The Life Sciences Lawyer

Issue 6

GLOBAL REACH, LOCAL KNOWLEDGE

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Decentralized clinical trials: five takeaways on the EU / UK legal landscape

Launch interactive document

Jaspreet Takhar and Julia Gillert of Baker McKenzie evaluate the most important aspects you should know about Decentralized Clinical Trials which are bringing clinical trials to patient's homes.

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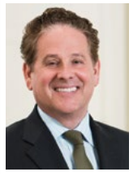

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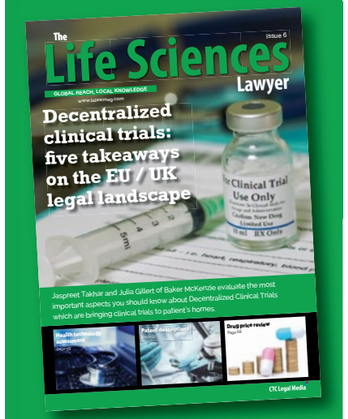
The Life Sciences Lawyer Magazine wishes to take this opportunity to thank the editorial board for their time and support.



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Editor's welcome

Clinical trails are crucial to the development of new treatments. With patients' needs at the centre of these trials, and perhaps inspired by the COVID-19 era, our cover story this issue discusses the decentralization of clinical trials to improve patient experiences. Bringing a larger proportion of a clinical trial to a patients' home may seem ideal, but it is also likely to complicate the legal position. Baker McKenzie provide five key points for the legal landscape of DCTs.

> **Baker McKenzie provide five key points for the legal landscape of DCTs.**

This issue also sees an evaluation on the new EU Regulation on health technology assessment, and how this correlates with Value-Based Healthcare. The new Regulation aims to contribute towards the formation of a safe and effective health policy delivering the best treatment at the best value.

Then, an explanation of the importance of accurate and detailed patent descriptions, with recent case examples including *Amgen v Sanofi (2021)* and *Juno Therapeutics v Kite Pharma (2021).* Failure to provide a sufficient description could result in damaging losses.

Also, an article reflecting on the Neurim Pharmaceuticals and Merck cases and what the outcomes may mean for the grant or refusal of interim injunctions moving forward.

Plus, an update on Canadian patented drug pricing review and its narrowing landscape.

Enjoy the issue.

Faye Waterford, 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.

Issue 6

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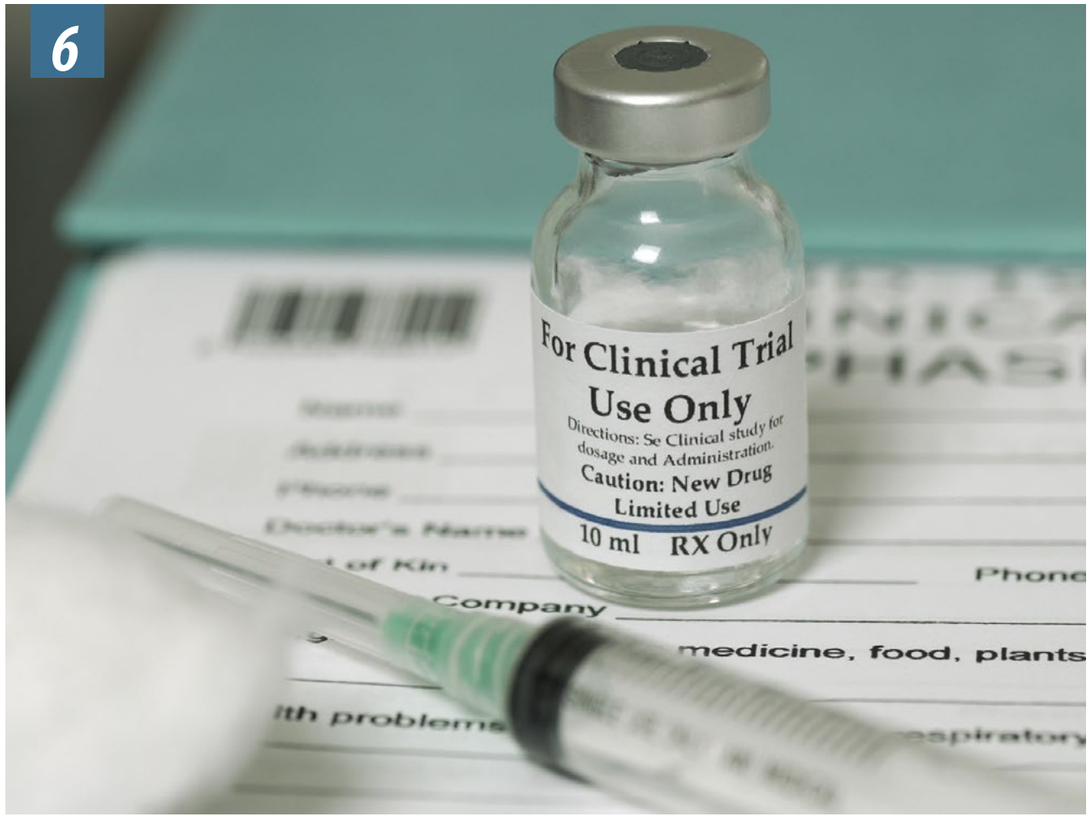


Decentralized clinical trials: five takeaways on the EU / UK legal landscape

Jaspreet Takhar and Julia Gillert of Baker McKenzie evaluate the most important aspects you should know about Decentralized Clinical Trials which are bringing clinical trials to patient's homes.

Résumés

Jaspreet Takhar, Senior Associate
Jaspreet advises market-leading tech and healthcare companies on issues at the cutting-edge of digital health.

She focuses on the development and regulation of healthcare technology. This includes assessing how digital health solutions can comply with the legal framework for data privacy, medical research and medical devices / pharmaceuticals. Jaspreet also advises clients on the regulation of clinical trials, accessing and using real world data, and the use and regulation of AI and other technologies in the healthcare space.

Julia Gillert, Of Counsel
Julia advises a broad range of tech and healthcare companies on issues across the healthcare ecosystem in relation to digital health.

She helps companies in the pharma, medtech, and healthcare sectors to navigate the strict regulatory regimes they face, often in the grey areas where innovative technological developments outpace the regulation. Julia's practice also focuses on advising companies to manage the regulatory challenges arising from Covid-19 and post-Brexit divergence. Julia advises both UK domestic clients as well as multinationals operating across borders.

