make things simpler for users and providers, or perhaps to provide additional aspects beyond the genetic resource.

Session 2
Synthesis

Philippe Desmeth
World Federation for Culture Collections & the Belgian Coordinated Collections of Micro-organisms

Desmeth's talk focused on microbial collections in particular, and how they can build trust. He identified trust as one of the most important things to build in collaborations, which must necessarily extend to any given system for material transfer. Culture collections are sometimes called "libraries of life." The common features of both culture collections and ex situ preservation is that at the same site you have material, data production and data processing, and expertise. These three elements - materials, data, expertise - constitute what are more broadly called biological resource centres, where you can find all the basics for research, research and development, basic science or applied science. The Belgian Coordinated Collections of Microorganisms (BCCM) are members of the World Federation for Culture Collections (WFCC), which has been active in putting in place systems that facilitate access and legitimate use according to the CBD and Nagoya Protocol.

In 1993 the WFCC began by introducing the MOSAICC code of conduct, including standard contracts (a Material Transfer Agreement). This established a basic process from taking the microbe sample in situ to its identification and use. This was done long before the Bonn Guidelines on access and benefit-sharing (2002), but you can see a lot of commonalities between the two. In particular, the Bonn Guidelines seem to have copied word for word the MOSAICS's list of monetary and non-monetary benefits.

In 2005 the WFCC moved on to MOSAICS. This introduced a Global Unique Identifier (GUID) for microbes - a permanent persistent label, linked to the internet that allows for up-to-date tracking of the microorganisms. The MOSAICS system also tried to value the microbial diversity, although this is difficult as a scale can start at zero value but there is no upper limit. Finally, the WFCC focussed on some legal concepts, working with colleagues who have created a microbial commons. The discussion began by asking the question 'do I own the microbes that I have in my collections?' From there they understood that the word ownership is not really the best word to use in terms of biodiversity. The WFCC used the concept of a bundle of rights, by which a set of rights and duties are apportioned among all the people dealing with microbial diversity.

More recently, around 2015, WFCC began developing the TRUST system. This system combines tracking with a search engine and data on the outcomes of research, all of which helps build trust among the participants. The main point of TRUST is the Global Catalogue of Microorganisms (*Fig. 2*), which is about facilitating access and legitimate use. It is a system that merges administrative and legal data as well as technical and scientific data. At the moment 108 culture collections, from about 43 countries, are signed up to the Global Catalogue, all merged in 1 portal. Each of these 108 collections required capacity building, including the training of their staff; 35 staff in total were trained on the new online catalogues.

Desmeth noted that access to microorganisms must be arranged so it can be accomplished quickly, as time is quite important for microorganisms, particularly for human and other pathogens. He also noted that they are seeing work on data taken from older collections, leading to the development of macromolecules through computer simulations. This has been made possible through the contribution of some key scientists, notably: Frederick Sanger, who established the reading of codes; J.

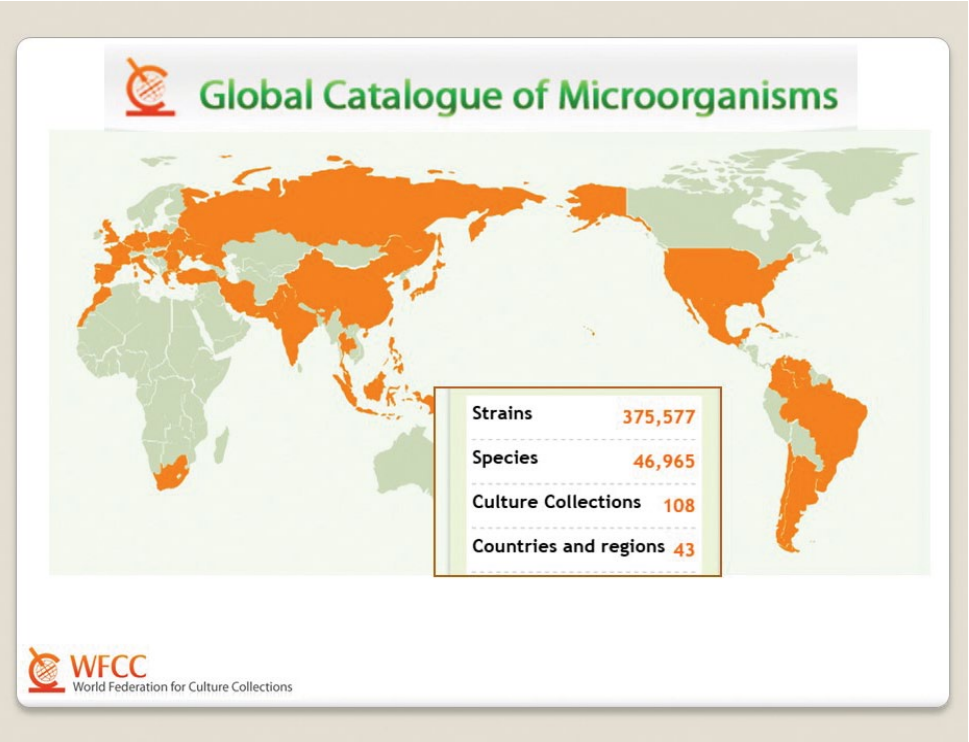

Fig. 2. WFCC map showing geographic coverage of the Global Catalogue of Microorganisms, courtesy of Philippe Desmeth

Craig Venter, who contributed the writing of codes; and most recently, Feng Zhang, who contributed editing and engineering.

For Desmeth, this brings us back to Ethical, Legal and Social Aspects (ELSA). ABS deals with legal aspects, but he cautioned that ethical and social aspects are just as important. Consider for instance the example of Botrytis cinerea, a pathogen for the strawberry which results in 'gray mold'. For the winemaker, this pathogen creates benefits, because it causes 'noble rot' which ensures the grapes make very sweet wine. And yet, for the wine growers' own personal health, it can lead to disease known as 'winegrower's lung'. So here we have an example of one microbe bringing three different kinds of costs and benefits.

At the end of Desmeth's talk, a participant asked for a further explanation of the evolution of the Material Transfer Agreements (MTAs) used by WFCC. Desmeth explained that initially their MTAs separated non-commercial from commercial use, but then changed to only one rule for access and exchange. Whether the use was commercial or non-commercial, their focus was on tracking the collection and its use. So the MTA says that those receiving BCCM collections can use it for any use, but in the case of commercial use they must report back. Desmeth acknowledged that this can lead to problems of confidentiality. When a partner reports that they are now intending to pursue some commercial use, BCCM informs the original depositor (who has already agreed that any use will be legal, as a condition of the depositing). They refer to this as an MAA 'Material Accession Agreement' (but this is slightly outdated language because it is really an act of depositing, rather than accessioning).

Graham Dutfield
University of Leeds

Dutfield's talk considered critiques of the concept of ABS, and how some of the challenges that synthetic biology presents to ABS amplify these critiques. He started by noting that the ABS concept might well be an attempt to solve a problem that mattered in the past, but that times may have moved beyond it. Thus, it might be worthwhile to be agnostic about ABS; one should have a strong sense of justice for develop-

ing countries and indigenous peoples, but acknowledge that ABS may not be the way to solve it.

The ABS approach of the CBD and Nagoya Protocol is informed in large part by the 'Green Gold' model. This incorporates a very linear model of discovery leading to research and development which leads to commercialisation. According to the model, this is expected to take 10-12 years, of which 1 in 10,000 projects will lead to a product. The Green Gold model often assumes that products are discrete, with single leads eventually arriving at single products. Discovery is understood to require access to single places of origin, and it's assumed that we'll know where the place of origin actually is. Moreover, it is often assumed that resources will be used as they are without some kind of transformation, or at least that they should be regulated as if they are. This model considers ABS as the primary means of rebalancing the costs and gains from conservation of tropical biodiversity, particularly in the developing world.

Dutfield proposed that the case of synthetic biology can help reinforce a critique of these assumptions. Are synbio products discrete technologies (more like drugs) or are they more like mobile phones and microprocessors (complex technologies)? The smartphone is a complex technology, composed of a large number of parts, from elements sourced from all over the world, manufactured in many countries, and incorporating a vast number of rights (copyright, patents, trade secrets, etc.). The ownership of these rights might be diverse, and thanks to their variety it is easy to infringe these intellectual property (IP) rights without realising it. Owners and developers of these kinds of technology are prone to seeing their IP rights being used strategically, including for bargaining. A single right might have trivial effects but can cause significant delays.

Dutfield asked whether similar kinds of problem might emerge from ABS claims. If one part of a marketed technology can be sourced to a developing country, can that be used to say they require a benefit-sharing arrangement? One good example

Members of the World Federation for Culture Collections (WFCC) have been active in putting in place systems that facilitate access and legitimate use according to the CBD and Nagoya Protocol.

to think with is the way that India pursues virtually every use of the Neem plant, as though it has a reach-through right on any use made of this plant. But Neem comes from Bangladesh, Pakistan, Myanmar, and Afghanistan as well. Why should it be India's? Over-emphasising such claims can lead us to some of the same problems associated with patents. If we consider the kinds of organism produced by an iGEM team, we can see that a cell is composed of various parts. As patents help to make markets for information, can ABS also help to create a right to the exchange of information? We do not yet know.

Dutfield ended by noting that we may need to explore more general queries. What precisely does 'use' actually mean? Should we take into account things like cognitive and material distance, or 'quantitative proportionality' (if a new product consists of many elements of knowledge and resources, should be reflected in benefit-sharing obligations)? Must genetic material be absolutely essential for, say, a new medicine for benefit-sharing obligations to be attached – what if the discovery is just one of many ways the product could have been developed?

At the end of Dutfield's talk, a participant requested that he speak more about "cognitive and material distance." To illustrate cognitive distance, Dutfield raised the connection between the use of Curare as an animal poison by indigenous peoples and Prozac. Understanding how Curare works meant that it could be used as a research tool for exploring chemical messengers in the brain. This research led not just to Prozac but actually a whole class of drugs. But such a learning trail can be extremely long, so how direct does a connection have to be in order for a benefit-sharing agreement to kick in? Particularly bearing in mind that it is increasingly less common

for a scientist to go into the rainforest to collect a sample or idea. Material distance, Dutfield explained, is a way to describe the modification of materials. In some cases, one might discover a chemical, but then eventually find another chemical that produces the same desired effect as the first but with a higher level of safety, etc. The material question here is how similar the eventual product is to the one collected, and does that difference take you outside of a benefit-sharing requirement.

Molly Bond
University of Bristol

Bond's talk reflected on the roles and perspectives of civil society organizations in debates around the Nagoya Protocol and synthetic biology. Civil society groups have played a significant role in the development of ABS regulations as we know them today, often bringing important critical voices to negotiations. They are also responding to the development of DNA synthesis, and some are working with the International Working Group on Synthetic Biology. They operate at a variety of different levels, working with policy makers, governments, and scientists, as well as on the ground with small farmers and local communities. The ability to bring otherwise marginalized stakeholders to the negotiating table is probably where the influence has been most significant.

Broadly, critical civil society organizations are reacting to DNA synthesis and the new uses of genetic resources on the grounds that these developments help to strengthen corporations' claims to intellectual property rights and at the same time to bypass ABS agreements, further exploiting genetic resources without sharing benefits. In particular, their concerns focus on the convergence of mass sequencing, online gene banks, and gene editing, which they see as enabling a new form of biopiracy, sometimes referred to as digital biopiracy or synthetic biopiracy. They often categorically state that these developments will completely undermine the Nagoya Protocol and ABS rules.

