The Life Sciences Lawyer

Issue 3 2020

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Pepper decision - plants and animals get chilli reception at EPO

Launch interactive document

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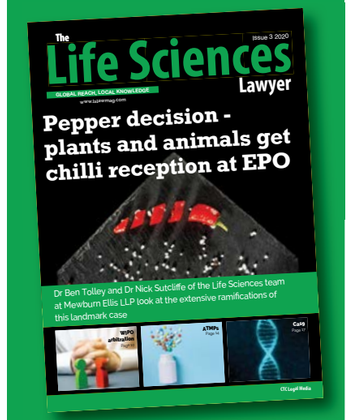

THE LIFE SCIENCES LAWYER
Issue 3 2020

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Published by:
CTC Legal Media Ltd,
23 Hedgers Way, Kingsnorth,
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Tel: +44 (0)20 7112 8862
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Design and Repro by:
Design and Printing Solutions Ltd
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Printed by:
Maxim
6 Hercules Way, Watford,
Hertfordshire, WD25 7GS UK

CTC Legal Media

Editor's welcome

Welcome to the third issue of *The Life Sciences Lawyer* magazine, and my first as Editor here at CTC Legal Media.

I am excited to make your acquaintance and look forward to bringing you the latest law developments in life sciences from hereon in. I have been working with *The Life Sciences Lawyer* since its launch earlier this year, so, with my background being in English (BA Hons), you can imagine my delight in becoming Editor. It will be great to hear from you, do get in touch.

I thank Matt Seex, my predecessor, for his insight and wish him well with his new beginning.

> **"We also touch on life sciences disputes from the specialists at WIPO"**

For this issue, our cover story, brought to us by Mewburn Ellis, explains the reason the G3/19 has suffered backlash from plant breeders associations, and how EPA both 'had its cake and ate it' in respect to the changes in patenting in the sector. Further, Janett Lumbreras discusses the uses for cannabis for medical and industrial use, and the modified production of cannabis to maximise yield and reduce THC properties. We also touch on life sciences disputes from the specialists at WIPO with a close glance at their experiences.

This and an in-depth analysis, from Baker McKenzie, of the changes enforced in pharmaceutical patent rights with the replacement of NAFTA with USMCA, plus more in the developments of life sciences law.

I hope you enjoy the issue.

Faye Waters

Faye Waters
Editor

Mission statement

The *Life Sciences Lawyer* educates and informs professionals working in the industry by disseminating and expanding knowledge globally. It features articles written by people at the top of their fields of expertise, which contain not just the facts but analysis and opinion. Important judgments are examined in case studies and topical issues are reviewed in longer feature articles.

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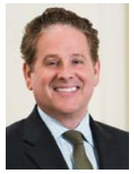

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Bob is a partner at Drinker Biddle & Reath LLP and Co-Chair of the Intellectual Property Group. In October of 2013, he was appointed to a three-year term on the CAFC Advisory Council, was reappointed for another three-year term in 2016, and reappointed in 2019 for an additional three-year term. He is currently serving on the Board of Directors for the American Intellectual Property Law Association.

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The Life Sciences Lawyer Magazine wishes to take this opportunity to thank the editorial board for their time and support.

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Pepper decision means conventionally bred plants and animals get a chilli reception at the EPO

Dr Ben Tolley and Dr Nick Sutcliffe of the Life Sciences team at Mewburn Ellis LLP look at the extensive ramifications of this landmark case.

Following decision G3/19 ("Pepper")[1] of the Enlarged Board of Appeal (EBA), plants and animals obtained from "essentially biological" processes will no longer be patentable before the European Patent Office (EPO). This decision only applies to pending European patent applications filed after 1 July 2017, when Rule 28(2) EPC was introduced.

For some time at the EPO, plant varieties and "essentially biological" processes for the production of plants and animals have been excluded from patent protection under Article 53 EPC (confirmed in "Broccoli" (G2/07)[2] and "Tomato" (G1/08)[2]). In this context, the exclusion of "essentially biological" processes is interpreted as encompassing processes for the production of plants based on steps of sexually crossing the whole genomes of plants and subsequently selecting plants (i.e. classical breeding), despite involving human intervention.

These exclusions to patentability are originally derived from Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions (The "Biotech" Directive)[3] and were subsequently incorporated into the EPC as Article 53(b) EPC. In contrast, claims to biotechnological methods (e.g. gene-editing, transformation, and regeneration) of producing transgenic plants or animals and to tools such as markers for use in methods of breeding, can be allowable.

Dr Ben Tolley

Dr Nick Sutcliffe

G3/19 – what has changed?

Until G3/19, it was possible to obtain patent claims to plants and animals or material thereof (e.g. fruit or seeds) resulting from biotechnological techniques and classical breeding techniques providing that the resulting product was new, inventive and could be reproduced reliably. This had been confirmed on several occasions including by the EBA; the highest decision-making authority at the EPO in the combined "Broccoli II" (G2/13)[4] and "Tomato II" (G2/12)[4] decisions, which concluded that the exclusion of "essentially biological" processes did not extend to products of those methods.

Despite providing much needed clarity and certainty, these decisions were not received favorably by some groups, especially plant breeders associations who argued that allowing the patenting of plants resulting from classical breeding is an unfair intrusion into the territory of plant variety rights (PVRs).

Whilst the EBA's decision in G3/19 significantly changes the situation regarding the patent eligibility of plants, the decision itself concerns Rule 28(2) EPC, which was introduced by the Administrative Council (AC) on 1 July 2017. Its introduction followed lobbying and pressure from the European Union to limit the extent of patent protection available in this field in the form of a resolution by the European Parliament in December 2015[5] and a non-binding notice from the European Commission in November 2016[6]. The change to the Rules was extremely controversial, particularly in the absence of a reference to the European Court of Justice on the matter[7]. The effect of the change was also unclear, with the Board of Appeal in T1063/18[8] ruling that Rule 28(2) EPC was, as many had anticipated, in conflict with Article 53(b) EPC (as interpreted by G2/12 and G2/13) and should therefore be ignored (and declaring their intention to reach a similar conclusion in T2734/18[9]). Following the issuance of T1063/18, the European Parliament issued a second resolution in September 2019 re-stating their view that the products of conventional breeding processes "must not become patentable"[10]. The vigor with which EU institutions have pursued this issue reflects the strength of the concerns of the plant breeding industry and various pressure groups about the monopolization of plant genetic resources.

In deliberating on this issue in G3/19, the EBA therefore faced considerable pressure from both inside and outside the EPO to find a way to maintain the validity of new Rule 28(2) EPC despite the existence of their own earlier case law. In the face of this pressure, the EBA found a way to maintain the validity of both new Rule 28(2) EPC and G2/12 and G2/13. In other words, the EBA both had its cake and ate it. The key to reaching this solution was adopting a so-called "dynamic interpretation" of Article 53(b) EPC. This allowed the EBA to conclude that the correct interpretation of Article 53(b) EPC was set out in G2/12 and G2/13 but was altered by the subsequent implementation of Rule 28(2) EPC. According to the EBA, the new interpretation that is set out in new Rule 28(2) EPC applies to applications filed after the rule was implemented on 1 July 2017. Applications filed before that date will not be affected by Rule 28(2) EPC and will continue to follow the previous interpretation of Article 53(b) EPC set out in G2/12 and G2/13.

Since the decision cannot be appealed, G3/19 therefore gives a clear-cut date for the prohibition on plants and animals produced by "essentially biological" processes, which does

1 G3/19 (http://documents.epo.org/projects/babylon/eponet.nsf/0/44CCAF7944B9BF42C12585680031505A/$File/G_3-19_opinion_EBoA_20200514_en.pdf)
2 Consolidated cases G2/07 (OJ 2012, 130) and G1/08 (OJ 2012, 206) ruling on the referrals in T83/05 (OJ 2007, 644) and T1242/06 (OJ 2008, 523)
3 Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions
4 Consolidated cases G2/12 (OJ 2016, A27) and G 2/13 (OJ 2016, A28)
5 European Parliament resolution of 17 December 2015 on patents and plant breeders' rights (2015/2981(RSP))
6 CA/D 6/17 Commission Notice on certain articles of Directive 98/44/EC of the European Parliament and of the Council on the legal protection of biotechnological inventions (2016/C 411/03)
7 Snodin et al. Are changes to rules 27 and 28 EPC illegal? CIPA Journal, 46, July-August 2017
8 T1063/18 ("Extreme dark green, blocky peppers")
9 T2734/18
10 European Parliament resolution of 19 September 2019 on the patentability of plants and essentially biological processes (2019/2800(RSP))

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Résumés

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at least provide some immediate clarity for patent applicants in the Agritech sector.

Although in some respects G3/19 provides a pragmatic solution to a thorny legal issue, the way the decision was arrived at may have some negative consequences for legal certainty at the EPO more generally. Whilst the EBA have always had the power to amend their own case law, in adopting the principle of "dynamic interpretation" the EBA appears to have jettisoned the principles of interpretation provided for in the Vienna Convention[11, 12], which led to a different conclusion in G2/12 and G2/13. If the EBA can take completely opposing positions on the interpretation of an Article of the EPC at different times, there can never be any certainty about the definitive interpretation of that Article. The EBA may even interpret Article 53(b) EPC differently again in a future decision if the legal and factual situation changes again. Therefore, whilst G3/19 brings an element of legal certainty to the patent eligibility of plants and animals in the short-term, the cost of this may actually be a reduction in the authority of EBA decisions in general, and the introduction of more widespread uncertainty in the longer term that extends beyond Article 53 EPC to other Articles of the EPC. Indeed, if the AC can overturn G2/12 and G2/13 by simply re-writing the Implementing Regulations, can they overturn other EBA decisions in the same way? Furthermore, the willingness of the EBA in G3/19 to support the position proposed by the President and AC brings into question the independence of the EBA. This seems like a high price to pay for expediency, especially considering that a statutory mechanism already exists for amending the Convention (via diplomatic conference under Article 172 EPC or unanimous vote in the AC under Articles 33(1)(b) and 35(3) EPC, which was not achieved by the AC vote that introduced Rule 28(2) EPC). If, as the proponents of the rule change allege, all the Contracting States were in favour of new Rule 28(2) EPC, an identical outcome could easily have been achieved without these potentially damaging consequences.

