## Grasping Frankenstein’s Monster: Uncertainty in the downstream scope of the Nagoya Protocol.

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**Abstract**

*The 2010 Nagoya Protocol to the UN Convention on Biological Diversity (the “Protocol”) is intended to assist the prevention of anthropogenic species eradication through habitat destruction, and preserve threatened indigenous culture, by creating rights over the access to, and utilisation of, genetic resources and traditional knowledge associated with genetic resources (“TKAGR”). This article explores and uncovers uncertainties in the drafting of the Protocol which relate to the downstream scope of the Protocol rights to control genetic resources and TKAGR used in genetic research and drug discovery. In particular, the work focuses on whether the rights control synthesis of, and research upon, human-made chemical derivatives of naturally occurring biochemicals and innovations still yet more distal from the original generic resource or knowledge. In looking at control over informational linkages within physiological and pharmacological research, the work also considers the uncertainties and challenges which may arise from Protocol-based claims asserted over the nucleotide sequence of genes within a genetic resource (so-called digital sequence information).*

**Introduction**

The Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (the “Protocol”) sets out mechanisms to allow countries, and indigenous peoples, to gain control over the use of genetic resources and, separately, indigenous peoples to gain control over the use of traditional knowledge associated with genetic resources (“TKAGR”). It is of significant practical importance to those seeking to operate the Protocol (and to scientific researchers working in many areas of biology) that the provisions of the Protocol are clear. As this paper will set out, in some vital, and practically relevant respects, the Protocol lacks the required clarity.

This is becoming particularly apparent in relation to the challenge posed by developments in synthetic biology. Synthetic biology allows the *de novo* synthesis of genetic material without the need for a primer or template which is *physically* derived from a genetic resource.[[1]](#footnote-1) New [DNA[[2]](#footnote-2) strands](http://en.wikipedia.org/wiki/Oligonucleotide_synthesis) are built from a [digital database of the required base](http://en.wikipedia.org/wiki/Nucleic_acid_sequence#Digital_format) pair sequences, so-called “digital sequence information” (“DSI”). Once generated, these synthetic DNA molecules work in an identical fashion to those created from a physical template and can be used in gene cloning, or even in the generation of entire synthetic genomes.[[3]](#footnote-3) It is not clear whether the Protocol could (or should) cover the downstream use of DSI. If it does not, there is an arguable case that the use of synthetic biology techniques would create an effective mechanism for evading the provisions of the Protocol. The question of the control over DSI was identified at the Thirteenth Conference of the Parties (“COP”) to the United Nations Convention on Biological Diversity (“CBD”) in December 2016[[4]](#footnote-4) as being one which required detailed investigation, and there is now a significant body of work being undertaken under the auspices of the COP to address this. In February 2018, the COP’s [Ad Hoc Technical Expert Group (“AHTEG”) on DSI of Genetic Resources](https://www.cbd.int/abs/dsi-gr/ahteg.shtml) presented a detailed report[[5]](#footnote-5) on the concerns raised under consultation, and this report will be further considered within the COP processes.[[6]](#footnote-6)

As will be briefly discussed in this work, if the Protocol is to be amended to cover the use of DSI, this uncovers further problems in terms of who should be entitled to ownership of the extended rights, and how they will be enforced.[[7]](#footnote-7) However, the aim of the current paper is to highlight, that notwithstanding the current focus on coverage of DSI, a further important ambiguity in the downstream scope of the Protocol should not be overlooked.

Mary Shelley’s 1818 work *Frankenstein; or, The Modern Prometheus* has come to symbolise the dangers in seeking to control nature and its protagonist has become synonymous with the “improper” creation of life forms.[[8]](#footnote-8) Popular culture has envisioned Frankenstein’s flawed creature as being incorrectly assembled from a “parts bin” of stolen human organs and limbs. This paper argues that, in its failure to clearly define the downstream limits to the use of genetic resources (particularly whether it covers the downstream use of human-made chemical derivatives of naturally occurring biochemicals) the Protocol is, in part, a similarly flawed creation.

This work will briefly examine the reasons behind the creation of the CBD and the Protocol, and outline the provisions of the Protocol which put the access and fair and equitable benefits sharing (“ABS”) objectives of the CBD into effect. It will then highlight the downstream complexities in modern drug discovery, and the fact that it is highly likely that the scientific (and commercial) benefits of using a piece of original TKAGR, or genetic resource, will be significantly distal to a complex process of mixing and dilution of the original information/resource. Although, as will be discussed, there are helpful doctrinal analyses of the Protocol within the existing literature, the aim of this work is to extend such analysis into the questions concerning of the Protocol’s reach into the more distal uses of genetic resources and TKAGR within drug discovery.

It concludes that the Protocol is something of a “Frankenstein’s monster”, bolted together from a number of “re-purposed” definitions from the Convention on Biological Diversity (“CBD”) in such a way that the scope of downstream protection offered in relation to human-made derivatives of biochemicals is unclear.

The paper then looks to downstream coverage of the Protocol in relation to *informational*, rather than *physical*, links. Here the paper firstly concludes that there is no inherent reason why amendment of the Protocol to cover DSI would change the current treatment of biochemical products of gene expression, or of human-made derivatives of such products.

It secondly concludes that, although the downstream scope of coverage of the Protocol in relation to TKAGR is likely to cover downstream use which is not covered by the provisions relating to genetic resources *per se*, where TKAGR serves as a research “lead” for further development the Protocol itself gives no clear guidance as to how far that knowledge can have a “reach through effect” into new scientific discoveries, or at what stage a researcher would be considered free of the traditional knowledge right. However, although the scope of such very distal reach of is unclear, it is likely that some synthetic biological work using DSI (where the route to obtaining the DSI has been stimulated by TKAGR) would fall under the ambit of indigenous peoples’ right to control such knowledge.

## Claims of misappropriation of genetic resources

Many compounds that have pharmacological effects in humans are derived from living organisms. In some cases these compounds have been honed by hundreds of millions of years of evolution to have exquisite selectivity and potency in biological systems. In some cases the biological effect produced by evolution has been harnessed by humans to provide beneficial therapeutic effects and many currently approved drugs have their origin in plants and fungi [[9]](#footnote-9) or animal venoms.[[10]](#footnote-10)

Often the Western understanding that a particular organism contained a compound of potential therapeutic benefit arose out of the knowledge of folk-healers or traditional medicine systems.[[11]](#footnote-11) In many historical cases, those Western ethnobotanists and scientists accessing and using TKAGR have treated this knowledge as a “public good” and have treated the originators of this knowledge to be undeserving of recognition, or reward, for its subsequent use, and similarly undeserving of any degree of control over the use of the information.[[12]](#footnote-12)

Longstanding political concerns as to the unfairness of the situation in which a genetic resource (and relevant TKAGR) obtained from indigenous peoples is used scientifically, or commercially, without their consent and/or without those indigenous peoples having received any benefit from the “downstream” use of said genetic resources and/or the related information, led to a movement to secure legal mechanisms by which: a) countries and indigenous peoples would gain control over genetic resources; and, separately, b) indigenous peoples would gain control over TKAGR, such that misappropriation could no longer occur.

It is worth noting that such resources are not easily protected through “classical” intellectual property rights (such as copyright, patents, utility models, trade secrets, trade marks, plant variety protection, or geographical indications), or through the law of confidence.[[13]](#footnote-13) For example, the multi-generational nature of much indigenous knowledge of the properties of a genetic resource would inherently render any potential patent protection for such “inventions” invalid for lack or novelty. Accordingly, protection of these rights has focused on the creation of a *sui generis* system which, independent of currently-established intellectual property rights, would ensure that genetic resources and related knowledge could only be controlled by those originally holding the resource or information.

The CBD came into force on 29 December 1993, having been ratified by 194 members of the United Nations.[[14]](#footnote-14) The CBD is a convention which looks to protect the biodiversity of the planet,[[15]](#footnote-15) ensuring sustainable use and fair and equitable sharing of the exploitation of biodiversity. It is toward that final end that CBD Article 8(j) requires that each contracting party shall “as far as possible and as appropriate”:

“...respect, preserve and maintain knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological diversity and promote their wider application with the approval and involvement of the holders of such knowledge, innovations and practices and encourage the equitable sharing of the benefits arising from the utilization of such knowledge, innovations and practices” [[16]](#footnote-16)

However, CBD Article 8(j) contains no detail as to how its aims should be met. In the years after 1993, attempts were made to develop consistent guidelines towards its implementation culminating in the (non-binding) 2002 “Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization.”[[17]](#footnote-17) The bringing into *binding* effect of CBD Article 8(j) had to await the adoption (in October 2010) of the Protocol, which came into force on 12 October 2014,[[18]](#footnote-18) and now has over 100 ratified parties.[[19]](#footnote-19)

The key aim of the Protocol is to provide a set of binding mechanisms for implementing the “ABS” objectives of the CBD. However, originating as it does from the CBD, the Protocol is deliberately limited in its scope: its focus is on the misappropriation of *genetic* resources (and the misuse of traditional knowledge which is related to a particular genetic resource), rather than attempting to create any sort of broader positive right in traditional knowledge *per se*, or in indigenous cultural expression.

The Protocol looks to apply two obligations (*access* subject only to prior informed consent and *use* subject to benefit sharing) to the users of two separate, but closely related, resources: genetic resources and TKAGR. The key operative provisions of the Protocol are summarised in Table 1.

**Table 1 Key elements of the Nagoya Protocol articles giving rise to positive rights**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Article** | **“Right holder”** | **Subject matter** | **Controlled activity** | **Condition** |
| 5(1) | Party | genetic resources | utilization(including “subsequent applications and commercialization”) | fair and equitable sharing upon mutually agreed terms |
| 5(2) | indigenous and local communities | genetic resources | utilization | fair and equitable sharing based on mutually agreed terms |
| 5(5) | indigenous and local communities | TKAGR | utilization | fair and equitable sharing upon mutually agreed terms |
| 6(1) | Party | genetic resources | access for utilization | prior informed consent |
| 6(2) | “indigenous and local communities” | genetic resources | access | prior informed consentor “approval and involvement” |
| 7 | “indigenous and local communities” | TKAGR | access | prior informed consentor “approval and involvement”and establishment of mutually agreed terms |

**Genetic resources, TKAGR and the problem of “downstream” use**

Were all downstream uses of a piece of TKAGR or genetic resource derived in a simple, linear, fashion from the original piece of knowledge or genetic resource, then the scope of a positive right in such a piece of TKAGR or genetic resource might be relatively easy to determine. This is rarely the case. It is, of course, entirely possible that the scientific (and commercial) benefits of using a particular piece of TKAGR or genetic resource may be relatively “proximal” to that TKAGR or resource. The history of pharmacology is full of the use of relatively simple plant extracts or compounds directly purified from such extracts to give a therapeutic benefit.[[20]](#footnote-20) However, the extraction and testing of a biochemical constituent of a genetic resource is, within modern drug discovery, far more usually merely the beginning, rather than the end, of a process of finding a safe and efficacious drug.[[21]](#footnote-21) From that point the development “trails” within drug development are often long, and very complicated.[[22]](#footnote-22) Indeed, the original contribution from biological source or traditional knowledge is often overestimated.[[23]](#footnote-23)

Biologically active compounds almost always act as “ligands” at biological receptor sites on (or within) cells and their behaviour is dependent upon how their 3-dimensional structure interacts with that receptor site (or family of such sites). Therefore, a key tool in the pharmacologist’s research armoury is to set about making structural derivatives of the extracted biochemical constituents of a genetic resource to determine how such changes will affect their biological behaviour.