The Third World Network (TWN) has been quite influential and participated to

We may need to explore more general queries. What precisely does 'use' actually mean? Should we take into account things like cognitive and material distance, or 'quantitative proportionality'?

the ABS debate from the 1990s. TWN has recently been conducting their own investigation of a large gene sequence sharing project known as Div-Seq. They began this when the Governing Committee of the International Plant Treaty (ITPGRFA) asked Div-Seq to report on how sequencing, synthesis, and so on are going to impact ABS. TWN has argued that, though Div-Seq promotes themselves as a politically neutral and pure science platform, they are actually highly politicised and are already developing significant ties to industry, for instance consulting with Syngenta and DuPont. They find that Div-Seq has sought to shape policy on access via analytic tools and subscriptions to genetic sequence data. TWN's concern is that the large amounts of data generated on materials, particularly those collected from farmers in the global south, are allowing companies to access and analyse new traits which they can then recreate for themselves using synthesis or gene editing. To support their position that synthetic biopiracy is already underway, civil society groups point to the example of a human influenza sequence uploaded in China appearing only a few months later on a patent application submitted by an American synbio company.

The underlying concerns held by civil society groups are quite varied. In general, they see part of their role as providing a critical voice that holds policy makers and companies to account. These organisations often explain themselves as representing historically marginalized stakeholders. In their view, benefit-sharing is exceedingly important to development to help promote sustainable livelihoods and thus conserve biodiversity into the future. So, on their terms, even if Syngenta were able to trawl through all the sequence information in the world and produce a super-seed that was drought tolerant, could handle high salin-

ity, produced the most nutritious fruit, etc, the concerns of civil society groups would not change much. They would remain concerned with questions of ownership, access, culture, sovereignty, retaining capability and knowledge within communities to produce their own crops, and equality in terms of who is benefiting and who is losing out. There is also a general suspicion of large multinational corporations, and of course many of these interests extend well beyond synthetic biology to a range of new technologies. Bond noted that civil society groups are not producing answers to how to ensure benefit-sharing from genetic resources, although in a recent letter in *Science* TWN said if user agreements were connected to public databases, these could be used to trigger benefit-sharing if information was used and commercialized. She highlighted that civil society groups were planning to campaign heavily around this issue at the upcoming CBD December negotiations, advocating a two-step process of another Ad Hoc Technical Expert Group on Synthetic Biology to consider the issue and then send it on to the Nagoya Protocol's decision-making body to consider if and how sequence information should be connected to ABS systems.

A participant asked Bond whether her sense was that debates around "synthetic biopiracy" were poised to become as polarized as they'd been 10 years ago during the negotiations for the Nagoya Protocol. She noted that there are similar underlying issues, and very similar concerns from the 1990s. A participant described scientists seeing it as the genie being out of the bottle, and civil society groups asking the genie to get back in the bottle. Bond noted that it wasn't the science or products themselves that were seen as a problem, but the related cultural, ethical and social issues.

Nicola Patron

Earlham Institute

Patron spoke from her experience with DNA foundries in the UK. She sees synthetic biology as moving away from the model of genetically modifying organisms found in nature, making single gene modifications, resulting in a modified organism

Critical civil society organisation's concerns focus on the convergence of mass sequencing, online gene banks, and gene editing, which they see as enabling a new form of biopiracy, sometimes referred to as digital biopiracy or synthetic biopiracy.

for which it is easy to trace where the original organism came from and who might have had some ownership over them. Synthetic biologists are instead making pathways and synthetic networks using many genes from many different sources, as well as mutagenising and editing genomes, putting things in different places, ultimately ending up with engineered organisms. The building of these kinds of organism is underpinned by the automated assembly of complex and bespoke DNA molecules. In order to help make the UK better at this, in 2012 the Biotechnology and Biological Sciences Research Council (BBSRC) invested £12 million in five institutes, four of which have now built DNA foundries in order to enable this vision.

The foundries work in roughly the same way. Whatever is being built, synthetic chromosomes or synthetic gene circuits, is constructed from 'parts', parts being small sequences of DNA. In the vast majority of cases, because assembly systems are automated, those parts have been standardised in some way. This usually means each part is flanked by a standardised sequence that allows for automation. Because of this ability to automate, and the drop in price in DNA synthesis, most parts are purchased from synthetic DNA vendors and come standardised for these assemblies.

The sequence of these parts might be identical to sequences found in nature, either cloned from an organism or synthesised from information held in a public sequence database, or from the private collections of sequences of academics of industrial partners that the foundry may be working in a collaborative agreement with. These sequences may have associated intellectual property (IP) owned by the user or have no IP-claims around their use.

Many parts of different origins and with different ownership claims can be used in combination. As well as nature-identical sequences, parts could also be designed, mutated, or degenerated. Knowledge of natural sequences might be used to build something new, not because the scientist is looking to avoid ABS regulations, but because they are looking to make something 'better' than what was found in nature e.g. a scientist might design parts that nature doesn't use, to look for novel functions. This raises the possibility that they might degenerate, mutate or design a sequence, and then later find out that this sequence does occurs in a living organism, even though that is not where they sourced the sequence from.

Once all the parts are identified, design software is used to determine the final assembly of these parts in the foundries. A collection of plasmids housing the DNA parts (that have themselves come from an automated production process) are used, some of which might come in the mail from a collaborator or from a synthesis company while others might be on hand in the freezer. The plasmids are used in the assembly reaction and this is then transformed into a chassis (organism), which is usually a bacteria that acts as an intermediary before the construct is delivered to the final cell or organism. At this stage, a series of validation and characterisation experiments are carried out to determine whether the circuit has assembled correctly. Ideally, all of the information collected from these characterisation experiments will be returned into a database known as a Registry, informing future and new users about the specific functions of DNA parts. These activities work towards both increasing understanding of organisms and may lead to the creation of new commercial products.

The Earlham Institute foundry was designed to exploit plants and microbes for the production of high value products; they are focusing on two things in particular. The first is using plants as factories for the production of high value commodities, particularly to meet global demands in vaccines and pharmaceuticals. An advantage of plants is that they enable distributed manufacturing because most countries in the world are able to build glasshouses to grow such plants and they have low inputs (light and water). The second is to engineer plant metabolism in order to increase agricultural yields and address food security.

Knowledge of natural sequences might be used to build something new, not because the scientist is looking to avoid ABS regulations, but because they are looking to make something 'better' than what was found in nature.

These goals lead us to another area of complication, however. The synthetic circuit may be created from a mix of natural and synthetic genes, but ultimately it is placed in a chassis organism. This chassis may be a model plant (or cell cultures of a model plant) or it may be a crop plant. In many cases this chassis organism or variety has its own benefit claims. So it's not just the sequences of the DNA parts; the chassis organism may have multiple kinds of potential benefit claims attached. This is often overlooked because crops and varieties come under their own set of regulations (the International Treaty for Plant Genetic Resources for Food and Agriculture). People are currently mining the biodiversity in seed banks as a way to overcome the reduction of biodiversity available in our agricultural crops – synthetic biology opens the door for engineering the biodiversity found in seed-banks into existing crop varieties, accelerating the crop-improvement process but potentially evading existing ABS mechanisms associated with those seed-banks.

Discussion from session 2

↠ *Synthetic biology's influences on ABS*

A participant started discussion by asking for examples, whether from academia, industry or otherwise, where synthetic biology and the capacity for DNA synthesis was changing the culture of and attitude towards ABS – whether by prompting

greater interest in and support for ABS, or the converse. One attendee suggested that there has certainly been a feeling of misappropriation within provider countries, with concerns of similar colonial patterns of access without sharing of benefits. They were unsure whether these concerns were founded in actual scientific practices, and wanted to know whether it was really the case that scientists no longer need access to material.

A participant identified an example of how synbio can raise the temperature around ABS-related issues. A book written in the 1980s about potential social and other dangers of biotechnology raised an alarm that vanilla was a natural product that would likely be replaced by biotechnology. Today, indeed, vanillin is about to be made by a Swiss company in yeast. Actual 'replacement' might not yet be happening, but there is a concern that producers in these countries will have their production completely replaced. This can directly push against the very kinds of thing that ABS is meant to address, if access to the sequences from material in provider countries is used to develop products for industrial production in user countries, which then supplants production altogether in the provider countries. Another attendee pointed out that an important additional factor to the story of vanillin is that under the EU regulatory laws synthetic biology-produced vanillin will be able to be marketed as "natural," which makes for a greater potential impact on the naturally produced vanilla market.

For one participant, this was understandable, as the final molecule will be exactly the same. For another, the example of vanilla brought into question the whole paradigm of the Nagoya Protocol. Vanilla was originally found in Mexico, and was transplanted to Madagascar, where it is now considered a native crop. Not only has the plant moved, but technologies today allow research to be carried out in lots of different places, with no need to rely on the natural environment, and ultimately resulting in a process that can be industrialised. This participant saw the opportunities to disassociate the physical from the conceptual as so huge that they wondered if the Nagoya Protocol was already working within an outdated paradigm.

↠ *ABS implications of sequencing and synthesizing extinct species?*

Related to synthetic biology's specific impacts on ABS, a participant introduced the question of sequencing extinct species, and the synthesising of those sequences. If the species are extinct, but the data is there, does anyone have a claim of ownership? An attendee responded that there are collections of extinct species, but these typically have collection records which would allow one to trace back to the country of origin – even if the legal framework for determining the country of origin wasn't pertinent because it had been collected in, say, the 1800s.

↠ *Nagoya Protocol and State ABS Legislation*

A participant noted that, regardless of whether or not the Nagoya Protocol was determined to include digital sequence data in its scope, individual countries can and are developing ABS legislation. If every country was to demand clear tracing of their genetic materials, what would be the implications for open science and international projects? To this person, there was a clear tension between open science and ABS.

In response, a participant pointed out that the Nagoya Protocol sets minimum requirements for signatories to adhere to – it acts as a floor – but that States may demand more. States may also interpret the requirements of the Nagoya Protocol differently. The EU's position is that digital information is not included within the Nagoya Protocol – so a due diligence declaration wouldn't be legislatively required by an EU Member State if a researcher is working from a digital sequence, but that researcher may have already had to put in place prior informed consent and mutually agreed terms depending on the terms of the provider country's legislation. (Another participant wanted to clarify that the use of the digital data was out of the scope of the EU legislation, but that the creation

of the digital sequence information might be within the scope.)

Later in the day, a participant asked whether material created from sequence data falls under the Nagoya Protocol. A participant responded that they believed not, at least in the EU. But again, one needs to look beyond Nagoya and consider countries legislating more broadly on ABS.

↠ *Shifting the focus from Nagoya's scope to larger objectives*

Another participant noted similar questions are being asked about ABS and digital information at the CBD in the marine context, in the case of ocean organisms in areas with national jurisdiction. Usually the negotiation focuses on whether these things lie within the scope of the Nagoya Protocol, but this participant felt that question might be missing the point. A better question is whether the Nagoya Protocol is really fit for purpose. Even if we agree it applies, how will it apply? For this, we need to know what is actually happening in terms of scientific practices.