Implications for the Agritech sector

The main impact of the EBA decision is that plants and animals obtained by classical breeding steps (i.e. those which only result in a mixing of genes of the parental lines) are no longer patentable before the EPO. The prosecution of European patent applications in this area, which had been stayed awaiting the outcome of this decision, will now resume at the EPO – those applications with filing dates prior to 1 July 2017 being allowed and those with later filing dates requiring amendment to avoid refusal. Although G3/19 allows those applicants to move forward with a degree of certainty, the change in position at the EPO will come as a disappointment to patent applicants in the Agritech sector with significant European markets, and those who filed patent applications based on G2/12, G2/13 and T1063/18. It is, however, likely to be well received by the European Parliament and Commission, who have devoted considerable time to this issue.

Plant breeders will also welcome the decision. To use plants encompassed by patent claims in a breeding program, plant breeders must acquire a license from the patent proprietor. This still applies to non-excluded plants, but the new legislation prevents future patent claims from covering plants obtained by classical breeding. Although these plants can still be protected by a PVR if the new traits are confined to a specific plant variety, a "breeders' exemption" allows the free use of plant varieties protected by PVRs for further breeding. As a result, the extent of overlap between patent and PVR protection has been significantly limited.

The situation is less clear in respect of granted patent claims to plants obtained by classical breeding. Despite prohibiting patents on plants and animals produced by "essentially biological" processes filed after 1 July 2017, G3/19 also confirmed the validity of patents covering such plants and animals that were filed before this date. These patents will be in force for years to come. Since this was a key concern of the EU Parliament and EU Commission, it remains to be seen how these institutions react to the existence of these patents. G3/19 is not binding on national courts, so whether granted claims to plant or animal products obtained by classical breeding can actually be enforced is unclear. Indeed, prior to G3/19, the national legislation of 10 of the 38 EPC contracting states[13-22], including those with the largest plant breeding sectors in Europe (the Netherlands, Germany, and France) already specifically prohibited patent protection for those products.

Agritech companies may now be forced to rely more heavily on the protection afforded by the PVR system to protect their products. However, the scope of protection offered by PVRs is much more limited than that afforded by patents, covering only traits confined to a specific plant variety. The lack of geographical alignment between EU and EPC territories also makes obtaining equivalent territorial coverage more complicated. Whilst a CPVR protects a variety in the 27 EU member states, separate national protection must be sought in EPC contracting states which are not EU member states. For example, the UK's departure from the EU (but not the EPC) means that from 1st November 2020, UKPVRs must be applied for separately, in addition to CPVRs. The fees for a UKPVR are comparable to those for a CPVR covering the whole of the EU. Consequently, protecting varieties in both the EU and UK will be more complicated and expensive for applicants, which could have detrimental effects on the UK Agritech sector, stifling innovation or increasing the cost of new varieties.

One unfortunate result of the EBA decision G3/19 might be that innovators are discouraged from developing new plants or animals, and plant or animal material of significant commercial, environmental, and humanitarian value. Importantly for Agritech innovation in Europe, transgenic plants, and animals, those produced by gene-editing techniques and the biotechnological methods of producing them remain patentable. Regrettably, the current European regulatory regime is anything but conducive to protecting innovative plants and bringing them to market. Innovators in Europe already face some of the most stringent regulations on genetically modified (GM) organisms, reflecting a disproportionate focus on how a plant was produced, rather than the benefits and risks of the traits that it delivers. This irrational situation has been exacerbated by the EU's treatment of precision gene-edited crops as "conventional" GM organisms (thereby limiting their planting and sale too), rather than a technological refinement of traditional mutagenic methods[23] - apparently also ignoring the difficulty in distinguishing gene-editing mutations from those which could occur naturally. As a result, Europe is out of step with regulators elsewhere, such as the US Department of Agriculture and others in South America, a situation which unfortunately results in inadequate protection for consumers and the environment. Whether the UK will implement a more favorable post-Brexit regulatory regime than the EU remains to be seen.

Although G3/19 will rightly meet with some criticism, it does demonstrate the power of political pressure in bringing about legislative change. If EU institutions can be convinced to devote a similar amount of time and resources to reforming the current regulatory framework in this area, Agri-technologies might start to realise their potential in addressing environmental and food security issues.

11 Vienna Convention on the Law of Treaties, Done at Vienna on 23 May 1969. Entered into force on 27 January 1980. United Nations, Treaty Series, vol. 1155, p. 331, Articles 31 and 3

12 Case Law of the Boards of Appeal of the European Patent Office, 9th Edition, III.H.1.1

13 Germany, § 2a (1) No. 1 German Patent Act 1936 (Patentgesetz), as published on 16 December 1980, § 2a (1) No. 1 introduced in October 2013

14 The Netherlands, Article 3(1), lit. c. and d., Dutch Patent Act 1995 (Rijksoctrooiwet 1995), valid from 5 June 2008

15 Italy, Article 45.4.b of the Italian Industrial Property Code (IIPC, Decreto Legislativo 10 febbraio 2005, n. 30 Codice della proprieta' industriale) as amended in 2010

16 Austria, § 2(2) of the Austrian Patent Law 1970 (Patentgesetz) in the version published in the Official Journal on 1 August 2016; - 53 – G 0003/19

17. Belgium, Article XI.5 § 1er, 3°, of the Belgium Code of Economic Law (Code de droit économique - Dispositions relatives au droit d'obtenteur) 2013 amended with effect from 1 June 2019

18. France, Article L611-19, I 3°bis, of the French Patent Act (Code de la propriété intellectuelle), as modified by Article 9 of the Law n° 2016-1087 of 8 August 2016 for the recovery of biodiversity, nature, and landscapes

19. Norway, Section C - chapter IV - 2a.3.2 of the examination guidelines of the Norwegian Intellectual Property Office, although Section 1(4) of the Norwegian patent law (Lov om patenter (patentloven) av 15. desember 1967 nr 9), last amended in 2013, does not deal with products obtained by essentially biological processes

20. Poland, Article 29(1)(ii) of the Polish Act of 30 June 2000 on Industrial Property Law (IPL), as amended by Article 1(4) of the Act of 16 October 2019 (Journal of Laws of 2019. Pos. 2309)

21. Portugal, Article 52(3)c) of the Portuguese Industrial Property Code 2018 (Código da Propriedade Industrial - IPC), Decree-Law 110/2018 of 10 December 2018, which entered into force on 1 July 2019

22. Serbia, Article 9(3) of the Patent Law 2011, in the version of 16 December 2018

23. Judgment of 25 July 2018, C528/16, ECLI:EU:C:2018:583 (http://curia.europa.eu/juris/documents.jsf?num=c-528/162018)

> **These decisions were not received favorably by some groups.**

> **Plant breeders will welcome the decision.**

Practical points for your intellectual property strategy in Europe

Patent applicants in this area should consider the following points when deciding their strategy for protecting inventions concerning plants or animals in Europe:

- Avoid claims directed to plants or animals, and plant or animal material produced by classical breeding techniques in Europe. However, retaining this subject matter in the specification is advisable because obtaining granted claims to these products may be possible, or may develop, in other jurisdictions.
- Although G3/19 only applies to patents granted on or after 1 July 2017 or pending applications filed on or after that date, it is not binding on national courts, so whether granted claims to plant or animal products obtained by classical breeding can be enforced is unclear. If your budget allows, adopting a "wait and see" approach might be advisable.
- If the characteristic traits are confined to a specific plant variety, then consider filing PVR applications covering key plant products.
- Avoid claims to methods including steps of classical breeding (i.e. crossing and selection). Technologies which improve the production of plants or animals or improve the steps of crossing or selection involved in classical breeding are patentable and should be claimed in their own right. Careful claim drafting may be required.
- Patent protection is available for:
- plant or animal derived products that are not propagation material, and in vitro plant or animal cell populations which are treated as microorganisms; and
- transgenic or edited plants or animals, plants or animals obtained by mutagenesis, and/or biotechnological (e.g. transgenic, gene editing) methods of producing them.

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WIPO arbitration and mediation for life sciences disputes

There are a number of different ways of solving a dispute in the life sciences sector. Examining these in detail are Chiara Accornero, Legal Officer and Representative of the WIPO Arbitration and Mediation Center in Singapore, Heike Wollgast, Head, IP Disputes Section, WIPO Arbitration and Mediation Center, and Sally Shorthose, partner in the Bird & Bird Life Sciences and Intellectual Property Group.

In this article we consider the particular challenges and opportunities which arise in the course of life sciences disputes, and the advantages and disadvantages of various types of dispute resolution. Given the investment in time and money that stakeholders invest in their products and collaborations, a simple win/lose situation is not necessarily a possible or desirable outcome. With skill and application, relationships can be mended, and reputations can remain intact without the cost, time, and publicity of a high profile, possibly multijurisdictional, court case.

Life Sciences Disputes

Life sciences disputes have distinctive characteristics that should be considered when designing the most appropriate dispute resolution strategy. For example, intellectual property (IP) is often the crux of development and exploitation and players will want to do their best to protect the value of that IP (whether patents, trademarks, know how or trade secrets). However, with regulatory and patent limitations, lifecycle of life sciences can be relatively short and therefore, avoiding costly and lengthy litigation is of prime interest for all parties involved.

Life sciences collaborations often involve multiple parties, some, or all of whom may be located in different geographic areas thereby bringing in the laws of multiple jurisdictions, as well as different business and legal cultures. This is particularly true as cross-border licensing becomes increasingly commonplace, or in the case of research and development projects, which often have a cross-border dimension. The choice of the appropriate forum is therefore of key consideration, to avoid conflicting results in simultaneous court proceedings in different countries, to ensure the neutrality of the court, avoiding unfamiliar procedural practices and a lack of enforceability of court judgments outside the jurisdiction where they were obtained.

The subject matter-involved in life sciences disputes is often specific, which makes legal and technical expertise essential for resolving such disputes. An understanding of the industry and market practice as well as regulatory aspects is also an important factor.

The issues surrounding life sciences disputes may involve sensitive information, such as a company's trade secrets. This is also crucial in highly sensitive research activities where scientific results must be kept confidential.

> **"The subject matter-involved in life sciences disputes is often specific."**

Collaboration and maintaining relationships are important considerations in the area of life sciences, for example when companies are collaborating to test a drug for licensing.

Alternative Dispute Resolution and Life Sciences Disputes

Mediation and Arbitration

Alternative Dispute Resolution encompasses a range of private dispute resolution mechanisms that allow parties to resolve their dispute in a more flexible, time and cost efficient way, giving parties control over the process and the possibility to select one or several independent mediators and arbitrators.

Mediation[1] is an informal procedure in which the parties request the mediator to assist them to settle their dispute. The mediator facilitates the settlement process by furthering dialogue between the parties and helping them to identify their underlying interests and to reach mutually satisfactory solutions.

Arbitration[2] is a more formal procedure, whereby parties submit their dispute to one or several arbitrators who render a final and binding decision, the arbitral award, which is normally final and not subject to appeal. Expedited Arbitration is an arbitration procedure that is carried out in a short time and at a reduced cost[3].

