THE ABS CAPACITY DEVELOPMENT INITIATIVE

L'INITIATIVE DE RENFORCEMENT DES CAPACITES POUR L'APA

Webinar report:

"Contribution of DSI in the development of commercial applications"

Wednesday, 16 June 2021, zoom (120 min)

I. Introduction

The webinar aimed to discuss how DSI can contribute to the development of commercial products including the opportunities and risks that can arise from its use.
The policy-science process under the CBD clearly showed that stakeholders are determined to keep the access to DSI in databanks open. However, open access does not necessarily mean that the access is for free. Future benefit-sharing models for the utilization of DSI are likely to be developed including terms and conditions at the level of access in data banks.
While many stakeholders specifically focus on benefit-sharing options for the commercial use of DSI, a definition of the difference between non-commercial and commercial research is not available, as yet. Many commercial products are based on initially non-commercial research with the research results then being used for commercial research.

This webinar aimed to inform about a 2-phase model of DSI generation and discussed the relevance of intellectual property (IP) to DSI and the role of patents. Examples of products which are already on the market or in the approval phase based on the utilization of DSI were presented. In the final part of the webinar the discussion was centred around the identification of individual benefit-sharing options in relation to the examples presented.

The discussion of the panellists and the participants was facilitated by Mr. Pierre du Plessis. The panellists were: Dr. Siva Thambisetty, Prof Marcel Jaspers and Mrs. Maria Julia Oliva. This report summarizes the input of the presentations, and the discussion of the panellists and the participants.
All presentations can be found here (https://www.abs-biotrade.info/topics/specific-issues/dsi/#c4665).

II. Presentations

Hartmut Meyer, team leader ABS Capacity Development Initiative: "*Contribution of DSI in the Development of commercial application"*

Dr Meyer briefly presented the approach of benefit-sharing of DSI in relation to the use of the Prior Informed Consent (PIC) and the Mutually Agreed Terms (MAT). If DSI sequences are involved, these are further transferred to open access data banks which can be accessed by potentially everybody. However, in principle, a MAT can forbid the use of the genetic resource for DSI or it can be the basis for the negotiations on benefit sharing from using DSI. The challenge is that a MAT itself cannot be uploaded to data banks. Whatever is negotiated at the provider level, therefore will not available for subsequent users. Consequently, if *subsequent* players use DSI for the development of commercial products a benefit-sharing becomes extremely difficult, and this causes a mayor "bottleneck" in the ABS system.

Pierre du Plessis *"Intellectual Property relevant to DSI"*

Mr. du Plessis provided input on emphasizing a series of challenges, which can become relevant for commercial applications of DSI. Researchers must deposit their data in open-access databases in order to obtain further funding. The credits and recognition will be received by the researchers rather than the community where the GR is originated. As most of the databases are based on open access there is no creative commons approach to create a formal benefit-sharing obligation for people who access databases. However, some databases are manually "curated" with terms and conditions or even subscription fees. Currently, plant breeders' rights on the use of DSI are widely discussed and most relevant for the DSI-discussion. On the one hand, breeders can obtain an exemption which allows subsequent breeders to use a protected variety for further development and further breeding, On the other hand, the number of patents for particular traits of a plant variety are increasing. In addition, trade secrets, (which are not publicly available) enable companies to hide the use of proprietary sequences for their product. The Traditional Knowledge, which helped to discover the phenotype of a genetic resource is not "encoded" in the DNA of a species and, thus not part of the knowledge and information shared in the databank with subsequent users. However, the genetic resource became what it is over centuries by applying the Traditional Knowledge through treatments and selections.

Hartmut Meyer *"DSI in patent applications"*

Dr Meyer presented an analysis (provided by Paul Oldham) about DSI in patent applications. The figure in the first slide shows the trends of the processes from the first applications on DSI until today. The number of sequences patented has grown exponentially until the 2000s, when this growth became more and more saturated. There are approximately 10,000 patents per year and high demand for patented DSI or applications. Further slides provided information on the applicants, the technology areas they work in and on the inventors. Patents are mostly developed by public institutions. The commercial sectors have brought in less patents as they benefit from the public institutions.

Examples presented provided information on vanillin and on the production of a perfume:

Vanillin-production in recombinant[1] yeast of the Swiss company Evola

Vanilla is originally a natural product coming from Madagascar, Indonesia, Mexico or elsewhere in the tropics. The natural product is expensive with prices growing constantly. Meanwhile, synthetic vanillin fully dominates the global market (around 99%). Several companies produce synthetical vanillin.

In 2014, Evola started its vanillin production in recombinant yeast. The ABS initiative analysed the role and the contribution of DSI in this case. The analysis focused on two main elements of DSI in patent documents:

- DSI involvement in the analysis of genetic material in order to identify new genes
- DSI involvement to synthesize new genes.

