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منظمة
الأغذية والزراعة
للأمم المتحدة

Submission of information received by the Commission on Genetic Resources for Food and Agriculture on the use of "digital sequence information on genetic resources for food and agriculture" and potential implications for the conservation and sustainable use of genetic resources for food and agriculture, including exchange, access and the fair and equitable sharing of the benefits arising from their use

I. Submissions by countries

Brazil

1. DEFINITION AND SCOPE

Digital Sequence Information (DSI) is data information contained in a digital file with a precise order of nucleotides or amino acids. The nucleotide sequence is the main structure of nucleic acid molecules, DNA and RNA, whose main function is the storage and transmission of genetic information.

DSIs can be obtained by sequencing the DNA of organisms already existing in nature, through inference by reverse translation.of amino acid sequences or fabricated through simulations and computer programs. In the first two cases they are called natural sequences (NS) and in the third case synthetic sequences (SS).

Public DSI information has been used to boost innovation through basic research, foster scientific collaboration and generate scientific knowledge. One of the most iconic examples is the National Center for Biotechnology Information (NIH-NCBI - https://www.ncbi.nlm.nih.gov/) Genbank database where researchers can currently download about 30 terabytes of data in a single day to make scientific and innovation discoveries – a resource which has been available since 1982. It was designed to provide and encourage scientific community access to DNA sequence information without imposing restrictions on the use or distribution of data. Another one is the European Molecular Biology Laboratory (EMBL). In both the genetic data of all living organisms can be deposited and freely accessed by different research groups, from all over the world.

The scientific community has recognized the benefits of open data, as this information serves as a source of both original and supplemental data for exploration and validation of findings and to make significant discoveries (https://ncbiinsights.ncbi.nlm.nih.gov/2013/09/16/ncbis-open-data-a-source-of-experimental-data-for-important-discoveries/). These international data repositories are fundamental to worldwide research, development and innovation (RDI) because they avoid duplication of efforts and expenditures and allow a much faster advancement of human knowledge. The exchange of digital sequence information is, therefore, essential to achieve important and highly relevant results for humanity. One significant example, in the medical area, is the influenza case (Dormitze,P.R., 2014). In agriculture, DSIs exchange and access might provide a fast response to pests that can devastate thousands of hectares, especially when compared to traditional breeding systems (without the use of molecular approach). It can also lead to a significant yield increase production in smaller areas. All those positive results lead to the achievement of the sustainable development goals (SDG).

2. DSI, CONVENTION ON BIOLOGICAL DIVERSITY, NAGOYA PROTOCOL AND FAO COMMISSION ON GENETIC RESOURCES

DSI discussion have started from considerations on Synthetic Biology (Synbio) at Twelfth Conference of the Parties to the Convention on Biological Diversity (CBD/COP12). COP13, serving as the meeting of the Parties to the Nagoya Protocol on Access and Benefit-Sharing (MOP2), adopted decisions on DSI on genetic resources in which they recognized the need for a coordinated and non-duplicative approach on this matter under the Convention and the Nagoya Protocol by decisions XIII/16 and NP2/14.

The FAO Commission of Genetic Resources understood the potential impact of DSI for the conservation and use of genetic resources for food and agriculture and therefore, decided to ask Members to submit information of “DSI on GRFA” and potential implications for the conservation and sustainable use, for the Secretariat to compile and submit this information to the Executive Secretary of the CDB. The Commission also requested the Commission Working Groups and the seven experts nominated for microorganism and invertebrate genetic resources to review and provide inputs to the draft exploratory fact-finding scoping study elaborated by the new work stream stablished at the last meeting, on “digital sequence information on GRFA” prior to its submission to the Commission for consideration at its next session - FAO, “CGRFA-16/17/Report” and “Follow-up to the 16th Regular Session” – FAO C/CBD-7, 22 May 2017.

3. TRACEABILITY, ACCESS and BENEFIT SHARING

In general, international public databases of digital sequence, such as those cited above (NCBI and EMBL) require the provision of several information of the submitted sequences. In most cases traceability data is required but it is not mandatory as it must be to safeguard the objectives of ABS international instruments. It is therefore important to understand that the traceability of public databases sequences is feasible, but not yet mandatory and to a large extent, available at the species level and subject to the information provided by the scientists.

Some difficulties for traceability could occur: genomes are composed by repetitive regions and those regions are even conserved between species from different kingdoms, which the vast majority is not endemic to a single country. In this way, identical DNA sequences can exist in several organisms originated from different regions of the world. Changes in taxonomic status are still common, with many papers being published every day (e.g., Maronna et al, 2016; Amirahmadi et al, 2016; Uribe et al, 2017; Eyun, 2017). However, on smaller databases, such as the CBOL (www.barcodeoflife.org), whose objective is to identify species and it is required the deposit of a specie voucher in an indexed herbarium/ museum (DNA barcode, Hartvig et al, 2015) traceability is essential. The Barcodes are short nucleotide sequences of a standard genetic locus for use in species identification and taxonomic reviews. It also has application to identify regulated species, including invasive species and to test the purity and identity of biological products. However, it is of the common knowledge that part of DNA research, which seeks to identify molecular markers associated with defense and resistance (abiotic, biotic) genes or adaptation do not need, a priori, the correct species identification.

The difficulty in tracking digital sequences becomes more evident in the case of the microorganisms, since these organisms are characterized by their great diversity, cosmopolitan distribution and fast adaptability to different conditions by evolutionary processes.

For provider countries and countries of origin of genetic resources, traceability is crucial for the full implementation of benefit sharing in the context of the utilization of digital sequence information. Traceability is also fundamental for countries that utilize this information, since a consolidated legal framework is considered favorable by institutions that study the possibility of investing in research in their domestic contexts.

Despite those difficulties it is important to ensure the traceability of sequences submitted in databases. Thus, it is necessary to: (i) establish mechanisms to ensure that the genetic databases require standardized information necessary to the traceability of submitted sequences; (ii) establish differentiated treatment for cases of sequences submitted in genetic databases prior to the definition of this mechanism or whose traceability is not yet possible.

Access and Benefit-sharing has been established under article 10 of the International Treaty on Plant Genetic Resources for Food and Agriculture and is at the core of the work of the Commission on Genetic Resources for Food and Agriculture as it has agreed on the importance of considering access and benefit-sharing in relation to all components of biodiversity for food and agriculture.

Considering the amount of sequence information available in online databases combined with the dramatic reduction of costs and difficulty for DNA sequencing, in the near future the use of a physical sample of genetic material will be unnecessary. Thus, the benefit sharing mechanism should be functional and article 15 of the CBD and article 10 of ITPGRFA are applicable even when the information on genetic resources is digitally obtained. Otherwise it would compromise the achievement of the general purpose of the Convention on Biological Diversity and the International Plant Treaty and the observance its principles, especially in megadiverse and developing countries.

4. POTENTIAL IMPLICATIONS OF DSI - THE BRAZILIAN EXPERIENCE

4.1. Conservation and sustainable use

Brazil is considered one of the most important megadiverse countries on the planet (Forzza et al., 2012). With the most diverse flora in the world, which represents 15% to 20% of the world´s plant diversity. The Brazilian flora include 46,442 species from which 4,753 of Algae, 33,052 of Angiosperms, 1,559 of Bryophytes, 5,722 of Fungi, 30 of Gymnosperms and 1,326 of Ferns and Lyophytes. Despite this, Brazil is far from knowing all the components of the Brazilian flora, given its complexity and dimension.

The relationship between conservation and the List of Brazilian Flora Species is exemplified when, in 2010, the country published the Catalog of Plants and Fungi of Brazil and launched the first online version of the List of Species of the Brazilian Flora, meeting Target 1 of the Global Strategy for Plant Conservation (GSPC-CBD). This botanical milestone was only achieved due to the commitment of more than 400 Brazilian and foreign taxonomists who worked on a platform where information about our flora was included and disseminated in real time. The "Brazilian List", as it was popularly known, closed in November 2015 with the publication of five papers and their respective databases dealing with the different groups of fungi and plants (Brazilian Flora 2020)

It is important to emphasize that the list of species of “Flora do Brasil” was evaluated based on studies of molecular phylogeny and taxonomic reviews. Other search results for "Legume Phylogeny Working Group-LPWG" (2017) on the known non-monophyly of the traditionally recognized subfamily Caesalpinioideae, now recognize not only three but six robustly supported monophyletic subfamilies. This new qualification uses as structure, a more comprehensive phylogenetic analyzes of the legumes up to the information based on sequences of plastid genes, and include almost the complete sampling of genera and ca. 20% (3696) of the known species.