Jaspreet Takhar

Julia Gillert

Decentralized clinical trials (DCTs) focus on bringing an increasing proportion of a trial's activities to the patient's home, as opposed to bringing the patient to a trial site. The ultimate aim is to meet patient needs and improve the patient experience, and the key to achieving this is technology i.e., utilizing tools like e-consents, telehealth solutions, and wearables that facilitate remote monitoring. However, when it comes to DCTs, the pace of innovation outstrips the pace of regulation.

The industry is moving rapidly to embrace this new approach, but there are key areas of uncertainty as to how DCTs sit within the legal and regulatory framework.

While we await more formal guidance from regulators, CROs and sponsors are already building on lessons from the pandemic to roll out elements of DCTs on a local, regional, and global basis.

We've set out five points on the legal landscape for DCTs below.

1) No formal statutory definitions (yet), but regulators agree that DCTs exist on a spectrum

Unfortunately, there is no statutory definition of DCTs yet, but several regulators such as the US FDA,[1] the Swedish Medical Products Agency,[2] and Germany's BfArM have acknowledged that DCTs exist on a spectrum.

In its most extreme form, a DCT may be fully decentralized or 'siteless', with a patient never physically setting foot in a trial site. The participant may be enrolled virtually, consent electronically, and self-administer medicines with assessments taking place remotely in the patient's home.

Although fully decentralized trials may not be commonplace yet, we are seeing a proliferation in the number of hybrid trials. These hybrid trials incorporate certain elements of DCTs, such as online recruitment portals, nurse home visits, direct-to-patient clinical supply, and remote monitoring.

2) There are several legal regimes at play

At the pan-EU level, DCTs involve several legal regimes coming together, some of which have not been adapted for DCTs (at least yet).

This means that bringing together these legal frameworks is one of the main challenges facing regulatory and compliance specialists when advising on DCTs. These regimes include:

- **The upcoming EU Clinical Trial Regulation (CTR) and Good Clinical Practice (GCP):** the CTR applies across the EU from 31 January 2022. There are no specific rules in the CTR or GCP prohibiting DCTs, so they are in theory possible, but the DCT must fulfil the requirements of GCP and the CTR, including the key underlying principles of ensuring patient safety and data integrity. (For completeness, the CTR will not apply in Great Britain, where the Medicines for Human Use (Clinical Trials) Regulations 2004 will continue to apply. However, the position is similar for Great Britain to that of the EU.)

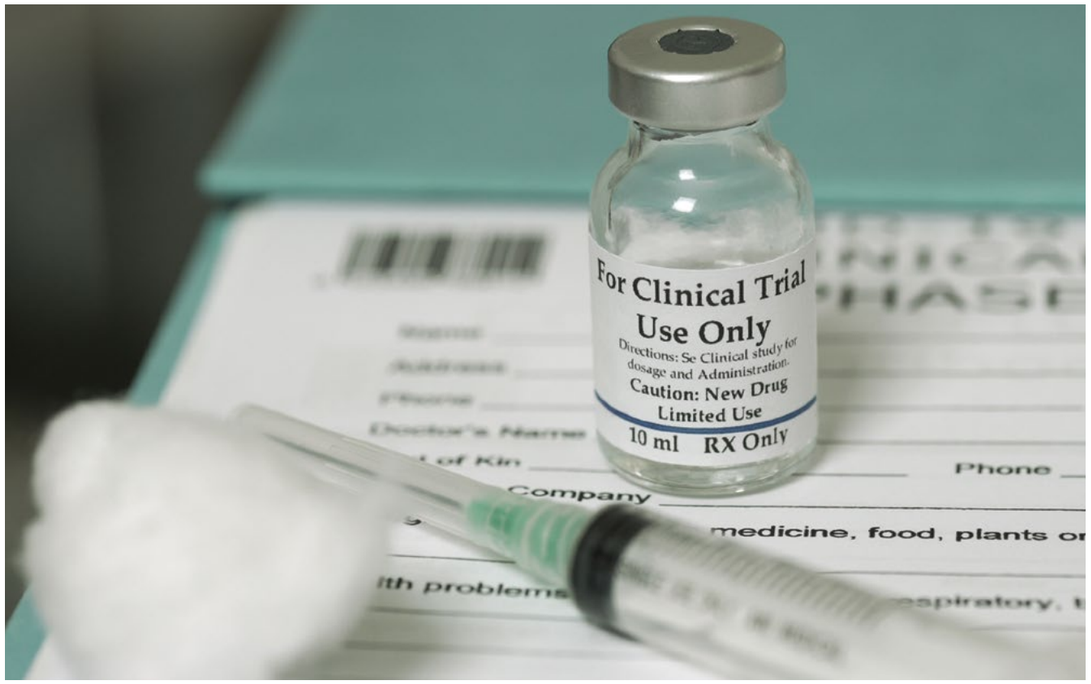
> **"We do not necessarily have robust and complete guidance from regulators on full DCTs, which means there are gaps, questions and grey areas emerging."**

- **The EU / UK GDPR:** data privacy often sits uncomfortably within the healthcare context. Its 'black-and-white' concepts such as data controllers and data processors do not fit neatly into the healthcare ecosystem where parties often assume nuanced roles, and they fit even less neatly into DCTs, where there are complex data flows and relationships between tech providers, hospitals, sponsors, and CROs. We've set out some tips on compliance below.

- **National laws and guidance:** including those issued in light of Covid-19, addressing issues such as dispensing, e-consents, remote access to electronic health records, how home health visits can be conducted, and local laws on medical secrecy and patient confidentiality.

3) Regulatory gaps exist

We are seeing regulators across the globe provide targeted guidance on specific elements of DCTs, such as e-consents, remote source data verification, and remote access to electronic health records. Examples are emerging of more general guidance relating to hybrid trials, including the Danish Medicines Agency's guidance on the implementation of decentralized elements in clinical trials with medicinal products.[3] The



Swedish Medical Products Agency is currently investigating how interventional clinical trials may be carried out on a decentralized basis in Sweden.[4]

However, we do not necessarily have robust and complete guidance from regulators on full DCTs, which means there are gaps, questions and grey areas emerging. Early engagement with the relevant ethics committee and regulator will be key.

4) Data privacy compliance must be built in from the outset

When assessing data privacy compliance, the first and most important step will be mapping the data flows involved in the DCT. This is a key initial question because DCTs typically involve increased access to non-coded patient data by vendors such as nursing service providers, app providers, and IT support.