Mediation and arbitration differ in terms of procedural formality, party control and finality, and each option offers benefits uniquely appropriate to particular circumstances. Mediation and arbitration can also be combined to accommodate the advantages of the different procedures, by having for instance a first mediation phase, followed, in the event of a failure to reach settlement within a designated period of time, by (expedited) arbitration. A first mediation phase allows parties to first put aside the legal merits of the case to mediate commercial interests in an informal setting, prior to resorting to a more formal arbitration procedure, if needed.

Advantages of Mediation and Arbitration for Life Sciences Disputes

The potential of mediation and arbitration in the field of life sciences is significant. Mediation and arbitration have features that, if well managed, can translate into substantial time and cost savings and commercially useful outcomes, making them a more affordable and flexible avenue for resolving life sciences disputes. Their main advantages include:

Party Autonomy: because of their private nature, mediation and arbitration offer parties the opportunity to exercise greater control over the way their dispute is resolved. Depending on their needs, they can select streamlined or more extensive procedures, choose the mediator or arbitrator, rules and procedures, place, and language of the proceedings. The WIPO Mediation, Arbitration and Expert Determination Rules (WIPO Rules) are entirely open to being modified by party agreement, while at the same time providing a firm procedural basis where the parties have not determined otherwise.

Single procedure: mediation and arbitration allow multiple issues and rights arising under several jurisdictions to be addressed in a single process, thereby avoiding the expense and complexity of multi-jurisdictional litigation, as well as the risk of inconsistent results. The international enforcement provided by the New York Convention[4] and more recently the Singapore Convention[5] ensures that arbitral awards and settlement agreements resulting from mediation are complied with internationally. The WIPO Mediation Rules have been updated in 2020 to facilitate the enforcement of settlement agreements as may be required under the Singapore Convention[6].

Time and cost: mediation and arbitration allow parties to save significant costs that the parties would otherwise incur in multi-jurisdictional court proceedings. The WIPO Center places emphasis on containing the time and cost of proceedings conducted under WIPO Rules. A typical WIPO Mediation takes four months but may be completed more rapidly at the request of the parties, for instance to ensure compliance with timelines in court referrals. Parties may also opt for the procedural framework established by the WIPO Expedited Arbitration Rules; WIPO expedited arbitration proceedings

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Résumés

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1 https://www.wipo.int/amc/en/mediation/.
2 https://www.wipo.int/amc/en/arbitration/.
3 https://www.wipo.int/amc/en/arbitration/what-is-exp-arb.html.
4 United Nations Convention for the Recognition and Enforcement of Foreign Arbitral Awards of 1958.
5 United Nations Convention on International Settlement Agreements Resulting from Mediation of 2018.
6 https://www.wipo.int/amc/en/rules/.

have been concluded with a final award in as little as five weeks.

Expertise: in mediation and arbitration, parties can select their mediator or arbitrator. The WIPO Center maintains a list of mediators and arbitrators specialized in all areas of IP (including life sciences) that parties can appoint in WIPO cases[7]. The WIPO Rules[8] contain specific provisions regarding technical evidence that may be useful in life sciences disputes, such as in relation to access to samples and testing, the scope of discovery, the selection of suitable technical experts and protection of trade secrets and other confidential information.

Confidentiality: except where otherwise required by law, mediation and arbitration allow parties to keep the proceedings and the outcome confidential. Confidential dispute resolution helps parties to focus on the merits of their dispute without fear of adverse publicity and to preserve the parties' business relationships and reputations. The WIPO Rules set out extensive provisions governing the confidentiality of the existence of the mediation and arbitration, disclosures made during the process and any outcome[9].

Preserving business relationships: mediation gives the parties the opportunity to go beyond the legalistic resolution of the dispute to negotiate creative solution that satisfy their business interests, including preserving existing business relationships, or forging new ones. 70% of WIPO mediation procedures settle and even in arbitration, 33% of WIPO cases are settled by the parties before any formal decision was issued[10].

How to Submit a Dispute to WIPO Mediation and Arbitration

Mediation and arbitration are consensual procedures, in that they can only be used if all parties consent to submit their dispute to it. For future disputes, such consent can be achieved through the inclusion of a mediation or arbitration clause into a contract, and for existing disputes through the conclusion of a mediation or arbitration submission agreement. To facilitate such party agreement, the WIPO Center provides recommended contract clauses and submission agreements[11]. It also offers access to an online Clause Generator[12] that proposes additional elements based on WIPO case experience.

To facilitate submission of a dispute to mediation in the absence of a mediation agreement between the parties (for example in infringement disputes or in cases pending before the courts), the WIPO Center offers the option for a party to submit a unilateral Request for Mediation to the WIPO Center[13]. The WIPO Center may then assist the parties to consider the Request or, upon request, may appoint an external neutral to provide the required assistance[14].

7 https://www.wipo.int/amc/en/neutrals/.

8 WIPO Arbitration Rules, Articles 50-54; WIPO Expedited Arbitration Rules, Articles 44-48.

9 WIPO Arbitration Rules, Articles 75-78; WIPO Expedited Arbitration Rules, Articles 68-71; WIPO Mediation Rules, Articles 15-18. In an expedited arbitration administered by the WIPO Center, the arbitrator issued a protective order pursuant to the WIPO Expedited Arbitration Rules to prevent the claimant from accessing certain confidential documents disclosing the respondent's business secrets.

10 Article 14(a) of the WIPO Mediation Rules allows the mediator to promote the settlement of the issues in dispute between the parties in any manner that the mediator believes to be appropriate. Also in arbitration, Article 67 provides that arbitrators can suggest that parties explore settlement at such times as they may deem appropriate; if the parties agree on a settlement of the dispute before the award is made, arbitrators may terminate the arbitration and record the settlement in the form of a consent award, if requested by the parties.

11 https://www.wipo.int/amc/en/clauses/index.html.

12 https://www.wipo.int/amc-apps/clause-generator.

13 Article 4 of the WIPO Mediation Rules. The Unilateral Request for Mediation is available at https://www.wipo.int/amc-forms/adr/mediation.

14 Article 4(b) of the WIPO Mediation Rules.

15 https://www.wipo.int/amc/en/center/specific-sectors/lifesciences/.

16 https://www.wipo.int/amc/en/center/role.html.

The WIPO Center's Experience in Life Sciences

The Role of the WIPO Arbitration and Mediation Center

The WIPO Center is part of the World Intellectual Property Organization (WIPO) and has offices in Geneva, Switzerland, and Singapore. The WIPO Center is the only international provider of specialized ADR services for IP and technology disputes.

To date, 15% of arbitration and mediation cases filed with the WIPO Center relate to life sciences[15], with a noticeable increase in recent years. These cases have involved research institutes, universities, hospitals, SMEs, and large-sized companies involved in the pharmaceutical, biotechnology and medical devices industries.

In its role as administering institution[16], the WIPO Center maintains strict neutrality and independence and administers mediation and arbitration cases under the WIPO Rules. This includes assisting parties in selecting a suitable mediator or arbitrator[17]; offering active case management, including guidance on the application of relevant procedural rules. The WIPO Center also makes available online case administration options, including an online docket – WIPO eADR[18] – and videoconferencing facilities[19]. While these tools have been used occasionally in the past, we observe a growing interest and use by parties in most recent cases.

Case Examples

Over the last years, the WIPO Center has administered several disputes in the area of life sciences. Some of these cases are summarized below, to illustrate the issues that can arise in such disputes and how they can be addressed by mediation and arbitration.

A WIPO Mediation of a Biotech Dispute

A French and a German company entered into a collaboration agreement for the development of a human antibody for the treatment of a major disease. Two years later, a US corporation acquired the French company. Alleging that the US corporation withheld certain payments required under the collaboration agreement, the German company filed an action for breach of contract against the US corporation in the United States. The US corporation filed counter-claims of rescission and breach of contract against the German company. After more than one year of prolonged and expensive court proceedings, the parties submitted a joint request for WIPO Mediation.

The WIPO Center suggested to the parties potential mediators with specific expertise in life sciences and mediation experience, as required by the parties in their mediation agreement. The parties agreed on a US IP lawyer with considerable mediation experience.

The mediator conducted meetings with the parties in the United States. As a direct consequence of the facilitative role played by the mediator, the parties settled their dispute six months after the commencement of the mediation.

A WIPO Arbitration of a Pharma Dispute

A European biotech company, holder of several process patents for the extraction and purification of a compound with medical uses, entered into a license and development agreement with a large pharmaceutical company. The parties included in their contract a clause stating that all disputes arising out of their agreement would be resolved by a sole arbitrator under the WIPO Arbitration Rules.

Several years after the signing of the agreement, the biotech company terminated the contract, alleging that the pharmaceutical company had deliberately delayed the development of the biotech compound. The biotech company commenced WIPO Arbitration claiming substantial damages.

The WIPO Center proposed a number of candidates with considerable expertise of biotech/pharma disputes, one of whom was chosen by the parties. Having received the parties' written submissions, the arbitrator held a three-day hearing in Geneva (Switzerland) for the examination of witnesses. This not only served for the presentation of evidence but also allowed the parties to re-establish a dialogue. In the course of the hearing, the arbitrator began to think that it would be in the interest of the parties to continue to cooperate towards the development of the biotech compound.

On the last day of the hearing, the parties accepted the arbitrator's suggestion that they should hold a private meeting (please add reference to Article 67 of the Rules). As a result of that meeting, the parties agreed to settle their dispute and continued to cooperate towards the development and commercialization of the biotech compound.

Conclusion

As has been described above, there are a number of different ways of solving a dispute in the life sciences sector. The advantages of alternative forms of dispute resolution are that they can provide flexibility, expertise, and a confidential forum within which transparency is encouraged and an opportunity to explore innovative solutions is provided, which solutions often result in a continuation of business relationships.

15 https://www.wipo.int/amc/en/center/specific-sectors/lifesciences/.

16 https://www.wipo.int/amc/en/center/role.html.

17 The WIPO Center maintains an international open-ended panel of mediators and arbitrators from around the world with expertise in intellectual property and technology, including in the area of life sciences.

18 WIPO eADR allows parties, mediators, and arbitrators in a WIPO case to securely submit communications electronically into an online docket. All case information filed in WIPO eADR is protected and encrypted to ensure confidentiality. Further information on WIPO eADR is available at www.wipo.int/amc/en/eadr/wipoeadr.

19 When parties and neutrals in WIPO cases are based in different locations, they have occasionally agreed to hold meetings or hearings remotely via online tools, including videoconferencing facilities, or telephone.