The above example illustrates the impact of molecular biology in conservation studies. This reality is straight related to cost reduction of DNA sequences generation, associated to the high quality and robustness of the analyzed data, providing greater efficiency in germplasm characterization, when compared to morphological traits. In addition, DNA data has been used to boost conservation studies in the following areas: (1) inbreeding depression, when selfing or crossing among relatives are more frequent than random crossing, resulting in high levels of endogamy; (2) deleterious mutations accumulation, which can radically reduce regeneration; (3) lost of genetic variation in small populations, when fragmentation (among other anthropomorphic actions) leads to a significant reduction in the genetic pool, causing a significant reduction in genetic variability; (4) adaptation to captive or isolation and its effect on reintroduction; (5) outbreeding depression, when the progeny shows lower fitness when compared to the parents in consequence of the high genetic distance between both parents; (6) fragmentation of populations and reduction in migration, when fragmentation causes isolation and prevents gene flow; and (7) taxonomic uncertainties and introgression (Frankham, 1995). To better understand those areas the free data access is very important to avoid duplication of efforts and to improve statistical robustness of analysis by considering data generated from multiple studies.

Regarding *ex situ* conservation, molecular characterization allows the generation of DNA data on a large scale, providing not only the optimization of conservation by enabling the elimination of duplicates, but also helping in the evaluation of the genetic representativeness of the germplasm banks, directing the needs of new introductions (e.g., Pessoa-Filho et al., 2007). Also allows comparison of representativeness among different germplasm banks, making it possible to identify access that may be at risk for being conserved in only one place. The DNA-based study greatly assists the formation of nuclear collections by allowing an accurate analysis of the collection's genetic diversity. It also assists in the formation of thematic nuclear collections by identifying genotypes resistant to biotic and abiotic factors. Still, it allows the differentiation of cultivars and the identification of landraces.

Microorganisms are an essential part of the biodiversity in nature and one of the greatest genetic reservoirs on Earth. These microscopic organisms are major players in the cycles of energy and matter, acting as protagonists of the biogeochemical cycles and the essential biochemical reactions that sustain the entire life in the planet. Understanding the role of microorganisms in the environment has provided conditions for the development of new biotechnological applications and the establishment of food security policies, sustainable agriculture and industrial development programs. However, scientists have only begun to understand this vast world, since a small fraction of the microbial diversity is known and/or can be cultured under lab conditions (Stewart 2012, Garza & Dutilh 2015). This fraction has been kept in culture collections, representing an important genetic resource for the countries, providing stocks of material for use in programs of interest to society. In Brazil, microorganisms have received more attention in the last decades, mainly due to their increasing importance for agriculture, food and environment, either in the form of bio-products or in different industrial and biotechnological processes.

Because of the advances in molecular biology and DNA sequencing techniques in the last decades, DSI of microorganisms available in different on-line databases grew at the same rate as sequencing costs were reduced. The availability of this information and free access to these sequences have been providing conditions for a huge scientific step in phylogenetic studies, biological characterization and ecology of microbial species. For most of the microorganisms, and despite of the importance of the morphological characterization, identification at the specific level depends exclusively on gene sequencing and phylogenetic analysis. The precise or correct identification of microbial strains deposited in culture collections is essential for conservation purposes and for the material exchange among institutions aiming its use in research programs of interest to society. It is noteworthy that advances in metagenomics have created the possibility of obtaining complete or nearly complete sequences from uncultured microorganisms, which can be collected directly from any environment, providing an important field for the study of biology, ecology, evolution and functional structure of microbial communities (Garza & Dutilh, 2015).

With regard to *in situ* conservation, the use of DNA sequences helps to determine priority conservation areas by studying the genetic diversity of species in different populations. It assists in evolution studies, taxonomy and biogeography. With the use of DNA sequences it is possible to identify populations with greater genetic diversity, populations with different gene pools, processes of evolution and adaptation. These molecular tools can aid in species identification (e.g., Nithaniyal et al, 2014) and the origin of the sample when the sequences obtained by different groups from different countries are made available in public databases and public articles. Another study case was identification of geographic origin of timber where researchers ensured that illegally harvested timber was traced (Degen et al, 2013). The mahogany logging in Brazil is illegal, but it is not in other countries of the Amazon region.

A new concept in conservation genetics is environmental DNA (eDNA). This makes reference to all genetic material that can be extracted from a bulk of environmental sample as soil, water and even air. This approach allows a significant and unprecedented ability to identify a range of species that are present in different areas and biomes and conduct analyzes for conservation, management and research. This kind of study has a high potential for helping in estimating population size, genetic diversity and also allow genomic analyzes, including biomolecules, such as eRNA and ePTNs (Barnes and Turners, 2016).

Knowledge about biodiversity is the first step towards conservation as well as a source of immense potential for economic use. To achieve these goals, the Brazilian Ministry of Environment's - Plants for the Future - initiative sought to promote the sustainable use of native species of Brazilian flora of current and potential economic value, used locally and regionally. Although today we have a considerable number of native species domesticated, or in process of domestication, the use of genetic resources of native species in commercial scale is still embryonic (Coradin et al.,2011). The use of the information already collected and published could help Brazil and other countries to reach a better nutritional status, also prompted by the SDGs (www.mma.gov.br/publicacoes/biodiversidade).

4.2. Breeding and exchange

The drastic reduction of arable areas coupled with extreme climatic events and the significant increase in the demand for food raise the awareness and dedication of genetic improvement in the development of cultivars/ breeds resistant to different biotic and abiotic factors such as pests and restriction of water use, respectively (Kage et al, 2016). The advance in DNA sequencing, with the new generation sequencing allows to integrate information of metabolomics, proteomics, transcriptome, together with mapping association studies, facilitating the identification of genes allelic variants, accelerating the breeding process through the development of functional molecular markers (FMMs) in plants or genomic selection in livestock.

The green revolution was achieved due to the development of dwarf and semi-dwarf cultivars of rice and wheat. Mutation points identified in two genes were identified in wheat, *Rht-B1b* on chromosome 4B and *Rht-D1b* on chromosome 4D. Markers for allele-specific PCR were developed and applied in selection of wheat genotypes with this characteristic of interest (Ellis et al, 2002). Deletion-based markers were developed for Dwarf8 gene coding region in maize for identification and selection of plant height and flowering time (Thornsberry et al 2001). There are hundreds of examples like these that make it clear that the use of DNA sequences is a reality for genetic breeding, since the research and development of a product goes far beyond the simple identification of a gene, but of its variables among different accesses. Each one of those accesses) may be originated in a different country. Most of the times scientific advances, specially for food and agriculture, are not due to the identification of a “magic gene”, that occur in only one species. If it occurs, it is the exception. Most of the times, scientific advances as those mentioned above, are due to a massive characterization of lots of different accesses in order to identify differences in genotypes, including known hundreds if not thousands of genes, most of them common in many different species and available in public databases.

The identification of genes and their functions, and the availability of this information as DSI, has been expanding the field of applied research in areas of interest for food production and bio-industry. There are several applications of the microbial genome sequences in industrial processes (bioenergy, biofuels, processed foods and derivatives), on the improvement of microbial strains or in the development of clones with specific genes of interest (Fávaro, 2012), and in plant transformation (Shelton et al. Al, 2002, Lemaux, 2008).