It will be essential to ensure there are appropriate agreements in place with such vendors. Sponsors are considered to be data controllers i.e., the party that determines the purposes and means of data processing. As controller, a sponsor is required to put in place data processing agreements with any vendors that process data on the sponsor's behalf.[5] To the extent such vendors may transfer personal data outside the EU or UK (as relevant), a valid international data transfer mechanism is required.[6]

As data controllers, sponsors will need to ensure there are appropriate technical and organisational measures to ensure a level of security appropriate to the heightened risk profile of DCTs.[7]

5) And patient confidentiality and medical secrecy must not be forgotten...

DCTs potentially involve the disclosure of confidential patient information to third party vendors, such as tech and app providers. This means that sponsors may need to consider any local laws on medical secrecy and medical confidentiality, and this may include identifying a basis for disclosure of such confidential information to third party vendors.

Local laws on medical confidentiality often run in parallel to data privacy laws. This means there may be certain overlap between data privacy laws and medical confidentiality laws, but in many jurisdictions, they are ultimately different regimes with different focuses. You may need to conduct separate exercises to ensure compliance under both regimes.

> **Early engagement with the relevant ethics committee and regulator will be key.**

1 https://www.fda.gov/about-fda/oncology-center-excellence/advancing-oncology-decentralized-trials
2 https://www.lakemedelsverket.se/en/permission-approval-and-control/clinical-trials/medicinal-products-for-human-use/decentralised-and-virtual-interventional-clinical-trials#hmainbody1
3 https://laegemiddelstyrelsen.dk/en/news/2021/guidance-on-the-implementation-of-decentralised-elements-in-clinical-trials-with-medicinal-products-is-now-available/~/media/5A96356760ED408CBFA9F85784543B53.ashx
4 https://www.lakemedelsverket.se/en/permission-approval-and-control/clinical-trials/medicinal-products-for-human-use/decentralised-and-virtual-interventional-clinical-trials
5 Article 28, EU GDPR; Article 28, UK GDPR
6 Article 44, EU GDPR; Article 44, UK GDPR
7 Article 32, EU GDPR; Article 32, UK GDPR

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The new EU Regulation on health technology assessment

Ricardo Costa Macedo, Partner, & Rafael Cunha Jóia, Junior Lawyer, of Caiado Guerreiro discuss how the new Regulation correlates with Value-Based Healthcare in the EU.

In the context of a global pandemic caused by the Covid-19 virus, the emergence of new health technologies, such as new vaccines created from mRNA, is a structural component, and as such, indispensable to health systems. In fact, the connection between technology and health has never been so close. This connection is enabling new technologies to treat new and old diseases, improving the quality of life of patients, and increasingly focusing the treatment on their individual needs and the outcome of such treatments.

> **In fact, the connection between technology and health has never been so close.**

The technological bases of care have increased dramatically in the last century, particularly in terms of equipment, medical devices, and medicines. While generating unequivocal health gains, health technologies also raised questions regarding financial sustainability of health systems with consequences for patient effectiveness as well as resource allocation.

The concept of health technology assessment

The expression health technology is used to cover any aspect of healthcare, including prevention programs (example: vaccination programs), diagnostic tests, a device or piece of equipment, a drug or a procedure, being that health technology assessment (HTA) is a form of a policy that examinates short and long-term consequences of using a healthcare technology. It is a multi-disciplinary process that summarizes information about the medical, social, economic, and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. This procedure aims to contribute to the formulation of safe and effective patient-centred health policies in order to deliver the best treatment that brings most value to the patient.

The goal of HTA is to inform the development of safe and effective, health policies that are patient focused and seek to achieve best value as defined by decision makers. HTA supports decisions such as:

- Should treatment A be reimbursed in a national healthcare system?
- For which patients should it be provided?
- What are the characteristics of the patient and the disease which best suit the treatment?
- What is its cost and effectiveness of such treatment?

HTA may look at the impact of a technology on an individual patient, on a group of similar patients, on the healthcare system as a whole, or on all of these. HTA may also use modelling, where specific assumptions are used to make an estimate or 'best guess' to predict, for example, the cost of using a technology in a certain setting or in a certain patient.

Correlation between health technology assessment and Value-Based Healthcare

Value-Based Healthcare (VBH) is accompanied by considerable ambiguity concerning the very meaning of the concept. Despite this ambiguity, it is safe to say that this new way of looking at health management argues that the value in health care consists of what matters most to patients, meaning, the health status they achieve (outcomes) and the price they must pay for it (costs). According to this new method of health care delivery, providers should focus on generating maximum value for their patients by helping them achieve the best possible outcomes and by doing so in a cost-efficient way. The use of this approach can include a reduction of costs to achieve better health and the increase of treatment efficiencies and patient satisfaction.

Given the fact that VBH focuses on health status (outcomes) achieved by a certain treatment and the price the patient must pay for it (costs), in a cost-efficient way, new technologies and the information available regarding the use of said new technologies plays a decisive role in implementing a VBH system. To that end, the process regarding health technology assessment can provide a precious help in assessing the added value of new or existing health technologies – medicines, medical devices and diagnostic tools, surgical procedures, as well as measures for disease prevention, diagnosis, or treatment – compared with other health technologies. HTA can be used not only to guide different authorities about whether a new treatment or other technologies should be available on the national health service, but also to assess if a certain treatment for a certain disease or a specific condition provides value in terms of health status for that particular patient in a cost-efficient way. HTA can therefore provide information to support decisions about priorities in healthcare or specific decisions about whether new treatments should be introduced, what is the cost-effectiveness of its use in certain patients and its positive or negative effects. By using this detailed information patients and health care providers can decide which of the available treatment options best meets their needs

> **This procedure aims to contribute to the formulation of safe and effective patient-centred health policy in order to deliver the best treatment that brings most value to the patient.**

HTA can also be used as a tool to implement a VBH system through a health economics assessment. In this regard, the assessment of a new treatment can be made through principles of economics that are applied to health and healthcare. In this perspective health economics can be used to provide evidence to support value for money considerations. Health economics data may cover both direct costs (such as the number of drugs used by a patient or the number of hospital visits in a given period) and indirect costs (such as the cost of time lost from work). The economic data combined with clinical effectiveness data leads to cost-effectiveness estimates.