They suggested that participants see this as an opportunity to step back and ask what we are trying to achieve in the first place. We become polarized around 'in or out' questions, but perhaps we should start with the bigger picture and ask: what are we trying to achieve? Not just money, but as a process of working together towards conservation and sustainable use – what is needed for that?

Here a participant began by pointing out that the CBD had multiple aims, including both ABS and conserving biodiversity. This person felt that many of the research programmes underway in synthetic biology were explicitly about sustainability. Some of the agricultural research is aiming to reduce the amount of resources we need to put into farming, so we can reduce the amount of land needed for farming, thereby creating space in which to preserve biodiversity.

↠ *Current practices in tracing sequence origins*

A participant wanted to know whether synthetic biology companies and university-based academics are giving much consideration to where the sequence data they use comes from. An initial response was that many of these actors primarily use freely available digital sequence information. Acknowledging this, the participant still wondered whether research was pursued in ways that recognize the history of the CBD, or the aims of ABS.

One participant pointed out that companies such as Ginkgo are actively and purposefully trying to push down the cost of synthesis, in fact that is one reason they are putting so many resources into synthesis. The situation changes somewhat if you move into the case of pharmaceutical companies, which are also working on critically important things such as new antibiotics. As was pointed out earlier with the Div-Seq example, there are ways in which every single contributed sequence can contribute to the overall product, but in ways that make apportioning credit to any individual sequence contribution exceedingly difficult – it's a collection of everything. These activities are underpinned by public databases and open science.

↠ *Futures of biotechnology and implications of associated promises*

At various points over the course of the morning, conversation returned to the question of the certainty of the trajectory of scientific practices. An attendee asked about how synthetic biology companies are 'forging a path', as though this was definitely the future. They wanted to ask the other participants whether they considered that this was the inevitable future of biological science. An immediate answer was 'yes'. Another participant responded by saying it was part of a general trend of biology turning into a programmatic science. Living systems have an architecture and properties, and DNA is the code that drives the whole process. It doesn't control or describe that process, but it guides it, which means there can be rational approaches to redesigning living systems. They argued that this is where biology is going.

Another participant wondered whether a similar vision of biology had been

present at the time the CBD was negotiated in the 80s and 90s. At that time there was a widely shared understanding that biotechnology was going to deliver on all the promises it was making, but this did not pan out as expected. Now, as others in the meeting were saying earlier, it feels as though we are being pulled back into the polarisation of the 1980s, and this participant wondered if one cause might be a new community pushing the promises of biotechnology.

One response was that polarisation today might indeed be worse precisely because of the strong expectations of the 1980s. There is now even more suspicion that each side will not get what it truly wants unless they really leverage the discussion. The participant saw this as a phenomenon underway across many levels of international negotiation, not just at the CBD.

↠ *ABS or other benefits?*

A participant wondered whether countries negotiating the terms of ABS weren't often asking for the wrong thing. They suggested that perhaps countries should be asking for investment in infrastructure to develop their own companies, through education and training. It seemed to them that most of the technologies coming out of synthetic biology make it easier for anyone to do it. In this context, they noted that any given DNA sequence stops being quite so important, and perhaps it would be worth taking the resources it would take to track these and putting them towards investing in new industries.

A response was that it was worth asking why such investment wasn't already happening. Conversations about ownership and tracking might seem a distraction, but they are being had in order to draw in people to try to ensure precisely these kinds of arrangement and agreements can be made. Intellectual property rights are also part of the picture, so that the individual DNA sequence can and does remain singularly important in some respects. The question then is about how to realise the changes inspired by ABS.

Another participant's response was that capacity building was an important part of the story, but not the only story. They had attended another meeting a few weeks ago in a country that had been attempting to track down instances of what they perceived as biopiracy. The country had discovered a company engaged in such practice, which they approached. The company responded by saying 'OK, we did not mean to infringe ABS', and offered to share the rights with the country. This offer was refused. So the company offered to give the country the patent, and this too was refused. It was an ethical position for this country - the patent should never have been granted in their view, so they were not interested in receiving it back, it was the whole thing that they wanted gone. So in some cases, it is not about wanting to build a country's own industry, but to critique the science and business practices underway.

↠ *Bilateral approach to ABS vs. global*

A participant argued that they were not in favour of bilateral agreements of benefit-sharing because there are broader benefits at the global scale, and a country outside of the bilateral agreement should not lose out on these. In response, a participant noted one reason a country of origin should get benefits is that, in the first place, a user probably has a bilateral contract with that country. There is then a legal obligation to share benefits. The only way to achieve global benefits would be to throw aside the Nagoya Protocol, which was not what this participant was interested in.

To another participant, it seemed the question of bilateral agreements could help us get to the heart of the digital sequence question. ABS works precisely because you have to have a bilateral agreement in place in order to gain access to materials. No such bilateral agreements are in place for the future use of that sequence information.

↠ *Questioning "dematerialization"*

A participant noted that it seemed as though a major animating concept behind what synthetic biology means for the CBD and the Nagoya Protocol is the idea that sequence information is infinitely and

immediately shareable. Thus, sequence information gets treated in a way that is very abstract. Perhaps instead, this person suggested, we should think of sequence data as a very material thing. It seemed to them that one thing which came across in this session was that there are key points at which work is being done by people on objects (from computers to plants), and that if those key moments were highlighted and pinpointed, one could start to build a system that would allow for a continuation or further exploration of frameworks in line with CBD and the Nagoya Protocol. For instance, even before you take the sequence of something, there are decisions about how you are going to do your research, which countries you are going to work with, and so on. Then when you do your sequencing, there are choices to be made about what kinds of information you are going to collect, then there is what kind of database you are going to put the sequence in, and then later on there is the question of what databases you are going to go to in order to select sequences for future work. This all covers just the first part of research, never mind eventually getting to the question of synthesis. The participant wanted to ask the others what they made of the suggestion that we should think of sequence data in these material terms.

One immediate response was "crazy". Another participant pointed out that, from previous experiences of setting up search engines, not all databases are accessed in the same way. There are indeed already rules. In the past, people experimented with database systems that automatically dug into other databases. This became recognised as a bad practice and not the appropriate way to develop resources. In most cases today, even when using public online databases, many actors proceed carefully so that the source of information remains open, and so that you are not putting yourself in a difficult position in terms of sharing.

Session 3
Continuity and change

Paul Oldham,
One World Analytics &
University of Manchester

On the day, Oldham was unable to attend. Instead, a presentation by Oldham was delivered by Chris Lyal. Lyal explained that this presentation was based on a paper he'd seen Oldham present at a meeting in Mexico a week earlier. This presentation was about three quarters the length of the original.

Lyal noted that participants had already heard about the difficulties countries face regarding knowing what has happened to their genetic resources and the products resulting from them once it has left their borders. The Nagoya Protocol is one system for monitoring that, but arguably it is in its early stages and has not yet been thoroughly tested. So there is interest in finding more detail in how it is working, but also interest in better understanding what benefits, in particular the non-monetary benefits, may follow from access to genetic resources and traditional knowledge. Likewise, there is interest on the user side to understand what can and cannot be done with genetic resources. There is also a huge challenge with regard to knowing what users need to do in order to get access in the first place, due to the variety of permits one might need to obtain.

Oldham is arguing for an international electronic system that would allow someone to get any permit they need from a central national website. He is currently in the process of designing such a candidate system, and the work in progress version can be found at http://abspermits.net, which outlines the basics of a reporting and monitoring system (*Fig. 3*). Lyal explained that Oldham is aiming to create one system that allows the providing country to really look at what is being requested, and therefore to automatically direct all interested parties to the correct permits and to the right kind of outline agreements. As ever, there may well be a need for further negotiation down the line, but this could streamline the process for the majority of cases, and thus reduce the burden on the user and the provider.

Such a system would also make monitoring easier. Each permit would be given a unique identifier which would not be a large undertaking, as it is already done by the CBD's ABS Clearing House and would be implemented at the country level. This identifier could then be the basis for global monitoring in databases, collection use, publications, patents, and so on. It would allow us to have a clearer idea of what happens to material once it has left the provider country. One further suggestion Oldham has made is that the unique identifier could be represented by a QR code (which connects to the permit), which would be attached to collection specimens, vouchers of samples, digital samples, and so on. The aim is a free and freely useable system.

Tracking is not just of use for ABS compliance, but also becomes a valuable source of information. One could look at a given country and learn what is being sourced there. One could also then turn to resources such as Crossref and learn about the publications that have been developed from these resources, tracking authors and their collaborators, what they are working on. It allows you to find out what is happening with the biodiversity of your own country and start mapping who is working with whom. This is particularly exciting because it allows you to begin to get a real idea of the benefits being generated thanks to access being granted.

At the moment Oldham is working with the Bahamas and Kenya to see how such a system could be worked into open access systems. There is a chance that the UK Natural History Museum and Kew will begin trialling the system, to help solve the problem of knowing what different specimens can and cannot be used for. The aim would be to roll this out for all user and provider

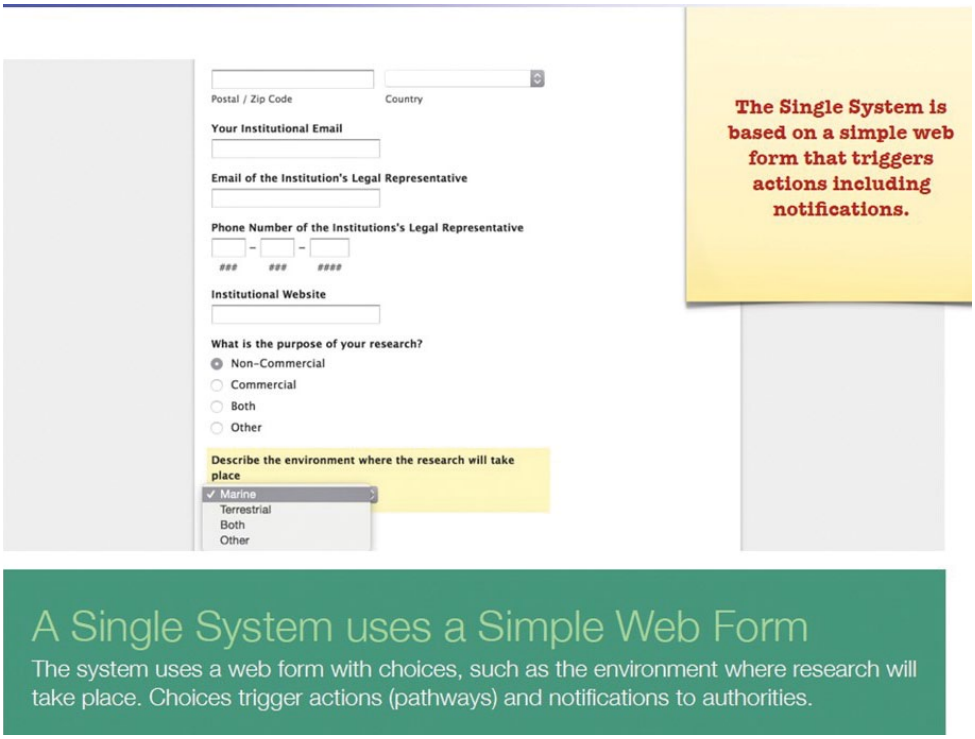

Fig. 3. Example of the web form for the Single System, courtesy of Paul Oldham

countries, building at the same time a network of people working on the monitoring and tracking of genetic resources and their use.