The same is true for animal genetic resources (AnGR) that are represented by all species (exotic and native, terrestrial or aquatic) with direct or potential use for food and agriculture. From a specific gene banking point of view, there is a growing trend to make germplasm (semen and embryos), genomic, and phenotypic information associated with the sample available to the public and private sector. In 2014, Brazil, Canada and the US launched efforts to incorporate genomic information into their joint database Animal-GRIN (http://nrrc.ars.usda.gov/A-GRIN/ or http://aleloanimal.cenargen.embrapa.br/) and to make it publically available through the internet (Paiva et al., 2016). This approach reduces duplication of genotyping efforts and leverages investments already made in genotyping. Sample acquisition coupled with digital curation of genomic and phenotypic information represents new areas of repository utilization.

From a general point of view, public DSI databases have played and will continue to play a significant part for FAO’s “Global Plan of Action” and “State of the World’s Animal Genetic Resources” publications and policy directions. Without those data bases it is not going to be possible, for example, to expand current knowledge about origin and diversity of all livestock and to fulfill the Strategic Priority 1: characterization, inventory and monitoring of trends as associated risks to AnGR.

Brazil is recognized to be one of the most important players in animal protein production and exportation (USDA-FAS, 2017). For example, the country is the biggest broiler meat producer and the second largest beef producer in the world. To keep up with those standards, Brazil and other countries are sharing genetic information to improve the breadth and reach of conservation and breeding programs (e,g., Bovine, Ovine and Swine Genomic Consortia). Impacts of controlling the use of genetic information obtained from digital sources and imposing benefit sharing obligations for non-commercial research are by far the most difficult to predict, monitor and manage. Therefore, operational procedures to obtain prior informed consent and monitoring the use of DSI should be facilitated and the most user friendly as possible.

Impacts of controlling the use of genetic information obtained from digital sources for development of new breeds with potential use for food and agriculture could specially impact the use of aquatic species with potential for aquaculture, as most of these are currently undergoing domestication. In this sector, many production and supply chains are under development, with high demands for new and innovative technologies.

Regarding exchange of genetic resources, the presence of public DSI data bases is essential to speed up germplasm movement and manage countries food security. For example, it is crucial to have preventive breeding actions, especially for resistance to economically important diseases/pathogens that are not present in a particular country or region. The growing frequency of extreme climate events is expanding disease zones very rapidly (mainly South to North). Mitigation of those events will just be feasible if DSI information and germplasm are available among countries to allow swift actions to be set in place before outbreaks can destroy entire production and supply chains. A Brazilian long-term experience, the Embrapa-Labex USA, a 20 years partnership and collaboration with USDA/Agriculture Research Service is proving to be very successful in this regard.

5. RELATED BRAZILIAN LEGISLATION

Brazilian Law 13,123/2015 defines genetic resources (or genetic heritage) as the genetic information from plants, animals, and microbial species, or any other species, including substances originating from the metabolism of these living organisms (Article 2, I). Furthermore, Decree No. 8,772/2016, in what concerns registration in the National System for Genetic Heritage - SisGen states:

"*Art. 22. For the **registration** of access to genetic heritage or associated traditional knowledge, the natural or legal person must complete the electronic form of SisGen that will require: …*
F) identification of the genetic heritage at the strictest possible taxonomic level or associated traditional knowledge, as the case may be, in particular:
*1. the origin of the genetic heritage, including georeferenced coordinates in the degree, minute and second format, from the place of in situ production, even if they have been obtained from ex situ or **in silico** sources; and...."*

…….

"§ 1 When it is not possible to identify the geo-referenced coordinate of the in situ sampling place, which is dealt with in item 1 of item "f" of item II of the caput, and only in cases in which the obtaining of the genetic patrimony occurred prior to the entry into force of Law 13,123, of 2015, the origin May be informed on the basis of the most specific geographic location possible by one of the following means:
*I - identification of the ex situ source of the genetic heritage, with the information Constants in the deposit register, when it comes from ex situ collection; or II - Identification of the genetic heritage origin database with the information In the deposit record, when it comes from an **in silico** database."*

Thus, the regulation of Law 13.123,2015 provides that research utilizing genetic information obtained *in silico* is to be carried out freely, and that registration is required only at the time of publication of the results, or upon application for a patent, or before introduction of a product on the market. The Brazilian legislation also brings facilitated mechanisms for access to genetic resources for food and agriculture, special considerations for scientific research for food and agriculture; economic exploitation as the point of incidence of benefit sharing obligation and the establishment of a benefit-sharing fund.

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Germany

Germany is of the view that the use and international exchange of digital sequence information (DSI) on genetic resources for food and agriculture should be considered in the overall context of conservation and sustainable use of GRFA as well as access and benefit sharing. In this context, Germany would like to highlight Articles 8b) and 8c) of the Nagoya Protocol which request Parties to pay due regard to cases of present or imminent emergencies that threaten or damage human, animal or plant health and to consider the importance of GRFA and their special role for food security.

International collaboration and common efforts in research and development are essential to achieve food security and sustainable development of agriculture worldwide in the context of poverty alleviation and climate change adaptation. In this regard, Germany wants to underline that it is important to maintain GRFA by widespread use and to support such use to achieve food security as envisaged in SDG 2.

Germany is of the view that access to DSI from public databases and publications does not constitute access to genetic resources in the meaning of the CBD and the Nagoya Protocol.
Including DSI in the concept and/or definition of genetic resources would result in insurmountable financial and administrative burden for both developing and developed countries and thus hamper research and development. This would be in contradiction with the objective of the Nagoya Protocol and the Convention itself.

Information exchange including digital sequence information is essential all over the world to strengthen efforts in conservation and sustainable use of GRFA, e.g. for,

- **identification** and **characterization** of GRFA, e.g. as an important step to prioritise target GRFA for *in situ*, on farm or *ex situ* conservation
- **conservation** of GRFA, e.g. by exploring population size and structure or to estimate relationships between populations, e.g. for classification of endangerment of species and to plan measures to minimise further genetic loss or to discover and monitor invasive alien species, e.g. invasive pest organisms in forestry and agriculture
- **breeding** and **genetic improvements**, e.g. by identifying key agronomic traits that can be useful for e.g. climate change adaptation of food crops (e.g. GENESYS and DIVSEEK, contributing to the Global Information System on Plant Genetic Resources according to Article 17 of the ITPGRFA), or for the further development of the aquaculture sector.

Apart from commercial considerations, the accessibility of reference data of DSI on GRFA is equally important for all countries in areas related to food and agriculture such as

- **food safety** (e.g. to test food products for the presence of contaminants, diseases or pests; in this context gene sequence information are an important tool to discover such contaminants etc.)
- **monitoring of plant and animal health** (e.g. reference data of DSI on GRFA facilitate urgently required tests)
- **quality controls of products in the food and feed sector** such as proof of authenticity and origin (e. g. reliable identification of fish species (aquagene.org database) that allows an unambiguous determination of fisheries products and obviates mislabelling and its negative consequences for consumers, traders and the environment)
- **testing of products** (based on genetic resources) to fulfil regulatory requirements (e.g. the EU Timber Regulation that aims to reduce illegal logging by ensuring that no illegal timber or timber products can be sold in the EU)
- **verification of the descent of certain breeding animals** (e.g. in order to implement the EU zootechnical legislation)

All abovementioned activities require continuous improvement or new development of methods, which are necessary worldwide. Internationally accessible databases including DSI on GRFA promote international research cooperation and global efforts in those fields. Therefore, Germany would like to stress that access to research information including DSI on GRFA constitutes a global benefit per se and is essential even for international research cooperation.

United States of America

Terminology

The United States understands the term “digital sequence information on genetic resources for food and agriculture” to mean the genetic sequence data (GSD) that describe the order of nucleotides in DNA or RNA in genetic material of actual or potential value for food and agriculture. We therefore will use the term GSD instead of DSI in our response.

We note that GSD are neither genetic material nor a genetic resource. It is essential to maintain a conceptual and definitional distinction between genetic material itself and data describing that material.

Use of GSD describing GRFA

Researchers around the world use GSD describing GRFA as a tool to advance scientific study and technological innovation, with enormous benefits for people and nature. The use and exchange of GSD describing GRFA are critical for efforts to improve agricultural productivity and resilience, which are essential for ending hunger and poverty around the world and achieving shared development goals. Any move to restrict or impede access to and use of GSD could slow or halt such research, with serious consequences for the conservation and sustainable use of GRFA, economic development and food security.