HTA process and its considerations about health economics, cost, effectiveness, application to certain patients and comparison with procedures, drugs or medical devices is shaping the way health care providers look at the needs of their patients. In doing so, HTA can serve as a precious tool of data that allows health stakeholders, including government decisions and hospital management, to implement a real

Ricardo Costa Macedo

Rafael Cunha Jóia

Résumés

Ricardo Costa Macedo, Lawyer and Partner at Caiado Guerreiro, head of the Life Sciences and Intellectual Property groups.

Mr. Macedo´s practice covers a wide range of contentious and non-contentious patent, trademark, and other IP-related rights, such as trade secrets and unfair competition, in particular in the pharmaceutical, home care, food, and insurance sectors. Moreover, he has vast knowledge in regulatory matters in these sectors.

Mr. Macedo graduated in 1998, from the Faculty of Law of the Catholic University of Lisbon. He undertook postgraduate studies in information society law at the Faculty of Law of the University of Lisbon in 2000 and in commercial law at the College of Law, London in 2003.

Rafael Cunha Jóia, Junior Lawyer at Caiado Guerreiro

Rafael Cunha Jóia is a member of the Life Sciences and Intellectual Property groups. Mr. Jóia has been focusing his practice on the health and insurance sector, in relation to which he covers a wide range of matters.

Mr. Jóia graduated from the Faculty of Law if Lisbon, University of Lisbon in 2019 and concluded his Master of Laws (LLM) in Commercial and Corporate Law in the Faculty of Law of the Catholic University of Lisbon in 2021.

VBH system, focusing on creating value treatments with good outcomes for the patients in a cost-efficient way, using new technologies or assessing from all the medical options that can be applied to a certain patient the ones who suits them better.

HTA Regulation in the EU

The HTA process is currently performed by 50 HTA agencies across Europe. Nevertheless, approaches vary from country to country which means a fragmentation of HTA criteria with serious negative impacts on the European health market and patients in its Member States.

To support cooperation between HTA bodies, the European Union has made substantial investments. Two Joint Actions have been carried out together with a number of projects. A third Joint Action was launched in June 2016 and run until 2020. This third Joint Action focused on developing common assessment methodologies, piloting, and producing joint clinical assessments and full HTA reports, and on developing and maintaining common criteria. In addition, following the adoption of the Cross-Border Healthcare Directive (Directive 2011/24/EU), the HTA Network was established in 2013 to provide strategic and political guidance to the scientific and technical cooperation at Union-level.

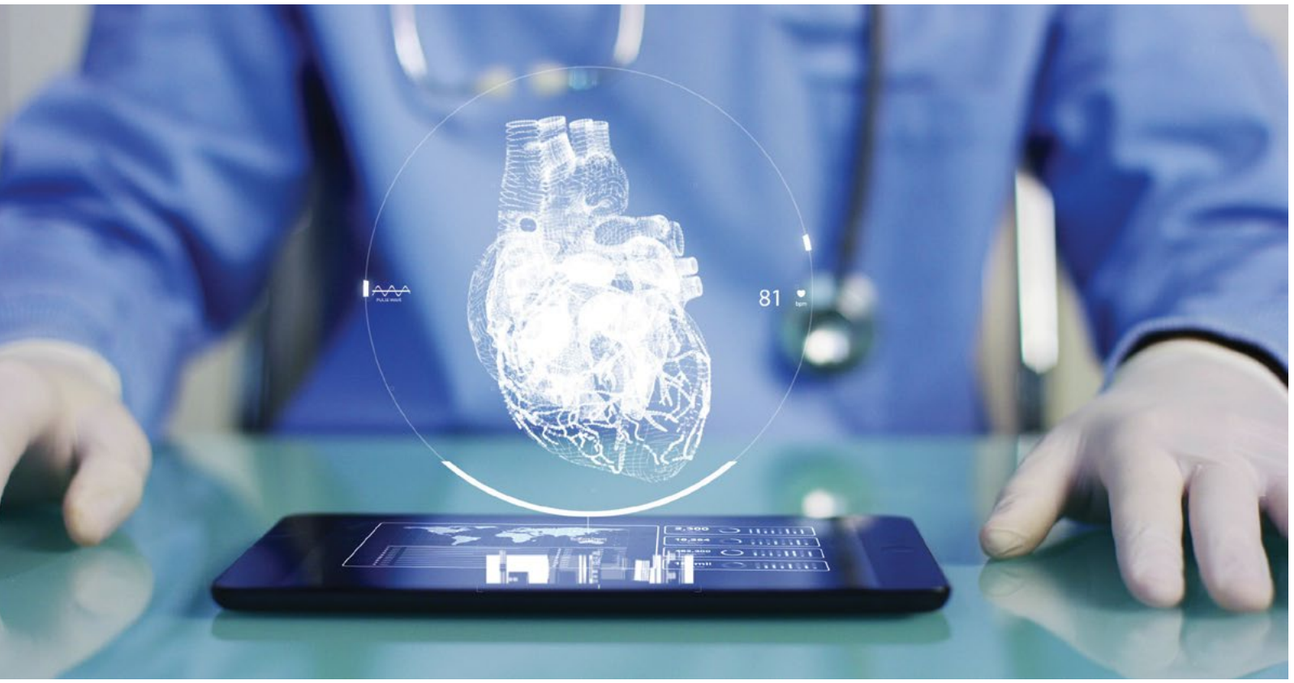
Following the negotiations set on June 22, 2021, the Council of the European Union and the European Parliament reached a provisional agreement on the European Commission's proposal for a European health technology assessment regulation (HTA Regulation), which aims to harmonize the clinical benefit assessment of health technologies across the EU.

> **Value-Based Healthcare (VBH) is accompanied by considerable ambiguity concerning the very meaning of the concept.**

This provisional agreement which now establishes the new Regulation (EU) 2021/2282 of the European Parliament and of the Council Of 15 December 2021 aims to achieve the following specific objectives:

- Improve the availability of innovative health technologies for EU patients;
- Ensure efficient use of resources and strengthen the quality of HTA across the EU;
- Improve business predictability.

This new Regulation establishes a **support framework and procedures for cooperation on health technology assessment at an EU level and common rules for the clinical assessment of health technologies** (article 1 of the regulation proposal). The Member State Coordination Group on Health Technology Assessment (the Coordination Group) is formally established in Article 3 along with its composition, roles, and responsibilities to oversee the joint work referred to in Chapter II. This joint work is based on the annual work program of the Coordination Group which is outlined in Article 4 of the Regulation. The annual work program provides clarity on the planned work of the Group and allows health technology developers to foresee any expected involvement they may have in the joint work for the year ahead.