Catherine Rhodes,
Centre for the Study of Existential Risk, University of Cambridge

Rhodes spoke on the broader governance of genetic resources, and how this speaks to the current debates around the Nagoya Protocol. The history of genetic resource governance dates back to at least the 1950s. A wide variety and large number of international agreements and rules relate to the use of genetic resources, some of which are found in *Table 1*.

Rhodes noted that, as scientific and technological advances have expanded the range of resources perceived to have actual or potential value, this has contributed to an expansion of the range of resources that fall under these rules. She identified a lack of responses to those changes as a general problem, and saw at the root of many of the current problems a reliance on systems established on patterns of exchange for plant genetic resources, extended to cover many different sources with different patterns of exchange.

How do we know if we are getting things right, and therefore whether we need to change anything in response to synthetic biology? Rhodes saw different ways to approach this question. One place to start is by thinking about the functions of international law. If the overall purpose of international law is coordinating state behaviour in areas where there is common interest and a high level of interdependence, where states can't handle an issue of common concern just by themselves, then various functions of international law will contribute to coordinating such state action. With particular regard to the Nagoya Protocol, important functions will include:

- *Providing predictability and reducing uncertainty*
- *Reducing costs of individual action and increasing efficiency*
- *Establishing and shaping expectations*
- *Simplifying and facilitating transactions*

Another way to begin is to assess the legal system against the goals that the governance is seeking to achieve. As there are a broad range of laws to keep in mind, not

Table 1. International agreemnents addressing genetic resources. Courtesy of Catherine Rhodes.

Convention on Biodiversity	International Plant Protection Convention	Convention on the Protection of New Varieties of Plants
Cartagena Protocol on Biosafety	Laboratory Biosafety Manual	Budapest Treaty on the Deposit of Microorganisms for the Purpose of Patent Procedure
Nagoya Protocol	Laboratory Biosecurity Guidance	UN Declaration on the Rights of Indigenous Peoples
International Treaty on Plant Genetic Resources	Guidance on Regulations for the Safe Transport of Infectious Substances	Indigenous and Tribal Peoples Convention
Interlaken Declaration and Plan of Action on Animal Genetic Resources	Pandemic Influenza Preparedness Framework	Universal Declaration on Bioethics and Human Rights
Convention on the Conservation of Antarctic Marine Living Resources	Codex Principles on Foods Derived From Modern Biotechnology	International Declaration on Human Genetic Data
Genebank Standards	Codex Guidelines Food Safety Assessment: Recombinant DNA Animals; Recombinant DNA Plants; Recombinant DNA Microorganisms	Universal Declaration on the Human Genome and Human Rights
Code of Conduct Plant Germplasm Collection and Transfer	Sanitary and Phytosanitary Agreement	UN Convention on the Law of the Sea
Convention on International Trade in Endangered Species	Trade Related Aspects of Intellectual Property Rights Agreement	Biological Weapons Convention
International Health Regulations		
Terrestrial and Aquatic Animal Health Codes and Manuals		

only do the goals of ABS and conservation of biodiversity matter, but also a whole range of goals for governing the use of genetic resources. If, for instance, you took the goal of improving food security, you could ask what elements would governance need to deal with in order to match that goal, and assess whether the elements of the law match up to that goal. A final way is to look at the actual impact governance will have in practice, and whether this matches with the intentions of the governance mechanisms.

Rhodes then moved on to consideration of power relations. She saw the interests of powerful states as having dominated the implementation of the international laws referenced in *Table 1,* and anticipates they will continue to do so. The extent to which laws will change in response to science and technology is thus bound up with whose interests will be served by such changes. In the specific case of synthetic biology and the Nagoya Protocol, Rhodes would ask who will benefit and who will lose out from the inclusion or exclusion of DNA sequence information from ABS regimes.

Rhodes noted many examples of new sciences and technologies coming up against existing rules, such as submersible technologies. These new technologies are opening up access to marine genetic resources in areas beyond national jurisdiction. They are very expensive technologies, and thus there are few companies and states that can afford to have an expedition. After about ten years, benefit-sharing arrangements are just now beginning to emerge in this example, which in itself tells us something about the power relations involved, and what comes onto the agenda then.

If asked to think of ways to improve governance, Rhodes would suggest de-linking access and benefit-sharing, albeit appreciating this is not necessarily a realistic goal. She recognized both access and benefit-sharing as essential, neither of which should stop, but she argued that they do not need to be closely connected. Indeed, looking at the range of rules, benefit-sharing appears in about half of them, but not many link this to access. While there is a continuing inequity in the concentration of benefits from the utilisation of genetic resources, Rhodes saw this as less to do with where resources are accessed from and then moved to, and more to do with the differences in capacity to utilise genetic resources with modern techniques, technol-

ogies and knowledge. By concentrating on bilateral contracts between States, Rhodes noted this risks weakening the more general demands for benefit-sharing internationally in terms of significant scientific and technological capacity building. The latter has been repeatedly asked for over a decade in international processes, and there are provisions saying it will be done, but such promises haven't been fulfilled. She was concerned that concentrating on bilateral contracts risks distracting from these on-going processes.

Petra ten Hoopen

European Bioinformatics Institute

Ten Hoopen's talk addressed scientific databases within ABS frameworks. The European Bioinformatics Institute (EBI) in Hinxton is an outpost of the European Molecular Biology Laboratory (EMBL). It covers a broad range of resources from genes and genomes, to transcripts, proteins, chemicals and services. One of the first of these services to be exposed to ABS was the European Nucleotide Archive (ENA), the European portal for the International Nucleotide Sequence Database Collaboration (INSDC). The latter collaborates with GenBank in the USA and the DNA Data Bank of Japan (DDBJ). The ENA quickly became involved in ABS because of projects it was involved in, particularly marine projects such as TARA oceans expedition and OSD, both sampling projects coordinated by large consortia that were interested in making sure best practice was formed concerning collections. Legal partners helped them design a system to ensure they collected samples in accordance with ABS and with local jurisdiction of the countries where samples were taken from.

ENA and EMBL-EBI data resources are open, unrestricted, and free. This means that no restrictions are connected to the data provided. The Terms of Use impose no constraints on the use of the contributed data other than those provided by the data owner. The data is owned by the depositors, not by the database; only the depositors can decide on the terms of access and use of those records. However, deposited data should be made public within two years from the date of deposition.

As there are a broad range of laws to keep in mind, not only do the goals of ABS and conservation of biodiversity matter, but also a whole range of goals for governing the use of genetic resources.

EMBLI-EBI scientific databases recognise the value of ABS and are contributing to discussions with regard to facilitating it. There are two aspects that databases are currently dealing with and to some extent pushing back on. One is that they are asked to track usage of data, which requires tracking use of information forward, into the future. This is very difficult to do: data become isolated because they are not integrated with other resources; it requires structures to pool information; and many other technical challenges. A second aspect is that databases are being asked to store all the legal information attached to the data created from samples.

Ten Hoopen said that, thus far, the position of the databases is to only track information backwards, i.e. tracking the provenance of the material used to sequence the data. They are aiming to work with legal databases to connect the legal information with the scientific information. The scientific databases feel that there is quite a fundamental difference between the legal and the scientific data, and that they do not have the expertise to manage the legal. Their solution is that the scientific databases are not keeping the legal information, but would like to connect to the legal databases. The scientific databases would like to prioritise provenance, which can then be used by the legal databases. In this backward tracking, a scientific discovery with benefits would be traced back through several layers of data analysis, assays, and ultimately a sample – if each individual user records their usage, one can trace back.

Thus, one of the most important best practices to establish is that of accurately and consistently recording provenance. EMBL-EBI is involved in data standards development and collaborations to pro-

duce such a best practice for provenance reporting. One example can be the CIESM Charter (www.ciesm.org/marine/charter/CIESMCharter.pdf), designed to cover marine organism research; it is meant to improve provenance and recording and reporting.

At the moment, ten Hoopen said that scientific databases see themselves as contributing to ABS in two key respects. The first is with regard to the organisation and presentation of data, which adds considerable non-monetary value. That this is shared with the entire international community is already a benefit being shared. The second is in the tracking of provenance, which can improve integration and compliance with ABS regimes.

Discussion from session 3

↠ *A focus on the material?*

Discussion immediately followed by picking up the question of whether, in light of ten Hoopen's presentation, it wouldn't be possible to treat data as something material, as suggested at the end of the previous discussion session. A participant responded that this raised two questions. First, could it be traced – this person saw it as possible to trace backwards, as described in the EBI presentation. Another question, however, was whether to treat sequences as data or as material. Sequencing is only one kind of analysis attached to a sample, from the same sample you can also get images. To this person, images should be treated as data rather than material, and thus, sequencing should be treated as data; it wouldn't make sense to treat images as data, but sequence information as material. The first questioner wondered whether sequence information wasn't actually different from images, because a product can be produced from the sequence but not from images.

Further discussion on the implications of treating data as material connected to the concepts of forward and backward tracking. An attendee noted that tracking data as material would require tracking every use going forwards, with each use treated as a separate event. They saw this as running the risk of losing truly important records in the proliferation of resulting records. Whereas if you require backwards tracking, you have an event which may produce benefits, and you only elaborate the chain that resulted in those benefits. To them, this seemed far more efficient in terms of the management and answering the concerns of the providers.

One of the most important best practices to establish is that of accurately and consistently recording provenance. One example is the CIESM Charter.

Another attendee emphasised that, even if you can track the provenance of the sequence, this doesn't touch on the question of how direct the connection is between the eventual product and the natural sequence. How close must the end product be to the natural organism to enable the benefit-sharing? If one used 10,000 sequences for inspiration for the final product, how does one decide which of the 10,000 connects to a benefit? By apportioning it back to an original sequence, this still then brings you to a system where it is more or less unenforceable. An additional challenge raised by another participant was that the same sequences occur across thousands of organisms. How, in such cases, can you prove which one was the true provenance?

To one participant, the answers to this could be found in focusing on the material aspects of data – the infrastructure around sequencing, sequence information, its sharing and use. This participant saw the foundries as an example of a new kind of infrastructure embedded in the UK, and wanted participants to consider other potential elements, such as EBI's system of maintaining provenance and BCCM's recognition of a "bundle of rights." These, they suggested, were examples of building into a system ways of dealing with the multiple contributions of different parties.

This led to a back and forth discussion between two participants. The second participant noted that, while one clearly could regulate data transfer from one centralized repository to another, synthetic biology was not just about simple transfer.

Rather, data is recombined, it is used as an inspiration – there was rarely a direct relationship between the data and final products, let alone the material sample and final product.

The first participant offered what they termed an "extreme example" to think through the material aspect of data. What if certain databases were blacklisted? What if there was a public declaration that such databases weren't doing sufficient due diligence to track provenance, or in terms of people putting their signature or tracking number on what they share? The second participant's response was that this seemed a rather Soviet way of managing things, and quite the antithesis to open science. Even regarding whether it should be done, how would one stop the leakage of information and free access, the liquid movement of information? This person took it as given that today we need distributed models, not centralised models. The first participant failed to see why this would be a centralising move. Rather, it was about looking at those moments and places where the biological became digital, and seeing those as moments for decisions, rather than assuming the digital is necessarily abstracted and free from the material.