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The future of medicine: ATMPs

Fieldfisher's Cliodhna McDonough, Legal Director, James Gallagher, Associate, and Emily Lockey, trainee solicitor, look at this critically important and rapidly developing area.

Patient medical treatments are seeing a paradigm shift towards one of cure from that of a traditional disease management approach. Advanced therapy medicinal products (ATMPs) are a group of medicines for human use that are based on genes, tissues or cells which hold promise as treatments for a variety of previously untreatable and high-burden diseases.

There are three main types of ATMP:

1. **Somatic cell therapy products** consist of cells or tissues that have been subject to substantial manipulation so that biological characteristics, physiological functions, or structural properties relevant for the intended clinical use have been altered.
2. **Gene therapy medicinal products** contain an active substance consisting of a recombinant nucleic acid used in, or administered to humans to regulate, repair, replace, add or delete a genetic sequence, with the therapeutic, prophylactic or diagnostic effect relating directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence.
3. **Tissue engineered products** contain or consists of engineered cells or tissues, and is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing, or replacing a human tissue.

In addition, some ATMPs referred to as **combined ATMPs** may also contain one or more medical devices as an integral part of the medicine e.g. cells embedded in a biodegradable matrix or scaffold.

In the EU, ATMPs are primarily governed by Regulation 1394/2007 ("the ATMP Regulation") which provides for classification and evaluation of these products by a specialized committee within the European Medicines Agency ("EMA"), the Committee for Advanced Therapies ("CAT"),

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who prepare a draft opinion before the Committee for Medicinal Products for Human Use ("CHMP") adopts a final opinion and a market authorization ("MA") is granted by the EU Commission. The ATMP Regulation also empowers Member States to permit the use of advanced therapies that are not authorized by the EU Commission, subject to certain conditions being satisfied, the so-called "hospital exemption".

Obstacles getting to market

However, there are tremendous challenges to the commercialization of these products, which require new and innovative approaches to ensure patient safety and efficacy of the products that is comparable to that of traditional pharmaceutical products. The success of ATMPs is dependent on the use of science and risk-based approaches to their development and manufacture. Over the next few years, the regulatory requirements and industry practices will continue to be significantly developed and become benchmarks.

At a development stage, recent research carried out by the Alliance for Regenerative Medicine (ARM) has highlighted that whereas the number of new ATMP clinical trials has increased significantly over a 4-year period on a global scale (+32% from Jan 2014 to June 2019), with notable growth in North America and Asia, this trend is not reflected in Europe. Within Europe, significant country-by-country variability in the number of clinical trials, speed of assessment, and time for approval of clinical trials has also been observed, with the UK, Spain, and France attracting the highest number of ATMP clinical trials during the same 4-year period (112, 102, and 101, respectively). Survey respondents also indicated that the most important criteria for selecting a clinical trial site and a host country are the availability of local clinical expertise and suitable healthcare facilities, followed by the speed of approval, the quality of review, and the expertise of local regulatory authorities. The authors also speculated that fragmentation of regulatory/ethical guidance and a lack of harmonization on various other factors (e.g. donor testing requirements, patient information consent forms, contracting agreements, etc.) across European countries may also make for a less attractive environment for clinical trials. As a further example, a possible cause of the relatively low number of gene therapy clinical trials in Europe compared to North America was also traced back to the classification of some of these therapies as GMOs, requiring specific approval by different national authorities, a step that adds complexity to the clinical trial authorization process and often extends the time required for approval.

From a commercial point of view, ATMPs present a different scenario to that of pharmaceutical medicines in that there is not a classic supply and demand model largely because ATMP therapies are more likely have a patient pull to fulfil an unmet medical need. In addition, the clinical development of ATMPs does not typically follow conventional clinical trial phases unlike traditional medicine. It is often the case with rare disease indications, that ATMP clinical programs are compressed into one or two clinical studies, followed by conditional approval with post-marketing commitments. To this end, ATMPs often utilize Early Access Programs, which allow for supply to patients prior to marketing approval.

Compliance with good manufacturing practice (GMP) is mandatory for ATMP products. New GMP guidelines on ATMPs from the European Commission (EC) came into force in 2018. These guidelines apply to ATMPs with market authorization, investigational ATMPs and those administered to patients under Article 3(7) of Directive 2001/83/EC (the "hospital exemption").

The guidelines seek to reflect the rapid technological and medical advancements being made in the field and recognize the need for a certain degree of flexibility so that manufacturers can implement measures most appropriate to the specific characteristics of their product. As such, the guidelines allow for a risk-based approach, giving manufacturers more autonomy over the production process.

The Pharmaceutical Inspection Co-operation Scheme Committee (PIC/S) has expressed concerns about the impact of the new GMPs on public health and the safety of patients, suggesting that the new guidelines lower the GMP standards.

The PIC/S produce their own GMP guidelines, which, until now, have been developed in parallel with EC guidelines. The development of stand-alone EC guidelines on ATMPs has therefore led to an internationally non-harmonized approach to GMP regulation.

Résumés

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Cliodhna is Legal Director at Fieldfisher specialising in Life Sciences, Food and Beverage, Cosmetics and Healthcare Regulatory Law.

James Gallagher
James is an Associate in the Public and Regulatory Department, based in Fieldfisher's offices in Dublin. He advises both private and public sector clients in relation to public and regulatory law issues, with a particular focus on healthcare, life sciences and food regulation.

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Emily is a trainee solicitor at Fieldfisher. She has a particular interest in the life sciences and healthcare sectors, having previously worked as a medical doctor in the NHS.

> **"ATMPs are a group of medicines for human use that are based on genes, tissues or cells."**

The PIC/S are currently developing revisions to their own guidelines to account for the international developments in the regulation of ATMPs, with particular attention given to the EC guidelines, whilst also addressing any concerns related to patient safety and the proportionate regulation of ATMPs.

The challenge for manufacturers will now be to check whether their current established processes are in accordance with the new guidelines, including any revisions made to the PIC/S guidelines, or whether any changes or additional activities will be necessary.

The ATMP field is rapidly moving from pure science focus, led by small industry and universities, to a focus on how to commercialize such therapies. The high cost of ATMPs is predominantly driven by the small scale of manufacturing, the high degree of scientific testing required for the products and the need

for ongoing patient monitoring testing which combined requires significant capital investment. Reimbursement of ATMPs is frequently mentioned as a major hurdle, both from a developer and health technology assessment (HTA) body point of view, as the manufacturing of ATMPs is considered more expensive by nature and is expected to pose pressure on healthcare budget. Combining the active ATMP pipelines with the prospect of healthcare budget constraints, sustainable ATMP reimbursement has become the next major challenge in this field.

Talking logistics: Supply chain challenges

One of the main barriers to commercial viability for ATMPs is the supply chain, which contributes significantly to the overall cost of goods and is limited by infrastructure, temperature requirements and, of course, the time frame for transportation taking into consideration cell viability. Poor co-ordination of supply and logistic conditions have the potential to negatively affect the quality of ATMPs.

Unlike traditional medicines, living cells have a short shelf life of between 1 to 3 days at ambient temperature conditions. Therefore, ATMPs require a quick delivery time from finished product to administration to a patient. Manufacturing constraints and the short shelf life of the product require the implementation of tight controls on logistical arrangements, which adhere to Good Manufacturing Practice (GMP), Good Distribution Practice (GDP) and ICH Q10 to ensure that patients receive these products safely at the correct time and within the shelf life.

Shipping logistics for example, require tailored temperature conditions, preservation techniques, and quality-control solutions. Due diligence must be performed to ensure that shipping companies have been evaluated to regulatory standards and that product quality oversight is a priority. Today, technology enables almost complete remote tracking of shipments while in transit be it with sophisticated geo-locating systems or sensors that automatically transmit while travelling with the product.

Clear traceability documentation is essential throughout the supply chain as is compliance with the trace-and-track regulations prescribed by GDP and the EU Falsified Medicine Directive to monitor and control the safety and supply of medicines for human use. For example, to minimize risk during transit, ATMP packaging labelling should indicate both the nature of the product and the special handling of product containers. It is also important that all customs paperwork and permissions are in order to ensure that the therapeutic agent is delivered to the correct clinical site, the correct patient and at the correct time.

> **“Combined ATMPs may also contain medical devices as an integral part of the medicine.”**

As part of the journey to the patient, the therapy must be delivered from the manufacturer into the relevant country's facility where it will be stored until Qualified Person (QP) release. The QP should be familiar with sample collection, supply chain and manufacturing processes. Clinical sites should also provide appropriate facilities and licenses for the storage and preparation of ATMPs. The absence of for example deep freezers, liquid nitrogen storage, cryopreservation, and GMO laboratories may restrict the use of clinical sites.

Traceability and control remains a consistent requirement throughout the supply chain. The challenge is that a therapy must not be administered to the wrong person; if that happens, the results could be catastrophic. Thus, a chain of custody is paramount, as the therapy changes hands among supply chain participants. The stakeholders of an ATMP supply chain are interdependent and must communicate and share data to provide transparency along the channel, while also assuring that sensitive patient data is appropriately protected. Manufacturers should outline a robust front-end supply chain and logistics planning strategy along with a thorough risk management assessment to help identify which factors in the chain might in turn influence manufacturing decisions.

As the shift from “one-size fits all” towards personalized medicinal strategies for biological therapies continues apace, the regulatory landscape associated with the development and commercialization of these treatments will continue to evolve. The challenges faced by manufacturers in adapting their processes and systems to ensure compliance with these requirements will also continue to change as new treatments and technologies are considered for scale-up and commercialization. For the organizations that can navigate this shifting landscape however, the rewards associated with successfully delivering life-changing and often lifesaving treatments to patients are within reach.

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The CRISPR-Cas9 gene editing system – non-complex technology; complex patenting

Osamu Yamamoto, patent attorney and partner at Yuasa and Hara, gives an IP overview of this important technology.

Inventor of CRISPR-Cas9

The CRISPR-Cas9 gene editing system has attracted attention in recent years due to its relative simplicity and its many potential applications, as a third-generation technique, following ZFN (Zinc Finger Nuclease) and TALEN (Transcription Activator-Like Effector Nuclease).

CRISPR is an abbreviation for “Clustered Regularly Interspaced Short Palindromic Repeat” and is a repeat sequence that was discovered in E. coli by Dr. Yoshizumi Ishino of Osaka University (now Prof. of Kyushu University) and others in 1987[1]. This sequence was known as a locus that served as a type of acquired immune system in prokaryotes, although its detailed role was not known. The research group of Prof. Jennifer Doudna and Prof. Emmanuelle Charpentier focused on the protein designated Cas9 (CRISPR associated protein 9), and discovered that:

(i) foreign DNA is incorporated into CRISPR domain by Cas9;
(ii) Cas9 forms a complex with guide-strand RNA; and
(iii) Cas9 cleaves double-stranded DNA complementary to guide-strand RNA.