The joint clinical assessments will be one of the main proponents of the future joint work, being those assessments limited to: **(i)** medicinal products undergoing the central marketing authorization procedure, new active substances and existing products for which the marketing authorization is extended to a new therapeutic indication, medicinal products undergoing the central marketing authorization procedure, new active substances and existing products for which the marketing authorization is extended to a new therapeutic indication **(ii)** certain classes of medical devices and *in vitro* diagnostic medical devices **(iii)** potential impact on patients, public health, or healthcare systems (e.g., burden of disease, budget impact, transformative technology) **(iv)** significant cross-border dimension, and **(v)** Union-wide added value.

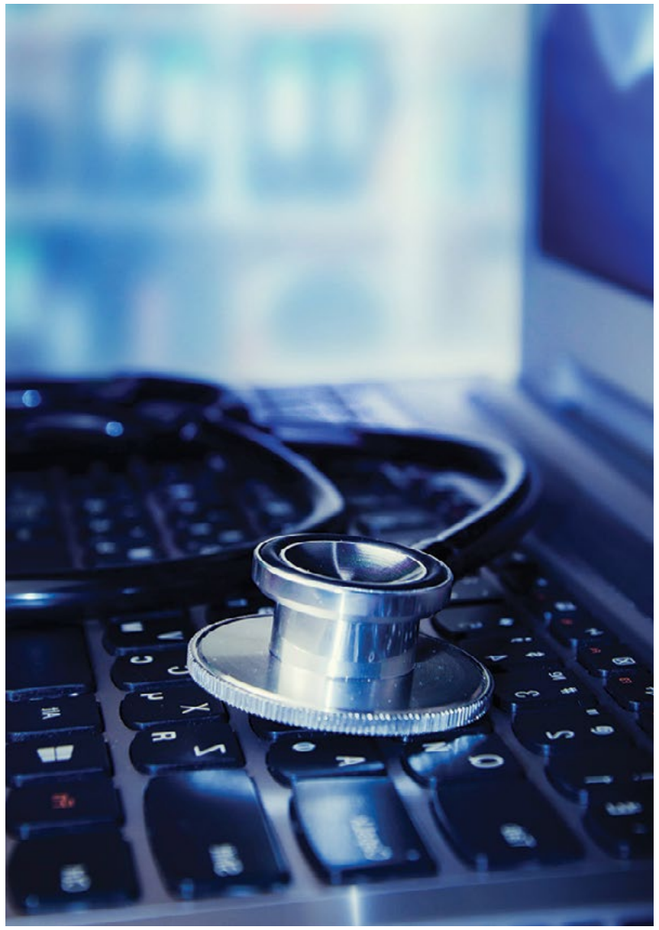
Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 provides for progressive implementation of the amount of joint clinical assessments during the transitional period. This means that the number of joint clinical assessments will increase gradually during the first three years after the date of application, considering specific selection criteria.

Chapter III of the Regulation lays down common rules for carrying out clinical assessments at Member State-level which will then be developed in detail in tertiary legislation. These rules will ensure a harmonized approach to clinical assessment across EU Member States.

Closing notes

Common rules in all EU Member States about HTA can serve as grounds for establishing a deeper VBH system. The correlation between, HTA criteria, mainly the criteria that sets rules to assess the health status (outcomes) achieved by a certain treatment and the price the patient must pay for it (costs), in a cost-efficient way, can be a precious help to implement a real VBH system in the European Union. With this regulation patients will be empowered, and medical personal better informed by having access to a Joint Clinical Assessment report that is of high scientific quality, transparent and accessible to the public.

To establish a VBH system it is necessary to provide the right tools that enable medical personnel as well as health care providers to compare various health care options, choosing among them the ones that offer a better treatment to the patient, with better results and at an efficient cost. The new EU Regulation could set equal criteria for different Member States, serving as a driver for the implementation of a European-wide VBH system.



> **These rules will ensure a harmonized approach to clinical assessment across EU Member States.**

Although we do not yet know the full extent of what the Joint Clinical Assessment report will present, this Regulation can establish a true cooperation in HTA, giving a real opportunity to relate the cost-benefit of each treatment to individual patient considerations, implementing what may be the beginning of a real VBH system.

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Deficient patent description can be fatal

DPS Parmar, Special Counsel at LexOrbis, explains why patent descriptions can be crucial for patent grant and enablement with reference to India and US cases *Amgen v Sanofi (2021)* and *Juno Therapeutics v Kite Pharma (2021).*

Résumé

Mr. DPS Parmar, Former Technical Member (Patents), erstwhile Intellectual Property Appellate Board; Special Counsel, LexOrbis

Mr. D.P.S Parmar heads the Patents Contentious Practice Group at LexOrbis. After joining the IPAB as Technical Member (Patents) in 2011, he has been instrumental in writing some path breaking and insightful decisions on Indian patent law issues. These include establishing legal positions on excluded subject matter under Section 3(d), 3(i) and 3(k), divisional applications, disclosure requirements under Section 8, working statements and compulsory license, to name a few. Before joining IPAB, Mr. Parmar worked with the Indian Patent Office (IPO) for over 27 years and played a vital role both at the administrative and policy levels. He represented India at various rounds of discussions organized by the World Intellectual Property Organization (WIPO) and attended follow-on programs at the European and Japanese Patent Offices. He was instrumental in the recognition of IPO as the 15th ISA and IPEA under the Patent Cooperation Treaty (PCT). He also served as the head of the Intellectual Property Training Institute (IPTI) in Nagpur, which was responsible for providing training to new examiners at the IPO.

Meeting the sufficiency of description is the primary requirement to obtain a patent and it serves well as a ground for invalidation of a patent. The courts of all patent jurisdictions are raising the standards of satisfying the statutory requirement for enablement and written description of a patent application in the context of inventions. For example, in two precedential decisions by the US Court of Appeals for the Federal Circuit, *Amgen v Sanofi (2021)* and *Juno Therapeutics v Kite Pharma (2021)* both involving invention relating to antibodies, the court ruled in the former case that "the claims are far broader in functional diversity than the disclosed examples" and in the latter case court held that "a person having ordinary skill in the art would not have been able to determine which scFvs would bind to CD19 in a way that distinguishes them from scFvs that do not bind to CD19 because the specification presented a limited number of examples, and did not disclose structural features common to the members of the genus to support that the inventors possessed the broader scope of claims." In both cases, the court favored opponents' assertion on lack of sufficiency of the description to enable the person skilled in the art to work the invention without undue experimentation and revoked the patents.