↠ *Potential lessons from sequence tracking for biosecurity*

The example of international coalitions of synthesis companies agreeing to check sequences for biosecurity risks was raised by several participants to make different arguments. One participant took this as an example of industrial actors choosing to set up a similar "whitelist/blacklist" system as previously discussed. The second participant saw this particular biosecurity initiative as not really working – they pointed to Chinese and Iranian synthesis companies not following the protocols, and noted that the initiatives were something of a paper tiger. In the case of ABS, the second participant considered that if a whitelist/blacklist system did work, it would effectively kill the European DNA synthesis industry as everyone would simply go the USA for synthesis. But in any case, they didn't think it would work – just as with the biosecurity protocols, they anticipated that biotechnology companies would simply drive a truck around such attempts at centralized control and limits to access, because there is no way to enforce such systems.

Another attendee wanted to suggest a further lesson from the biosecurity screening example. People have argued that the costs of such screening means that only large synthesis companies are able to be compliant. They saw similar risks for the Nagoya Protocol, in which smaller institutions might be at a disadvantage without the necessary infrastructure and capacity to comply.

↠ *ABS and databases*

One participant wanted to know what an "awareness" of ABS issues among database owners meant in practice. A response was that in most cases databases do not take responsibility for use, rather responsibility lies with the depositor to make sure any collection agreement allowed for the uploading of the sequence information. This is why it is so important to have best practices, so that collectors know what to do, that when they enter data into a database, they know what they are allowed to do with the material they collect.

The first participant wondered what would happen in the future if provider countries choose to restrict the right to reproduce sequence data. If PIC and MAT do not explicitly cover sequence information, and such changes are made, might this dramatically shrink existing public databases? Another attendee noted that many countries remain quite silent on their terms of use, so it is already difficult to know what is required. One saving grace is that if a country says you can put it in an open database, you have to carry with that data the identification of the collection event. That might make them feel more secure about the ongoing use of that data, but it doesn't answer the point raised, which is the control of the use of the endpoint, when the user of the end point has never signed an agreement.

↠ *Separate system for data?*

This conversation led to the question of whether sequence data necessitated a separate system of compliance than the current one dealing with the physical transfer of material.

An attendee explained that, already, some collectors provide a sheet of paper with a list of all the things they might do with material, including sequencing and putting on public databases. This is already being made available to provider countries, attached to the permit. This helps to provide more substance and legal clarity to permits that are rather vague on what is actually allowed. To this attendee, it seemed possible that, as sequences from that material was uploaded, this could be combined with a link to the identifier, collection event, and relevant permits; future users would then know the conditions of the permit.

To this attendee, the big step was to then determine what type of responsibility from that point would be on subsequent users to address benefit-sharing. Would this responsibility be legal or ethical? They clearly saw an ethical responsibility, but perceived legal responsibility as a little more hazy. A strong ethical framework – something various organizations already have – was perhaps what we should focus on expanding. A legal framework for use of sequence data might be too far away, no matter what provider country legislation says, utilization of sequence data takes place far away from where it is collected.

Speaking to how an "ethical" framework might be perceived, one participant noted parallels with Corporate Social Responsibility agreements that in practice don't seem to stop human rights abuses. Thus, non-binding frameworks might be viewed with scepticism.

↠ *Drivers and implications of ABS legislation*

Throughout the day, participants raised questions of how countries and companies could and were responding to the Nagoya Protocol and ABS requirements. One participant said that there was the opinion in the biotech industry that the ability to freshly synthesis and not have material transfer was liberating, facilitating innovation and commercial activity, and freeing commercial entities from the constraints of the Nagoya Protocol. At another point, a participant asked whether new practices of "synthetic biopiracy" had been provoked by the Nagoya Protocol.

A participant raised the point that some user countries simply say that if a provider country makes their ABS terms too burdensome, they will refuse to use their genetic resources – and indeed, throughout the day several participants raised examples of countries and companies where this has reportedly already happened (for example, a particular case was explained of a company that once had a very good relationship with scientists in Brazil, and had invested in Brazilian universities and training programmes, helping to increase Brazil's own capacity to pursue research. Following the Nagoya Protocol, this company decided to withdraw from all of these agreements). On the other hand, some countries really do have unique genetic resources that can't be obtained elsewhere. Furthermore, the question was raised of what might happen if all provider countries legislate on access to genetic information.

One response was that user organizations have sufficient genetic resources in their collections in many cases to simply go forward with research, without having to share benefits. If no access takes place, there is no benefit-sharing, and ultimately a loss to provider countries.

Another participant pointed out an economic driver for a legal framework is the security it gives companies that they can invest because they know their legal claims to material and its information. One could create a system where, say, x, y, and z are required to establish legal provenance otherwise products are threatened, this might be the sort of economic driver to focus on, rather than ethics.

Another participant picked up the challenge of determining what kind of system to put in place. They suggested thinking about this by breaking down benefit-sharing and asking what kinds of benefits

people are interested in. If we work on the details, perhaps that is where we can find an arrangement that works. For example, in the ITPGRFA, an agreed upon benefit is facilitated access. The same treaty seeks to accrue money by restricting access to material, so that money is distributed from patents. It seems that the drafters of the treaty didn't see this inconsistency – on the one hand, wanting to facilitate access and, on the other, basing the benefit-sharing system on restricting access. Thus, from the start, we should ask: which benefits are more meaningful? In this case, which benefit will we focus on – for resources and knowledge to remain public, or to privatize and restrict in order to trigger benefits? We need to acknowledge that there are trade-offs among benefits.

They suggested the ITPGRFA, and the way challenges in that treaty are being grappled with, might help shed new light on entrenched discussions around the Nagoya Protocol. Databases may be seen as a threat, but the ITPGRFA is trying to see if it can be a way to enhance benefit-sharing, by linking databases, by giving a different sense of control to providers. Their development of a Global Information System in particular might be worth study, to know what shortcomings they are dealing with and how they are responding.

The session closed with a participant raising the point that any system of tracking costs money, and that many organizations are willing to follow ABS but simply do not have the resources – financial and human resources, hardware, software, etc.

Session 4
Reflections and final discussion

↠ *Synthetic biology and the Nagoya Protocol – what questions are raised?*

Initial reflections focused on disconnects between conversations and assumptions within communities in synthetic biology and around the Nagoya Protocol. Many synthetic biologists see themselves as engaged in work to produce organisms completely orthogonal to the natural world. In this case, of what relevance is the Nagoya Protocol to them? Similarly, a popular metaphor within synthetic biology is that of writing DNA and being creative in doing so – from this perspective, claiming that countries may own the "words" scientists want to write with may seem quite alien.

On the other hand, some criticisms of synthetic biology may apply equally to the Nagoya Protocol – most notably, that both rely on a decontextualized, reductionist view of genetic information, as opposed to acknowledging the importance of context for gene expression.

↠ *Open science and ABS – how to connect?*

Another participant reflected on the open science vision, and the potential connections and disconnects with the Nagoya Protocol's vision for ABS. They noted that the current model for biotechnology research and commercialization could be heavily criticized for failing to broadly disseminate the benefits of its products, in part because of significant corporate consolidation in agriculture. An open science model is trying to challenge this model, recognizing that most large scale engineering projects depend upon open technologies, open standards for compatibility, open software, etc. They see most fields as existing on two levels – a private, monetized layer that is supported by an open layer that promotes innovation. Biotechnology, as a young field, is still developing this open layer.

However, this participant saw the open science vision as departing from the Nagoya Protocol's in a number of significant ways: global instead of bilateral; free use rather than attempting to monetize; supporting basic research rather than applications; and focused on sharing data rather than the transfer of material. They proposed that the Nagoya Protocol may want to try to incorporate recognition of the need for that "open" layer. When faced with the dematerialization of biology, then, it would be relatively straight forward to liberate certain data to the "open" layer and free it from ABS requirements.

When asked how ABS could work in the face of such an "open source" vision, they suggested that it might be a matter of focusing on *when* in a process patents are applied. Delaying this works quite well with the model of open sharing of technologies. When pressed on whether there were economic drivers from open science that could convince industries to engage with the ABS system rather than seeking to avoid it, they said that purely economic drivers were likely not enough. Rather, they saw the closest analogy as fair trade.

They argued that open systems can make sense domestically, because intellectual property protection costs money. A patent application is something like $ 100,000, so there is a benefit if you have a collective arrangement of sharing materials. You see this already in the software industry, in computer hardware; where there are open standards and resources viewed as mutually beneficial, industry supports such activities. A similar commercial incentive ought to apply in biotechnology, but this process and procedure needs to be developed.

Another attendee suggested that, while this contrasting vision of open science and the Nagoya Protocol may accurately reflect the emphasis thus far, most of the elements of the "open" vision are indeed present

in the Nagoya Protocol; the question is how we go about putting them in place. Furthermore, they raised the question of whether the labels of "open" and "global" science are accurate. It may be open and global in aspiration, but not equally open and accessible across the globe. This participant saw it rather as a club – albeit a widespread club - of people who make use of open science, and noted that it may not include those scientists in countries where they want the Nagoya Protocol to reach its objectives. When pushed on whether limitations in access and training shouldn't be seen as distinct from "closed" science, they noted that the Nagoya Protocol is precisely about building the capacities of those who currently can't take advantage of what is out there in order to really benefit. Many of the things mentioned in the vision for open science - making resources open and accessible, building capacity - these are non-monetary benefits. So in many ways the Nagoya Protocol is about precisely the kinds of thing being discussed here, although perhaps not with sufficient emphasis. Perhaps it is the case that some people attached to the discussion have spent too much time talking about patent-triggered benefits, and we should focus on non-monetary. But this discussion may also highlight blind spots in the open science community – that work is needed to ensure that what claims to be "open" is really open, and if it is not accessible, that perhaps more guidance and efforts to build capacity are needed for open science to be genuinely beneficial.

Later in the discussion, another attendee noted that, while there may well be a clamour for open access, to them it seemed this clamour was much louder in developed countries than developing countries. The perception here, in Cambridge, would perhaps be rather different if this meeting were taking place in Nairobi. Listening to some of the things being said, they suggested that a representative from a developing country might be pretty enraged by now, because of the underlying assumptions of the discussion. What might seem self-evident and obvious from a biotech industry point of view is quite the reverse in some cases from a developing country point of view. They called on participants to be aware that what may seem logical and natural to them will bump up against others for whom that is anything but.

↠ *National sovereignty of genetic resources*

Building from the open science discussion, a participant noted that we currently have an opportunity to begin valuing things never before valued and including them in our estimations of overall cost and benefit, such as environmental services. They see the Earth as a giant workshop full of evolved systems that we are now starting to pull out and modify. If there are ways to recognize the worth of this, that has to be good. But they failed to see how a national model was a rational way to deal with global resources, as we should be using benefits to aid the global community.

An initial response was that the Nagoya Protocol exists, and it is based on a bilateral model for the most part, and it cannot go away. When the first participant noted that therefore the Nagoya Protocol would likely not work, another attendee reminded the room that the Nagoya Protocol did not introduce the concept of national sovereignty of natural resources. This goes back to the CBD's entry into force in 1993, and even earlier; the international legal framework regarding sovereign rights of biological resources is very well established.

A response to this was that international law can be changed. Indeed, this participant saw a need to get rid of sovereign rights to genetic resources. An immediate response was that sovereign rights over resources are part of what it is to be a sovereign country. That said, it's about how sovereignty is used, what is done with sovereign rights. Furthermore, genetic resources are hybrid, material and information, and it doesn't seem as though information can be included in sovereign rights.