In addition, the finding of a new pharmacologically active compound within a genetic resource may uncover an as yet unknown biological mechanism within humans (or at least previously unknown ways of affecting known systems) which can give rise to further lines of research, both in terms of new chemical entities, and new therapeutic benefits. In this way it is highly likely that the scientific (and commercial) benefits of using a piece of original TKAGR or genetic resource will be significantly distal to a complex process of mixing and dilution of the original information.

Accordingly, a piece of TKAGR can take many routes within the drug discovery process – there are many pathways and feedback loops. The original information may be admixed to a greater body of existing information regarding the clinical problem, and there may be yet further admixture to the original information of discoveries derived from it and subsequent admixture to other “parallel” information which is not derived from it. In such a way, the original source is “diluted” or “attenuated”. Figure 1 is a much-simplified schematic showing some of the potential steps that a genetic resource/piece of traditional knowledge may take within a drug discovery process.

**Figure 1. Simplified schematic of path taken by a piece of TKAGR/GR within the drug discovery process.**

Despite its potential scientific complexity, none of these processes are mysterious. However, as we will see, the Protocol is not obviously orientated towards dealing with the problem of distal downstream use within drug discovery. Since the Protocol arises out of the CBD, unsurprisingly much of its focus is upon the control of *genetic* *resources* in their simplest sense. Accordingly (as can be seen in Table 1 above) at the heart of the Protocol’s positive rights are concepts of “access” to, and “utilization” of, “genetic resources”. Determining how these terms can be used to apply ABS principles to downstream use within drug discovery requires doctrinal analysis of these terms alongside application to the relevant science. Accordingly, each of these terms will be dealt with in turn, and their significance explained.

## What does “access” to a genetic resource mean?

Notwithstanding the importance of the term, “access” is not defined within the CBD, or the Protocol.

In relation to a *physical* resource, it is clear that accessing that resource could simply mean taking *physical* possession of the resource. An ethnobiologist being given plant samples by a group of indigenous peoples (or a government department) is clearly “accessing” those samples. However, is a geneticist who is later given that plant by the ethnobiologist (and goes on to extract DNA from it) equally “accessing” that material?

“Access” could conceivably mean the first-time physical apprehension of a physical resource or the *continued* physical apprehension of a physical resource. Whether access refers to the first accessing or to a continued/ongoing access is important. If it is the latter, one could see access as extending beyond mere *physical* access within the jurisdiction in which the genetic resources are held, to a broader concept of *legal* access - this being a permission for the continued holding of a genetic resource that would be otherwise be prohibited. The debate on this point is far from settled and has been the subject of some polemic debate. [[24]](#footnote-24)

During the negotiation of the Protocol the view of many genetic “user” countries was that genetic resources are “accessed” when a biological sample crosses a national boundary. The view of genetic “provider” countries was that access occurs when biological material is *used* – regardless of whether it crosses a national boundary.[[25]](#footnote-25) If this broader interpretation of access, encompassing subsequent activity, is not correct, then the requirement for consent/approval from the rights holders would arguably be restricted solely to the *very first* occasion upon which the subject matter of the rights in question were acquired. At first sight this may seem unduly limited. However, one has to appreciate that the Protocol does, within Article 5, contain other provisions ensuring that the “utilization” of the resource is subject to mutually agreed terms. This narrow interpretation is arguably also consistent with the overriding objective of the Protocol set out at Article 1:

“The objective of this Protocol is the fair and equitable sharing of the benefits arising from the utilization of genetic resources, **including by** appropriate access to genetic resources and by appropriate transfer of relevant technologies, taking into account all rights over those resources and to technologies, and by appropriate funding, thereby contributing to the conservation of biological diversity and the sustainable use of its components.” [emphasis added]

Indeed, if anything, Article 1 could be said to envisage “access” as something of a narrower subset of broader “utilization”, rather than being required to be co-terminous with it.

However, even if we do take a broader interpretation - wherein Article 6 envisages a positive right controlling some sort of *ongoing* legal access - we are left with the question: what is it access *to*? Does it relate only to use of genetic material containing DNA, the DNA alone, or does it envisage something yet further, such as “access” to other chemical compounds found within an organism - for example a plant-derived, therapeutically-active ligand? To address that question we need to look to the meaning of “genetic resources”

## The meaning of “genetic resources”

The concept of “genetic resources” is clearly at the heart of the Protocol. It is the subject matter which is “utilized”, “accessed” and “accessed for utilization”. Given the importance of the term, the definition provided within the Protocol is surprisingly brief. Indeed, the definition of “genetic resources” is taken in its entirety from the definition provided in Article 2 of the CBD. During negotiation of the CBD there was little discussion of the meaning of “genetic resources” and (due to time pressures) a “lowest common denominator” definition, legally ambiguous, but acceptable to the majority, was decided upon.[[26]](#footnote-26) That definition is as follows:

“Genetic resources" means genetic material of actual or potential value.”

where:

“Genetic material" means any material of plant, animal, microbial or other origin containing functional units of heredity.”[[27]](#footnote-27)

The first point to note is that the definition of “genetic resources” is not coterminous with that of “genetic material” but is “genetic material of actual or potential value”. It is not entirely clear what this limitation to “actual or potential value” achieves. One might ask what is meant by “value” and indeed further ask: “actual or potential value” to whom? However one answers these questions, it is arguable that the definition is flexible enough to provide for changes in what constitutes actual or potential value as science and technology develop.[[28]](#footnote-28)

The term “functional units of heredity” is not defined in either the Protocol or the CBD itself. However, on the face of it, a functional unit of heredity would seem to refer to a gene; the Merrion Webster dictionary[[29]](#footnote-29) defines a gene as:

“a specific sequence of nucleotides in DNA or RNA[[30]](#footnote-30) that is located usually on a chromosome and that is the **functional unit of inheritance** controlling the transmission and expression of one or more traits by specifying the structure of a particular polypeptide and especially a protein or controlling the function of other [genetic](http://www.merriam-webster.com/dictionary/genetic) material”. [emphasis added]

In its very narrowest sense, “material of plant, animal, microbial or other origin containing functional units of heredity” could refer solely to DNA extracted from the cells of an organism (this being the a part of the original organism which contains functional hereditary units) whether that DNA encodes for the entire genome of the organism, or encodes for only a sub-set of genes of interest.

However, one might additionally argue that the term “material” could more broadly refer to an entire organism (or any part of an organism) which contains “functional units of heredity”. If this were the case, “genetic material” of an organism would include *any* element of the organism which would enable it to be propagated – which in a plant would include either a cutting, or a seed, or a spore. Such a definition of “genetic material” would also appear to be broad enough to encompass eukaryotic cells (such as erythrocytes) containing only mitochondrial DNA[[31]](#footnote-31) (arguably a “functional unit of heredity”, if only of the mitochondrion itself).

The CBD does go on to provide a, potentially helpful, separate definition of "Biological resources" which:

“includes genetic resources, organisms or parts thereof, populations, or any other biotic component of ecosystems with actual or potential use or value for humanity.”[[32]](#footnote-32)

This separate definition of “biological resource”, which includes “genetic resources” within a broader definition, alongside separate mention of “organisms or parts thereof” would seem to suggest that the narrower (DNA-only) interpretation of “genetic resources” is correct. There otherwise seems little additional work for a broader (part of organism) definition of “genetic material” to do (other than to distinguish parts of organisms which do not contain units of heredity such as structural proteins, although this is a small subset of the parts of an organism).

This narrow interpretation is supported by Correa[[33]](#footnote-33) who notes that it is consistent with the prevailing thinking in the early 90’s (when the CBD was agreed) that manipulation of large or small sections of DNA would be the crucial element in exploitation of genetic resources.

## The products of genetic expression

Genes (the CBD’s “functional units of heredity”) are the way in which an organism encodes the instructions for making the proteins which make up the structural components of cell and tissues, and which regulate and catalyse reactions within the cells. Where such protein is an enzyme, it will (subject to regulatory messages) catalyse the conversion of other biochemicals within the cell.[[34]](#footnote-34) In this way the (non-DNA) biochemical components of an organism are an *expression* of the genetic material of the cell, even if they are not *themselves* functional units of heredity.

The question of whether “non-DNA” biological components of an organism fall within the scope of “genetic resources” for the purpose of the Protocol is an important one. If they did not, potentially important substances found within an organism – including the biologically-active ligands which have biological effects in other organisms (such as the prokaryotic and eukaryotic toxins from which many medicines or pharmacological tools are derived) would arguably be excluded from the access and benefit sharing provisions of the Protocol.

If one takes a narrow interpretation of “genetic resources” to include only the DNA of an organism, then one might argue that “use” of that DNA will, of necessity, include only those techniques in which that piece of DNA itself is manipulated. These might include taking the entire genome of an organism (that could be expressed in its entirety through nuclear transfer cloning) or a sub-set of genes of interest which can be spliced into the genome of another organism.[[35]](#footnote-35) Such a sub-set of genes could be used to provide the recipient (genetically modified) plant, animal, fungus or microorganism with a beneficial advantage (*e.g.* drought, pest, or herbicide resistance) or to stimulate the recipient organism to synthesise a particular molecule (which molecule itself may be used to provide a therapeutic benefit). Although these are undoubtedly powerful and commercially important techniques, they do not include “use” which takes a product of genetic expression (such as a protein or a metabolite produced through enzyme catalysis) as a starting point.

The fear that such products of genetic expression would be excluded from the access and benefit sharing provisions of the Protocol was a major driving force for the advocates for the “provider” countries at the negotiations of what would become the Protocol. [[36]](#footnote-36), Aubertin & Filoche[[37]](#footnote-37) report that provider country negotiators argued that:

“the creation of wealth (and thus of benefits which may be shared) does not take place as result of the use of DNA, or the genes themselves, but (in 89% of cases according to the megadiverse group of countries) as a result of research and development regarding biochemical components (which include not only natural molecules, but also synthetic products which copy a natural molecule, medicines and so on).”

and that:

“a Protocol dealing only with the use of genetic resources in the strict sense of the term, and not derivatives, would therefore be meaningless”.