DPS Parmar

> **The opponent must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention.**

Sufficiency and enablement requirement in India

The statutory requirement for written description, support, and enablement can be found in section 64 (h) of Patents Act, 1970, which states that "the complete specification does not sufficiently and fairly describe the invention and the method by which it is to be performed, that is to say, that the description of the method or the instructions for the working of the invention as contained in the complete specification are not by themselves sufficient to enable a person in India possessing average skill in, and average knowledge of, the art to which the invention relates, to work the invention, or that it does not disclose the best method of performing it which was known to the applicant for the patent and for which he was entitled to claim protection".

Accordingly, where insufficiency and lack of enablement are taken as a ground to revoke a patent, the opponent must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without undue experimentation.

Determinants of lack of sufficiency requirement

The determination of sufficiency at the examination stage is guided by the statutory requirement relating to presenting the description in the complete specification under section 10 (4) which states that:

"(4) Every complete specification shall—

(a) Fully and particularly describe the invention and its operation or use and the method by which it is to be performed;

b) Disclose the best method of performing the invention which is known to the applicant and for which he is entitled to claim protection; and

(c) End with a claim or claims defining the scope of the invention for which protection is claimed."

The Patent Rules lay no further guidelines to ascertain how this statuary requirement can be determined. But in practice, the examiner normally uses various factors for determining the adequacy of the disclosure in the specification. These factors may depend upon their knowledge in the field, the extent and content of the cited prior art. This means that at the examination stage sufficiency requirement determination is purely linked to determine the scope of the claims. It further means that at the examination stage it is not linked to the determination of lack of the enablement requirement. Therefore, if the applicant describes the invention and its operation or use, and the best method by which it is to be performed, it is sufficient for examination purposes in the Indian context. However, if this requirement is not met it may be used as a ground to oppose the patent at pre-grant (section 25(1)(g)) or post-grant stage (section25(2)(g)).

Position in the US

In the US, the examiner is guided by judicial rulings relating to the determination of the sufficiency of description and enablement. For example, in re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988), the court set forth that this determination requires a conclusion reached by weighing the following factual considerations (popularly known as the "Wands factors"):

"Factors to be considered in determining whether a disclosure would require undue

> **Simply stated, a patent application is said to be enabled if the application provides sufficient details that enable a person of ordinary skill in the field of the invention to practice the invention.**

experimentation have been summarized by the board in re Forman. They include-

(1) The quantity of experimentation necessary,

(2) The amount of direction or guidance presented,

(3) The presence or absence of working examples,

(4) The nature of the invention,

(5) The state of the prior art,

(6) The relative skill of those in the art,

(7) The predictability or unpredictability of the art, and

(8) The breadth of the claim."

Accordingly, the patent description satisfies the written description requirement when it reasonably conveys to those skilled in the art how to practice or work the claimed invention without undue experimentation. Simply stated, a patent application is said to be enabled if the application provides sufficient details that enable a person of ordinary skill in the field of the invention to practice the invention. Any deficiency in the description entails the refusal of a patent by the examiner. In case the patent is granted the deficient description carry the burden of invalidation at any stage of the patent. However, in order to invalidate a patent for lack of enablement, in the US a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation'. This is what happened in the recently decided invalidation of antibody patent case viz *Amgen v Sanofi (2021)* and *Juno Therapeutics v Kite Pharma (2021).*

> **Any deficiency in the description entails the refusal of a patent by the examiner.**

A word of caution

Deficient description can prove fatal to the granted patent as it is likely to face invalidation on the ground of insufficient description or lack of enablement. The patentee must ensure that the specification is well-drafted disclosing the complete scope of the claimed invention and providing at least one working example sufficient to enable a person skilled in the art to make and use the invention without exercising inventive skill. A well-drafted specification can minimize the risk of refusal during the examination of the application and at subsequent stages when a patent is challenged on the grounds of not meeting sufficiency of disclosure and enablement requirements. This is particularly required for the complex inventions that are directed to antibody technologies and other unpredictable technologies as we have seen invalidation of such patents above. The more complex and unpredictable inventions are, the more cautious approach in presenting a specification that meets the enablement and written description requirements is desirable. The first aspect of drafting particularly antibody applications would be to give a sufficient number of representative examples across a broad range of the claimed significant features of the invention. Secondly, it is advised to have one claim with a narrow scope that can trace back the support from the specification and examples. Finally, the drafter should avoid using functional elements in the language such as 'binds', 'blocks bindings' or 'interact with' as such terms in the language are normally construed narrowly during the interpretation of the claims. The cautiously drafted specification with examples of the common elements is no doubt beneficial to rebut enablement or sufficiency of description challenge at any stage of the patent. In the Indian context, the examiner is not guided by the elaborate guideline like "wands factors" for determination of enablement, but the ground of insufficient description or enablement is a major line of attacking a patent. In the past, the erstwhile Intellectual Property Appellate Board (IPAB) has refused to allow amendment of claims as the proposed amendments were not supported by description in an appeal case *Diamcad N.V. BELGIUM vs Asstt. Controller [Order no. 189/2012]*. This clearly shows that the addition of new matter in the specification is not allowed and the failure to disclose the 'best mode' remains a solid ground for challenging the validity of a patent in India.

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Interim injunctions for patent infringement in the aftermath of Neurim Pharmaceuticals and Merck

Professor Mark Engelman, Barrister at The Thomas Cromwell Group, reviews the outcome of recent cases and what they mean for interim injunction in the field of life sciences.

Not all infringements of intellectual property rights involve the same class of causes of action. For example, passing off is a form of deceit/malicious falsehood and its roots live there. There is no requirement to establish damage in order to consummate the cause of action. Damage is to be inferred. Patent infringement, by contrast, is a statutory tort and damage is an essential ingredient.

Damage of course is also an essential ingredient in the successful prosecution of an interim injunction. The test has long been laid out in *American Cyanamid v Ethicon [1975] AC 396.* It reads as a sequence of steps to be decided by the Court when determining whether an interim injunction should be granted or refused. Those well-known steps comprised consideration of: (i) whether there existed an arguable case; (ii) whether if the injunction were not granted the Claimant would incur a loss unquantifiable in money terms, if not then the injunction would be refused. If so, then the Court goes on to consider whether if the injunction was granted the Defendant would incur a loss unquantifiable in money terms, if that is then established, the injunction would be refused. On the premise that both parties suffer an unquantifiable loss, the Court will proceed to the next step and consider the balance of convenience. In essence, the test took the form of, in computer science terms, a logic tree.