The outcomes of protein sequences mentioned in the patent were presented as follows:

- 25 DNA and protein sequences mentioned in the patent were analysed in a Gene Bank;
- 19 cases of the sequence were uploaded more than 10 years ago; and
- Only in 5 cases information was available on the country of origin of the respective genetic resource (Spain, USA, Japan, Germany, Italy).

The analysis has also shown that three sequences were cloned from genetic resources and two new genes were synthesized based on DSI accessed in databanks. Dr Meyer estimated that more DSI was used during the R&D processes of the company.

Clearwood – Parfume – Firmenich

The second example was based on the scent of patchouli, which was developed through producing the scent molecules in transgenic yeast. It was patented in 2011, and introduced on the market as "Clearwood" in 2014. The original synthase[2] of Patchouli was obtained from a nursery garden in Switzerland.

III. Panel

The moderated was done by Mr Pierre du Plessis who had prepared specific questions for each of the panellists.

Dr Siva Thambisetty, *associate Professor in intellectual property Law at the London School of economics*

As an IP Law expert, what problems do you see when it comes to IP that can be relevant to the commercial application of DSI?

The first panellist, Dr Thambisetty highlighted that it is important in the DSI discussion to create or maintain public commons, while the term "commons" remains being a challenge.
The characteristics of commons were described as follows:

[1] Artificially produced, often in cell cultures or with the help of genetically modified microorganisms.
[2] Enzymes catalize the synthesis of two specific molecules.

1. **In principle, they can be accessed and used by everybody,** however if some people lack the capacity of using them, the use of commons leads to an unequal access to data and disadvantages for those who cannot access the data. In this case nobody should be allowed to take property rights from the commons.
2. **If no property rights can be obtained through** this approach, it remains unclear what will happen to rights regarding with DSI used in a patent application. To what extend will these rights, which are freely available through the commons be re-appropriated?
3. In order to create commons, it is very important to be **free from prior claims**
4. To create a "real DSI" there **should not be any defection**.

Creating commons can be interpreted as a way of watering down property rights. If the knowledge or the data is part of the commons, then nobody else should be able to re-appropriate it.

Most of the upcoming cases cannot be regarded as "one sequence = one patent". There are multiple patents on the same sequence which are used in different forms. With regard to patenting gene sequences in their natural form Dr Thambisetty gave the example of the marine eukaryotic microorganism ONC-T18 which itself is patented, just the same as the nucleic acids, which were isolated from the organism. If the use of a certain organism can be identified, the degree of alteration, which can lead to patentability is very low.

Prof Marcel Jaspers*, director of marine biodiscovery centre of the university of Aberdeen*

How representative are the examples presented by Hartmut? Do you have an additional perspective to add on the use of DSI for commercial applications?

The second panellist, Prof Jaspers provided a short summary on how DSI is applied in his company (Ripptide Pharma) by giving an example:

A specific alga is producing a medicinally interesting compound. The chemical compound cannot be isolated respectively this is very expensive. To develop a special compound, it is difficult to trace a chemical structure back to the protein from which it originated– and it is even more difficult to trace it back to the original DNA sequence. Consequently, other ways are used to achieve the desired result.

Therefore, researchers took the sequences of the protein which is producing the desired chemical compound and searched for analogous structures using GSD (Global Species Database). An analogous protein has to be 30-40% similar in order to possibly have the same function as the desired protein. Then the modifications on the protein are implemented. Example for modifications are: a better temperature range, stability at a certain pH value, changes specific towards a specific substrate, etc. For a company it is important that the implemented modifications are patentable.

To produce a functional protein that can work in another organism, (as it the case for E. coli with its codon usage), optimization has often been the first step. It also needs to be noted that industrial production of a desired chemical compound is only possible with an engineered enzyme that is functional in another organism. The process replaces toxic, highly wasteful, chemical processes and is

thus faster, cleaner, greener, and less costly. The chemical process may take 6 months to produce the same end product. In comparison, the process that Prof Jasper introduced takes two weeks, only. Hence, this use of DSI speeds up drug discovery in a much cleaner way.

Mr Du Plessis pointed out that this process deserves to be protected as an inventive step. It shows the massive potential of DSI to improve everyone's life. On the other hand, it shows the disruptive potential of DSI.

Maria Julia Oliva *deputy director and coordinator for access and benefit sharing policy at the union for ethical bitrade (UEBT)*

The third panellist was Mrs Oliva. She was requested to share some perspectives of the ABS complications companies are facing even when they are willing to comply with Benefit sharing obligations? What problems arise when a single product uses a range of sources, with different ABS stages and IP protection attached? Do you have any examples how they solve the problem through mutually agreed terms or other creative ways?

Mrs. **Oliva** explained that the challenges faced are very much linked to the original purpose of ABS, which, in the beginning was created for situations in which there is only one provider and one user. Which in reality is rarely the case. Often the process starts with a single user and then there are kinds of subsequent users. Another challenge can be seen in the varying scope of ABS requirements around the world.