Correa[[38]](#footnote-38) reports that the result of the negotiation was the addition to the Protocol of the concepts of “utilization”, “biotechnology” and “derivative” which were not present in the CBD and states that:

“the common understanding among all Parties was that the definition of “Utilization of genetic resources” held the key to determining whether the scope covered derivatives or not*”.*

Greiber *et al.* also report that:

“Late in the protocol negotiations, it became clear that many of the contentious technical issues could be solved if there were a clear understanding of the concept of utilization. ...the Parties included Subparagraph (c) defining the term “utilization of genetic resources”. This definition helps to provide legal certainty through specific indicators that make a clear test for determining when the Nagoya Protocol governs a particular activity and when it triggers the obligation to share benefits.”[[39]](#footnote-39)

So, it is to the definition of “utilization of genetic resources” that we must now turn. As will be seen, some of the confidence in the clarity of the definition shown in the last quote is, for this author, optimistic.

## What does “utilization of genetic resources” mean?

Throughout the Protocol genetic resources is used in tandem with the term “utilization”. Article 3 of the Protocol which deals with scope adds little. It merely states:

“This Protocol shall apply to genetic resources within the scope of Article 15 of the Convention and to the benefits arising from the utilization of such resources. This Protocol shall also apply to traditional knowledge associated with genetic resources within the scope of the Convention and to the benefits arising from the utilization of such knowledge”.[[40]](#footnote-40)

Article 5(1) refers to the sharing of benefits “arising from the utilization of genetic resources as well as subsequent applications and commercialization”, Article 5(2) refers to benefits arising from the “utilization of genetic resources” and Article 6(1) refers to access to genetic resources for their “utilization”. So what does “utilization” mean here?

The relevant definitions are provided in Article 2 of the Protocol:

(b) “Utilization of genetic resources” means to conduct research and development on the genetic and/or biochemical composition of genetic resources, including through the application of biotechnology as defined in Article 2 of the Convention;

(d) “Biotechnology” as defined in Article 2 of the Convention means any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.

(e) “Derivative” means a naturally occurring biochemical compound resulting from the genetic expression or metabolism of biological or genetic resources, even if it does not contain functional units of heredity.

Our starting point for analysis is the term “research and development on the genetic and/or biochemical composition of genetic resources”.

Research and development on the “genetic composition of genetic resources” would seem relatively clear – meaning analysis of the DNA sequences found within the particular genetic resource. What, though, does research and development on the *biochemical* composition of genetic resources mean?

As we have seen above, the definition of “genetic resources”/“genetic material” in the Protocol (via Article 2 of the CBD) is rather scant. As is also highlighted above, the “material...containing functional units of heredity” within the definition of “genetic resources” can possibly be interpreted in two ways:

1. functional units of heredity *alone*; or
2. more broadly as “material” of the organism in question which contains “functional units of heredity”.

If one assumes for the moment that the first (functional units of heredity *alone*) interpretation is correct, this leaves us with a difficult question over the meaning of research and development on the *biochemical* composition of genetic material/resources. If we reasonably assume that “genetic composition” means the nucleotide sequence within a strand of DNA, then we are left looking for *other* biochemical elements of the DNA strand(s) which may be the subject for investigation. What could these be?

Within eukaryotic organisms, nuclear DNA is wrapped around structural proteins called histones to form a composite material called “chromatin”. These structures (together with non-histone chromosomal proteins) are used to assist the organised coiling of DNA within a chromosome, protecting it, ensuring it fits within the nucleus and regulating gene expression.[[41]](#footnote-41) Modification of histones[[42]](#footnote-42) (together with DNA-methylation[[43]](#footnote-43)) are mechanisms for bringing about long-lasting heritable (so-called “epigenetic”) changes to the way in which the genome of an organism is expressed which are distinctly separate from modification of the nucleotide sequence.[[44]](#footnote-44) So, studies of chromatin structure and epigenetics would arguably meet the narrow definition of non-nucleotide sequence research on units of heredity. However, (although they are very important areas for study in their own right) in the light of broader concerns over the scope of “utilization of genetic resources”, it would seem perverse to give the term “research and development on the biochemical composition of genetic resources” such a narrow interpretation.[[45]](#footnote-45)

In contrast, if we interpret “genetic material” to not be limited to DNA (with or without histones), but to more broadly include that “material of plant, animal, microbial or other origin” which contains the “functional units of heredity” (that is *any* part of an organism which contains genetic material), it would logically follow that research and development on the *biochemical* composition of genetic resources would appear to mean research on the biochemical composition of such “material of plant, animal, microbial or other origin containing functional units of heredity”.

Since the DNA nucleotide sequence element of the resource would appear to be dealt with by the first part (genetic composition) of the definition, the reference to “biochemical composition” could arguably mean all those *other* biochemical elements present in the material which are created through genetic expression. For this author, this interpretation seems by far the more realistic - even though the narrow interpretation of “genetic resources” (as is discussed above) would seem to be the correct one when looking at the CBD *alone*.

Indeed, examining the meaning of “research and development on genetic resources”, Correa follows a similar line of reasoning:

“...Interestingly, this definition [of utilization] alludes to research and development on the ‘biochemical composition’ of genetic resources, that is, the arrangement of the chemistry of the compounds of living tissues and the processes in a living organism, and not to research and development on biochemical compounds as such. It may be understood, however, that any study of a ‘biochemical composition’ may include that of the individual components.” [[46]](#footnote-46)

Such a broad interpretation is supported by the 2008 Report of the Meeting of the Group of Legal and Technical Experts (“GLTE”) on Concepts, Terms, Working Definitions and Sectoral Approaches, which sets out a non-exhaustive list of kinds of R&D that could be included as utilisation.[[47]](#footnote-47) This list is instructive. Although most activities are equally consistent with a DNA-only interpretation of “genetic resources”, the GTLE suggestion of “Propagation and cultivation of the genetic resource in the form received” is clearly more consistent with a broader “part of organism” interpretation, as this would clearly include propagation of seeds, spores or cuttings of plants.

Within the European Union, the provisions of the Protocol were brought into effect through Regulation 511/2014 of 16 April 2014 (the “ABS Regulation”). Since the ABS Regulation, in part, mirrors the Protocol, and given the lack of clarity in the Protocol, in August 2016 the EU Commission issued its guidance on the scope and meaning of terms within the ABS Regulation through Notice 2016/C313/01 (the “Notice”). Of interest to our analysis, the Notice seeks to provide some explanation for the positions taken. In relation to “utilisation of genetic resources”, the Notice states that the Protocol definition is:

“…quite broad and covers various activities relevant for many sectors, without providing for a list of specific activities to be covered ... so as not to pre-empt changes in the rapidly evolving knowledge and technology in this domain”.[[48]](#footnote-48)

The Notice appears to see the definition of “research and development” as being key to understanding the scope of the Protocol.[[49]](#footnote-49) Noting that these are not defined in the Nagoya Protocol, the Commission states that interpretation of these terms:

“…should be based on their ordinary meaning in the context they are used and in the light of the purpose of the Regulation”.[[50]](#footnote-50)

The Commission appear to be particularly concerned that so-called “upstream” activities (such as the maintenance and management) of a genetic collection for conservation purposes should not be caught.[[51]](#footnote-51) However, in relation to “downstream” activities the Notice is arguably less clear, but proposes that researchers use a ‘litmus test’ where users should ask themselves whether what they are doing with the genetic resources:

“creates new insight into characteristics of the genetic resource which is of (potential) benefit to the further process of product development. If this is the case, the activity ... should be considered research and therefore falls under the term ‘utilisation’” [[52]](#footnote-52)

## The Meaning of “Biotechnology” and “derivatives”

As stated above, given the overall context, a reading of “conduct research and development on the biochemical composition of genetic resources” to include non-DNA biochemicals appears to be the interpretation which avoids outcomes which seem counter to the overall spirit of the Protocol.

Morgera *et al.*[[53]](#footnote-53) suggest that “biochemical composition of genetic resources” in Article 2(c) does not, in fact, clarify the object of the utilisation “self-evidently”, but go on to state that the combined reading of Article 2(c) with the other “new” definitions provided in the Protocol, “in particular that of derivatives”, leads to the conclusion that utilization of genetic resources includes research on the products of genetic expression.

As will be seen below, for this author the definition of “derivatives” falls far short of providing clarity. (Although as will be explained, since that lack of clarity is found in a non-limiting example it arguably does not actually serve to effectively limit the scope of the definition of “utilization of genetic resources”.)

If one performs a simple “de-nesting” of the nested definitions found within “utilization of genetic resources” one arrives at the following:

“Utilization of genetic resources” means to conduct research and development on the genetic and/or biochemical composition of genetic resources, including through the application of [any technological application that uses biological systems, living organisms, or [naturally occurring biochemical compounds resulting from the genetic expression or metabolism of biological or genetic resources, (even if they do not contain functional units of heredity)] thereof, to make or modify products or processes for specific use]].”

(NB. The square brackets show the nesting of the definitions)

The complexity, and lack of clarity, is obvious.

“Biotechnology” is provided as a (non-limiting) example of one of the means *by which* to conduct research and development on the genetic and/or biochemical composition genetic resources; that is it is described as a mechanism or *tool*.

The general understanding of biotechnology as a technique is broad and such technology has a long history.[[54]](#footnote-54) However, notwithstanding the different means used, one of the recurring similarities of all types of biotechnology is the production of a final “product”, whether that be a disease-resistant crop, a monoclonal antibody, an antibiotic, a beer, or a stilton cheese. This focus on products is, of course, reflected in the definition originally provided in the CBD:

“A technological application that uses biological systems, living organisms, or derivatives thereof, to **make or modify products or processes** for specific use” [emphasis added] [[55]](#footnote-55)

If we assume that the original CBD definition of genetic material intended to capture DNA alone, we can see that the definition of “Biotechnology” was entirely consistent with that narrow interpretation. It would be consistent the use of transgenic whole organisms (“living organisms”) whose genome has been modified by the insertion of particular genes to manufacture a particular proteins (or downstream products from those proteins where those proteins are enzymes). It would certainly include (but not be limited to) the application of “*In vitro* nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles.”[[56]](#footnote-56)

However, if we assume that “genetic material” should be read as (also) meaning “parts of organisms which contain functional units of heredity” then in terms of “conducting research and development on the *genetic* composition” such an interpretation would be consistent with techniques which do not specifically seek to move DNA through *in vitro* nucleic acid techniques, but which attempt the:

“Fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection.”[[57]](#footnote-57)

Such techniques could include the production of monoclonal antibodies through the creation of hybridoma cell lines made by fusing B-lymphocytes with a myeloma cell line.[[58]](#footnote-58)

In both the examples above, one might argue that the “Biotechnology” is being used to exploit the *genetic* composition of the “genetic resource”, rather than being part of the research and development on the (non-chromatin) *biochemical* composition of the “genetic resource”.

If this is correct, how then might these “biotechnology” applications be used in the research and development of the *biochemical* of the genetic resource? As we have seen, the understanding of biotechnology extends beyond what the Cartagena Protocol on Biosafety to the Convention on Biological Diversity calls “Modern Biotechnology”[[59]](#footnote-59) (essentially *in vitro* nucleic acid techniques and cell fusion techniques) and the definition within the CBD is certainly not so limited.[[60]](#footnote-60) Such research into the biochemical composition of genetic resource would certainly include the use of cell and tissue cultures using *unmodified* organisms to assist in the making of greater amount of the substance in question.