Professor Mark Engelman

Focusing more precisely upon the two questions associated with the respective parties' losses, the questions the Court poses, is whether the respective party's losses could be compensable by damages as an "adequate" remedy. Two recent judgments have changed not merely how the questions are framed but the step-wise nature of the test itself.

Within the space of 11 months The Irish Supreme Court and English Court of Appeal have both dissembled the American Cyanamid test turning it from a four-step sequence to a multifactorial test in which the stages vary from those laid down in American Cyanamid and then questions what is meant by the term "adequate" as it relates to a party's damages. Both judgments

Résumé

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concerned pharmaceutical patent disputes however both have repercussions in the approach a Court should adopt to the grant of interim injunctions across all areas of law.

Damages in patent disputes have historically accommodated a number of different heads of loss. The most obvious represented by the loss of business profits caused by the diversion of the patentee's sales in his invention to the Defendant. Damages in respect of a Defendant's unlawful sales would be calculated on the basis that the patentee would have made equivalent sales to those of the Defendant.

Damages have also been recovered for the loss of a patentee's network of distributors arising from loss of product turnover.

It is also often been successfully argued that a patentee has suffered a loss of profits through a reduction in the price of his products which otherwise enjoyed a market monopoly when that reduction is necessitated in order to compete with the infringer's products.

In *Neurim*, the English and Welsh Court of Appeal, considered an appeal against the grant of an interim injunction brought by the Neurim for infringement of its patent for melatonin, an hypnotic, marketed under the brand name Circadin. Upon learning of the imminent launch of a generic pharmaceutical, Sylento, by Mylan, which fell within Neurim's patent claims, Neurim sought injunctive proceedings to prevent its sale. It was alleged for the purposes of the then existing American Cyanamid test that Sylento would cause Neurim to lose sales of Circadin, the diversion referred to earlier, and also depress the price at which Circadin could be sold. Harm would also be caused to Neurim's distribution networks. Consequential losses would arise from the closure of Neurim's R&D programmes and associated redundancies. These, Neurim said, were unquantifiable heads of loss.

Mylan, as respondent to the injunctive proceedings, also laid claim to unquantifiable losses. It claimed the loss represented by missing the opportunity to launch a product for which Mylan had obtained marketing authorisation during a period over which Mylan would have enjoyed (without other generic competitors) a valuable "first mover" advantage in the hypnotics market place. Its price of Sylento would be significantly higher in those circumstances.

The High Court below had decided that *Neurim's* damages associated with both diverted sales and price suppression could be estimated from the respective sales data of both parties such that they could "properly be calculated". As to *Neurim's* consequential losses, it was rich enough to absorb them. The High Court found they would arise in any event when

> **It reads as a sequence of steps to be decided by the Court when determining whether an interim injunction should be granted or refused.**

Nuerim's patent expired in 2022, some two years following the date of the hearing before the High Court judge.

Similarly, Mylan's "first mover" losses were considered by the High Court to be merely transitory in nature because, were the interim injunction refused, many other generic companies would be fast behind it. The first instance judge recognised such damages would be difficult to quantify but that did not mean, however, that a damages remedy to Mylan would be "inadequate" for that reason alone.

The injunction application failed because the patentee failed at step two, its damages were considered to be an adequate remedy and not unquantifiable.

The Court of Appeal applied the four-stage test of American Cyanamid. Floyd LJ when addressing Neurim's claimed unquantifiable loss stated that whilst in some cases "damages as a remedy falls so far short of the perfect, that the remedy can no longer be described as adequate", but going on to decide, this case was not one of them.

Floyd LJ, in the lead judgment of the Court of Appeal, focused upon the central issue under appeal: whether the calculation of the damages to which Neurim and its distributer Flynn would be entitled, were they to succeed in obtaining a permanent injunction at trial, was of such complexity as to render their remedy in damages inadequate. He pointed out that the patentee had put into evidenππnce both its actual and forecast sales turnover. The Defendant had also evidenced its "actuals". Those were sufficient to quantify the patentee's losses in price suppression. Whilst Floyd LJ accepted that after the period of launch of Mylan's drug estimates of *Neurim's* price depression would become more difficult, in Floyd LJ's words: "damages are, however, to be "assessed liberally", from which one is to infer, any estimation of damages is not intended to be an exact science. It upheld the High Court's refusal to grant the interim injunction."

The Court of Appeal made no reference to a very significant earlier judgment of the Supreme Court of Eire in *Merck Sharp & Dohme Corporation v Clonmel Healthcare Limited S:AP:IE:2018:000107* which had been handed down 11 months earlier. Naturally, judgments of the five-man Supreme Court of Eire are not binding upon the English and Welsh Court of Appeal. But the Merck judgment might well have had impact. It opened with the ominous words: "this appeal raises important questions as to the proper approach to the application for an interlocutory injunction, which is an important remedy in many different disputes."

Merck held two patents for simvastatin and another for ezetimibe, statins for the treatment of cholesterol. It marketed its patented invention under the brand Inegy which combined the two ingredients.

The High Court had granted Merck an interim injunction against a generics company on a without-notice basis but refused it when it returned on-notice. The High Court found Merck's damages to be an adequate remedy despite the emergence of a generics company into its market. A judgement which aligned with that of the later judgement in Neurim. It also considered whether the generics company would lose its first-mover advantage were the injunction to be granted. It concluded it would but such losses were also quantifiable.

The Court of Appeal upheld the judgment of the High Court and Merck appealed to the Supreme Court.

Again, before the Supreme Court, the generics company argued that damages were an adequate remedy for the patentee, and once that had been decided, it was argued that on American Cyanamid principles, the High Court need have progressed no further into the stepwise test. It also queried the entire approach to the American Cyanamid test.

The Supreme Court thus went on to discuss the principles governing the grant of interim injunctions in general as laid down in American Cyanamid. O'Donell J. stated:

> "It should not, in my view, be approached as though it (American Cyanamid) were the laying down of strict mechanical rules for the control of future cases. It is apparent, for example, that there is some ambiguity in the judgment about a matter which arises in this case, which is whether the question of adequacy of damages is part of or antecedent to the balances."