↠ *Benefit-sharing and proprietary technologies*

Another attendee raised the question of access to research tools. They saw much of the discussion of benefit-sharing focused

on training and perhaps funding, but they wondered about a separate problem of gaining access to the proprietary technologies (equipment, reagents, etc.) necessary for work that exploits genetic resources. At present, one has to deal with large multinational corporations in order to get the equipment needed to pursue the research that might lead to benefits. They also pointed out that gene and genome synthesis technologies are in the hands of proprietary companies in the developed world. It is currently a centralised system. Nobody is developing large synthesis capacity in developed companies. These are benefits that need sharing, and they could not see how bilateral agreements with researchers or companies could ease that path to equitable access.

A participant suggested that nothing in the Nagoya Protocol would stop these kinds of benefits being included in the ABS agreements. The openness of the Protocol's list of possible benefits allows room for a genuine understanding to develop on what is needed, whether in fact these technologies should be part of the benefits. You need good faith engagement, so that such needs can be identified. They also noted that the Nagoya Protocol presumes a bilateral arrangement in the absence of anything else, but more creative solutions are possible; a regional approach may be developed, and there is a provision in the Protocol to consider a multilateral mechanism.

↠ *Strategic ambiguities and DSI*

The day ended with one of the participants noting that, from the start, the text of the Nagoya Protocol was understood to include "strategic ambiguities" (Bavikatte & Robinson 2011). Necessary to achieve a consensus text, these ambiguities allowed room for interpretation and jurisprudential growth. The synthetic biology negotiations have opened up space for the CBD and Nagoya Protocol processes to address the broader issue of changes in technologies and practices in the life sciences. This, in turn, may provide a space for Parties to probe the protocol's ambiguities, while in the context of the treaty's third objective.

From Cambridge to Cancun: Making connections

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In this second part of the report, co-authors Deborah Scott and Dominic Berry reflect on the November workshop in light of the December 2016 UN Biodiversity Convention. One of the co-authors, Deborah Scott, was at the Cancun negotiations (as were quite a few of the workshop participants), and collaborated collecting data there with Molly Bond. We use her notes from the negotiations to consider differences and similarities in these deliberations, and to highlight issues that were raised at our workshop but not in the negotiations, and vice versa. Our workshop did not provide answers to the conundrum of whether and how ABS systems could address DSI. But this report serves to highlight some issues not yet addressed in formal negotiations and to provide additional texture to conversations already underway.

The 2016 UN Biodiversity Convention brought more than 8,000 delegates to Cancun, Mexico. This was the 13th meeting of the Conference of the Parties to the CBD (COP), a gathering that acts as the decision-making body of the treaty. It was also the first time that a CBD COP met concurrently with the decision-making bodies of the two protocols - the Conference of the Parties serving as the Meeting of the Parties for the Cartagena Protocol on Biosafety (COP-MOP 8) and for the Nagoya Protocol (COP-MOP 2). Holding these meetings concurrently was intended to help integrate the work of the CBD and its protocols.

"Digital sequence information on genetic resources" and its potential impacts on benefit-sharing was quickly recognized as a cross-cutting issue for the treaty and protocols. Earlier in 2016, the CBD's Subsidiary Body on Scientific, Technical and Technological Advice (SBSTTA) developed a Recommendation to the COP that essentially served as a draft COP Decision on Synthetic Biology. Among the bracketed portions of the Recommendation (brackets indicating that consensus had not been reached) were the following:

> [(o) Invites the Conference of the Parties serving as the meeting of the Parties to the Nagoya Protocol to clarify, if and how, the use of digital sequence information on genetic resources relates to access and benefit-sharing]
>
> Annex: Terms of Reference for the Ad Hoc Technical Expert Group on Synthetic Biology, 1(e) [Propose elements to the Conference of the Parties serving as the meeting of the Parties to the Nagoya Protocol to facilitate the clarification of, if and how, the use of digital sequence information on genetic resources relates to access and benefit-sharing;]

These two sentences turned out to be some of the most contentious of the negotiations. Digital sequence information (DSI) was discussed in at least three meetings of the Contact Group on synthetic biology and was spun off into a cross-cutting

(CBD and NP) Contact Group specifically dedicated to DSI. It was brought up in the NP COP-MOP discussion on need for and modalities of a global multilateral benefit-sharing mechanism.

Ultimately, those two bracketed sentences led to two Decisions of the COP and COP-MOP specifically on DSI and one COP-MOP Decision including DSI:

- Digital Sequence Information on Genetic Resources (CBD/COP/DEC/XIII/16). The 14th COP (to be held in 2018) will consider "any potential implications of the use of DSI on genetic resources for the three objectives of the Convention." Thus, DSI will be considered not just in terms of access & benefit-sharing, but also implications for conservation and sustainable use. The Secretariat will invite views and relevant information as well as commission a fact-finding and scoping study to clarify terminology and "assess the extent and terms and conditions of the use" of DSI. An Ad Hoc Technical Expert Group (AHTEG) specifically on this issue is established (a meeting will be convened in February 2018). The SBSTTA is requested to consider the outcomes of the AHTEG to make a recommendation for the next COP.
- Digital Sequence Information on Genetic Resources (NP/MOP/DEC/2/14). The Nagoya Protocol's COP-MOP passed an almost identical Decision as the CBD COP, although noting that this issue may concern the NP's objective (as opposed to the CBD's three objectives), and asking the AHTEG to also serve the NP and thus to consider the NP in its work.
- Cooperation with International Organizations (NP/MOP/DEC/2/5) - This NP COP-MOP Decision lists a number of international organizations, including the World Health Organization, the World Intellectual Property Organization, the Commission on Genetic Resources for Food and Agriculture of the Food and Agriculture Organization of the United Nations, and the International Treaty on Plant Genetic Resources for Food and Agriculture, that the Executive Secretary is to continue to engage with in order to collect information on current discussions on the relationship between the use of DSI and ABS.

These Decisions can be seen as commitments to procedural processes leading up to the next COP/COP-MOPs in 2018, establishing processes of information gathering and analysis that may lead to substantive decisions.

Interactions between Cancun negotiations & our workshop

A number of aspects of the interplay between DSI and ABS that were grappled with at our workshop came up in Cancun as well. An overview of these areas is included below. This is followed by issues raised in our workshop but not in the formal negotiations, and then those raised in Cancun but not our workshop. Throughout, we refer to the people in Cancun - the negotiators, civil society representatives, businesspeople, scientists, youth, and others - as 'delegates', and those persons taking part in the Cambridge workshop as 'participants'.

Issues addressed in Cambridge and Cancun

↠ *The importance of provider country national regulations*

At our workshop, participants who had been engaged in the Nagoya Protocol for a number of years kept reminding the room that the protocol was only one relevant instrument, and that provider countries may choose to base their regulatory regimes on more than just the protocol. Furthermore, where the Nagoya Protocol is ambiguous, such as around this question of DSI, provider countries could choose to interpret the Nagoya Protocol in ways different from the EU. In discussion, a participant raised the question of what might happen if all provider countries decided to treat DSI as genetic resources, and therefore covered by ABS regulations. The room did not have an answer to this question.

At Cancun, delegates of countries primarily identifying as providers of genetic resources raised the prospect of DSI as a loophole to benefit-sharing. In the course of negotiations, a few delegates repeatedly noted that, if this forum would not take ac-

tion, provider countries might coordinate in changing their standard ABS contract's Mutually Agreed Terms (MATs) to disallow genetic sequencing of materials being accessed until a multilateral solution was developed. In other words, if the COP and COP-MOP will not adapt benefit-sharing frameworks to acknowledge changing scientific and commercial practices, provider countries might be forced to change their terms of access. Such a move would impact all potential bioprospectors, whether or not they came from countries party to the Nagoya Protocol.

These delegates were quick to add they did not see this as a desired result - they recognized it could hamper scientific research. Nonetheless, this was a sign of how seriously they consider the threat of DSI technologies and practices to benefit-sharing systems. It seems highly unlikely that this is the last we will hear of the potential for coordinated provider country domestic action as a response to DSI.

Our workshop did not provide any responses to such a potential strategic move. We want to highlight here simply that this is indeed on the table. Any scientific or commercial entities seeking to avoid Nagoya Protocol obligations by looking to countries that have not joined the protocol should be aware that domestic action is possible regardless of protocol commitments. An awareness of the possibility of coordinated provider country action if no multilateral action is taken might push some actors to the negotiating table.

↠ *Open science: global benefit or threat to national sovereignty?*

At our workshop, some participants saw open science as a necessary challenge to the current model of biotechnology research and commercialization. Cancun delegates did not use such language, but several framed open science - specifically, publicly accessible genetic sequence information - as a public good that would be threatened if DSI was found to fall within the Nagoya Protocol's scope.

At our workshop, it was often stressed that the power of open science had yet to be tapped. Some participants offered a vision of the future in which the Nagoya Protocol would essentially provide an exemption to material being used in "open" science, much as fair trade operates alongside conventional trade arrangements. This was seen as not only practical, as the locations of biological material used in research will be numerous, but beneficial for developing countries who would be at less of a disadvantage with IP-free materials. At Cancun, open science was described as already positive, indeed, as a public good in itself - one delegate described making genome sequences publicly available as an act of custodianship, while another didn't see why such information shouldn't belong to the world, for the benefit of students across the globe.

At both the negotiations and in our workshop, these statements received push-back - not disputing its positive potential, but challenging open science's role as an automatic or global good. At our workshop, it was noted that "open" did not equate with accessible, and that what may seem as indisputable goods to those sitting in Cambridge may be seen quite differently from other parts of the world. The Cancun negotiations displayed this shift in perspective, as numerous delegates noted that if open science led to patents, it was a path to sabotaging the Nagoya Protocol and promoting biopiracy.

Going forward, it seems there is a need to address the tension between openly available data and resources on the one hand and commercialization on the other. The tension exists not only because some stakeholders aim to prevent certain kinds of business practice, such as the use of patents to assert ownership over biological resources, but also because of disparities in capacity to commercialize between states with different levels of access to capital. Because of these tensions, invocations of the need to protect open science in relation to DSI and ABS will likely continue to be challenged. If proponents of open science want to ensure current trends in publicly available data continue, they would do well to address this relationship. In addition, as was raised at the end of our workshop, "open science" is broader than publicly

available data, and could include hardware such as technologies for gene and genome synthesis.

↠ *A global multilateral benefit-sharing mechanism*

Article 10 of the Nagoya Protocol says that Parties "shall consider the need for and modalities of a global multilateral benefit-sharing mechanism" for transboundary situations or where it is not possible to grant or obtain prior informed consent (PIC). At the time of our Cambridge workshop, the Nagoya Protocol had commissioned an expert study and held two expert meetings (2013 and 2016).

At our workshop, the possibility of a global mechanism was raised at various points throughout the day but not extensively explored. Rather, it led to discussion of other global benefit-sharing mechanisms - namely, the WHO's Pandemic Influenza Preparedness framework and the ITPGRFA's multilateral mechanism - and whether those were successful or relevant examples. To some participants, the narrow focus of these mechanisms alone disqualified them as being of any relevance. But for others these mechanisms, while developed for unique instances, were useful for current discussions within the Nagoya Protocol, whether looking at the ITPGRFA's successes in benefit distribution or the WHO's work to determine how to make their fee-based system attractive to industry.