In practice, however, there is no split in the use of biotechnology techniques as between *genetic* and *biochemical* composition - *all* biotechnology techniques are available for research on the (non-DNA) biochemical composition of a resource, notably the use of genetically modified bacteria, or eukaryotic cell lines, to produce a sufficient quantity of a substance for analysis and study. One might imagine here the production of human interferon through the use of transgenic bacteria.[[61]](#footnote-61)

To conclude, the un-amended definition of “Biotechnology” in the CBD is entirely consistent with a broad interpretation of “genetic resources” to mean “parts of an organism containing functional units of heredity” and “biochemical composition of genetic resource” to include the non-DNA products of genetic expression. It is, however, equally consistent with a narrower chromatin-only interpretation of “genetic resource” or a chromatin-only interpretation of “research and development on the biochemical composition of the genetic resource”.

### Does the “new” definition of “Derivative” assist?

As we have seen, the Protocol introduces a definition of “Derivative”:

“a naturally occurring biochemical compound resulting from the genetic expression or metabolism of biological or genetic resources, even if it does not contain functional units of heredity.”[[62]](#footnote-62)

In itself, the definition of “Derivative” is clear. Had it been inserted as an expansion of the definition of “genetic material” at Article 2 of the CBD it would have unambiguously expanded that term to include any protein (such as an enzyme) produced through genetic expression or any naturally occurring compound produced through enzyme-catalysed metabolism within the organism in question. This is not, however, how the phrase is used. Indeed it is not used as a capitalised defined term *anywhere* within the Protocol.[[63]](#footnote-63) Instead it is arguably used as what appears to be a clarificatory example of the term “Biotechnology”.

As we will see, the way in which “Derivative” entered into the Protocol is complex. However, if we understand the mention of “derivatives” within the Article 2 CBD (and Article 2 Protocol) definition of Biotechnology as being a reference to “Derivative” as a defined term within Article 2(e) of the Protocol, then its effect is (arguably) to amend the definition of Biochemistry to the following:

“any technological application that uses biological systems, living organisms, or **[naturally occurring biochemical compounds resulting from the genetic expression or metabolism of biological or genetic resources, (even if they do not contain functional units of heredity**)**]** thereof, to make or modify products or processes for specific use” (bold text denotes substitution).

With the substitution in place, it is not entirely clear what work the “thereof” is performing in that sentence. Reference to a derivative (undefined) of biological systems or living organisms suggests that the system or organism has been manipulated is some way. Genetic manipulation of such systems or organisms to make products or processes is, of course, “classic” biotechnology. Here the “thereof” seems sensible. However, once one makes the substitution of “derivative” with its new definition, the presence of the “thereof” becomes more confusing. The substituted definition makes reference to “genetic expression or metabolism of biological or genetic resources” so why does that need to further particularised to be “of” biological systems or “of” living organisms? Such further particularisation is arguably otiose. It certainly does not enhance clarity. One might charitably conclude that the presence of the “thereof” is vestigial - having been left behind during a rushed negotiation. As will be discussed below, the reality is more complex.

With or without the “thereof”, one might argue that what is being described is the use of a “naturally occurring biochemical compound resulting from the genetic expression or metabolism of biological or genetic resources”within a technical application used in research upon genetic resources. This interpretation is incomplete - as we saw above, the underlying constant of Biotechnology is that it is a *process* for producing product and this requirement is still present within the definition. However, putting that requirement to one side for the moment, we need to recognise that the application of a “naturally occurring biochemical compound” here is a description of the *actor* upon a *subject*, rather than a description of the *subject itself.*

If this use as a *tool* was the intention of the negotiators of the Protocol, then the definition of “Derivative”, and where it is inserted, works relatively clearly. There are, indeed, very many such “naturally occurring biochemical compounds resulting from the genetic expression or metabolism of biological or genetic resources” which are used as tools in the conduct of research upon the “genetic and/or biochemical composition of genetic resources”. There does not appear in these definitions to be a requirement that the genetic resources from which the tool is taken has to be the *same* genetic resource upon which the tool is being used. As such, the definition would include the use of DNA probes taken from other organisms, dyes and stains derived from plants, animals, fungi and microbes, inhibitors of intracellular metabolism, and ligands at intracellular or extracellular receptors. Nor is there, of course, any restriction on using a tool obtained from one organism (“genetic resource”) upon the biochemical composition of *the same* genetic resource – one might imagine here the (admittedly narrow) use of tetrodotoxin obtained from a *Tetraodontidae* puffer fish to examine voltage-gated sodium channels in the same species of puffer fish.[[64]](#footnote-64)

Although the definition of “Derivative” as a tool clearly works in this (limited) way, it hardly seems a necessary clarification, given that the use of such compounds have long been a mainstay of biological research techniques. In addition, such a detailed explanation hardly seems “in character” given the other, rather sparse, definitions provided within the CBD and Protocol.

We also have the remaining problem that in the definition of Biotechnology the application using the “naturally occurring biochemical compound” should “make or modify products or processes for specific use” which is clearly not the case with all biological research tools. So, what then is the purpose of the expanded definition of “Derivative”?

**What is the purpose of the expanded definition of “Derivative”?**

During the negotiation of the Protocol, developing nations sought to ensure that the Protocol included specific reference to “derivatives”, arguing that this is where the main interest of modern biological research lies.[[65]](#footnote-65) In contrast, (perhaps for the same reason) some developed nations sought to ensure that the provisions of the Protocol merely applied to functional units of heredity (i.e. DNA).[[66]](#footnote-66)

As a result of this impasse, the term “derivative” did not find its way into the operative terms of the Protocol but it was understood that by way of compromise the term “utilization of genetic resources” would include the “notion” of derivatives.[[67]](#footnote-67)

As we have seen, the word “derivative” was already present in the existing (1992) CBD definition of “Biotechnology", namely:

“any technological application that uses biological systems, living organisms, or **derivatives** thereof, to make or modify products or processes for specific use” [emphasis added].

As discussed above, what appears to be referred to here is derivatives of biological systems or living organisms (which have most likely been created through modification of the genetic material within them), rather than to the biochemicals produced through translation of genes into proteins. Notwithstanding that (very) distinctly different use, the presence of the word “derivative” at that position appears to have acted as an easily negotiated route for insertion of the new definition of “Derivative”, without the parties becoming involved in a potentially fractious confrontation over a new definition of “Biotechnology”.

For this author using a strict doctrinal interpretation, the taking of that route has left us with the rather limited effect of “Derivative” as a non-limiting example of a tool to be used on genetic resources (and a strange hangover requirement to directly produce a product or process as would be the case with a Biotechnology application). The result is certainly difficult to untangle.

Morgera *et al.*[[68]](#footnote-68) refer to this outcome as “puzzling”. Notwithstanding this they state that the relevance of the definition of “Derivative” to the interpretation of “utilization of genetic resources” can be argued on two grounds:

1. ““utilization” **implicitly**refers also to research and development through the application of biotechnology **on** derivatives” [emphasis added]; and
2. “The definition of “utilization” makes reference to the “biochemical composition of genetic resources” which arguably relates to the reference to compounds in the definition of “derivatives” as it is only the latter that provides the necessary elements to circumscribe this otherwise vague concept”.[[69]](#footnote-69)

With regard to point b) Morgera *et al.* appear to suggest that the term “biochemical composition of genetic resources” is unclear. Although understandable, as discussed above, this author believes one can interpret that term clearly enough when one broadly interprets “genetic material” to include the cells of an organism which contain “functional units of heredity”. However, even assuming uncertainty in this regard, given that “Derivative” is used as an example of a tool (“Biotechnology”) used to act *upon* the subject of “biochemical composition of genetic resources” it is hard to see how one can easily use the reference to “biochemical compound” in the definition of Derivative to guide us as to the overall meaning of “biochemical composition of genetic resources”.

This use of “derivative” as somehow clarificatory of, or integrated within, “genetic resources”, notwithstanding rules of interpretation is prevalent. Vogel *et al.*[[70]](#footnote-70) are highly critical of this approach:

“Despite the introduction of ‘derivative’ in Article 2 (e), ‘derivative’ is not incorporated into Article 3 which defines the scope. Nevertheless, many delegates and scholars are not disheartened. They have inferred ‘derivative’ in the phrase ‘utilisation of such sources’. Unfortunately for the advocates, such an inference is not obvious and would morph ‘utilisation of such sources’ into a “panchrestron”, Garrett Hardin’s neologism for something that signifies everything and therefore means nothing” [[71]](#footnote-71)

Morgera *et al.*’spoint a) is, for this author, the stronger. They suggest that if your understanding of “biotechnology” is a narrow one, meaning merely the use of organisms to make products following manipulation of their genetic material, then such an understanding would not be entirely consistent with research on the products of genetic expression found within a genetic resource. They suggest that expanding the meaning of biotechnology to include the use of “Derivatives” (as newly defined) is consistent with “biotechnology” meaning a broader range of activities and, in particular, including research on the products of genetic expression found in a genetic resource.

At first blush, this may seem a reasonable interpretation. Indeed, as we have seen the original definition of “Biotechnology” in Article 2 of the CBD (without the expansion of the term “derivative”) appears to refer only to the use of biological systems or of living organisms (which have most likely been created through modification of the genetic material within them) *to make products*. However, although that interpretation is certainly consistent with a narrower understanding of biotechnology, as was discussed above, the use of those “narrow” techniques is still entirely consistent with a broad interpretation of “genetic resources” and a broad interpretation of “research and development on the genetic or biochemical composition”.

In addition, the inclusion of the new definition of “Derivatives” within the definition of “Biotechnology” is consistent with a broad understanding of the term biotechnology and with research on the products of genetic expression found within the cells of a genetic resource. However, if this were the aim of the inclusion of a specific definition of “Derivative”, it seems a relatively imprecise way of achieving the end, and we are still left with the problem of reconciling the need for the application to directly produce or modify a product or process.

Although concluding that the operative effect of the new definition of “derivative” is to further clarify that research and development on “naturally occurring biochemical compounds resulting from genetic expression or cellular metabolism and not containing DNA” can fall within “utilization of genetic resources”, Morgera *et al.* are (unsurprisingly) concerned that “the unfortunate drafting may raise doubts in interpreters and as a consequence lead to variations in national legislation implementing the Protocol”.[[72]](#footnote-72)

Overall we might broadly conclude that the new definition of “Derivative” though, in itself, clear, is poorly placed within the definitions provided within the CBD and the Protocol. As part of the definition of “genetic material” or “genetic resource” it would have provided welcome clarification. As part of the definition of “Biotechnology” (which is itself merely a non-limiting example of research and development) perhaps all we can really say with regard to the use of the term “Derivative” is that it is at least not-inconsistent with the definition of “biochemical composition of genetic resources” including naturally occurring products of genetic expression.

##  “Isolated” derivatives

Morgera *et al.* raise the problem of what they refer to as an “isolated derivative”, that is a derivative “acquired and utilised without physical access to genetic resources, such as those isolated from their natural environment and available *ex situ.*”[[73]](#footnote-73) Although they argue that such compounds fall within the scope of “utilization of genetic resources” they are concerned that there may be variations in national legislation implementing this aspect of the Protocol.