Broadly speaking, researchers can use GSD describing GRFA to (1) define populations, (2) characterize genetic diversity within and between populations, and (3) better understand traits of interest; all of which can inform decisions related to the conservation, management and use of GRFA in a manner that promotes food security and economic development.

GSD can be used to define populations of interest based on genetic sequence signatures. Therefore, researchers can use GSD to distinguish between populations that may seem identical in appearance, behavior, and other properties but are genetically distinct. For example, crop genebanks look at differences in diagnostic nucleotide sequences to identify unknown samples, maintain these samples genetically true-to-type, and choose the best samples for specific research or breeding purposes. In aquaculture, researchers have used GSD to define populations released for commercial production, facilitating the identification and management of those fish populations.

In addition to defining specific distinct populations, researchers use GSD describing GRFA to establish the degree of genetic divergence and diversity within and between populations. As diversity within a population is essential for adaptation; researchers can use GSD to determine whether a population has the ability to adapt to environmental changes, contributing to the development of resilient production systems.

Knowledge of the genetic diversity within and between populations is also useful for maintaining genetic diversity and reducing inbreeding, both of which are important for selective breeding and conservation activities, such as cryopreservation. In aquaculture, researchers have used GSD to develop breeding programs for rainbow trout with increased yield and production efficiency. And in forestry, researchers use GSD to develop robust ex-situ collections of at-risk species by identifying distinct natural populations and those with increased diversity. In plant breeding, knowledge of genetic interrelationships of parental lines is a prerequisite for producing hybrids of maize, sorghum, sunflowers, and certain vegetable and fruit crops. Hybrid vigor in these crops results in yield and product quality that substantially exceed those of non-hybrid plants.

Researchers also use GSD describing GRFA to study traits of interest in agricultural products, such as disease resistance, product quality, production efficiency, and resilience to extreme conditions. GSD can be used to advance discovery and development of new crop and livestock varieties, with enhanced outcomes for food security. For example, researchers used GSD to identify genetic sequences in hybrid catfish associated with tolerance for low oxygen conditions. Similarly in cattle GSD are useful in determining adaptability to high altitudes and reduced pulmonary edema as well as increasing tolerance to high ambient temperatures and humidity. Researchers also use GSD to determine milk production potential in dairy cattle, which enables selective breeding for increased milk yield with less time and money required to assess genetic merit. Greater productivity and lower costs contribute to greater availability for consumers.

GSD is also being used extensively in all crop development, and especially for production of drought- and pest-resistant crops and crops altered for enhanced nutritional and economic value. Use of GSD has enabled researchers to rapidly identify markers for genes associated with drought tolerance in sorghum, maize, wheat and other crops. Scientists are also using GSD to breed beans that cook more quickly, which could reduce fuel use and therefore economic and environmental costs associated with this food staple. In summary, researchers can use GSD describing GRFA to accelerate the progress of genetically improving dietary staples, enabling yield and productivity gains that underpin food security by providing more abundant food to humanity.

The generation and exchange of data and information associated with GRFA are important modes of benefit-sharing. As part of research best-practices, GSD are openly available via international data repositories such as GenBank and the International Nucleotide Sequence Database Collaboration, as well as in journals found in print and online. Additionally, scientists make large amounts of GSD freely available through sector and species specific online databases, such as Gramene (link: http://www.gramene.org/), GrainGenes (link: https://wheat.pw.usda.gov/GG3/), TreeGenes (https://dendrome.ucdavis.edu/index.php) and SoyBase (link: https://www.soybase.org/), to name a few.

These repositories and journals further engender collaboration by providing a free flow of GSD to both researchers and to the general public. This open access and collaboration are key benefits of the use of GSD. Regulations that would restrict or preclude access to and sharing of GSD would likely lead to a significant reduction in data sharing through these and other such mechanisms, stifling innovation, slowing agricultural research and development, and potentially impeding responses to crises affecting agricultural production, with negative impacts for food security.

II. Submissions by International Organizations

African Centre for Biodiversity

We write to you from the African Centre for Biodiversity (ACB). The African Centre for Biodiversity (previously 'Biosafety') was established in 2003 and registered in 2004 in terms of the laws of the Republic of South Africa. ACB carries out research, analysis, capacity and movement building, and advocacy, and shares information to widen awareness and catalyse collective action and influence decision-making on issues of biosafety, agricultural biodiversity and farmer-managed seed systems (FMSS) in Africa. The ACB's work both informs and amplifies the voices of social movements fighting for food sovereignty in Africa.

We make these submissions based on our grave concerns about the implications stemming from the ability of corporate 'breeders' to use genetic engineering technologies such as Clustered regularly interspaced short palindromic repeats (CRISPR), which edit DNA, to access genetic sequence data pertaining to genetic resources, and convert this data back to DNA or RNA and to use it in living organisms, and the risks this poses to the conservation and use of biological diversity and access and benefit sharing international and national regimes and agreements.

Genetic sequence data can be accessed on the internet or in an email, this means that it may no longer be a need to access and exchange of the physical genetic resources/biological materials. Crop traits can be accessed in this way as well as genes that encode for active compound in medical plants, and be used in the manufacture of pharmaceuticals. This gives rise to the possibility that genetic resources can be accessed without prior informed consent and in the absence of a benefit sharing agreement. This would thus undermine several international agreements, including in particular the 3rd objective of the Convention on Biological Diversity (Convention), the Nagoya Protocol on Access and Benefit Sharing (Protocol) and the International Treaty on Plant Genetic Resources for Food and Agriculture (Treaty). Indeed we will go so far as to say that current benefit sharing regimes may be rendered redundant as we go into the future particularly those of the Protocol and Treaty. The rationale underpinning objective 3 of the Convention, and the central imperatives underpinning the Protocol and the Treaty to prevent biopiracy or the misappropriaton of genetic resources will be totally eroded.

Today, what are commonly referred to as the "Big Six" mega seed and agrochemical corporations - namely: BASF, Bayer, Dow, DuPont, Monsanto and Syngenta - together control 75% of the global agrochemical market, 63% of the commercial seed market and over 75% of all private sector research and development (R&D) in the sector.

However, three mega-mergers in input supply underway between ChemChina and Syngenta, Dow and DuPont and Monsanto and Bayer are set to entrench the existing global oligopoly built on a cartel-like technological platform in biotechnology traits, commercial seed and patented agrochemicals. These mergers are indicative of broader processes and the threats they pose to economic participation, social equity and ecological sustainability.

These multinational corporations are making major strides in the new genetic engineering technology that will supersede 'aging' technologies such as transgenic crops: CRISPR, genome editing technology and synthetic biology, which are cheaper and quicker to develop, and for now, unregulated.

Recommendations

1. Parties and all other relevant stakeholders and interested parties to the Convention, the Protocol and the Treaty must ensure that a legally binding decision is taken to unequivocally require that sequence data be considered equivalent to its physical biological counterparts.

2. Sequence data in this regard, must be broadly defined, because it is not necessary to

synthesize an entire genome in order for the data to be useful and profitable. Individual genes synthesized from data and inserted into living organisms can be of enormous commercial value, particularly in industrial and medical applications. Sequence data includes DNA, RNA and amino acid sequences as well as accompanying characterization information. Parties and all other relevant stakeholders and interested parties to the Convention, the Protocol and the Treaty must thus pay attention to the scope of digital sequence data. The hereditary material of an organism is not just DNA but in some cases it is RNA. Since the complementarity between molecules, and their important functions, the sequences of both must be covered. The sequences of amino acids that nucleotides encode are similarly valuable and can be used to replicate and modify natural compounds and in design of biological systems. These sequences too need to be addressed with respect to benefit sharing, see below.

3. Further, Parties and all other relevant stakeholders and interested parties to the Convention, the Protocol and the Treaty must agree to measures to be taken at the national level, to ensure that access and benefit sharing laws and agreements not only apply to the physical transfer of biological material but also to sequence data. In this regard, the scope as mentioned above in point 2, must be broad enough to ensure that all relevant data is caught in the benefit sharing net.