In addition, every single ABS case itself is very complex and has to be treated individually. For example, most of the traded vanillin is synthetic. And most of the natural vanilla is imported from countries where vanilla not a native species. It is less the R&D that causes the major challenges but rather the supply chains, as vanilla is exported from poor communities, countries and regions that face a series of challenges.

It also needs to be further discussed how products that have different biological resources can be managed? For example, fragrances include the ingredients of dozens of various genetic resources, and some are natural, some synthetic. There are all kind of different challenges to be addressed in cases like this.

The ABS system of Brazil demonstrates that it could be better to focus on value of a final product than on the initial use. Based on a law from 2015, Brazil developed a registration system with which the approach from the access is traced. However, not every access to a genetic resource leads to benefit sharing. Benefits thus are shared only if a final product is developed and sold - and the genetic resource adds significant value to this product or is of key functional relevance to this product. The genetic resource could also be of importance with regard to the marketing strategy and market value of the product. The discussion should more consider this approach when discussing DSI. The question thus is: where is the value and how is the genetic resource contributing to the product?

Question to Prof Jaspers: Under which conditions would you use a sequence that is linked to PIC and MAT negotiations and agreements?

Prof Jaspers doubted that there is a case, in which a single sequence found in the database is unique and therefore has to be used (and cannot be replaced by any other sequence. In general, the same sequence can always be found somewhere else, too. For example, his research team found a sequence in arctic moss that was identical to one they found in Australian sea squirt. These species are differing a lot and are not even related to each other. Molecular biologists have a saying that "everything is everywhere and the environment selects." Prof Jasper emphasized the importance to develop a system that acknowledges the fact that the same sequence can be found at multiple locations or even in multiple organisms- adding even more complexity to the questions discussed. Companies and researchers will always go for the simplest legal aspect. Hence, if there are restrictions in the future, they will always tend to use the sequence which is similar enough to work with but implies fewer restrictions. A multilateral system thus would be the most feasible.

To Dr Thambisetty: How can we overcome the problem, that users bypass ABS using a similar sequence?

While trying to create creative commons licences, it needs to be acknowledged that there is the influence of many others factors that preclude a "real" common. With investment, commons can be engineered. It is important that patent officers seriously consider publicly available sequences as an element of trail art.

Furthermore, Dr Thambisetty recommended to focus on small-scale commons that can be created, making a distinction between the public domain (free for all) and more carefully engineered ("curated") commons. For example, companies might regard the value of precluding the of property rights of individuals higher compared to the value of individuals obtaining these property rights on particular sequences. In this case smaller commons should be engineered.

What has to be enclosed in patent application?

Dr Thambisetty explained that researchers do have the information from where DSI was originated that is now used for their work. They do not disclose it because nobody asks them to do so.
Prof Jasper added to this statement that Good Scientific Practice would always comply with those standards. If there was a place where DSI information could be displayed, a scientist would displace it. However, Prof Jaspers negated that the information has to be part of a patent. He recommended to create a system in which scientists can fill in the relevant sequence information.

There is an asymmetry of power when it comes to DSI: what are your ideas to avoid this?

Prof Jasper emphasized that it is not just capacity development or inclusive innovation. All actors of a research project should be included right from the beginning. In this framework, it would be equally important to integrate people who gave access to t information. The aim of the research should be discussed with them and a research program should be set up that involves to everyone.

Is there a way to solve the ABS question around DSI?

Prof **Jaspers** stressed that there are solutions to connect ABS with DSI, using the world sea project as one option how to solve this challenge. Still, future questions are already being raised, like: what to do regarding designer sequences downloadable from databanks? What can be done with proteins entirely designed or with designed molecular compounds that do not exist in nature? These "synthetic" compounds exist due to lessons learned from big data of databases. However, the designed compound

is not derived from a database anymore. How can these challenges be addressed? Contributions as well as the usage of information from databases, need to be recognized and rewarded. According to Prof Jaspers this can only be achieved by using a big multilateral system.

Mrs Oliva highlighted the importance of exchanges like the one today. It is also important to develop ideas that match the real situations and, based on this develop a concept that can finally contribute to the conservation of biological diversity.

Dr Thambisetty raised the question whether a law is the right tool to achieve the desired changes for the protection of biodiversity or the conservation of endangered species as both scientific innovations and climate degradation move far quicker than any new law that will be created. The topic has been discussed for decades, while discussion continue about the correct use of terms of language. For example, people disagree on basic terms, like “innovation”, while an innovation for one person might result in the harm of another.

Even if a new law will be created, there are many different ways of interpreting it. The system, which we will create will never provide the final answer to the topics discussed in the webinar. It was thus recommended to rather have a look at options that can be implemented into practice by now (such as, for example, tracing of origin or improving technology transfer). More ambitious aims, such as open access models are taking more time and require different sorts of conversation.

Dr Thambisetty does not see a way how to get around a multilateral system. This multilateral system will have to be established in parallel to the existing bilateral system with the hope the multilateral system will be so functional enough that there will be less need for the bilateral system.