Osamu Yamamoto

Based on their discovery, the University of California and the University of Vienna (UC *et al*) filed a US provisional application on 25 May 2012. Earlier than UC *et al*, Vilnius University in Lithuania filed a US provisional application relating to the technology on 20 March 2012. Neither of the US provisional applications included any data showing application of CRISPR-Cas9 in eukaryotic cells.

Shortly after the filings by the two groups, three other groups filed US provisional applications showing practical application of CRISPR-Cas9 to eukaryotic cells. The three groups to file were: Toolgen Incorporated, on 23 October 2012, Sigma Aldrich Corporation, on 6 December 2012, and Broad Institute Inc. and MIT (Broad *et al*), on 12 December 2012. Each of the three groups filed PCT applications claiming priority from the first filed application (and some others).

Patents in Japan

Please refer to the table (above right) showing the status in Japan of the PCT applications.

PCT/US2013/032589, filed by UC *et al* entered the national phase in Japan and was allowed on 8 May 2018 (JP 6343605). It covers broader concepts than the applications by the other groups. Additionally, a divisional application was recently granted patent as JP 6692856, and one further divisional application remains pending.

Résumé

Mr. Yamamoto

Mr. Yamamoto is a patent attorney, and a partner of YUASA and HARA. He has extensive experience in pharmaceutical and biotechnology research and development at a chemical company for ten years before specializing in intellectual property. He has represented a variety of companies in the fields of pharmaceuticals, biotechnology, diagnostics, and food and beverages. He is experienced in all aspect of patent issues, including drafting patent applications, dealing with Office Actions, providing expert opinions, defending or attacking patent rights in invalidation trials and oppositions, and patent infringement litigations.

[1] J. Bacteriol. 169, 5429 - 5433 (1987)

	Vilnius Univ.	UC *et al.*	Toolgen	Sigma Aldrich	Broad *et al.*	
First filing	Mar. 20, 2012	May 25, 2012	Oct. 23, 2012	Dec. 6, 2012	Dec. 12, 2012	Dec. 12, 2012
PCT	PCT/US2013/033106	PCT/US2013/032589	PCT/KR2013/009488	PCT/US2013/073307	PCT/US2013/074819	PCT/US2013/074743
Japan						
Granted	JP6423338	JP 6343605 JP 6692856	JP6517143	JP6620018	JP 6203879 JP 6495395 (Opposition 2019-700804) JP 6420273 JP 6726225	JP 6545621 (Opposition 2020-700032) JP 6723094 (Case 2: Hei 31 Gyo-ke 10011)
Pending	Application 2018-196574	Application 2019-210828	Application 2017-155410 (Appeal 2020-000013) Application 2020-000091	Application 2018-183815	Application 2019-039723 Application 2019-039724	Application 2019-035911
Rejected			Application 2015-176407 (*Appeal 2017-019510)	Application 2017-115672 (*Appeal 2018-006381)	Application 2015-547573 Application No. 2016-117740 (Appeal 2017-013795, Case 1: Hei 31 Gyo-ke 10010)	

* In both cases, the aplications were rejected due to lack of inventive step over Science; Aug 2012; Vol. 337; pp. 816 - 821

As for Broad *et al*, a divisional application derived from the national phase application entered in Japan from PCT/US2013/074819 was allowed on 31 July 2017 (JP 6203879) and was the first granted patent on CRISPR-Cas9 system in Japan among the five groups. From PCT/US2013/074819, as of the end of June 2020, one divisional application and two second generation divisional applications have been granted as JP 6420273, JP 6495395, and JP 6726225, respectively; two divisional applications are pending at the examination stage. Further, one divisional application (Application 2016-117740) was rejected by the JPO appeal board (Appeal 2017-013795), and the case was brought to the Intellectual Property High Court (IPHC), and the IPHC rejected the demand (Case 1 below).

Broad *et al.* also filed the national phase applications from PCT/US2013/074743 as shown in the table.

The IPHC decisions on the two patent applications of Broad *et al*, rendered on 25 February 2020, are explained below.

Case 1

As stated above, one divisional application was rejected by the JPO appeal board (Appeal 2017-13795). The reasons for rejection were prior art effect rejection* under Article 29(2) of the Patent Act and lack of inventive step under Article 29-2 of the Patent Act. A lawsuit for revocation before the IPHC was filed against it (Hei 31 Gyo-ke 10010).

The Claim in question is shown below.

Claim 1

An engineered, non-naturally occurring CRISPR-Cas vector system, comprising one or more vector systems comprising:

(a) a first regulatory element operably linked to a nucleotide sequence encoding a CRISPR-Cas system polynucleotide sequence comprising a guide sequence, a tracrRNA and a tracr mate sequence, wherein said guide sequence hybridizes to one or more target sequences in a polynucleotide locus in a eukaryotic cell;

(b) a second regulatory element operably linked to a nucleotide sequence encoding a type II Cas9 protein; and

(c) recombination template,

wherein components (a), (b), and (c) are located on the same or different vectors of the system, and the system further comprises one or more nuclear localization signal(s) expressed with the nucleotide sequences encoding Cas9 protein, and thereby the guiding sequence targets the one or more polynucleotide loci in a eukaryotic cell, and Cas9 protein cleaves the one or more polynucleotide loci, whereby the sequence of the one or more polynucleotide loci is altered.

The IPHC focused on the issue of prior art effect rejection under Article 29(2) of the Patent Act. Broad *et al* asserted that Citation 1 (WO2014/089290; Sigma-Aldrich PCT/US2013/073307) did not provide any experimental evidence on sequence modifications of the target site and did not provide any reasonable basis of feasibility for adapting CRISPR-Cas9 technology to eukaryotic cells. However, the IPHC dismissed Broad etc. assertion stating that the facts "guide RNA leads Cas9 protein to a target part in genome sequences in eukaryotic cells, and Cas9 leads cleavages of double strand genome DNA at the target part, and the cleavage of the double strand is repaired in the process of DNA repair in a manner the genome sequences are modified" is substantially disclosed in Citation 1. The IPHC did not judge the issue of inventive step in view of Citation 2 (Science; Aug 2012; Vol. 337; pp. 816-821: by group of Prof. Doudna).

> **"The reasons for rejection were prior art effect rejection."**

Case 2

The national phase application entered in Japan from the Broad et al application. PCT/US2013/074743 was allowed on 20 May 2019 (JP 6545621) and an opposition was subsequently filed against the patent on 17 January 2020 (Opposition 2020-700032). The patented claims set forth "tracr sequence has a length of 40 or more nucleotides".

The subject of Case 2 is a divisional application (Application 2016-128599) derived from the national phase application of PCT/US2013/074743.

The JPO appeal board rejected the application on ground of prior art effect under Article 29(2) of the Patent Act and lack of inventive step under Article 29-2 (Appeal 2017-13796). A lawsuit for revocation was filed before the IPHC (Hei 31 Gyo-ke 10011).

The Claim in question is shown below.

Claim 2

An engineered, non-naturally occurring CRISPR-Cas vector system, comprising one or more vector system comprising:

(a) a first regulatory element operably linked to one or more nucleotide sequences encoding one or more CRISPR-Cas system guide RNAs which hybridize to a target sequence in a polynucleotide locus in a eukaryotic cell, said guide RNAs comprising a guide sequence, a tracr sequence and a tracr mate sequence; and

(b) a second regulatory element operably linked to a nucleotide sequence encoding a type II Cas9 protein, wherein the protein comprises nuclear localization signal(s),

wherein components (a) and (b) are located on the same or different vectors of the system, the tracr sequence has a length of 30 or more nucleotides, thereby said one or more guiding RNAs targets the polynucleotide loci in a eukaryotic cell, and the Cas9 protein cleaves the polynucleotide loci, whereby the sequence of the polynucleotide loci is altered, wherein the Cas9 protein and the guide RNAs do not naturally occur together.

As for prior art effect rejection, the JPO appeal board did not admit that defining the length of tracr sequence "30 or more nucleotides" constitutes a substantial difference from the invention of Citation 1 (WO2014/089290; Sigma-Aldrich PCT/US2013/073307), and rejected the application under Article 29(2). On the other hand, the IPHC judged that the technical idea of defining the length of tracr sequence per se did not appear in Citation 1, and consequently defining the length of tracr sequence "30 or more nucleotides" does constitute a substantial difference from the invention of Citation 1. The IPHC concluded that the JPO decision was erroneous.

As for inventive step, the JPO appeal board did not admit inventive step over Citation 2 (Science; Aug 2012; Vol. 337; pp. 816-821: by the group of Prof. Doudna) with respect to the length of tracr sequence. The length disclosed in Citation 2 is "26 nucleotides," whereas that disclosed in the claim of the application is "30 or more nucleotides". However, the IPHC concluded that the JPO decision was erroneous, and stated that the effect of improving the efficiency of genome-modification in eukaryotic cells by

adopting the length of tracr sequence "30 or more" should be regarded as an effect exceeding the expectations of a person skilled in the art, since there were no science papers or patent documents available at the time of the priority date disclosing that CRISPR-Cas system were applicable to eukaryotic cells.

As a result of the IPHC decision, the case was brought back to the JPO appeal board and then patented by the JPO appeal board as JP 6723094.

Patent pool

The foregoing relates to foundational patents on CRISPR-Cas9 technology. Subsequently, as in many other countries, a considerable number of patent applications have been filed in Japan concerning CRISPR-Cas9 technology. If any person wishes to apply CRISPR-Cas9 technology to pharmaceutical developments etc., it will be necessary to use not only the foundational concept, but also a number of improved techniques. This means that it will be necessary to obtain licenses from many patentees, which is likely to be both time consuming and costly. Under such circumstances, use of a patent pool system that facilitates collectively obtaining licenses for patents relating to CRISPR-Cas9 technology has attracted attention. One example is that MPEG LA in the US has begun calling for participation in the patent pool for CRISPR-Cas9 technology. However, license situation remains opaque, and to achieve success a considerable number of obstacles will need to be resolved and overcome.

> **A number of obstacles will need to be resolved.**

Technological developments in Japan

Although Japan does not hold an initiative in gene editing technology, many groups are actively conducting research and development. For example, Modalis Therapeutics Corporation (formally EdiGENE, a venture to develop pharmaceuticals using CRISPR-Cas9 technology) has developed new platforms CRISPR-GNDM (Guide Nucleotide Directed Modulation) that is effective for the development of efficacious therapeutics for hereditary genetic diseases[2].