4. Parties and all other relevant stakeholders and interested parties the relevant international agreements must ensure that a legally binding decision is made to require that repositories of sequences and databases in turn require their users to up front agree to benefit sharing as a pre-condition to accessing any sequence information. In this regard, Parties and all other relevant stakeholders and interested parties to the relevant international agreements must be asked to elaborate rules and procedures to govern such user agreements.

5. Turning to the first and second objectives of the Convention, we make the following submissions:

5.1 The gene foundry and synthesis equipment industries are largely unregulated, and this creates risks to biodiversity. Since synthesis equipment does not care what it is synthesizing, and companies are generally not under any legal obligation to consider the safety of the nucleotide sequences they are producing, much less the ecological impacts, invasive and harmful organisms may be produced and thereby pose a risk to biodiversity. This needs urgent attention by the Parties and all other relevant stakeholders and interested parties to the Convention, including to take into account emerging newer equipment such as “digital-to-biological-converters” that are smaller, faster, cheaper, more portable and able to synthesize ever longer sequences.

5.2 The misuse of sequence data may also impact negatively on the conservation of biological diversity. The ability to synthesize organisms, or modify organisms with synthesized genes (creating a new sub-species/strain) presents a serious and novel challenge to efforts to curb the negative effects of invasive species. While traditional efforts to prevent invasive species have focused on physically preventing introductions-e.g. phytosanitary measures and border protection-the use of genetic data can leapfrog these controls, resulting in the introduction of invasive species from within a country rather than from outside its borders.

5.3 A link may be drawn between sequences and sustainable use of biological resources. The unregulated and free access to sequences of genetic resources such as natural medicinal compounds and “climate smart genes” (sequences conferring drought or salt tolerance for example) may harm communities and decrease the perception of the importance of maintaining and developing the resiliency of the genetic resources in situ and within context specific and appropriate ecological environments.

5.4 We make mention here that we do not accept that the recording of sequences in databases is sustainable use. The potential for the disruption or collapse of small farmers’ markets particularly in Africa, where 80% of the food is produced by small-scale farmers farming on average of 2 ha, engendered by unfettered and unrestrained use, is a real and grave danger. This will have severe negative impacts on the conservation and sustainable use of biological diversity by economically and culturally undermining indigenous peoples and local communities conserving and sustainably utilizing a wide pool of biodiversity.

We trust that these comments will contribute to the further work by Parties and other stakeholders towards realizing the goals and objectives of all three international agreements referred to in this submission.

CABI response on potential implications of the use of digital sequence information (DSI) from genetic resources for the three objectives of the Convention, and for the objective of the Nagoya Protocol.

At its thirteenth meeting, the Conference of the Parties to the Convention on Biological Diversity (CBD) considered the issue of digital sequence information on genetic resources and adopted decision XIII/16, in which it decided to consider, at its fourteenth meeting, any potential implications of the use of digital sequence information (DSI) on genetic resources for the objectives of the Convention on Biological Diversity.

Summary statement

CABI believes that amendments to the Nagoya Protocol are **not** necessary in respect to Digital Sequence Information (DSI) as it is already captured in the definition of the genetic resources and genetic material covered by the Convention on Biological Diversity (CBD). “Genetic resources‶ means genetic material of actual or potential value. “Genetic material‶ means any material of plant, animal, microbial or other origin containing functional units of heredity. CBD 19 Mar 2010; https://www.cbd.int/doc/meetings/abs/abswg-09/information/abswg-09-inf-01-en.pdf. DSI describes the resource or material and in a functional form would be a “derivative” and its use and benefits can be treated at a country level at the point of access to genetic material. However, it would be helpful to have a common agreement on the generation of DSI and how it can be used in order not to impede innovation in the life sciences.

CABI position

- Generating and publishing sequence data is considered by CABI as the production of descriptive information on the organism and therefore not utilisation. As such, it is out of Nagoya Protocol regulatory scope.
- Publishing the sequence as electronic data is an act of sharing such descriptive information and thus meets any benefit-sharing commitment required from access to sequence the organism.
- DSI can be used at many non-exploitative levels: for example, it is used to confirm identification and in the CABI understanding this is an observation; in most cases the sequence is published.
- if DSI is used for financial benefit then this could be considered utilisation and the full benefit sharing aspect would be negotiated with the provider country as would be done for access to the organism
- The generation and use of DSI must be considered at the point of access and be expressed in the Mutually Agreed Terms (MAT) and presented in any Material Transfer Agreement (MTA) for clarification on what can and cannot be done regarding DSI.

CABI reasoning

The debate continues within the regulator and stakeholder communities, on whether access to Digital Sequence Information (DSI) should be treated in the same way as would accessing the genetic resource or material (organism) itself. It is obvious they are not the same thing as currently more can be done with the organism than with a partial sequence or even an entire genome. In essence, generation of a sequence requires the genetic resource, itself, to be accessed; the DSI is a product of that access, a “derivative”. However, generating and publishing sequence data is considered by CABI as descriptive information and therefore not utilisation and, as such, it is out of regulatory scope. Publishing the sequence as electronic data is an act of sharing such descriptive information with the wider community – including the provider country. DSI can be used at many non-exploitative levels; for example, it is used to confirm identification and in the CABI understanding this is an observation; in most cases the sequence is published. European draft guidance indicates that taking the sequence information and using it to develop a product or tool is out of scope but we are aware that other countries are not of that opinion (this is still in debate at COP). However this does not negate the need for benefit sharing and in this case it is the actual publication of the DSI that shares the benefits of access to the genetic resources from which it was generated.

Selected DSI are becoming standard tools for identification and phylogenetic characterisation of species and populations: mitochondrial CO1 ‘barcodes’ for animals; plastid matK and rbcL barcodes for plants;16S ribosomal DNA for bacteria, and ITS for many eukaryotes (including Fungi), have become standard tools in modern taxonomy and identification, although the real power of this approach becomes most obvious when sequences from multiple individuals and sources (countries) is freely shared and duly acknowledged. In the future, whole genome sequencing will, without any doubt, have a similar impact on taxonomy. We argue strongly that DSI generated for taxonomic or descriptive purposes needs to be freely shared in the public domain to help address the taxonomic impediment that the CBD recognises, as well as to meet the needs of agriculture and other sciences.

Conclusion

Generation and use of DSI should be considered when accessing the genetic resource to the extent that benefit-sharing is required under the CBD. However, the generation and publishing of such data is not “utilisation” and should not trigger the Nagoya Protocol. Further, we suggest that such generation and publishing of DSI should be considered as part of a country’s responsibilities under Article 7 (Identification and Monitoring) and 17 (Exchange of Information) of the CBD. As new technologies develop, DSI may have additional uses that could trigger benefit-sharing and this should be subject to equitable sharing of benefits. Requirements will vary from country to country but should include placing the DSI in the public domain and its subsequent use can be defined in standard Material Transfer Agreements. Likely benefits could include sharing the developed tool or enabling access to the generated product but in most cases the benefit is likely to be facilitating access to the published data and no more. It would be preferred that a single common global understanding was reached to ensure full compliance and thereby reduce confusion.

NOTE FOR SUBMISSION IN UK and to EC: In Europe there is an additional problem because the EU in their guidance documents are using the Frascati definition of research and development http://www.oecd-ilibrary.org/science-and-technology/frascati-manual-2002_9789264199040-en to help define “utilisation” and this includes the generation of knowledge. In this case generating DSI would consequently be “utilisation” and trigger benefit-sharing. However, the guidance documents go on to describe sequencing as a descriptive step or confirming identity which is NOT utilisation – there is still work needed to clarify.