This author sees no realistic difficulty in interpreting “research and development on the genetic and/or biochemical composition of genetic resources” as encompassing work on such an isolated derivative. The mere fact that a naturally occurring compound has been physically isolated from its genetic resource source makes it no less a constituent part of biochemical composition and *in vitro* (or indeed *in silico*) study of it no less study of the biochemical composition of genetic resource source.[[74]](#footnote-74)

## The problem of “Chemical Derivatives”

The analysis provided above would appear to strongly suggest that research and development on the naturally occurring biochemical compounds resulting from genetic expression (or cellular metabolism of a genetic resource) falls within the scope of “utilization of genetic resources” for the purposes of the benefit sharing provisions of Article 5 of the Protocol.

However, as discussed, the identification and isolation of such a compound (though often of great importance) is often merely the beginning of a research and development trail aimed at the production of chemicals, which though based upon the original compound, are chemically modified such as to enhance their biological efficacy and bioavailability and reduce their side-effect profile relative to the original compound. Within the field of biochemistry such compounds are referred to as chemical derivatives (or more simply as just “derivatives”) of the original biochemical.[[75]](#footnote-75)

One might suggest that, in the light of the long-standing use of the term “derivative” within the field of biochemistry, the use of the term “derivative” within the Protocol is unfortunate and potentially confusing.[[76]](#footnote-76) Notwithstanding this potential confusion, we need to be absolutely clear; the reference to “Derivative” within the Protocol is *not* a reference to human-made chemical derivatives, but (as we have seen) has a very specific given meaning in the Protocol, being:

“a naturally occurring biochemical compound resulting from the genetic expression or metabolism of biological or genetic resources, even if it does not contain functional units of heredity.”[[77]](#footnote-77)

By definition then, the meaning of the phrase “naturally occurring” excludes any human-made, non-naturally chemical derivatives. However, we should not be confused into believing that this limitation could assist us in the broader question of whether chemical derivatives fall within the scope of Article 5. The operative effect of the term “Derivative” has been examined above, and, as this term is used within Article 2 of the Protocol (as a non-limiting example of “Biochemistry”), it would not operate to extend the scope of the meaning of research and development on genetic resources. Crucially, however, neither would its limited scope (of itself) operate to limit the scope of meaning of research and development on genetic resources to research and development upon naturally occurring compounds alone.[[78]](#footnote-78)

The answer to this question of interpretation (if there is one) has to lie in the definition of “utilization of genetic resources” and particularly the phrase “research and development on the biochemical composition of genetic resources”.

Assuming “biochemical composition of genetic resources” to mean the products of genetic expression, we can be reasonably confident that the following broad classes of substances created by the metabolism of a genetic resource would fall within the provisions of Article 5:

1. a naturally occurring RNA strand produced directly from the transcription of the DNA of the organism;
2. a naturally occurring protein produced from the transcription/translation of the DNA of the organism;
3. glycosylated protein (such as a functional enzyme) produced from the metabolism of the protein produced in (b) above; and
4. biochemical compound (“X”) whose synthesis was catalysed by the enzyme in (c) above.

Clearly, a chemical derivative of the biochemical “X” above is not a member of the set of endogenous compounds which are naturally produced within a cell by genetic expression and it would not be part of the “biochemical composition” of the genetic resource.

Could, however, the production of a chemical derivative of “X” (called hereafter “X-A”) be considered to be part of the “research and development” on X? The use of chemical derivatives of an endogenous biochemical can be used to enhance our understanding of the interaction between X and the intra- or extra-cellular target through which X has a biological effect. Is this sufficient to constitute research on the *original* substance? Although Correa is comfortable that a broad definition of “research and development” would mean that the benefit sharing obligations of the Protocol would encompass work upon a naturally occurring biochemical compound, he states that:

“the extent to which it would apply to downstream products derived, in turn, from such compounds is less clear.[[79]](#footnote-79)

Aubertin & Filoche[[80]](#footnote-80)are somewhat more certain, and state:

“By presenting derivatives as nothing more than a biochemical compound from a living organism, claims relating to synthetic molecules with a structure similar to a natural substance fall outside the scope of the Protocol. It would therefore appear that a natural molecule which has been synthesized and altered does not fall within the scope of the Protocol, even if it was “inspired” by nature.”

As discussed above, the GTLE arrived at a non-exhaustive list of “typical uses” of genetic resources.[[81]](#footnote-81) Amongst that long list there was one use that could arguably be construed as encompassing a chemical derivative namely:

“Use of genetic material as a "factory" to produce organic compounds, such as: Active compounds for pharmaceutical production”

However, since the list of organic compounds to be manufactured concludes with “Other naturally occurring compounds” it would appear that the active compounds envisaged are *naturally occurring* rather than human-made derivatives. Overall the uses are entirely focussed on work on naturally occurring substances. A similar approach is taken in respect of a discussion on the meaning of “derivatives”. So, although an opportunity was there for the drafters of the Protocol to specifically identify human-made *chemical* derivatives of the biochemical composition of genetic resources, that opportunity was not taken.

In relation to “derivatives”, for this author the Commission Notice glosses over the doctrinal problems outlined above. It states that:

“through the concept of ‘biotechnology’, the definition of utilisation is interlinked with the definition of ‘derivatives’ in Article 2(e) of the Protocol, which clarifies that ‘derivative’ means ‘a naturally occurring biochemical compound resulting from the genetic expression or metabolism of biological or genetic resources, even if it does not contain functional units of heredity”.[[82]](#footnote-82)

The Commission go on to conclude that:

“research and development on derivatives (whether or not containing functional units of heredity) is within scope where they are derived from genetic resources accessed under the Protocol”.[[83]](#footnote-83)

It is however clear from the examples set out by the Commission that the derivatives they refer to are *naturally* occurring products of genetic expression, not human-made chemical derivatives thereof.

Overall, therefore, one has to conclude that the question of whether “utilization” within the meaning of the Protocol includes work on *human-made* chemical derivatives of naturally occurring biochemicals remains entirely unclear. So, if it is unclear whether the Protocol directly covers human-made chemical derivatives, we need to consider whether more indirect *informational* linkages will lead to downstream use of such derivatives falling within the scope of the Protocol. It is to those informational linkages that we will now turn.

**Informational Linkages 1: Digital Sequence Information**

As seen, there remain significant uncertainties over what constitutes “research and development” on “genetic resources”. However, one clear constant in the discussion on “utilisation” set out above is that the research is done upon DNA (or biochemicals) which have physically originated *from the genetic resource itself*. What if, however, the subject for research and development did not *physically* originate from the genetic resource itself, but was independently synthesised using information gained from the original genetic resource?

Such a situation could arise where one had made *de novo* DNA or “synthetic DNA” on the basis of the DSI of the original genetic resource. As mentioned in the introduction, the concern that such a synthetic route would allow for an evasion of the ABS principles of the Protocol has stimulated the COP to investigate whether DSI should be covered by the Protocol.[[84]](#footnote-84) Indeed, such fears are well founded. The Commission Notice clearly takes the position that:

“as the reference to Derivatives in the Protocol is to *naturally occurring* biochemical compounds the definition does not cover material such as synthetic gene segments.” [[85]](#footnote-85)

In addition, they go one to state that:

“…the Protocol deals with access to and utilisation of genetic resources *as such* and therefore does not regulate issues concerning digital information obtained from genetic resources.” [[86]](#footnote-86)

Since the focus of this article is on the downstream scope of the Protocol in relation to non-DNA human-made chemical derivatives this work will not seek to examine in detail the arguments for and against coverage of DSI under the Protocol. However, extending control over “genetic information” could potentially extend the scope and nature of access and benefit sharing provisions under Article 6 and Article 5(1) and (2) of the Protocol rather than merely fixing a lacuna in current provision. Certainly, moving to control over *information* leads to significant questions of allocation of the right to control such information, and to questions of what might constitute “infringement” of the right. These questions less obviously arise when looking at control over a *physical* genetic resource – in that case one knows that the physical genetic resource at least came from (a perhaps traceable) physical *something*.

In relation to wholly, or very closely, conserved DNA sequences, these sequences may have been preserved across aeons and taxonomic groupings – just because the original sequence was determined from a sample taken from, say, a *liana* from a megadiverse nation, it is entirely possible for the same sequence to have been determined from a yeast,[[87]](#footnote-87) a mouse, or an elephant. Indeed, “*75% of human expressed genetic make-up is the same as a pumpkin - 57% the same as a cabbage*”.[[88]](#footnote-88)

One might then ask why a particular nation (or indigenous group) should have a right to control “access” to a nucleotide sequence which has been determined from an organism (our *liana*) which was found within a certain nation state (say Ecuador) when that sequence could have equally, and as easily, been determined from a yeast in Burton-on-Trent.[[89]](#footnote-89) In what way is the code from the *liana* unique or special, such that a right to control access is justifiable?

We need also to ask: If the nucleotide sequence is entirely conserved across taxonomic groups then what would happen if the “accessor” of the nucleotide sequence argued in their defence that the sequence information actually used by them had originated not from the Ecuadorian *liana*, but from the defendant’s independent determination from the genome of the Burtonian yeast? In this case would control over the sequence reside in the party which controls the resource from which the nucleotide sequence information was *first* determined – akin to a path-independent monopoly right to the sequence? Or is there to be an *originality* requirement (akin to copyright) where independent (non-path dependent) determination of the sequence by a third party constitutes a defence to “infringement”? What if the defendant (although truly independently sequencing the nucleotide sequence) had been in some way been directed toward that gene by an understanding of functionality of sequence by work done on the *liana*?

In addition, what if the nucleotide sequence were not exactly conserved across species? How similar would the “copied” sequence need to be to be considered an “accessing” of the original sequence. Would infringement/accessing in some way rely upon some measure of “functionality” of the unit of heredity [[90]](#footnote-90) and how would one begin determine or compare such “functionalities”?

One definition of functionality is the affect that the presence or absence of a gene has on the phenotypic characteristics of the host organism. In some cases that may be simple; in others it could be far less determinable.[[91]](#footnote-91)

A related, but more granular, definition of functionality could mean the ability of a gene to make a protein which then goes on to perform a particular function. That function may itself be to synthesise a further (non-protein) molecule which goes on to have a downstream function within the biochemistry of the cell. According to that definition, the claim to a particular genetic sequence would be rooted in the biochemical “product” produced by expression of the sequence (and potentially the biological effect of that product).