That statement made early in the leading judgment heralded an attack by the Supreme Court upon the mechanistic approach which had routinely been undertaken by the Courts when applying the American Cyanamid test. He stated:

> "In my view, the preferable approach is to consider adequacy of damages as part of the balance of convenience, or the balance of justice, as it is sometimes called."

Concluding:

> "While a structured approach facilitates analysis and, if necessary, review, any application should be approached with a recognition of the essential flexibility of the remedy and the fundamental objective in seeking to minimise injustice, in circumstances where the legal rights of the parties have yet to be determined."

> **As to adequacy of damages to either applicant or respondent, O'Donell J. considered it unnecessary to treat it as a science.**

As to adequacy of damages to either applicant or respondent, O'Donell J. considered it unnecessary to treat it as a science. Putting it prosaically: "The fact that it is in theory possible to gather every feather does not mean that it is not more convenient to stop the pillow being punctured in the first place."

The Court decided that the inadequacy of damages to both parties was balanced and that other factors operated in determining where the balance of convenience lay. They, like the evaluation of the prospects of success at trial, should be taken into account. Had the stepwise approach in American Cyanamid been deployed, the Court would not have got that far down the logic tree, but would have stopped at whether damages were inadequate for the patentee and gone no further. But it didn't.

O'Donall J. concluded his lead judgment with what would be heretical to the doctrine enshrined in American Cyanamid, a step-wise sequence of the American Cyanamid factors but entirely out of step to that envisioned by American Cyanamid: a determination was to be made on the merits of success at trial, and if positive, whether the action would in fact proceed to trial. Then the court would consider the balance of convenience. That would include a consideration of the adequacy of damages to both parties. He commented that in commercial cases that question should be approached with some scepticism. Any difficulty in their calculation was to be consigned to operate merely as a factor which might point in favour of the grant of an injunction.

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The scope of Canadian patented drug price review narrows

Noel Courage and Nyrie Israelian, of Bereskin & Parr, summarize a recent case which reviewed the pricing of the Alexion drug Soliris, resulting in a strengthened position for innovator drug companies undergoing pricing review.

The Canadian Patented Medicine Prices Review Board regulates prices of patented medicines. Any thread of connection between an approved medicine and a Canadian patent can trigger the Board's jurisdiction to review price. For this reason, companies sometimes weigh a trade off between having Canadian drug patent protection and triggering price review versus dropping their drug patents and avoiding price review.

The Board was recently reined in by the Federal Court of Appeal (**FCA**) in a case involving the Alexion drug Soliris.[1] The Court held that the Board must stay within its mandate of preventing excessive pricing. The Board does not have the power to pursue a more general mandate of ensuring reasonable pricing, price-regulation, or consumer protection at large. As well, the Board's decision was unreasonable by making an unprecedented departure from its *Compendium of Policies, Guidelines, and Procedures* ("*the Guidelines*") to require that the price of Alexion's drug Soliris be lower than that of all seven comparator countries. The Board decision was quashed, and the case was sent back to the Board for redetermination.

Noel Courage

Nyrie Israelian

In its initial decision, the Board found that Alexion priced Soliris excessively and ordered Alexion to forfeit excess revenues earned between 2009 and 2017. In making this decision, the Board relied upon the list price of Soliris being higher than the price in one of the seven countries used for comparison purposes. In other words, the price of Soliris had to be lower than all seven comparator countries. This was the first time the Board had ever imposed that requirement. Alexion applied for judicial review to the Federal Court.

The FCA stressed in its decision that case law establishes that the excessive pricing provisions in the *Patent Act* are directed at controlling patent abuse, and not reasonable pricing, price regulation, or consumer protection at large.[2] The FCA rejected the Board's arguments that the case law and certain statements in Parliamentary debates established a "consumer protection" or "reasonable" pricing mandate for the Board.

In making its initial Soliris decision, the Board considered the price of Soliris on provincial budgets, the fact that the price of Soliris had been under scrutiny in other jurisdictions, and that Soliris was priced lower in the United States. The FCA found that the Board did not, in a satisfactory manner, explain why these reasons were relevant to "excessive" pricing under section 85 of the *Patent Act*, indicating that the Board exceeded its statutory powers by pursuing a general price regulation mandate.

Further, the FCA took issue with the Board's explanation for its significant and unprecedented departure from the *Guidelines*. The Board justified this departure by citing "unique circumstances", but it did not specify what those circumstances were to an extent satisfactory to the FCA. The Board noted that a report from the United Kingdom criticized the price of Soliris as potentially unreasonable and that while Canadian prices for drugs were generally lower than those in the United States, Soliris in Canada exceeded the price in the United States at some points. The FCA described these reasons as "thin and impoverished", stating that "it is not enough to allude vaguely to 'unique circumstances' and then just name two circumstances that do not appear to be unique and that fall short of logically supporting the sort of significant, unprecedented departure from the Guidelines the Board took here".

The FCA also found that the Board failed to provide an adequate explanation for its inconsistent decision to use, under section 85 of the *Patent Act*, the lowest international price of the seven comparator countries as the benchmark to determine if a price is excessive, and then under section 83 of *the Patent* to order a remedy based on the highest international price.

The Federal Court of Appeal granted Alexion's application for judicial review, quashed the Board's decision, and remitted the matter to it for redetermination. The FCA concluded by stating that on redetermination, the Board is free to make whatever decision seems appropriate based on a reasonable interpretation of the legislation, but cautioned that in making its decision, the Board must ensure that a reasoned explanation is discernable on the key issues.

> **"The Board must ensure that a reasoned explanation is discernable on the key issues."**

The Board has requested leave to appeal to the Supreme Court of Canada. Alternatively, the Board may just redecide the case in the manner required by the FCA. In the meantime, this case strengthens the position of innovator drug companies that are undergoing pricing review and negotiations with the Board. We will monitor the effect of this case on the Board's interpretation of its mandate, as well as any implications for the Board's draft new guidelines and regulations that the federal government continues to postpone.

Résumés

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[1] *Alexion Pharmaceuticals Inc. v Canada (Attorney General)* [2021] FCA 157. Leave to appeal to the Supreme Court of Canada has been requested.

[2] The FCA stated that the PMPRB excessive pricing provisions may be constitutionally suspect as outside the power of the federal government if they were aimed at reasonable pricing, price-regulation, or consumer protection at large.

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