As noted above, since both the foundational patents of Broad etc. and UC *et al* recite Cas9 in the Claims, use of other Cas polypeptides may not infringe the patents. Prof. Tomoji Mashimo *et al* of Osaka University developed an E. coli - derived TypeI-ECRISPR system (CRISPR-Cas3) and found that the system is more efficient in gene editing than Cas9 system, with no prominent off-target effects[3]. To confirm the therapeutic potential of the system, the group carried out Cas3-based repair of the DMD gene in induced pluripotent stem cells from a patient with Duchenne muscular dystrophy.

Target-AID invented by Prof. Keiji Nishida *et al* of Kobe University is a gene editing technique that introduces mutations by transforming nucleotides without cutting DNA[4]. New gene editing tools are being developed in Japan.

**note: prior art effect rejection (or secret prior art rejection) arises due to the existence of a prior filed application disclosing the same invention in the specification but not published as of the filing date of the application in question*

2 https://www.businesswire.com/news/home/20200331005248/en/Modalis-Obtains-Access-Foundational-CRISPR-IP
3 Nature Communications 10 Article number: 5302 (2019)
4 https://www.nature.com/articles/d42473-019-00325-y

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The impact of the United States, Mexico, and Canada Agreement (USMCA) on the Pharmaceutical industry: patent rights and test data exclusivity

Marina Hurtado-Cruz, Partner at Baker McKenzie and Head of the Patent Practice in Mexico, discusses the life sciences impact of USMCA.

The new agreement between the United States, Mexico, and Canada, came into force as of 1 July 2020. The USMCA is one of the most complex and complete agreements that these three countries have ever negotiated. This agreement replaced the North American Free Trade Agreement (NAFTA) that had been in place since 1 January 1994.

The year 1994 marked the beginning of a process of regional integration of the countries of North America. Canada, Mexico, and the United States had subscribed to NAFTA, the main objective of which was to create a free trade area and eliminate several product tariffs. NAFTA incorporated the regulation of goods, services, IP rights, and provisions to safeguard investment in the three countries.

NAFTA and the agreement on Trade-Related Aspects of Intellectual Property (TRIPS), which were negotiated at the same time, were paramount for Mexico in terms of IP rights. In the 90s, during the NAFTA and TRIPS negotiations, a new regulation for industrial property was introduced in Mexico in order to meet commitments with its commercial partners. Of the three countries, Mexico had to make the most changes to its local regulation with significant changes in the patent field. Changes were positive and included granting protection for a broader range of inventions, including pharmaceuticals, and extension of patent protection period to 20 years.

Intimate economic ties had been developed between the three countries after NAFTA came into force. Trading volume had been significant. Every day, the United States conducted more than US $3.6 billion in trade with Mexico and Canada. From 1997 to 2017, trade under NAFTA increased almost four times, which allowed companies in the region to take advantage of

Marina Hurtado-Cruz

Résumé

Marina Hurtado-Cruz

Marina Hurtado-Cruz leads the Baker McKenzie's Patent practice in Mexico. With more than a decade of experience handling sophisticated intellectual property matters, she advises on a broad range of areas including technology transfer, licensing, patent linkage, prosecution and litigation of patents, utility models and industrial designs. In addition to this, she practices in the areas of health law and consumer goods and regularly advises clients on advertising and promotion law. Marina manages the patent portfolios of international consumer goods and pharmaceutical companies. She coordinates prosecution, audits, due diligence, freedom to operate and infringement opinions, licensing, and strategy development for the protection, prosecution and defense of these rights. She is well acquainted with the relationship between the Patent Office and the Healthcare authorities. Marina has an LLM from the Munich Intellectual Property Law Centre and holds a Diploma in Sanitary Regulation for the Pharmaceutical Industry. She covered the absence of a Legal Director in an international pharmaceutical company in agreement with Baker Mckenzie. Recently, Marina was appointed by the Secretary of the Mexican Ministry of Foreign Affairs, as ad honorem external advisor on intellectual property issues to collaborate in the development of IP public policies in Mexico.

the elimination of tariffs, save costs, have protection of their investments under a system of rights and dispute settlement, and in turn become more competitive.

Over the years, NAFTA began to lose competitiveness in the face of the economic reality of the North American region. There was a need to modernize and update the agreement to make it more consistent with the new economic situation and include cutting-edge elements in terms of a new generation of trade agreements. The reason behind modernizing NAFTA is to strengthen trade relations in the region, and to become more competitive against other economic integration phenomena, particularly those that have been developing in Asia.

Thus, in 2017, the United States decided to renegotiate NAFTA because of a campaign promise of the Donald Trump administration. After more than 13 months of negotiation, the new agreement was signed by the parties during the G20 Summit that took place in Buenos Aires, Argentina, at the end of 2018.

USMCA reinforces regulatory systems, E-commerce, and the protection of IP rights. It will affect a number of sectors, healthcare being one of them. Within the healthcare industry, patents and test data exclusivity protection were among the most controversial topics during the negotiations.

The most relevant issues regarding patents and test data exclusivity are the following:

Patents

Patents are an indispensable tool for the protection of inventions and the investments that goes into them. Therefore, strengthening the protection and enforcement of IP rights, including patents, was a priority during the USMCA negotiations. The USMCA states that the three countries shall process patent applications in an efficient and timely manner, provide procedures to expedite examination and avoid unreasonable or unnecessary delays in the issuance of a patent.

In this regard, for some years, these countries have implemented Patent Prosecution Highway (PPH) programs to speed up patent prosecution. Under this program, the claims of an application have to be adapted to the claims granted by the other participant patent office. If the examiner considers that the new claims comply with local law, the patent may be issued in the short term. In Mexico, the PPH can be requested at any time before substantial examination starts and will be analyzed once the application is published and the third-party observation period has concluded.

The PPH has been a very useful tool in accelerating the granting of patents in Mexico. Currently, Mexico has signed agreements with various patent offices including not only the United States Patent and Trademark Office (USPTO) and the Canadian Intellectual Property Office (CIPO), but also with the European Patent Office (EPO), the Japan Patent Office (JPO), the Spanish Patent Office, among others. To strengthen this point, in January 2020, the USPTO and the Mexican Institute of Industrial Property (IMPI) representatives signed an agreement to increase investment, stimulate innovation, speed up patent prosecution and combat infringement of IP rights.

> **The USMCA is one of the most complex and complete agreements that these three countries have ever negotiated.**

Furthermore, the USMCA states that a patent term adjustment proceeding must be implemented to compensate for unreasonable delays of patent offices to grant a patent (in any field of technology). An unreasonable delay is when the patent is issued more than 5 years from the date of filing or 3 years after a request for examination, whichever is later.

In addition to patent term adjustments granted by patent offices, the USMCA establishes the possibility of another patent term adjustment for pharmaceutical products. In order to commercialize a pharmaceutical product, a marketing authorization must be obtained from a health authority. The USMCA outlines that each country shall make best efforts to process applications for marketing approvals in an efficient and timely manner, avoiding unreasonable or unnecessary delays. Furthermore, each country will make available patent term adjustment proceedings (when the pharmaceutical product is protected by a patent) to compensate the patent owner for unreasonable delays in obtaining marketing authorization that affect patent rights.

This has been a sensitive issue for Mexico since the responsible authorities in the country have shown some resistance to establishing procedures to correct patent validity terms. In Mexican legislation, patent protection is granted for a non-renewable term of 20 years starting from the date on which the application is filed. Although under the USMCA the parties are obliged to compensate for unreasonable delays, in practice, this is not a relevant issue for IMPI. This is because during the negotiations of the USMCA, IMPI issued internal guidelines for examiners stating that the resolution of a patent procedure should not take more than 5 years from the filing date.

This provision included in IMPI's internal guidelines was further confirmed in the New Mexican Industrial Property Law that was published in July 2020 and will became effective in November 2020. However, in this new Law, the obligation to compensate pharmaceutical patent terms for unreasonable delays in the issuance of a marketing authorization was not also included. In the case of Canada, a patent term restoration for up to

two years was only implemented for the first time in 2017. This was not for all patents, only for some patents related to human and veterinary drugs. The United States did not need to make any changes to its legislation to comply with this requirement.

In addition to the foregoing, the New Mexican Industrial Property Law recognizes that new uses can be patented. Although in practice IMPI already grant protection for new uses, there is now greater legal certainty for their protection.

Furthermore, USMCA establishes that parties shall maintain a regulatory review exception for pharmaceutical products that permits a third person to make, use, sell, offer to sell, or import a product covered by a patent solely for the purposes to generate information to request a marketing authorization. This provision was also included in the new law approved last month by Mexico.

The USMCA asserts that patents shall be available for any invention, whether a product or process, in all fields of technology, provided that it is new, it has an inventive step and industrial application. In addition, and in contrast with NAFTA, USMCA expresses that inventions derived from plants can be subject to protection. This has the objective of increasing protection for plant-derived inventions and provide legal certainty, because even though these inventions were already granted in the region, this provision was not included in local regulations, like in Mexico. Finally, in the final version of the USMCA, a section outlining the exclusions from patentability was eliminated, the purpose of which was to strengthen the protection of a broader range of

> **USMCA reinforces regulatory systems, E-commerce, and the protection of IP rights.**

inventions, as long as they comply with the other cited requirements.

Recognizing the benefits of transparency in the patent system, the USMCA endeavors to publish pending patent applications promptly after the expiration of 18 months from the filing date or, if priority is claimed, from the earliest priority date. In order to comply with this requirement, Mexico amended its law in 2018 to allow the publication of complete patent files. Before this reform, the complete file was only made public after the patent was granted.

Many of the obligations established by the USMCA in patent matters, were implemented by Mexico in 2018, during the negotiations of the agreement. Some others, such as compensation for patent terms as a result of IMPI delays, and the regulatory review exception for pharmaceutical products were included in the New Mexican Industrial Property Law that came into force in July 2020. For some other cases, the USMCA establishes certain transition periods.

Test data exclusivity

As previously mentioned, to market a pharmaceutical product, it is necessary to obtain a marketing authorization, for which the applicant of an innovative product must present undisclosed information regarding the efficacy and safety of the same. Data protection is the exclusivity period in which third parties cannot rely on or use information from the innovator to market the same product.

The original text of the USMCA signed by the parties in 2018, included a ten years protection term for biologics, which exceeded the

available protection under both Canada and Mexico's domestic regimes. In United States law however, there was already a 12-year protection term. Biologics were defined by the USMCA as "a product that is produced using biotechnology processes and that is, or alternatively, contains, a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, for use in human beings for the prevention, treatment, cure or disease or condition". Considering that production of biologics is costly, and protection of biologics through patent rights is limited, data protection is an important means for maintaining exclusivity and recover the investment in time and resources.