Unfortunately, gene expression (in eukaryotes) is rarely simple. There are many levels of gene regulation, and the same string of genetic code on a chromosome can, through the process of alternative splicing of the DNA, code for a number of different protein isoforms. In this way the “mere” 20,000 or so genes in the human genome can code for the very much greater number different proteins found in a human.[[92]](#footnote-92) In humans it may be that around 95% of multi-exon protein-coding genes produce alternate-spliced protein variants.[[93]](#footnote-93) In some cases, the different parts of a protein are even coded for on entirely different chromosomes.[[94]](#footnote-94)

The correlation between protein amino acid sequence and the gene coding for it is yet further complicated (in both prokaryotes and eukaryotes) by the process of messenger RNA “editing”. Here the nucleotide sequence in the messenger RNA is altered *before* protein synthesis, such that the amino acid in the final protein will differ from that which would ordinarily have been predicted from the nucleotide sequence in the encoding gene. [[95]](#footnote-95)

Given sufficient understanding of the relevant genome-proteome linkage, reading back from the biochemical “product” to the code is perhaps not impossible. However, the complexity, and required level of understanding of the relevant gene expression-protein linkage, may well significantly complicate claims to a particular DSI. In particular, since many different proteins can be manufactured from the same gene, claims over DSI based upon protein functionality may give rise to multiple separate (and competing) claims over a single gene.

Yet further complication may arise where third parties claim a degree of difference in the functionality and structure of “their” protein relative to that found in the claimed genetic resource. As between different species (say the *liana* and the yeast), even where the primary peptide sequence of a protein is identical, there would very likely to be a difference in the types and nature of post-translational modification/glycosylation of the protein. Essentially, although they would appear *similar*, they would not be identical and they may have subtle differences in function. How much functional similarity would be required for the protein in the yeast to be considered the same as that in the *liana*?

These are not insurmountable difficulties when looking at medicines regulation (for example see the treatment of “biosimilars” by medicines regulatory agencies[[96]](#footnote-96)), or indeed in patent litigation. However, in both cases, the definition of the required functionality has been established by the regulatory applicant, or patentee, in very detailed terms and that detail forms part of the basis of the grant of exclusivity to the right holder. It is not at all clear how such a requirement could be accommodated within the Protocol as it stands.

So, moving from control over *physical* genetic resources to *informational* genetic resources will likely require an appreciation of concepts of “firstness” and detailed claims to functionality – concepts more at home within the ambit of patent law and apparently not envisaged (and certainly not currently legislated for) within Articles 6 and 5(1) and (2) of the Protocol.

In the light of this analysis, would a move to permit the coverage of DSI within the Protocol impact upon the question of ABS control over the biochemical product of gene expression or of human-made derivatives of such products? The answer to that question is dependent upon how the Protocol was amended to bring coverage of DSI into effect. However, for this author, there is no inherent reason why Articles 6 and 5(1) and (2) of the Protocol would require to be amended in a way which would change the current treatment of biochemical products of gene expression, or of human-made derivatives of such products.

Although, as we have seen, control over genetic information is potentially problematic with regard to genetic resources *per se*, there already are provisions of the Protocol in which the concept of information is at the very heart of the right. These are Articles 7 and 5(5) in relation to TKAGR. It is possible, therefore, that the downstream scope of protection offered by these provisions will be more flexible (and more extensive) than the protections offered by Article 6 and 5(1) and (2), (and quite clearly some informational link was entirely intended by the formulators of the Protocol). It is to these positive protections that we will now turn.

## Informational Linkages 2: The right to control “access” to TKAGR resources under Article 7

TKAGR has no internationally accepted definition.[[97]](#footnote-97) However, in relation to potentially useful genetic resources it is perhaps best described as the knowledge (however held, whosoever held by, and however widely) that tells us that any type of genetic resource may be useful, and the ways it can be used and prepared to give that usefulness. Crucially (and obviously) for our current analysis, traditional knowledge is not a *physical* resource but an *informational* one and this changes the very nature of how it can be “accessed”.

Access in the form of mere *physical* acquisition cannot apply. Although traditional knowledge can be recorded in physical form, it is certainly not limited to such form. The “acquisition” here is instead conceptual, and the acquiring of the concept could certainly be argued to be access to the information. However, does this mean that it is only the *first* acquisition of the concept from the holders of the information which is the “accessing” event? One might imagine here that an ethnobiologist obtains the first disclosure from a particular indigenous group in Ecuador of the anti-tumour effects of ground-up *liana* seeds. It is hard to argue that such an event is other than an “accessing” for the purpose of Article 7. However, what about the case where our ethnobiologist publishes her findings and a third-party uses them to find the appropriate *liana* for anti-cancer research purposes? Is the initial reading the “accessing” or is it the acting upon that reading to source the *liana*?

Given the overall purpose of the Protocol (and the access provisions of Article 6) it would seem perverse to limit access to the very *first* accessing event - a “one-off” event, a single dipping into the “well” of indigenous information, after which all further use of the information is permitted. Indeed, given the overall context of the Protocol, it would seem more consistent that each new user should require consent to access (and that for each user continued “access” to a piece of TKAGR requires *continual* ongoing consent from the holders of the traditional knowledge for use of the knowledge). If this were not the case the provisions of Article 7 would be limited, and easily evaded.

However, where one creates a requirement for ongoing consent to “access” in relation to something as intangible as an idea, there is potential for the scope of control to be very broad indeed. Does the reference to prior informed consent here mean that that consent must encompass *all* continued usage of the information, and that *any* new use of the information, howsoever remote, requires permission? What about the pharmacologist who tests the *liana* extract against tumour cells? What about the synthetic chemist who makes a chemical derivative of that extract, and so on? When is the information no longer being *used*? The Protocol is silent as to these questions.

Notably, however, in relation to Article 7, there appears to be no requirement in the Protocol that a piece of traditional knowledge should be connected to a *specific* physical sample of genetic resource – indeed, such a requirement would be overly restrictive, and would again potentially lead to the Article 7 right being easily evaded.

Article 7 also contains no express requirement for the information to be used in any particular way. There is no requirement within Article 7 (unlike Article 6(1)) that the genetic resource to which a piece of traditional knowledge is associated should simultaneously be “utilised” as seems to be the case under Article 6(1). Accordingly, TKAGR can realistically only mean information which relates to the characteristics and properties of a “genetic resource” more generally. Genetic resource here, of course, means material of plant, animal, microbial or other origin containing functional units of heredity which is of actual, or potential, value. Presumably, *any* information relating to a particular plant, animal, microbe or other organism (presumably also covering fungi) containing functional units of heredity will be covered.

## Informational Linkages 3: TKAGR and the right to benefit-sharing under Article 5(5)

The key term in relation to understanding the scope of the right under Article 5(5) is clearly “utilization of traditional knowledge associated with genetic resources”. Unlike utilization of genetic resources, this term is not expressly defined within the Protocol (or the CBD). As with “access” to TKAGR under Article 7, it is clear that such use does not have to relate to a specific *physical* sample of a genetic resource.

Morgera *et al.*[[98]](#footnote-98) suggest that “utilization of traditional knowledge associated with genetic resources” needs to be understood “by combining different elements of the Protocol” and that the term can be “interpreted along similar lines to the definition of utilization of genetic resources”. This approach has much appeal, however, as we have seen in the analyses above, the meaning of “utilization of genetic resources” (and also “access to genetic resources”) is far from clear (particularly where the purported causal link is *informational* rather than physical).

We should also note that although there is no doubt that the provisions of Article 7 and Article 5(5) should work together with Article 6 and Article 5(1) and (2) where appropriate, the meaning of *“*utilization of traditional knowledge associated with genetic resources” does not seem to be expressly linked to, or restricted by, the definition of “utilization of genetic resources”. Nor is there any requirement that “utilization of genetic resources” should occur alongside the “utilization of traditional knowledge associated with genetic resources” (although there will, of course, be many occasions when both will happen concurrently).

Morgera *et al.* actually go on to imply that “utilization of TKAGR” is something distinctly different from (and, for this author, clearly broader than) “utilisation of genetic resources”. They suggest that the traditional knowledge should:

“serve as lead information for the utilisation of genetic resources, it can be understood as hinging on the same intent (research and development) as genetic resources.” [[99]](#footnote-99)

Here they reflect the view of the Ad Hoc Open-Ended Inter-Sessional Working Group on Article 8(j) and Related Provisions of the Convention on Biological Diversity who state that:

“In essence, traditional knowledge that sparks the process or provides the lead to the properties of a genetic resource although it may not be reflected in the end-product it remains associated to that product.” [[100]](#footnote-100)

and also the view of the Group of Technical and Legal Experts on Traditional Knowledge Associated with Genetic Resources in the Context of the International Regime on Access and Benefit-Sharing who state:

“...traditional knowledge often provides the lead to genetic resources with potential properties, even if the traditional knowledge does not match the end product. Thus it should nevertheless be covered by the International Regime. Although the traditional knowledge used for the final product may not match the body of traditional knowledge, traditional knowledge adds value to genetic resources by providing a massive increase of efficiency in identifying genetic resources with potential properties. Traditional knowledge can therefore be considered as an indicator of the potential properties of a genetic resource. At the same time, it was noted by some that traditional knowledge does not always provide useful leads to genetic resources.”[[101]](#footnote-101)

However, the work of these UNEP[[102]](#footnote-102) expert groups was not incorporated into the operative provisions of the Protocol, so we are left to look at general principles and the overall context of the Protocol (and of Article 8(j) of the CBD).

What seems clear is that the rights under both Article 5(5), and Article 7, and are about control over *information* rather than the utilisation of a particular physical resource and although one might expect that the “downstream” scope of a right to information may extend further than one rooted in a physical resource, we have no guidance from the Protocol itself (or the CBD) as to whether the scope of Article 5(5) or Article 7 should extend to all downstream products, in all circumstances.

At first blush, one is tempted to take the absolutist view that *any* benefit which derives from (or accessing of) a piece of TKAGR, no matter how distantly far down the drug discovery pathway, is covered by the provisions of Article 5(5) or Article 7 respectively. Whether such a far-reaching scope is philosophically justifiable the subject of work currently being undertaken by this author.

What about where the determination of a DSI has been arrived at by following the experimental “lead” provided by a piece of TKAGR? There seems an at least arguable case to be made for saying that the use of that DSI is subject to Article 5(5) or Article 7. This may, in part, solve the problem of Protocol avoidance arising out of the use of synthetic biology, but it would be a right limited to indigenous peoples (as opposed to Parties to the Protocol). Again, however, the question of whether it is justifiable for a DSI to be covered by the Protocol when that DSI has been derived from TKAGR via very circuitous routes is again the subject of work currently being undertaken by this author.

## Conclusions

So, is the Protocol a flawed creation? As we have seen, the Protocol was born out of, and is heavily reliant upon, the CBD. This work argues that definitions which were put into the CBD for one end have been “repurposed” for use in the Protocol. This is particularly true of the definition of “Derivative” and of “Biotechnology”, and the results are confusing. This reuse of parts was perhaps understandable given the conflicting views of, and time pressures upon, the negotiating parties who had a desire to achieve mutual acceptable agreements between conflicting camps. However, for those following in their wake, who are required to understand and bring into effect the rights and duties created by the Protocol, this “Frankensteinian” model of treaty drafting has been unhelpful.