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Institute for Agriculture and Trade Policy

The Institute for Agriculture and Trade Policy (IATP) appreciates this opportunity to submit a short comment on an issue of critical importance before the Commission. We offer the following comment on digital sequence information to the Commission to assist it to “compile and submit this information to the Executive Secretary of the CBD [Convention on Biological Diversity], as a timely contribution to the process set by decision CBD COP XIII/16.”[i] IATP is a non-profit, non-governmental organization

(501.c3, in U.S. law) headquartered in Minneapolis, MN (U.S.) with offices in Washington, DC and Berlin, Germany. Since IATP's founding in 1986, we have participated in numerous meetings organized or co-organized by the Food and Agriculture Organization, including those of the Committee on World Food Security and the Codex Alimentarius Commission. IATP staffer Shiney Varghese and advisor Sophia Murphy have participated in the High-Level Panel of Experts advising the Committee on World Food Security.

Much of the discussion about governance of advanced techniques of genetic engineering, such as genome editing, in relation to the conservation and sustainable use of genetic resources, has concerned potential impacts of gene drives on biological diversity.[ii] Part of that concern derives from the inability of those who would release gene drives to forecast the biological diversity impacts of suppressing one or more species and/or to reliably program the self-termination of the gene drive before biological resistance to the gene drive has formed.[iii]

Similarly, it is difficult to forecast the impact of the cross-border transfer or "trading" of digital sequence information derived directly or indirectly from genetic resources on the conservation and sustainable use of those resources, including fair and equitable Access and Benefit Sharing (ABS) resulting from the use of those resources, including their digital sequencing. Sequence data includes DNA, RNA, and/or amino acid sequences as well as the accompanying characterization information for those sequences. Current ABS governance in domestic regulation is implemented through a material transfer agreement (MTA) that requires signing of the agreement prior to transfer of the biological materials containing DNA, RNA or amino sequences and characterization information.

However, MTAs are already subject to abuse and circumvention.[iv] The cross-border transfer of digital sequence data via the internet or even on a bootlegged thumb drive, which can be subsequently be synthesized as organisms either for non-commercial research or commercial purposes, will circumvent the current ABS and prior informed consent requirements of the CBD's Nagoya Protocol. The simplest form of circumvention is to claim that utilization of digital sequencing data is not "access" to genetic resources, and therefore no ABS for use of those data is required. A corollary argument for not recognizing and meeting ABS obligations is that to so will inhibit innovation.[v] Such circumvention, however commercially advantageous in the short term, will deprive CGRFA members of adequate resources to conserve *in situ* and *ex situ* the genetic resources upon which digital sequences to develop agricultural traits depend.

To prevent the potential misappropriation of genetic resources via circumvention in the digital sequencing of those resources, IATP urges CGRFA Members and the Commission Secretariat to respond to the CBD decision on digital sequence information[vi] by informing the CBD Secretariat that the CGRFA Secretariat will consider doing the following:

1. Request that FAO Members inform the CBD Executive Secretary of both governmental and non-governmental digital sequence data bases in their jurisdictions of genetic resources that can be used for food and agriculture, per the Strategic Goals and Objectives of the CGRFA.[vii]

2. Request that FAO members inform the CBD Executive Secretary of measures that govern access to and use of those data bases, both within their jurisdictions and across borders, per Goals 1 and 5.

3. Request that FAO Members inform the CBD Executive Secretary of voluntary guidelines, mandatory rules or proposed rules in their jurisdictions concerning digital sequence information of genetic resources for food and agriculture, including guidelines and rules pertaining to the cross-border transfer of such information.

4. Request that FAO members support the recommendation of the CGRFA ABS Expert Team "that the Commission convene an international workshop on Access and benefit-sharing for genetic resources for food and agriculture, to be jointly organized, as soon as practicable after the 16th

Regular Session of the Commission, by the Secretariats of the Treaty and the Commission, possibly in collaboration with or supported by the Secretariat of the CBD."[viii]

5. Request that FAO members support the convening of this international workshop with the collaboration of the Secretariat of the CBD.

6. Request that this workshop include a discussion of digital information sequence, as was begun by the ABS Expert Team at its September 2016 meeting.[ix]

7. Request that the CBD Secretariat recommend to CBD Members that the next Meeting of the Parties of the Nagoya Protocol agree on a further specification of the term "utilization" for use in the ABS Clearing House and elsewhere in the CBD. Further specification, including the CBD's understanding of the utilization of digital sequence information, will help the CBD respond to the CGRFA ABS Expert Team's view that "the Nagoya Protocol does not provide any specific guidance as to the nature or type of research and development activities covered by the term "utilization"[x] as they are applied generally, and more specifically to genetic resources for food and agriculture. The CBD's work on and definitions of the utilization of digital sequence information may assist the CGRFA in the international workshop recommended by the ABS Expert Team to further the CGRFA's Strategic Objectives and Goals.

8. If the next CBD Conference of the Parties decides that in principle digital sequence information is equivalent to biological material to enable implementation of the objectives of the CBD, the Secretary of the CGRFA should recommend to CGRFA Members that they invite the Secretary of the CBD to explain such a Decision and its possible follow-up at the international workshop, as recommended above. The CBD's ABS Expert Team should likewise be invited to meet with the CGRFA ABS Expert Team to discuss how a CGRFA Decision on digital sequence information may assist the realization of the CGRFA's Strategic Objectives and Goals.

The Institute for Agriculture and Trade Policy thanks the CGRFA for its consideration of these actions to inform the CBD of work by FAO members and the CGRFA on digital sequence information in mutual support of CBD and CGRFA goals and objectives.

Third World Network

Sequence information on genetic resources for food and agriculture (SI)[1] 1 has long-term implications across the mission, strategic goals and objectives of the Commission, including for the loss of genetic resources, food security, conservation, and sustainable use, as well the fair and equitable sharing of benefits derived from their use. For example, it might be argued that placement of SI in databases "in silico" constitutes a form of protection against loss of genetic diversity. Yet, at at the same time, undue reliance on SI as a conservation (or even use) mechanism may sap government resolve and even drain away what little resources that are available for *in situ* conservation, interrupting and devaluing the work of small farmers, pastoralists, fishers, indigenous peoples, and others who create, conserve, and develop GRFA.

Sequence information and fair and equitable sharing of benefits arising from the use of genetic resources

Most urgently at present, however, are questions regarding SI and the fair and equitable sharing of benefits arising from the use of genetic resources. Gene segments, genes and, indeed, entire organisms

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[1] We note decisions by the CBD and discussion at the Commission that terminology should be carefully reviewed and possibly modified. "SI" is used here in the interest of clarity.

of high economic value (e.g. vaccine viruses) are now synthesized from SI that may have been exchanged via the internet or email, meaning that organisms and genetic variants can effectively cross borders without physical biological material changing hands. In the area of microbial genetic diversity, for example, in 2002, synthesis of poliovirus from data was considered a significant technological advance. Yet poliovirus is a mere ~7750 bases long. Fifteen years later, at the end of 2017, the Synthetic Yeast Genome Project anticipates creating an entire 12 million base yeast strain from sequence data. The length of the largest wholly synthetic genome will have grown in 15 years from 7,750 bases to 12 million – over 1500 times as long. Or course it is not necessary to synthesize an entire genome in order for SI to generate benefits. Individual genes synthesized from SI and inserted into living organisms can be of enormous value, particularly in industrial, agricultural and medical applications. For example, the gene(s) encoding a valuable industrial enzyme may be synthesized from SI and inserted into microbes for production in fermentation vats. Such uses of SI may be accomplished without accessing the microbe (or plant, animal, etc.) itself or obtaining prior informed consent (PIC) from the originators of the genetic resources and knowledge holders. Most benefit sharing agreements, policies, and laws are predicated on physical transfers of material and may not be applicable to SI in their current forms. This is a large problem for ensuring fairness and equity in use of GRFA and it is poised to continue growing as the cost of sequencing diminishes and tools for storage and manipulation of SI are further developed.

Recommendations

1. In addressing the obvious threat that the combination of SI and synthesis technologies pose to fair and equitable sharing of benefits, the Commission should adopt the approach that sequence data be considered the equivalent of biological material. In other words, users of SI should, in general, be subject to the same benefit sharing obligations as users of the biological materials that are the source of that SI. Alternatively, some genetic resource providers may choose to make SI available without the underlying biological material and, in such instances, these providers should be fully enabled to ensure the application of obligations that will result in fair and equitable benefit sharing.