In addition to biologics, further provisions, such as a protection period of at least three years with respect to new clinical trial information for new indications or formulations, and at least 5 years for new pharmaceutical products that contain a chemical entity that was not previously approved, were included in the original text of the agreement. This certainly was good news for innovators.

Interestingly, USMCA was amended in December 2019 in order to update several sections. The pharmaceutical industry had the most significant impact. The protection of biologics and new uses and methods were eliminated from the agreement as a result of pressure from democrats in the United States who argued that longer protection terms may raise prescription drug prices for patients.

In the case of Mexico, there is currently no local law or secondary regulation providing data exclusivity for biologics. In fact, NAFTA granted such protection for a period of no less than 5 years from the regulatory approval of pharmaceutical products. This protection for both small molecule drugs and biologics could only be obtained through litigation. The original text of the USMCA signed in 2018 would have provided legal certainty regarding the protection of data exclusivity. However, the protection of data exclusivity in the final version of the USMCA was restricted to at least 5 years for new pharmaceutical products and new chemical entities, which include biologics, similar to the protection already granted by NAFTA. Like Mexico, there is no local law or secondary regulation in Canada providing data exclusivity specifically for biologics. Canada currently has an 8-year data protection term for pharmaceutical products that contain new chemical entities, and biologics.

> **"The PPH has been a very useful tool in accelerating the granting of patents in Mexico."**

Conclusions & keynotes

The USMCA has provisions that impact many sectors, pharmaceutical being one of them. Among the relevant takeaways are the following:

- Like NAFTA, the USMCA states that members shall grant at least five year's data protection for new pharmaceutical products including new chemical entities. Specific provisions for data exclusivity protection of new uses and formulations, and biologics, were eliminated from the original version of the USMCA.
- The parties shall provide patent term adjustment proceedings to compensate patent owners from unreasonable delays of the patent offices to issuance a patent in all fields of technology. In addition, for pharmaceutical products, another patent term adjustment shall be provided to compensate unreasonable delays of the health authorities to grant marketing approvals.
- Members shall provide patent regulatory review exceptions to make, use, sell, offer to sell, or import a product covered by a patent for the purpose of requesting a marketing authorization.
- --Also, in the patent field, patents shall be available for any invention, whether a product or process, in all fields of technology, provided that it is new, it has an inventive step and industrial application. In addition, and in contrast with NAFTA, the USMCA states that inventions derived from plants can be subject to protection.

Although there were considerable changes in the version of the USMCA originally signed in 2018 in contrast with the amendments approved in 2019, which affect mainly the protection of clinical data, there are positive changes in the field of patents that may create a balance and benefit pharmaceutical patent owners. Furthermore, although some data protection provisions were eliminated from the USMCA, protection may be granted or increased locally in each of the countries. In Mexico, for example, local pharmaceutical associations will seek to increase test data protection for biologists.

Without a doubt, of the three countries, Mexico is the one that has had to and will continue to implement the greatest number of changes to make its local legislation comply with the USMCA obligations, followed by Canada. The United States will not have to make relevant changes.

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Improvements in production of cannabis for medical and industrial uses and their protection

Janett Lumbreras, Senior Associate, Uhthoff, Gomez Vega & Uhthoff S.C, tackles a high-profile and fast-moving area of IP law.

The use of Cannabis has been stigmatized due to its psychoactive effects; however, it has several uses in industry and medicine.

Cannabis contains more than 500 components. Two of these have been the subject of scientific investigation due to their pharmacological properties: Δ9-tetrahydrocannabinol **(Δ9-THC)** and cannabidiol **(CBD).** Other plant-derived cannabinoids include cannabinol (CBN).

Cannabis as a drug and industrial hemp both derive from the species Cannabis sativa and contain the psychoactive component tetrahydrocannabinol (THC), yet they are distinct strains with unique phytochemical compositions and uses. **Hemp** has lower concentrations of THC (0.3% or less) and higher concentrations of cannabidiol (CBD), which means minimal to no psychoactive effects. The legality of industrial hemp varies widely between countries. Some governments regulate the concentration of THC and allow only hemp that is bred with an especially low THC content.

The discussion on the use and legality of each of these plants, even if they are from the same family, must be carried out for each of them. Separating it into the legal, productive, and social fields would also make it possible to differentiate the recreational, medical, and wellness uses of marijuana from the industrial, medicinal, and useful properties of hemp.

Janett Lumbreras

This would, in turn, motivate research, health, industrial, and economical advancement, improving the quality of life for hundreds of patients.

Uses of cannabis

Recent reports indicate that Cannabis production is increasing and that cannabinoid formulations have been changing over the last two decades, especially with regard to their THC and CBD concentrations.

Therapeutic applications of Cannabis and cannabinoids

THC is the psychoactive principle of Cannabis, inducing the Cannabis inebriation sought by many users. Its addictive potential and negative consequences are now well known. The effects of CBD are distinct and, in many cases, the opposite of THC's effects. CBD seems not to induce euphoria and seems to have antipsychotic, anxiolytic, antiepileptic, and anti-inflammatory properties.

According to an evaluation (in 1999) by the Institute of Medicine in the United States, on Cannabis as a medication, the future of medical Cannabis lies in isolating its cannabinoid components and their synthetic derivatives. The variable composition within the raw Cannabis plant and especially the differing THC/CBD ratios make therapeutic applications of these products quite complex.

The following medical applications have been described for Cannabis:

THC
Analgesic
Anti-bacterial
Anti-cancer
Anti-inflammatory
Anti-spasmodic
Appetite Stimulant
Bronchodilator
Neuroprotective

THCV
Anti-convulsive
Appetite Suppressant
Bone Stimulant

CBD
Analgesic
Anti-anxiety
Anti-bacterial
Anti-cancer
Anti-convulsive
Anti-depressant
Anti-emetic
Anti-inflammatory
Anti-insomnia
Anti-ischemic
Anti-psychotic
Anti-spasmodic
Bone Stimulant
Immunosuppressive
Neuroprotective

CBDV
Anti-convulsive
Bone Stimulant

CBC
Analgesic
Anti-bacterial
Anti-cancer
Anti-depressant
Anti-fungal
Anti-inflammatory
Anti-insomnia
Bone Stimulant

CBG
Analgesic
Anti-bacterial
Anti-cancer
Anti-depressant
Anti-fungal
Bone Stimulant

Industrial uses

Hamp has been refined into a variety of commercial items, including the following listed below:

TEXTILES
Clothing
Diapers
Handbags
Denim
Shoes
Fine Fabrics

INDUSTRIAL TEXTILES
Rope
Canvas
Tarps
Carpeting
Netting
Caulking
Molded Parts

PAPER
Printing
Newsprint
Cardboard
Packaging

BUILDING MATERIALS
Oil Points
Varnishes
Printing Inks
Fuel
Solvents
Coatings
Fiberboard
Insulation
Acrylics
Fiberglass Substitute

FOODS
Hemp Seed Hearts
Hemp Seed Oil
Hemp Protein Powder
EFA Food Supplements

BODY CARE
Soaps
Shampoos
Lotions
Balms
Cosmetics

> **The use of Cannabis has been stigmatized due to its psychoactive effects.**

> **The future of medical Cannabis lies in isolating its cannabinoid components.**

Production of cannabis

Millennia of selective breeding have resulted in varieties that display a wide range of traits; e.g. suited for particular environments/latitudes, producing different ratios and compositions of terpenoids and cannabinoids (CBD, THC, CBG, CBC, CBN...etc.), fiber quality, oil/seed yield, etc. Hemp grown for fiber, for example, is planted closely, resulting in tall, slender plants with long fibers.

The high THC concentrations obtained from the various Cannabis varieties result from technical advances in production, such as genetic manipulations, cross-breeding, and improvements in indoor hydroponic cultivation. As advanced techniques and more potent seeds have become more widely available, a steady increase of THC concentrations in Cannabis has been made possible.

Genetic modification and engineering could enable industrial-scale production of cannabinoids that have pharmaceutical potential and provide more efficient alternatives.

The PCT application No. PCT/US2019/017433 describes *a method of increasing the cannabinoid levels in a genetically modified Cannabis sativa plant which includes genetically modifying the plant to induce the overexpression of the gene that controls the expression of tetrahydrocannabinolic acid (THCA) synthase and/or cannabidiolic acid (CBDA) synthase.*

The PCT application No. PCT/IL2019/050653 discloses *methods of in vitro clonal propagation, regeneration and transformation in Cannabis.*

Some researchers and biotechnology companies are aspiring to replace Cannabis plants with microorganisms that have been genetically enhanced to produces THC, the non-psychoactive compound cannabidiol (CBD) and many other cannabinoids of pharmaceutical

Résumé

Janett Lumbreras - Senior Associate, Uhthoff

Janett has a Pharmaceutical Chemistry-Biology Degree from UNAM, Diplomats in Access to Worldwide Scientific and Technological Information and in Industrial and Intellectual Property Law from UNAM. She is a Senior Associate at Uhthoff, working with patent matters for more than 20 years. She is an active member of AMPPI, AIPLA and CNQFBM.

interest. Others are aiming to modify chemical synthesis in the Cannabis plant by genetically altering its cells to make the desired molecules from shoot to tip, thereby boosting yield.

US patent application No. 16/594,733 discloses a *method of generating and selecting mutant new varieties of Cannabis plants through chemical mutagenesis of Cannabis cell suspensions.*

Benefits of microbial synthesis include the ability to mass-produce rare cannabinoids that are usually present in plants only in trace amounts or even molecules not found in nature. Transgenic plants can also be engineered for superior resistance to pests and environmental stresses.

Ploidy manipulation is a valuable tool in plant breeding. Important consequences of genome doubling can include larger organs and improved production of secondary metabolites, often linked to increased tolerance to biotic and abiotic stress. Polyploid forms also provide a wider germplasm base for breeding. Polyploids have yet to be implemented in most breeding programs for Cannabis.