As demonstrated in this paper, the drafting of the Protocol creates serious problems in determining the downstream scope of its protection. It seems reasonably clear that the Protocol envisages that a genetic resource includes, not only the genome of that resource, but the biochemical compounds found within the resource which are created by the expression of that genome. What is less clear is whether the scope of protection extends to the human-made chemical derivatives of such biochemical compounds. For patent practitioners used to arguing infringement cases involving small differences in chemical composition, the existence of such potential “loop-holes” will be surprising.

Still more surprising is the confusion surrounding protection of genetic information under the Protocol. If a synthetic gene which is informationally (but not physically) derived from a genetic resource is not considered to be part of that genetic resource, the potential for evasion of the provisions of the Protocol are potentially great. Given recent advances in synthetic biology and the prospect of using mere digital sequence information in gene and protein engineering,[[103]](#footnote-103) the prospects for evasion are yet greater.

Some of the potential for such evasion may be prevented by the existence of rights in TKAGR under Article 5(5) or Article 7. Given the inherent *informational* nature of TKAGR it is conceivable that the rights in TKAGR created by the Protocol could extend well beyond those provided for genetic resources *per se*. Certainly, TKAGR is of an unrelated type to the informational component of a genetic resource, and the definition of a genetic resource in the Protocol does not delimit the meaning or scope of the traditional knowledge associated with that genetic resource.

However, what seems to be missing from the positive rights in relation to TKAGR under the Protocol is any principle or guidance for determining a balance which combines fair protection for the traditional knowledge/genetic resources rights holders with a reasonable degree of legal certainty for third parties. Where such knowledge serves as a research “lead” for further development, the Protocol itself gives no clear guidance as to how far that knowledge can have a “reach through effect” into new scientific discoveries, or at what stage a researcher would be considered free of the traditional knowledge right.

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 For an accessible review of the history of the development of synthetic biology techniques see: J C Venter, *Life at the Speed of Life, From the Double Helix to the Dawn of Digital Life* (Abacus, London 2013) 250 [↑](#footnote-ref-1)
2. Deoxyribonucleic acid [↑](#footnote-ref-2)
3. [DG Gibson](http://www.sciencemag.org/search?author1=Daniel+G.+Gibson&sortspec=date&submit=Submit) et al., “Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome” (2010) 329 (5987) Science 52 [↑](#footnote-ref-3)
4. CBD/COP/DEC/XIII/16 (16 December 2016) [↑](#footnote-ref-4)
5. CBD/DSI/AHTEG/2018/1/4 [↑](#footnote-ref-5)
6. Including the Fourteenth Conference of the Parties, November 2018. See CBD/NP/MOP/3/1/Add.2, 33 [↑](#footnote-ref-6)
7. See Comments of the Life Science Committee of the Chartered Institute of Patent Attorneys (2017) 47(1) CIPA Journal 9 and also (2018) 47(10) CIPA Journal 9 [↑](#footnote-ref-7)
8. Jon Turney, *Frankenstein’s Footsteps: Science, Genetics and Popular Culture* (Yale University Press 1998) 26 [↑](#footnote-ref-8)
9. Paul A Cox, “The ethnobotanical approach to drug discovery: strengths and limitations” in Derek J Chadwick and Joan Marsh (eds), *Ethnobotany and the Search for New Drugs* (John Wiley & Sons 1994) (Ciba Foundation Symp 185) 25, 27; Norman R Farnsworth, “The role of ethnopharmacology in drug development” in *Bioactive compounds from Plants* (John Wiley & Sons 1994) (Ciba Foundation Symp 154) 2 [↑](#footnote-ref-9)
10. Glenn F King (ed), *Venoms to Drugs: Venom as a Source for the Development of Human Therapeutics* (Royal Society of Chemistry, Abingdon, 2014 [↑](#footnote-ref-10)
11. Londa Schiebinger, *Plants and Empire, Colonial Bioprospecting in the Atlantic World*  (Harvard University Press 2004); Michael J Balick and Paul A Cox, *Plants, People, and Culture: The Science of Ethnobotany* (Scientific American Library 1997) [↑](#footnote-ref-11)
12. Philip Schuler, “Biopiracy and Commercialization of Ethnobotanical Knowledge” in J Michael Finger & Philip Schuler (eds) *Poor People’s Knowledge* (World Bank and OUP 2004) [↑](#footnote-ref-12)
13. Graham Dutfield, *Intellectual Property Rights, Biogenetic Resources and Traditional Knowledge* (Earthscan Publications, London and Sterling, VA 2004), 101 [↑](#footnote-ref-13)
14. <http://www.cbd.int/information/parties.shtml> (Accessed November 2017) A notable omission is the United States of America which signed the convention in June 1993 but has so far failed to ratify; the only signatory to do so. [↑](#footnote-ref-14)
15. Tobias Kiene, *The Legal Protection of Traditional Knowledge in the Pharmaceutical Field. An Intercultural Problem on the International Agenda*  (Waxmann, Münster 2012), 198 [↑](#footnote-ref-15)
16. <http://www.cbd.int/convention/articles/default.shtml?a=cbd-08> (Accessed November 2018) [↑](#footnote-ref-16)
17. CBD COP Decision VI/24 [↑](#footnote-ref-17)
18. [http://www.cbd.int/doc/press/2014/pr-2014-10-12--protocol-en.pdf](http://www.cbd.int/doc/press/2014/pr-2014-10-12-nagoya-protocol-en.pdf) (Accessed November 2018) [↑](#footnote-ref-18)
19. A history of the development of protection of TKAGR can be found in Frantzeska Papadopoulou, *The Protection of Traditional Knowledge on Genetic Resources* (Edward Elgar, Cheltenham 2018) [↑](#footnote-ref-19)
20. One can see this where particular endogenous toxins are simply extracted and used. One example is the use of the puffer fish toxin, tetrodotoxin as a research tool. CH Lee and PC Ruben, “Interaction between voltage-gated sodium channels and the neurotoxin, tetrodotoxin” (2008) 2(6) Channels (Austin) 407 [↑](#footnote-ref-20)
21. DG Grahame-Smith and JK Aronson, *Oxford Textbook of Clinical Pharmacology and Drug Therapy* (Oxford University Press, Oxford 1992), 3; John Hall, “The drug development process” in Ignazio Di Giovanna and Gareth Hayes (eds) *Principles of Clinical Research* (Wrightson Biomedical Publishing, Petersfield UK 2001) 1 [↑](#footnote-ref-21)
22. See Hugo Kubinyi in Enrique Raviña, *The Evolution of Drug Discovery: From Traditional Medicines to Modern Drugs* (Wiley-VCH, Weinheim, Germany, 2011), 463 [↑](#footnote-ref-22)
23. Graham Dutfield, “A critical analysis of the debate on traditional knowledge, drug discovery and patent-based biopiracy” (2011) 33(4) EIPR 238 [↑](#footnote-ref-23)
24. Pierre Du Plessis, “Disclosure of origin of biological resources and potential effects of the Protocol” (2011) 40(5) CIPA Journal 331; Tim Roberts, “CBD and Nagoya – a rejoinder” (2011) 40(6) CIPA Journal 403; Pierre Du Plessis, “CBD and Nagoya” (2011) 40(7) CIPA Journal 466 [↑](#footnote-ref-24)
25. MW Tvedt, and OK Fauchald, “Implementing the Protocol on ABS: A Hypothetical Case Study on Enforcing Benefit Sharing in Norway” (2011) 14(5) JWIP 383 [↑](#footnote-ref-25)
26. Carlos M Correa “Implications for BioTrade of the Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization” (2012) paper prepared for the BioTrade Initiative on UNCTAD (UNCTAD/DITC/TED/2011/9) [↑](#footnote-ref-26)
27. CBD Article 2 [↑](#footnote-ref-27)
28. Thomas Greiber et al.  *IUCN Explanatory Guide to the Protocol on Access and Benefit-sharing*. (IUCN Environmental Policy and Law Paper No.83, 2012) , 64

([https://cmsdata.iucn.org/downloads/an\_explanatory\_guide\_to\_the\_\_protocol.pdf](https://cmsdata.iucn.org/downloads/an_explanatory_guide_to_the_nagoya_protocol.pdf)) (Accessed November 2018) [↑](#footnote-ref-28)
29. “Gene” in Merriam-Webster.com.

<http://www.merriam-webster.com/dictionary/gene> (Accessed November 2018). [↑](#footnote-ref-29)
30. Ribonucleic acid [↑](#footnote-ref-30)
31. Francisco J Iborra et al. “The functional organization of mitochondrial genomes in human cells” (2004) 2 BMC Biology 9  [↑](#footnote-ref-31)
32. CBD Article 2 [↑](#footnote-ref-32)
33. Correa (n 26) [↑](#footnote-ref-33)
34. See Christopher K Mathews, KE van Holde and Kevin G Ahern *Biochemistry* (Benjamin Cummins, San Francisco, 2000), 875-1110 [↑](#footnote-ref-34)
35. Including (but certainly not limited to) CRISPR/Cas9 gene editing technology; See F Zhang, Y Wen, X Guo “CRISPR/Cas9 for gene editing: progress, implication and challenges” (2014 23 Human Molecular Genetics R40; PD Hsu, ES Lander, F Zhang “Development and applications of CRISPR for gene engineering (2014) 157(6) Cell 1262 [↑](#footnote-ref-35)
36. EC Kamau, B Fedder, and G Winter, “The Protocol on Access to Genetic Resources and Benefit Sharing: What is New and what are the Implications for Provider and User Countries and the Scientific Community?” (2010) 6(3) Law, Environment and Development Journal 246, 251; Correa (n 26), 14; Elisa Morgera, Elsa Tsioumani and Matthias Buck, *Unravelling the Protocol: A Commentary on the Protocol on Access and Benefit Sharing to the Convention on Biological Diversity* (Brill/Nijhoff, Leiden 2014), 66; Greiber (n 28), 63 [↑](#footnote-ref-36)
37. Catherine Aubertin and Geoffroy Filoche “The Protocol on the use of genetic resources: one embodiment of an endless discussion” (2011) 2(1) Sustentabilidade em Debate – Brasília 51 [↑](#footnote-ref-37)
38. Correa (n 26), 14 [↑](#footnote-ref-38)
39. Greiber (n 28), 63 [↑](#footnote-ref-39)
40. Article 3 of the Protocol [↑](#footnote-ref-40)
41. See Mathews (n 34), 1075: Arthur M Lesk, *Introduction to Genomics* (Oxford University Press, Oxford 2012), 10 [↑](#footnote-ref-41)
42. T. Kouzarides, “Chromatin modifications and their function” (2007) 128 Cell 693; T Jenuwein and CD Allis, “Translating the histone code” (2001) 293 Science 1074 [↑](#footnote-ref-42)
43. J D Lewis et al. “Purification, sequence, and cellular localization of a novel chromosomal protein that binds to Methylated DNA” (1992) 69 Cell 905; X Nan et al. “Transcriptional repression by the methyl-CpG-binding protein MeCP2 involves a histone deacetylase complex” (1998) 393 Nature 386; NL Adkins and PT Georgel “MeCP2: Structure and Function” (2011) 89 Biochem Cell Biol 1 [↑](#footnote-ref-43)
44. Adrian Bird, “Perceptions of epigenetics” (2007) 447 Nature 396; Gary Felsenfeld, “A Brief History of Epigenetics” in C David Allis et al. (eds) *Epigenetics* (Cold Spring Harbor Laboratory Press, New York 2007), 15; Nessa Carey, *The epigenetics revolution. How modern biology is rewriting our understanding of genetics, disease and inheritance* (Icon Books, London 2012), 178 [↑](#footnote-ref-44)
45. This approach is consistent with the rule of interpretation set out in Article 31(1) of the 1969 Vienna Convention on the Law of Treaties namely: “A treaty shall be interpreted in good faith in accordance with the ordinary meaning to be given to the terms of the treaty in their context and in the light of its object and purpose”. [↑](#footnote-ref-45)
46. Correa (n 26), 14 [↑](#footnote-ref-46)
47. Report of the Meeting of the Group of Legal and Technical Experts on Concepts, Terms, Working Definitions and Sectoral Approaches, UN Doc UNEP/CBD/WG-ABS/7/2 (12 December 2008) <https://www.cbd.int/doc/meetings/abs/abswg-07/official/abswg-07-02-en.pdf> (Accessed November 2018): See also discussion by EC Kamau, B Fedder, and G Winter, “The Protocol on Access to Genetic Resources and Benefit Sharing: What is New and what are the Implications for Provider and User Countries and the Scientific Community?” (2010) 6(3) Law, Environment and Development Journal 246, 251 [↑](#footnote-ref-47)
48. Commission Notice 2016/C313/01 para 2.3.3 [↑](#footnote-ref-48)
49. Ibid. [↑](#footnote-ref-49)
50. Ibid. [↑](#footnote-ref-50)
51. Indeed this was a major concern of industry actors during the consultation period of the Commission Notice (see Elisa Morgera and Miranda Geelhoed, Consultancy on the Notion of “Utilisation” in the Nagoya Protocol and the EU ABS Regulation for the Upstream Actors” <http://ec.europa.eu/environment/nature/biodiversity/international/abs/pdf/ABS%20Final%20Report%20upstream%20users.pdf> ( Accessed November 2018)) [↑](#footnote-ref-51)
52. Commission Notice (n 48) para 2.3.3 [↑](#footnote-ref-52)
53. Morgera, *Unravelling the Protocol* (n 36), 65 [↑](#footnote-ref-53)
54. Dutfield, *Intellectual Property, Biogenetic Resources and Traditional Knowledge* ( n 12), 14 [↑](#footnote-ref-54)
55. Protocol Article 2