Thus, when GRFA is sequenced – for example, a collection of the diversity of farmers' varieties of a particular crop species – if and when such information is shared and/or placed in databases, due consideration must be given, and steps taken, to ensure that users of that data are obligated to share benefits, and that Farmers' Rights and other rights of genetic resource providers are protected.

2. Importantly, providers, especially in developing countries, need to maintain awareness that transfers of non-reproductive materials – e.g. leaf matter or killed cell cultures – typically are potential transfers of SI (if the recipient extracts and sequences nucleic acids, at the time of transfer or if the samples are preserved at a future date). Thus, even transfers of "dead" biological materials can give rise to the generation of SI that may lead to the utilization of those genetic resources in biological systems again.

3. SI should be understood to include sequences of DNA, RNA in all their forms, as well as the sequences of amino acids and accompanying characterization information. Like DNA and RNA sequences, the sequences of the amino acids that nucleotides encode are valuable and can be used to replicate and modify natural compounds and in design of biological systems.

4. The Commission should explore how repositories of SI, such as the databases operated or provisioned by international agricultural research centres (IARCs), microbial collections, botanical gardens, etc, and databases such as Genbank and the European Nucleotide Archive, can require users to agree to benefit sharing as a precondition of access to SI. The Commission may, in collaboration other relevant intergovernmental bodies, consider the development of provisions for such user agreements (e.g. "click-wrap" terms and conditions) for databases, and develop recommendations on how databases should be required to implement them.

5. The Commission should study and consider developments in the gene foundry and synthesis equipment industries and their implications for SI and fair and equitable benefit sharing. The gene

foundry and synthesis equipment industries are largely unregulated, even to the extent of copies of some of the world's most dangerous pathogens being reproduced from SI, causing alarm in security circles. Put simply, synthesis equipment does not care what it is synthesizing, from neither safety nor fairness perspectives, and companies that commercially synthesize SI generally do not consider Commission-relevant obligations associated with the nucleotide sequences they are producing.

Further, efforts are underway to create smaller, faster, cheaper, and more portable machines to synthesize ever-larger molecules from SI, including machines that synthesize double stranded DNA and that can be directed by e-mail. These so-called "digital-to-biological converters" aim to expeditiously and easily complete the loop from biological to SI and back to biological. These aim to be portable and easy to operate, broadening the possibilities to use SI to modify and recreate organisms – particularly microorganisms – anywhere.

6. Socio-economic and sustainable use impacts of the use of SI – e.g. on vanilla and vetiver farmers – have been described. The Commission will continually need to bear in mind that the recording of SI is not sustainable use *per se*, and that the potential disruption or collapse of small farmers' systems engendered by unrestrained use of SI could more broadly impact conservation and sustainable use of genetic resources by economically undermining communities that conserve and sustainably utilize a wide variety of GRFA.

Thank you for the opportunity to make these comments. Third World Network looks forward to the result of this information gathering exercise and will continue to monitor the Commission's work on SI.

III. Submissions by others

Associate Professor Jens Sundström, Faculty Professor Pär Ingvarsson, Department of Plant biology at the Swedish University of Agricultural Sciences in Uppsala: Digital Sequence Information (DSI); its use and importance for agricultural research.

Global research commons

Digital Sequence Information used for research and breeding are to a large extent stored at, and maintained by the global DNA database consortium GenBank/Embl/DDJB[2]. This is an open source format which builds on the principles that 1) results from publicly funded research should be published in open access, 2) that knowledge assets should be governed as common gods on a global scale, and 3) that data-sharing that contribute to global research commons is a legitimate form of benefit-sharing[3].

What is Digital Sequence Information?

The heritable material *i.e.* the DNA of any living organism is in principle built up by four different nucleotide bases (Adenine, Cytosine, Thymine and Guanine) that are held together by a sugar-phosphate backbone. The order in which the nucleotide bases appear on the DNA-strand can be determined using different sequencing techniques and the resulting sequence (ACTGCTT…etc.) can be stored in a digital form. In its most simplistic form the term Digital Sequence Information refer to such a sequence of nucleotide bases.

The global research community have built up databases of Digital Sequence Information that harbor information from many different organisms. The information can be in the form of **genomic DNA** that provide information on the different genes as well as the chromosomal regions in-between the genes. It can also be in the form of Expressed Sequence Tags (ESTs) or coding sequences, which correspond to the **RNA transcript** of a gene. Complementary to the nucleotide sequence of a gene, the translated **amino acid sequence** of the corresponding protein is also often deposited in the same database.

Digital Sequence Information can also be in the form of **Single Nucleotide Polymorphisms**, often abbreviated as SNPs. A SNP is a variation in a single nucleotide that occurs at a specific position in the genome. Each SNP is present to a variable degree in a population. For instance, at a specific position in the wheat genome the base C appear in most cultivars, whereas in a few cultivars the position is occupied by the base A. There is a SNP at this specific base position, and the two possible nucleotide variations – C or A – are said to be alleles for this base position. Information about SNPs can be directly or indirectly coupled to different traits and are, hence, widely used in plant breeding.

During recent years, a deeper understanding of the importance of how the DNA is packed into the cell nucleus has emerged. Epigenetic modifications, in form of *e.g.* **acetylation and methylation of the DNA** nucleotides, influence the three-dimensional structure of the DNA, which in turn may affect transcription and, hence, cellular functions. Digital information about acetylation and methylation patterns of the DNA are often deposited alongside with the DNA-sequence in the public databases.

Technology development

In 1977, Frederick Sanger and colleagues developed a method for DNA-sequencing; termed Sanger sequencing. Sanger sequencing gives relatively long reads (>500 nucleotides) with high accuracy, at a

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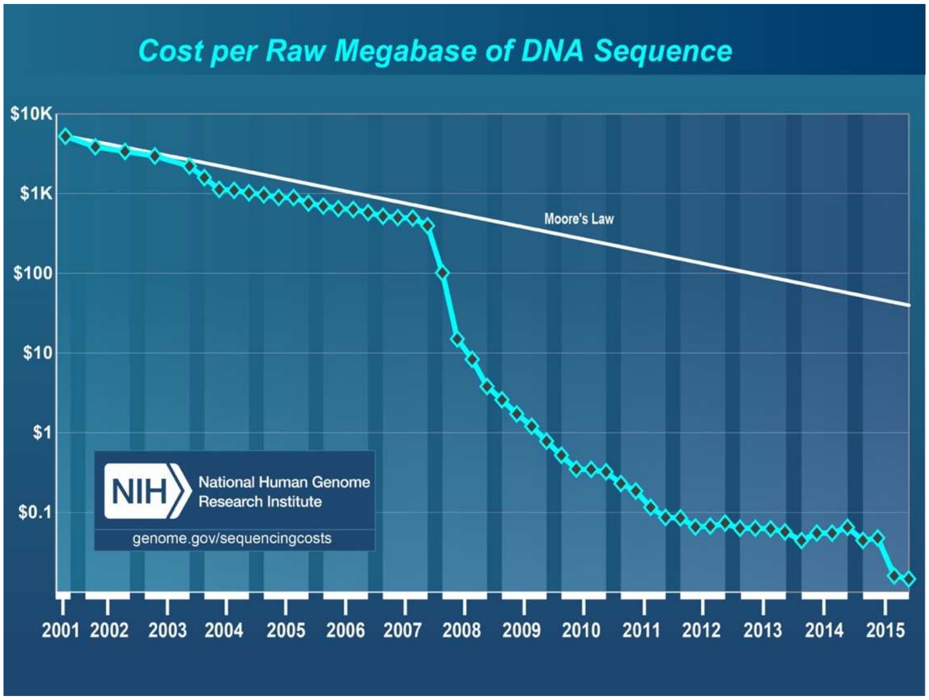
[2] http://www.insdc.org

[3] Common Pools of Genetic Resources, Equity and Innovation in International Biodiversity Law (2013) Eds. E.C. Kamau and G. Winter, Routledge

relatively high cost. During recent years technology development have drastically reduced the costs for sequencing, as illustrated by the graph provided by NIH[4].