US patent application No. 16/357,999 describes a *method for inducing polyploidy in a Cannabis plant, the method comprising treating the Cannabis plant or a part thereof with an amount of a dinitroaniline compound effective to induce polyploidy.*

The PCT application No. PCT/US2017/027643 *discloses a plant of the genus Cannabis that does not require flowering in order to produce trichomes comprising secondary compounds. The disclosed plants have a high mass% of secondary compounds and a high degree of trichome coverage on the surface of the plant.*

> **Cannabis contains more than 500 components.**

US patent applications Nos. 16/560,260 and 16/510,032 *describe the identification and use of particular CBDa synthase alleles, more particularly the use of these alleles to produce Cannabis plants having very high rations of CBGa to CBDa and/or THCa.*

IP rights of cannabis

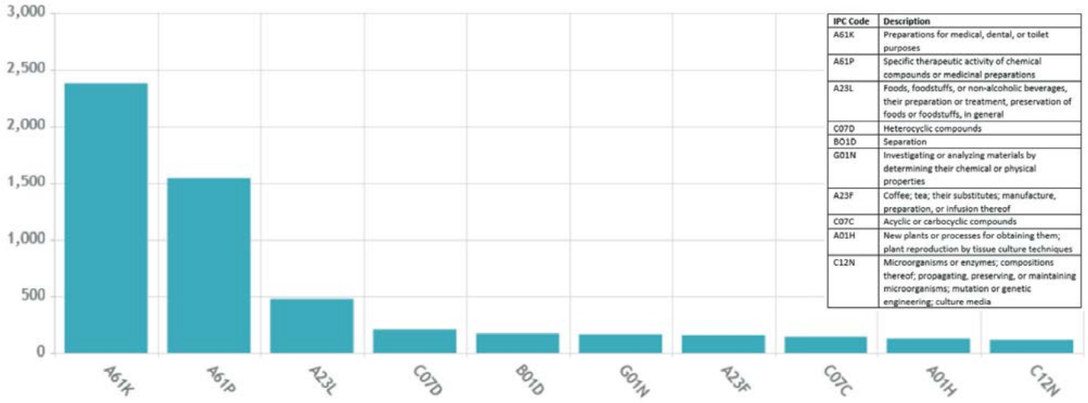
In recent years, the protection of products, methods, productions, etc. of Cannabis has increased, being China the main country in terms of filed patent applications related to Cannabis. Also, the main field of protection is that related with medical applications.

Statistics obtained with data published by WIPO show who is using PCT system and how it is being used.

Applications filed by Country

Country	No. of applications
China	1,842
USA	691
PCT	424
Canada	233
European Patent Office	151
Australia	119
United Kingdom	55
Republic of Korea	50
Mexico	**37**
Israel	27

Applications filed according to IPC Code



[1] Pertwee R. ed. Handbook of Cannabis. Oxford University Press; 2014. Available at: http://www.oxfordscholarship.eom/view/10.1093/acprof:oso/9780199662685.001.0001/acprof-9780199662685. Published online January 2015. Accessed May 21, 2017

[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5741114/#__sec1title

[3] HEMP Gazette. The Big List of Cannabis Cannabinoids

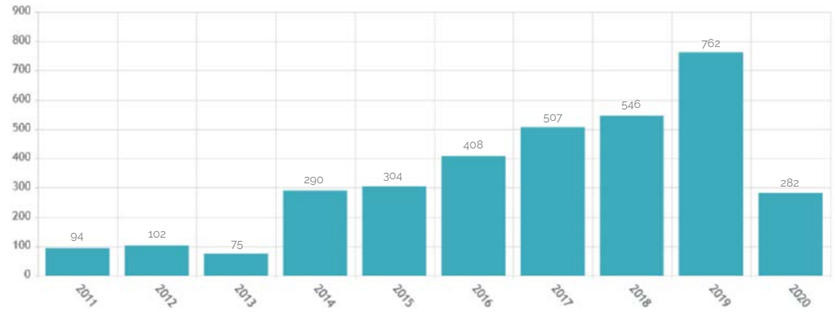
[4] https://www.forbes.com.mx/140-dias-para-cambiar-a-mexico/

[5] https://www.forbes.com.mx/marihuana-vs-hemp-lo-que-tienes-que-conocer/

[6] Elie Dolgin. A boosted crop. 29 August 2019. Vol. 572. NATURE S7 - https://www.nature.com/articles/d41586-019-02525-4

Number of applications by Publication Date

This graph shows how the number of publications associated to Cannabis is growing; the significant increase during 2019 is notable



Examples of filed PCT applications referred to improvement of Cannabis production are cited hereinbelow.

No.	No. PCT Publication	Title
1	WO2020102905A1	Dual droplet aeroponic systems and methods for growing plants
2	WO2020102905A1	Cannabis variety which produces greater than 50% female plants
3	WO/2020/035869	Modulation of cannabinoid profile in Cannabis
4	WO/2019/186568	Physical means and methods for affecting Cannabis plants
5	WO/2017/051398	Methods for the production of different Cannabis product compositions
6	WO/2017/181018	Enhanced Cannabis plants and methods of making and using the same
7	WO/2019/164689	Genetically modified Cannabis sativa plants and modified cannabinoid compounds for treatment of substance addiction and other disorders
8	WO/2020/084455	Post-harvest optimization
9	WO/2019/234750	Methods of regenerating and transforming Cannabis
10	WO/2019/113497	High cannabigerol Cannabis plants, methods of producing and methods of using them
11	WO/2020/093103	Cannabis plants with a cannabinoid profile enriched for Δ-9-tetrahydrocannabinol and cannabigerol
12	WO/2019/069309	A novel Cannabis production process and products thereof

*In **Mexico** there have been few patents granted, but there are several patent applications pending to be examined. These cases involve all the fields related with Cannabis. It also should be noted that during 2019 the number of applications increased.*

No.	No. MX Publication	Title
1	MX/a/2019/015673	Veterinary granules composition containing hemp extract
2	MX/a/2019/015315	Sleep disorder compositions and treatments thereof
3	MX/a/2019/014715	Use of cannabidiol in the treatment of tuberous sclerosis complex
4	MX/a/2019/012109	Cannabinoid extraction process using brine
5	MX/a/2019/009708	Method and cell line for production of phytocannabinoids and phytocannabinoid analogues in yeast
6	MX/a/2019/011583	Process for purification and separation of cannabinoids from dried hemp and Cannabis leaves
7	MX/a/2019/012779	Cannabis fiber, absorbent cellulosic structures containing Cannabis fiber and methods of making the same
8	MX/a/2019/009463	Methods and apparatus for low-pressure radiant energy processing of Cannabis
9	MX/a/2017/005833 Pat. MX 369078 B	Cannabis fiber, absorbent cellulosic structures containing Cannabis fiber and methods of making the same
10	MX/a/2019/003063	Trichome specific promoters for the manipulation of cannabinoids and other compounds in glandular trichomes
11	MX/a/2019/001968	Plants and methods for increasing and decreasing synthesis of cannabinoids
12	MX/a/2019/001121	New Cannabis tablet formulations and compositions and methods of making the same
13	MX/a/2014/003310 Pat. MX 367758 B	A pharmaceutical composition comprising the phytocannabinoids cannabidivarin (CBDV) and cannabidiol (CBD)
14	MX/a/2019/003269	Leak resistant vaporizer device
15	MX/a/2019/001286	Cannabis composition
16	MX/a/2019/001285	Cannabis composition
17	MX/a/2017/015304	Cannabis plants having modified expression of THCA synthase
18	MX/a/2014/000535 Pat. MX 346923 B	Genes and proteins for alkanoyl-CoA synthesis
19	MX/a/2015/013202	Breeding, production, processing and use of specialty Cannabis

The following Variety Plants of Cannabis has been filed at ***UPOV.***

Applications filed by Country

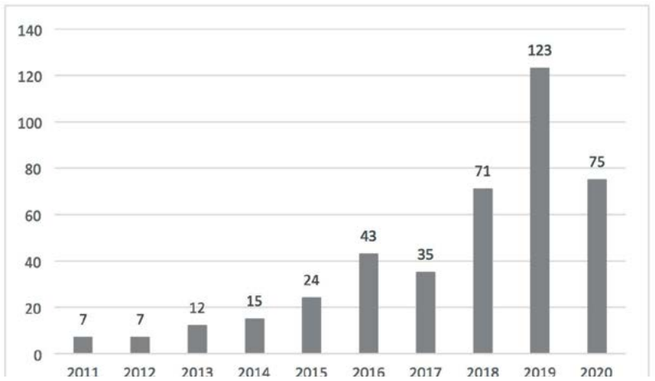
Country	No. of applications
NL	351
IT	313
HU	309
PL	303
FR	302
CZ	298
GB	292
SI	291
RO	289
DE	288

Applications filed according to UPOV Code

UPOV Code	Botanical Names	No. of applications
CANNB	Cannabis L.	7
CANNB_SAT	Cannabis sativa L.	807
CANNB_SAT_IND	Cannabis sativa L. subsp. indica (Lam.) E. Small & Cronquist Cannabis indica Lam.	1
CANNB_SAT_SAT	Cannabis sativa L. ssp. sativa	53
CANNB_SIN	Cannabis sativa ssp. sativa x Cannabis sativa subsp. indica	1

Number of applications by Filing Date

This graph shows how the number of applications associated to Cannabis is growing; the significant increase during 2019 is notable.



[7] Jessica L. Parsons, Sara L. Martin, Tracey James, Gregory Golenia, Ekaterina A. Boudko, and Shelley R. Hepworth. Polyploidization for the Genetic Improvement of Cannabis sativa. Front Plant Sci. 2019; 10: 476.

[8] S.H. Fox, in Encyclopedia of Movement Disorders, 2010

[9] https://patentscope.wipo.int/search/es/search.jsf

[10] https://www3.wipo.int/pluto/user/en/

[11] https://siga.impi.gob.mx/newSIGA/content/common/principal.jsf

Conclusions

Known uses of Cannabis and new medical and industrial uses thereof have raised an interest to improve Cannabis production to increase industrial-scale production of cannabinoids. The use of different methods has allowed for these improvements. The methods include, for example, genetic modifications, cultivation methods that increase the content of the substance in interest (CBD), and obtaining plant varieties. It follows that new technologies developed in order to achieve such objectives need to be protected through patents, plant varieties, or any other industrial property rights.

Furthermore, due to the nature and psychoactive effects of Cannabis, there is the need of domestic regulations for the production, use, and marketing of Cannabis for medical and industrial uses.

In recent years, the number of patent applications related to Cannabis around the world has grown significantly and will continue increasing as legal frameworks progress in each country. The research and development of new applications of Cannabis will promote such increase. It is also expected for other ways of protection to increase, e.g. Plant Variety, or Seed Certification.

In Mexico, the legalization for the use of *Cannabis sativa* for medicinal and research purposes has been approved. The laws regarding this subject-matter will apply to the following activities:

I. The sowing, harvesting, production, transportation, distribution, marketing, carrying, and consumption of Cannabis and its derivatives for personal, therapeutic, and scientific purposes.

II. Public Health control of Cannabis.

In consequence, Universities, Research Centers, and Pharmaceutical Companies will now be able to do research on *Cannabis sativa.*

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