 [↑](#footnote-ref-55)
56. Article 3(i) (a), Cartagena Protocol on Biosafety to the Convention on Biological Diversity [↑](#footnote-ref-56)
57. Ibid. [↑](#footnote-ref-57)
58. César Milstein, “The hybridoma revolution: an offshoot of basic research" (1999) 21 (11) *BioEssays*  966 [↑](#footnote-ref-58)
59. Article 3(i), Cartagena Protocol on Biosafety on Biosafety to the Convention on Biological Diversity [↑](#footnote-ref-59)
60. Indeed the presence of a narrower definition for “Modern Biotechnology” within the Cartagena Protocol on Biosafety to the Convention on Biological Diversity supports a broader interpretation for “biotechnology” within the CBD and Protocol. [↑](#footnote-ref-60)
61. D Riesenberg et al., “High cell density fermentation of recombinant *Escherichia coli* expressing human interferon alpha 1” (1990) 34(1) Appl Microbiol Biotechnol 77 [↑](#footnote-ref-61)
62. Nagoya Protocol Article 2(e) [↑](#footnote-ref-62)
63. It is interesting to note that “derivatives” may have been used in this way in the indicative list of typical mutually agreed terms set out at Paragraph 44(i) of the pre-Protocol (non-binding) Bonn Guidelines: “Provisions regarding the sharing of benefits arising from the commercial and other utilization of genetic resources and their derivatives and products.” (COP 6 Decision VI/24 “Bonn Guidelines” Part D Paragraph 44(i)). However, even here it is not really evident what is meant by a “derivative” of a genetic resource in this context. [↑](#footnote-ref-63)
64. Lee and Ruben (n 20) [↑](#footnote-ref-64)
65. Morgera, *Unravelling the Protocol* (n 36), 66 [↑](#footnote-ref-65)
66. Matthias Buck and Claire Hamilton, “The Protocol on Access to Genetic Resources and Benefit-sharing Arising from their Utilisation to the Convention on Biological Diversity” Review of European Community and International Environmental Law (2011) 47, 56 [↑](#footnote-ref-66)
67. Ryo Kosaka, *The Negotiating History of the Protocol on ABS: Japanese Perspective* (2012) <http://www.ipaj.org/english_journal/pdf/9-1_Kohsaka.pdf> (Accessed November 2018)

 [↑](#footnote-ref-67)
68. Morgera, *Unravelling the Protocol* (n 36), 66 [↑](#footnote-ref-68)
69. Morgera, *Unravelling the Protocol* (n 36), 67 [↑](#footnote-ref-69)
70. Joseph Henry Vogel et al., “The Economics of Information, Studiously Ignored in the Protocol on Access to Genetic Resources and Benefit Sharing” (2011) 7/1 Law, Environment and Development Journal 52 [↑](#footnote-ref-70)
71. Garrett Hardin, ‘Meaninglessness of the Word Protoplasm’ (1956) 82/3 Scientific Monthly 112 [↑](#footnote-ref-71)
72. Morgera, *Unravelling the Protocol* (n 36), 68 [↑](#footnote-ref-72)
73. Ibid. [↑](#footnote-ref-73)
74. Correa (n 26) 14 [↑](#footnote-ref-74)
75. Derivative : “a chemical substance related structurally to another substance and theoretically [derivable](http://www.merriam-webster.com/dictionary/derivable) from it” (<http://www.merriam-webster.com/dictionary/derivative>) (Accessed November 2018 ) [↑](#footnote-ref-75)
76. Though as we have seen, it was perhaps originally used for an entirely different purpose within the CBD. [↑](#footnote-ref-76)
77. Nagoya Protocol, Article 2(e) [↑](#footnote-ref-77)
78. Although the operative effect of the definition of Derivative does not assist us in this regard, we can at least note that if the broad aim of introducing the term “Derivative” had been (as Morgera *et al.* (n 36) suggest) to ensure that compounds naturally produced within a cell by genetic expression were caught within the access and benefit sharing provisions of the Protocol the concept of derivative would not include a chemical derivative. [↑](#footnote-ref-78)
79. Correa (n 26) [↑](#footnote-ref-79)
80. Aubertin and Filoche (n 37) [↑](#footnote-ref-80)
81. UNEP/CBD/WG-ABS/7/2 (n 47) [↑](#footnote-ref-81)
82. Commission Notice (n 48) para 2.3.3 [↑](#footnote-ref-82)
83. Ibid. [↑](#footnote-ref-83)
84. CBD/COP/DEC/XIII/16 (16 December 2016); CBD/DSI/AHTEG/2018/1/4 [↑](#footnote-ref-84)
85. Commission Notice (n 48) para 2.3.3 [↑](#footnote-ref-85)
86. Ibid. [↑](#footnote-ref-86)
87. For example, even though the common ancestor of yeast and humans was alive at least one billion years ago, many human and yeast genes are functionally interchangeable. AH Kachroo et al “Systematic humanization of yeast genes reveals conserved functions and genetic modularity” (2015) 348 Science 921 [↑](#footnote-ref-87)
88. Gillian K Ferguson, *The Human Genome: Poems On The Book Of Life*

<http://www.thehumangenome.co.uk/THE_HUMAN_GENOME/Primer.html> (Accessed November 2018 ) [↑](#footnote-ref-88)
89. An English town renowned for its brewing. [↑](#footnote-ref-89)
90. [Peter Johan Schei](http://www.fni.no/cv/cv-pjs.html) and Morten Walløe [Tvedt](http://www.fni.no/cv/cv-mwt.html) “ ‘Genetic Resources’ in the CBD: The Wording, the Past, the Present and the Future” Fridtjof Nansen Institute Report 4/2010 ([http://www.fni.no/doc&pdf/FNI-R0410.pdf](http://www.fni.no/doc%26pdf/FNI-R0410.pdf) ) (Accessed November 2018); Morten Walløe [Tvedt](http://www.fni.no/cv/cv-mwt.html)  and [Peter Johan Schei](http://www.fni.no/cv/cv-pjs.html) “The Term 'Genetic Resources': Flexible and Dynamic while Providing Legal Certainty?” in S Oberthür and GK Rosendal (eds), *Global Governance of Genetic Resources: Access and Benefit Sharing after the Protocol* (Routledge , London/New York, 2014), 18 [↑](#footnote-ref-90)
91. Particularly where the phenotype is the result of the interaction of a number of separate genes. [↑](#footnote-ref-91)
92. Nessa Carey *The epigenetics revolution. How modern biology is rewriting our understanding of genetics, disease and inheritance* (Icon Books, London 2012), 53 [↑](#footnote-ref-92)
93. Lesk, *Introduction to Genomics* (n 41), 8 [↑](#footnote-ref-93)
94. S Schoenfelder et al. “Preferential associations between co-regulated genes reveal a transcriptional interactome in erythroid cells” (2010) 42 Nature Genetics 53 [↑](#footnote-ref-94)
95. Lesk, *Introduction to Genomics* (n 41), 9 [↑](#footnote-ref-95)
96. See for example such treatment by the European Medicines Agency: <http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/general/general_content_001832.jsp&mid=WC0b01ac0580bb8fda> (Accessed November 2018). [↑](#footnote-ref-96)
97. Commission Notice (n 48) para 2.3.2 [↑](#footnote-ref-97)
98. Morgera, *Unravelling the Protocol* (n 36), 74 [↑](#footnote-ref-98)
99. Ibid. [↑](#footnote-ref-99)
100. Report of the Sixth Meeting of the Ad Hoc Open-Ended Inter-Sessional Working Group on Article 8(J) and Related Provisions of the Convention on Biological Diversity, Conference of the Parties to the Convention on Biological Diversity Tenth Meeting Nagoya, Japan, 18-29 October 2010, 36

<https://www.cbd.int/doc/meetings/cop/cop-10/official/cop-10-02-en.pdf> (Accessed November 2018) [↑](#footnote-ref-100)
101. Report of the Meeting of the Group of Technical and Legal Experts on Traditional Knowledge Associated with Genetic Resources in the Context of the International Regime on Access and Benefit-Sharing Montreal 9-15 November 2009 (UNEP/CBD/WG-ABS/8/2), 8

 <http://www.cbd.int/doc/meetings/abs/abswg-08/official/abswg-08-02-en.pdf> (Accessed November 2018) [↑](#footnote-ref-101)
102. United Nations Environmental Program [↑](#footnote-ref-102)
103. For a review of potential directions for development see: JC Venter (n 1), 250 [↑](#footnote-ref-103)