Throughout the workshop, a number of participants questioned whether bilateral arrangements for ABS were the most efficient, realistic, or just solution. These comments were often followed by other participants noting that, regardless of their usefulness, this was the reality of the Nagoya Protocol. It's fair to say that there was more freedom to question the underlying tenets of the Nagoya Protocol at our workshop than there was at the UN Biodiversity Convention. Perhaps because of this, our conversation gravitated to the utility and appropriateness of the national sovereignty of genetic resources, while the COP-MOP discussions focused on procedural next steps, and specifically whether

At both the negotiations and in our workshop, statements that conceived of open science as an inherent good received push-back.

there was sufficient evidence to determine a need for a global mechanism. Delegates arguing that DSI must be interpreted as included within the CBD and Nagoya Protocol's "utilization of genetic resources" often gestured to Article 10 as a possible way for the Protocol's system to address related challenges of regulating DSI.

NP COP-MOP Decision 2/10 on the need for and modalities of a global multilateral benefit-sharing mechanism establishes a process by which the Executive Secretary will compile information submitted on: the implementation of NP provisions related to traditional knowledge associated with genetic resources; practical experiences where it is not possible to grant or obtain prior informed consent; and views on the way forward on Article 10. The Subsidiary Body on Implementation (SBI) is requested to explore the need for a global multilateral benefit-sharing mechanism and make recommendations for the next COP-MOP.

↠ *Starting points*

The starting point for any negotiation is important, as it shapes the course of discussion. When faced with the issue of DSI and ABS, one can start with the question of what a regulatory solution would look like: is it a phenomenon that can be governed? At our workshop, some saw the ability to radically disassociate the physical from the conceptual as a major paradigm shift, leaving the Nagoya Protocol already outdated. From this perspective, the Protocol rests on a fundamental assumption of physical access and use, leaving DSI out of its scope, and will only become less relevant as sequencing and synthesis continues (or, as was raised by a workshop participant, as companies are 'driven' to these practices in order to avoid ABS responsibilities).

A different starting point is to ask whether DSI represents a potential path for biopiracy: does this situation fall with-

in the scenarios for which the CBD calls for fair and equitable benefit-sharing? For the most part, delegates arguing for DSI to be addressed as a form of utilization of genetic resources started here. They acknowledged changes in scientific and commercial practice since the CBD had come into force - one delegate described it as regulating VCR technology in the age of YouTube - but they held that the principle of fair and equitable benefit-sharing had not changed. Science would not leave the CBD (and its Protocols) behind; it was rather up to delegates to bring the system into alignment with new practices.

Starting with the question of whether the principle of the CBD's third objective still applied also meant that delegates rarely ventured into details of how to govern DSI for ABS. At this point, they saw the only question before delegates as whether DSI fell within the ABS system, not how that could then be governed. When challenged that this was a problem with no solution, they exhorted the room to trust the treaty and protocol processes - that if agreement could be reached on the principle, experts would find a proper response.

If you are in a community of interest currently grappling with these questions of ABS and DSI, it might be useful to identify if your deliberations have taken for granted one of these starting points.

Issues raised in our workshop but not in Cancun

The CBD is a treaty notable for its culture of openness and transparency; formal small-group meetings, such as Contact Group and Friends of the Chair sessions, are almost always open to observers. In Cancun, high interest in the synthetic biology negotiations (and the spin-off issue of DSI) led to sessions in packed rooms of over 100 people for which Secretariat staff had to control entry in order to keep room numbers within fire safety rules. Still, each of the formal meetings of the synthetic biology and DSI Contact Groups were open to observers. This section addresses issues not addressed in these formal negotiating spaces. Of course, negotiation happens outside of these formal multilateral settings as well, in bilateral discussions and informal groups of negotiators; it's not to say that these issues were not raised there, or in some of the many side events, but rather that they largely stayed off the formal agenda in Cancun.

↠ *Distance from original genetic resource*

In Cancun, negotiators grappled with whether genetic sequence data should be considered equivalent to its material organism, like a "hard copy" or a "soft copy" of a document. This issue was not resolved, as delegates went back and forth on whether a thumb drive and an ear of corn could/should be considered the same for the purposes of ABS. Both sides of this debate focused on the question of equivalency of a genetic resource and the sequence information corresponding to it.

Our workshop repeatedly raised a different question: what are the ABS implications of trends in increasing distance from one "original" genetic resource? Synthetic biologists often see the DSI of an organism as a jumping-off point, from which they may engage in modifying metabolic pathways, making multiple edits to the genome, or combining with sequences from many sources. When working like this, how does one trace ABS responsibilities back to defined collection moments? And what if 10,000 sequences are used? How do we make sense of processes like a BLAST search, which relies on millions of sequences to provide the necessary context for the alignment of sequences?

If Parties are going to seriously engage with bringing the CBD and Nagoya Protocol into alignment with contemporary scientific practices, these are an important aspect of the utilization of genetic resources, now and into the future. Nature is often referred to by synthetic biologists as an "inspiration" for the constructs and organisms they produce. What would an ABS system need to look like in order to ensure this approach to life doesn't allow (or rely upon) biopiracy? Changes in how DSI is used may require the focus to be shifted from individual samples (whether

material or information) to something else – whether that is relationships between institutions, flows of material/information, or transparency.

↠ *Innovation is not a pipeline*

Our workshop raised the question of whether the Nagoya Protocol frames ABS based on a decontextualized, reductionist understanding of innovation. And if so, is there flexibility in the notion of ABS, as captured in the CBD and Nagoya Protocol, to incorporate other understandings? If the linear "Green Gold" model of discovery leading to research and development leading to commercialization is recognized as an incredibly rare path to innovation, are adjustments to the governance framework necessary, or possible?

Any object of governance must be first defined such that it is governable. There seems to be broad agreement that, in the quest to make the utilization of genetic resources a process that can be governed to ensure fair and equitable benefit-sharing, negotiators of the Nagoya Protocol relied on a linear model of innovation. The challenge of DSI may be offering an opportunity for CBD and Nagoya Protocol Parties to explore how to conceptualize ABS in light of greater complexity.

↠ *Reclaiming the materiality of digital sequence information*

Some of our workshop participants were interested in pushing back on the "dematerialization of biology" narrative. Throughout the day, various participants asked whether physical materials / physical access had actually lost their importance. Was discovery and access through databases already a reality? Was it a possible future? Was there a chance that we are basing these debates on promises from scientific communities that may fail to unfold, much as high expectations of bioprospecting in the early 1990s were disappointed? Do synthetic biologists never need access to physical biological materials?

It should be noted that there was strong confidence among some participants that this was indeed the future of biology, if not the current reality. Others, however, were interested in ways of conceptualising the materiality of DSI by looking at the way it is curated in databases, manipulated through software, transferred to synthesis companies, and so on - to explore whether ABS of DSI could be approached from these material infrastructures rather than treating it as abstract, disembodied information. It might be an exercise worth seeing through, either by the consultants hired by the Secretariat or by academics, to identify the infrastructure through which DSI is made, held, shared, and used, and to consider whether this could connect with moments for decision-making and thus be incorporated into emerging models of ABS.

If the linear "Green Gold" model... is recognized as an incredibly rare path to innovation, are adjustments to the governance framework necessary, or possible?

Issues raised at Cancun but not in our workshop

↠ *Treaty and protocol processes and boundaries*

Unsurprisingly, a substantial portion of the DSI-related negotiations focused on questions of institutional processes, including: whether these negotiations and subsequent actions took place under the auspices of just the Nagoya Protocol or also the CBD; what types of actions were possible and appropriate by different bodies, such as the SBSTTA, AHTEG, and COP; and the potential legal impacts of a COP Decision.

Delegates also discussed the evidence base for decision-making: what kinds of information were needed in order to make decisions on this issue; how best to gather such information, whether through an open submission for information or a commissioned study; what entails a "scientific" study and what kinds of aspects can be within the scope of such a study.

In the second week, some delegates began to question the scope of the term DSI – wondering whether specifying "digital"

might close off future ways of storing information, and whether "genetic sequence" might leave out important aspects such as proteins, methylation, etc. Ultimately, the term was footnoted in the COP and COP-MOP Decisions with the note that the terminology is subject to further discussion in the study and expert group.

↠ *Driving urgencies*

Fears have been expressed regarding what synthetic biology can or will do to the aims and ambitions of the CBD. At our workshop, a number of participants expressed concern that their work might be restricted or threatened by a stringent ABS system that included DSI. This viewpoint was also expressed in Cancun, by negotiators as well as delegates from business, public sector researchers, and others. Missing from our workshop, however, was the palpable sense of urgency that a number of delegates of self-identified provider-countries brought to Cancun. They expressed fear that, without action, benefit-sharing would continue to fail as it had since 1992. One delegate noted that in 2002, when the Bonn Guidelines were agreed upon, gene banks contained 17.4 million genetic sequences, while as of June 2016 they held 196 million, with the number "doubling every 4 months." The negotiations were interspersed with such statistics as reason for an urgent need to take action. It should be noted that this urgency was countered by other delegates, some of whom described the issue as "important but not urgent," or who questioned whether enough was known to describe it at all.

These are very different sources of urgency: on the one hand a concern that existing and potential research and business practices will be curtailed by regulation; and on the other a concern that opportunities for biopiracy will multiply without action. The point here is not that one of these sense of urgency is more legitimate than another. Rather, we would simply like to note that in the context of discussions within a country such as the UK, or within synthetic biology communities, it is far more likely that the first set of concerns will be palpably present. These discussions shouldn't lose sight of the second set of concerns.

ABS & DSI after Cancun

This section is not endorsed by or representative of the views of workshop participants.

In this last section, we identify key themes that can be explored going forward and make an effort to highlight the ways in which multiple interpretations of these issues were available at both the Cambridge workshop and in Cancun. As with the rest of the report, this is intended as a resource for future debate and discussion, but does not aim to provide solutions.

This discussion should not be seen as only important to those who identify as synthetic biologists. Synthetic biology is useful to think with because it places itself squarely within scientific and commercial practices involving DSI and DNA synthesis. The following points are therefore made with this narrow community directly in mind, but should be read as also applying to biological science and technology institutions and organisations more broadly.

↠ *Beginnings*

Our workshop was organised with a commitment to addressing the topic from as diverse a range of perspectives as possible, allowing participants to begin the conversation in a manner of their choosing. When it comes to situating ourselves in relation to the history of ABS, beginnings matter.

We can, for instance, begin with developments in molecular biology and the eventual arrival of practitioners who identify as synthetic biologists. Doing so we are likely to end up discussing scientific methods, technologies, and ambitions, concluding with recognition of large economic disparities between different states. This might lead to appeals to these same disparities as motivation for scientific research in the first place.

Alternatively we can begin with the economic development of states. Doing so we de-centre science and technology, seeing them alongside a wide range of other factors impinging upon the economic security and health of citizens, acknowledging power differentials in international agreements. This leads to seeing the aims and motivations of ABS in competition with a host of other agendas playing out in international governance.

Or we can begin with the history of international sponsorship and growth of the sciences, recognising the persistent aspiration to collect and bring to the centre of powerful states (or empires) examples of organisms considered valuable for a whole host of reasons. This leads to recognising that systems for the collection and dissemination of valued resources recreate social and political arrangements, opening up the question of what kinds of arrangements should be aspired to.