In 2007, the first method for high-throughput sequencing was developed, also called next-generation sequencing. Several different technology platforms for high-throughput sequencing have since been developed. These methods typically give fairly short reads (around 100 nucleotides) that subsequently have to be assembled into longer continuous sequences. Using these modern methods, it is now possible to sequence the entire genome of a whole organism at a relative low cost. It is likely that all crops covered by the FAO international treaty on plant genetic recourses for food and agriculture will be sequenced within the next few years. In addition, transcriptomes (all RNA transcripts present in a sample) from many different crops, cultivars, strains or wild crop relatives are already published and made publicly available. In fact, sequencing of a transcriptome is now often considered a standard procedure, and may in many research areas only be included as part of a larger study, if published in high ranking journals.

Still, most sequencing techniques demand large sequencing facilities and require adequate computer capacity to handle the large data sets that are generated. Recently, portable real-time nanopore sequencing (RTnS) has become available. This technique gives long reads from a sequencing device in the size of a USB-stick, and offers opportunities to rapidly collect and analyze genomic data anywhere. It was used to monitor the Ebola outbreak in 2015[5] and has recently been used to analyze SNP variation among closely related plant species during ongoing field work[6].

As stated above, a publication in peer reviewed scientific journals often requires that digital sequence information is presented according to internationally agreed standards and is made public through *e.g.* the global DNA database consortium GenBank/Embl/DDJB. In many cases, species or genera specific databases are also built up that harbor genomic sequence along with transcriptomes, information about SNPs and other genetic tools that facilitate further research[7,8]. It is important to note that these

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[4] https://www.genome.gov/sequencingcostsdata/

[5] Nature. 2016 Feb 11;530 (7589):228-232.

[6] *Scientific Reports* **7**, Article number: 8345

[7] http://www.arabidopsis.org

databases often are global research commons. The databases are the results of joint efforts by the scientific community, and the open source format is essential for the curating of the databases.

Digital Sequence Information and the species concept

One of the lessons learned from evolutionary studies and the collective sequencing of different species is that many genes are shared even between distantly related species. This is not that surprising since all living organisms originate from a common ancestor. Sequencing of genomes from different species have shown that while there may be genes that are unique to a species, a majority of the genes have counterparts in other species and may not differ substantially in function or sequence composition. For instance, the genes that determine reproductive organ identity *i.e.* stamen- and carpel-identity are highly conserved within all flowering plants, and it is in principal possible to move those genes in-between species without changing either form or function of the flower. This implies that the species concept is not relevant on the gene level. This has implications for the handling and the regulation of digital sequence information since it is not, by necessity, possible to assign a specific digital sequence to a specific species.

Examples

Digital Sequence Information is part of what in general terms are called Big Data. The digitalization of sequence data facilitates cross comparisons within and between species. Genetic diversity in e.g. the field of population genetics has increasingly become a tool for understanding basic biological processes and is equally important for plant breeding.

Since many genes are shared between different organisms, model systems are often employed to study basic biological functions. Generation of databases with digital sequence information, along with genetic tools and seed collections greatly facilitate the transfer of knowledge gained in a model system to crops covered by the FAO international treaty on plant genetic recourses for food and agriculture

Arabidopsis - a model system for plant breeding

Arabidopsis thaliana is a small weedy plant that belong to the Brassicaceae family. The genome of *Arabidopsis thaliana* was fully sequenced already in 2001[9] and it now serves as plant model species, not only for other Brassicaceae family members but for all seed plants. Digital Sequence Information is made available through the Arabidopsis Information Resource (TAIR). Arabidopsis is used to study almost all aspects of plant life such as development, metabolic pathways, disease resistance and adaptation. The knowledge gained using this model system and the Digital Sequence Information made available through TAIR have influenced breeding and helped to breed for a wide variety of traits such as *e.g.* salt tolerance in Rice[10], flowering time in Sugar beet[11] and resistance to clubroot disease in *Brassica napus*[12]. Important for the success of such breeding efforts, that in essence build on a comparative analysis between a crop and a model species, is of course that a database with Digital Sequence Information is available also for the crop species.

Digital sequence information in population genetics

Population genetics as a discipline dates back to the 1930s and has over the last century developed a rich theoretical understanding of how various evolutionary processes interact to shape genetic variation within and between species. Access to data from real populations has, however, always been scarce and largely limited a few special cases in model systems. The technological advances in DNA

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[8] http://www.plantgdb.org
[9] *Nature (2000)* 408, 796–815
[10] Plant Molecular Biology (2007) 64:49-58
[11] Current Opinion in Biotechnology (2015) 32C: 121-129
[12] Front Plant Sci (2016) 7: 1483
[14] Genetics (2017) 205:1003-1035
[15] Molecular Ecology 25:2337-2360

sequencing over the last few decades have yielded unprecedented levels of genomic information that can be applied to test and extend existing theories in population genetics on just about any organism. It is therefore now feasible to study entire genomes on population level scales with hundreds or thousands of samples. This has allowed for a much better understanding how genetic diversity varies across the genome of an organism and how this diversity is shaped by various evolutionary processes, such as natural selection, genetic drift and recombination[14]. Population-level genomic data from closely related species has also facilitated studies of speciation and how this process shape genome divergence[15]. Free access to Digital Sequence Information from published studies, such as whole-genome DNA sequences, through GenBank/EMBL/DDJP has been instrumental in many of these studies.

The use of Digital Sequence Information in genomic selection

The continuous decline in sequencing costs greatly facilitate the discovery of genome wide SNPs that can be used as markers for breeding purposes. In parallel high-throughput sequencing, breeders are increasingly using large scale phenotyping to couple those markers to desired traits. Hence, genome wide selection is a breeding method which use high-throughput methods for both phenotyping and genotyping. It has the advantage over traditional selection methods, since it in a cost-effective manner allows the breeder to simultaneously select for several complex traits. The availability and free access to curated reference genomes of via GenBank/EMBL/DDJP is very important for the implementation of Genome Wide selection, and often a prerequisite for the adoption of this powerful breeding technique in national or local breeding programs[16]

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[i] Commission on Genetic Resources for Food and Agriculture, "Follow Up to the 16th Regular Session, C-CBD-7, 3. May 22, 2017, referencing https://www.cbd.int/doc/decisions/cop-13/cop-13-dec-16-en.pdf

[ii] E.g. Nicole Gutzman et al, "CRISPR-based gene drive in agriculture will face technical and governance challenges," *EMBO Reports*, August 7, 2017. http://embor.embopress.org/content/early/2017/08/07/embr.201744661

[iii] Robert L. Unckless, Andrew G. Clark, Phillipp W. Messer, "Evolution of resistance against CRISPR/Cas9 gene drive," *Genetics*, Early online December 10, 2016. as 10.1534/genetics.116.197285

[iv] E.g. Tasnia Bubela, Jenilee Guebert and Amrita Mishra, "Use and Abuse of Material Transfer Agreements: Lessons in Proportionality from Research, Repositories and Litigation," *PLOS Biology*, Published online February 3, 2015. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4315468/

[v] Steve Burgess and Dominic Berry, "Regulating the Use of Genetic Sequence Data," *PLOS Synbio Community*, December 15, 2016. http://blogs.plos.org/synbio/2016/12/15/regulating-the-use-of-genetic-sequence-data/

[vi] https://www.cbd.int/abs/dsi-gr.shtml

[vii] http://www.fao.org/nr/cgrfa/cgrfa-vision/en/

[viii] "Third Session of the Technical and Legal Experts on Access and Benefit Sharing," Commission on Genetic Resources for Food and Agriculture, Food and Agriculture Organization of the United Nations, 13-15 September 2016, CGRFA/TTLE-ABS-3/16/Report, paragraph 39. http://www.fao.org/3/a-bp766e.pdf

[ix] Ibid., paragraph 38.

[x] Ibid., paragraph 16.

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[16] Front Genet. 2016; 7: 221