All those whose work depends upon and deals in biodiversity need to be aware of this multiplicity. There are a range of potential interpretations of scientific and industrial work, and the one that any particular group chooses is likely to be the most self-serving. This holds true for all life scientists and related industries, not just the

community of practitioners who identify as synthetic biologists. Ignoring this multiplicity is likely to lead to increased confusion in discussions and impede potential points of agreement.

↠ *The culture of ABS*

One feature of the workshop was its involvement of a range of persons from different kinds of institution and discipline. Each had varying levels of understanding when it came to the history and origins of ABS agreements. Indeed, the work of learning about and understanding ABS, where it has come from and why such agreements are struck, is unequally dispersed throughout the biological sciences and associated academic and commercial institutions. It was important therefore that we had participants who had been involved with the implementation of ABS compliance procedures from the earliest years, who could be directly brought into discussion with scientists working in newer disciplinary spaces.

When it comes to the daily life of something like synthetic biology, particularly on the public stage, it does not often invite direct comparison and contrast with anything historical. Synthetic biology is much more commonly framed as entirely new, cutting edge, and - to use a phrase with multiple meanings in the context of DNA synthesis - de novo. But historical comparisons are essential, as they allow us to see what it has taken to achieve ABS gains thus far (i.e. at a minimum systematised training and education of practitioners working with biodiversity), and thus what might be needed to continue growing and strengthening these efforts (i.e. the training and education of anyone working with biodiversity on the history of ABS and its goals).

Right now ABS is being encultured in labs, departments, museums, and businesses. There is no essential reason for synthetic biologists and those working with synthesised DNA sequences not to embrace and explore the range of opportunities for international cooperation that the Nagoya Protocol has opened up. A purported abstraction from a material to an informational level ought not to discourage practitioners from engaging in fair and equitable collaborations with international partners. However legal framings and procedural recommendations capture (or fail to capture) the specifics of actual practices, the ability to use DSI rather than directly accessing material collections does not create an essential bar to embracing the culture of ABS.

If on the face of it some scientists are alarmed about the kind of work this might require, that is perhaps because they are picturing having to do it all themselves. They will not be expected to implement these systems in isolation, and indeed broad participation across a range of organisations has already been, and will remain, a characteristic of ongoing ABS implementation.

↠ *Practicalities*

Various speakers at our workshop provided a range of practical tools and guides already in place for the implementation of ABS and told of more that are on the way. One key feature of these tools is that many of them have been created bespoke for particular communities of researchers, to deal with the area of the CBD and Nagoya that most directly affects them. Governments have not intervened to produce such tools universally, and there are few actors who take part in every single aspect of research and development (i.e. very few organisations sponsor expeditions, manage collections over time, share them with external partners, use them for research, and also create new products from them). Labour is divided, and accordingly ABS resource and tool creation has been partial.

At the outset, this dispersed approach – relying on the innovativeness and entrepreneurial spirit of those learning to comply with ABS – fits very comfortably with much of the ethos expressed by synthetic biologists. Think of Paul Oldham's permit collecting software, the increasing reliance on samples with QR codes at institutions such as the NHM as explained by Chris Lyal, and EMBL-EBI's CIESM charter as explained by Petra ten Hoopen. These attempts to find solutions to ABS

requirements are precisely the kinds of entrepreneurial activity that synthetic biologists (who tend to be positioned close to technology hacker and DIY bio spaces) often choose for themselves. There is clearly an opportunity here for synthetic biologists to acknowledge and incorporate ABS compliance as part of their own agenda, in ways that help them achieve their own ambitions. To give one example, tracking systems are not only a good way to ensure ABS is being complied with, but can also help to acknowledge and record credit for scientific work.

At the same time, we were informed of working practices that do not seem compatible with ABS as it is currently widely understood. Examples include organisms being produced from a large number of sequences taken from across multiple species in multiple collection locations and BLAST searches that rely on large datasets again taken from an incredibly large number of samples from different locations. While such practices undoubtedly pose challenges, there is flexibility within the Nagoya Protocol, both within and outside Article 10, to explore new arrangements that better address DSI and related practices.

As was repeated by a number of participants throughout the workshop, the CBD and Nagoya Protocol are about establishing long-term and strong relationships between providers and users. They provide an opportunity to enter into two-way, iterative discussions about what benefits might be and what sharing can look like; they are meant to establish processes to allow relationships to evolve that are fair and equitable, while leading to conservation and sustainable use. The grounds for such relationships can be healthy even in the face of considerable uncertainty about the value of the specific biological materials contributing to research and development.

The extent to which any agreement maps directly (or can map directly) onto the biological resources at hand becomes less important if we build a system in which all sides are receiving the returned benefits that they expect. As our workshop participants repeated that ABS is about building trust over the long term. Shared understandings of new working practices and the expectations that surround them will need to be built in collaboration, not just between scientists in different states, but between many invested areas of society.

↠ *Inspiration*

Synthetic biologists may see their main relationship to DSI as one of being "inspired" by genetic sequences, but this framing can lead to certain problems. When it comes to ABS, the suggestion that scientists are only 'inspired' by DSI, which in the process gets unrecognisably transformed into their own creative productions, may be interpreted by others as self-serving rhetoric. Those developing novel organisms through genetic modification and incorporating sequences from a vast range of material collections could perhaps find better ways in which to conceptualise their activities than 'inspiration', 'art', and 'craft'. Rather than considering their work as an individual creative process, they could learn to see their individual activities embedded in and dependent on a wider context, one that includes decades of collection, curation, sequencing, and management of genetic resources.

Are there not other terms in which synthetic biologists could describe their dependency on DSI? Could these alternatives not point more clearly in the direction of arrangements between provider and user countries that contribute to the aims of ABS? The improving ethos underlying much of synthetic biology, for instance, would lead us to understand creative products as essentially temporary, open for further improvement by others. Emphasising these aspects of construct design and development could help build the longer term and reciprocal arrangements to which ABS aspires.

Annex: Workshop documentation

Timetable

9:30–10:00	**Friday, 28 November 2016**
	Coffee and registration
	Board Room, Sainsbury Laboratory,
10:00–10:10	*University of Cambridge Botanic Gardens*
	Introduction and welcome to the workshop
	A brief description of the workshop's origins, its aims
10:10–10:30	*and ambitions.*
	Session 1: Genetic resources before and after Nagoya
	Alan Paton (Royal Botanic Gardens, Kew)
	Chris Lyal (Natural History Museum, London)
	Katie Beckett (UK BIS)
	Elisa Morgera (University of Strathclyde,
11:30–11:45	BENELEX project)
11:45–13:00	*Coffee Break*
	Session 2: Synthesis
	Philippe Desmeth (Microbial collection group –
	Belgian BCCM)
	Graham Dutfield (University of Leeds)
	Molly Bond (University of Bristol)
13:00–14:15	Nicola Patron (Earlham Institute)
14:15–15:30	*Lunch*
	Session 3: Continuity and Change
	Paul Oldham (One World Analytics /
	University of Manchester)
	Catherine Rhodes (University of Cambridge,
	Centre for Existential Risk)
15:45–16:30	Petra ten Hoopen (European Bioinformatics Institute)
	Reflections and final discussion

Workshop participants

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Original workshop proposal

Genetic resources in the age of the Nagoya Protocol and gene/genome synthesis

To provide an open forum for discussion on: the current range of practices of genetic resource collection, circulation, and use; the implementation of the Nagoya Protocol to date; and the possible changes or challenges that may arise as a result of gene and whole genome synthesis.

↠ *Proposal Overview*

Biological resources are valued in numerous ways by multiple stakeholders, from local communities employing traditional uses, to research institutions navigating commercial and non- commercial spaces, to corporations prospecting for new products, to governments seeking to build a bioeconomy. The confluence of science, nation building, and geopolitics have always been subject to considerable tension, though in the case of biological resources, it was only in the late twentieth century that grievances with certain practices gained broad attention. Politicians, representatives of indigenous communities, civil society organisations, and academic actors identified problems with the collection, circulation, and use of historic and contemporary biological resources. They drew particular attention to bioprospecting, the pursuit by an individual, company, or national institution, of biomaterials located outside of their own state or immediate research context (for example, the pursuit of landraces in one's own country). Some cases of bioprospecting involve unmediated collecting expeditions, but often a prospector relies upon local knowledge and expertise. These collecting activities are pursued with the intention of reaping multiple benefits, whether revenue from industrial processes, advancement in one's research, or contributing to conservation campaigns. The most controversial cases have involved the imposition of intellectual property rights, which secure such benefits for a select few, without return to the communities or countries of origin.

These debates culminated in a number of international agreements, most notably the Convention on Biological Diversity (CBD, effective since 1993). The Convention's objectives are the conservation of biodiversity, its sustainable use, and the fair and equitable sharing of benefits arising from the utilization of genetic resources. The CBD established that genetic resources were not a common heritage of humanity, but for the most part under the sovereign control of countries. The Convention established principles for "access and benefit-sharing" (ABS) of genetic resources, which were further developed in the Bonn Guidelines. The adoption of the Nagoya Protocol in 2010 provided a specific, binding legal framework for ABS of genetic resources and associated traditional knowledge. Parties to the Nagoya Protocol must take measures including clear access procedures (such as prior informed consent), that the benefits arising from the utilization of genetic resources are shared with the country of origin, and that Parties support compliance. In late 2015, the UK passed regulations to implement EU regulation 511/2014, providing measures for compliance with the Nagoya Protocol.

But do these legal frameworks reflect recent developments and trends in the utilization of genetic resources? Late twentieth and early twenty-first century debate seems to have often assumed that valuable biological material would always need to be physically transferred. The on-going improvement of gene and whole genome sequencing and synthesis technologies presents possibilities of new practices, and demands discussion and debate in light of the long history of global bioresource management. The proposed workshop acts as a venue for collecting information on current developments, sharing views, highlighting potential areas of concern, and establishing grounds upon which to build better understanding of the interactions

between and implications of the Nagoya Protocol and gene synthesis for collection, circulation, and use of genetic resources.

Research questions

↠ *Legal*

What are the underlying goals of the Nagoya Protocol, and the means of compliance in the UK and EU?

Some practices are not covered by the UK & EU's implementing regulations (for instance, materials collected before the Nagoya Protocol came into effect are explicitly not included, while those stored digitally and used to reproduce the original sequences at a distance through DNA synthesis are not addressed). Does this lack of explicit legal coverage undermine the goals of ABS?

In what ways might achieving the ABS goals of the Nagoya Protocol also require attention to other areas of international law, such as intellectual property, trade, and the environment?

↠ *Social*

What are the existing practices of collection, circulation, storing, and use of genetic resources? What role, if any, is played by the digital transfer of genetic information in the collection and circulation of genetic resources?

How do practitioners anticipate sourcing of genetic resources will change (if at all) in the near future?

What range of practitioners have responded to the Nagoya Protocol, and how?

To what extent are those in the biosciences aware of ABS rules on bio-resource management and use, and how are they responding?

How are those working within the field of synthetic biology relating to, or distancing their work from, existing practices of international bio-resource management and use?

How do regulators and lawyers expect gene and genome synthesis to relate to the goals of the Nagoya Protocol?

↠ *Historical*

How have international biomaterial collecting, sharing, and use practices developed over the course of the 20th and 21st centuries?

In what ways have these changes related to broader political and economic considerations? How significant, or insignificant, are the possibilities of gene and genome synthesis within the course of this history?