NEW DAWN FOR LIFE SCIENCES IP STRATEGY

How technological, regulatory and legal changes are transforming biotech and pharma IP management approaches

IAM SPECIAL REPORT

FOREWORD

Life sciences IP strategies are being remoulded – not just by the ordinary ebb and flow of case law, but by more fundamental shifts that are changing the way IP is protected, enforced and monetised in the healthcare space.

The traditional pharma IP paradigm – of seeking patents to fend off generic competition and maximise the period of exclusivity – remains vital for much of the industry. But cutting-edge biotechnologies are creating new IP landscapes where different strategic thinking is needed. The rise of artificial intelligence and digital healthcare, moreover, has created a significant overlap between the previously highly distinct worlds of the life sciences and high-tech, and is reshaping the way value is created from intangible assets.

Even where the old models continue to apply, the rise of new technologies – notably biologics and biosimilars, as well as personalised/precision medicine – is posing fresh legal and strategic quandaries for IP professionals.

Meanwhile, shifts to the legal, regulatory and policy environments in which all life sciences innovators must operate add to the strategic recalculations that IP professionals must make.

This Special Report seeks to provide insights into the areas where life sciences IP strategy is being reshaped most radically. It zooms in on IP developments in cutting-edge areas of innovation, such as mRNA and CRISPR, where complex, contested and multi-layered patent landscapes pose distinctive licensing and freedom-to-operate challenges and must be navigated in new ways. It considers strategies for overcoming patent protection and enforcement challenges in the fast-growing field of personalised/precision medicine. It examines how litigation strategies have evolved in recent biosimilar-related patent disputes. And it puts forward ideas about what innovators can do to avoid IP pitfalls and capitalise on IP opportunities in the fast-changing medical device space.

The rise of digital healthcare and the convergence of life sciences and high-tech IP strategies is also a major theme of the report. As well as creating a need for hybrid/cross-disciplinary IP teams, this is generating new opportunities to obtain and license valuable patents, as well as boosting the importance of trade secrets, and making data into a precious form of intangible asset.

An interview with the Chief IP Counsel of the Dana-Farber Cancer Institute, a major patent owner in the cutting-edge immuno-oncology space, shines a light on how recent developments in US case law and looming policy shifts are threatening the future of fundamental, early-stage life sciences innovation. And in-depth articles provide insights into how seismic shifts in the European legal and regulatory framework are changing the strategic outlook for pharma and biotech innovators.

IAM is grateful to all the authors for their contributions to the report. IAM

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Developments in biotechnology – such as in CRISPR and mRNA vaccines – have created several multi-layered, fast-changing and highly-contested patent landscapes where new kinds of life sciences IP strategy are necessary. Innovators must be adaptable: freedom-to-operate analyses and licensing decisions must be undertaken on a continuous basis throughout the product development process.

The widespread application of artificial intelligence and other digital technologies in drug development and patient care is altering IP strategies among life sciences companies and creating an ecosystem of high-tech businesses with a stake in the healthcare sector.

This is leading to a convergence of high-tech and biopharma IP strategies. Patent monetisation strategies traditionally seen in the computing and telecommunications spaces are beginning to be seen in the life sciences space. A growing number of biotech/pharma companies require patent professionals with subject matter expertise in high-technology, while hybrid IP teams are increasingly sought after.

Data has become a valuable intangible asset in its own right. But realising the value of healthcare data is difficult, calling for new approaches to the collection, organisation and presentation of information. These must overcome privacy and data-protection barriers while offering commercial value to innovators.

Life sciences IP strategies must also adapt to shifts in the legal and political landscape. In Europe, the Unified Patent Court has already made its mark on pharma patent strategies, while a slew of imminent regulatory changes will impact innovators' IP management approaches. In the US, political political hostility to pharma-related patents has led to policy proposals which could damage innovation, especially among smaller organisations.

NEW TECHNOLOGIES, NEW STRATEGIES

IP strategies must reflect the nature of the technologies involved; and as technology changes, so do ways of protecting, enforcing and monetising IP rights. This has proved to be especially true in the life sciences where a wave of technological developments – particularly in biotechnology – has created new patent landscapes where traditional pharma IP strategy paradigms do not apply.

The articles that follow examine the multi-layered and highly contested patent landscapes that have emerged in the CRISPR and mRNA spaces. They ask how these dangerous terrains can best be navigated by drug development companies and explore how IP owners in these areas can maximise the value of their patents through enforcement and licensing.

The articles in this section also provide insights into the fast-changing strategies and tactics being used by companies in US biosimilars litigation. They explore how best to protect personalised medicines in a somewhat hostile legal environment, and how to capitalise on IP opportunities in the evolving medical device space.

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EVOLVING CRISPR PATENT LANDSCAPE REQUIRES COMPANIES TO BE ADAPTABLE

The complex and contested CRISPR patent landscape requires companies to be both diligent and adaptable, says HLK's Catherine Coombes

CRISPR technology has already caused a paradigm shift in gene-editing and, according to BCC research, the global market for CRISPR technology is already worth more than $3.4 billion – a figure that is predicted to grow to $7.5 billion by the end of the decade.

Though the earliest patent applications adapting and applying CRISPR systems as a gene-editing toolkit were filed as recently as 2012, a multi-layered and highly-contested IP landscape has emerged over the past decade. This situation has arisen because several parties made the same breakthrough of applying CRISPR technology to the gene editing of eukaryotes at similar times. Moreover, the fluid ever-shifting foundations of the early CRISPR patent landscape have been added to by a deluge of follow-on patent applications. These cover new Cas enzymes and systems, new evolutions in techniques, such as base-editing and prime-editing, incremental improvements in the components used, and a vast array of applications and guide RNAs.

The result is a vast and dynamic patent landscape to navigate for those considering licensing and freedom-to-operate. Organisations navigating this complex and fast-changing patent terrain need to be diligent from the outset but should also be willing to adapt their IP strategy throughout the product development process.

Foundational rights remain contested in Europe and the US

Multiple parties filed their earliest patent applications in 2012 to subject matter that encompassed using Type II CRISPR/Cas systems as toolkits for carrying out site-specific, targeted gene-editing in eukaryotes. These parties included Vilnius University, CVC (a collaboration between UC Berkeley, University of Vienna and Charpentier), Broad (a collaboration between the universities of Broad, Harvard and MIT), Sigma Aldrich and ToolGen. Unusually, the apparent strength of each of their earliest IP portfolios have ebbed and flowed over time.

In Europe, most parties managed to get broad claims granted. This was followed by rounds of oppositions and appeals from third parties. All these early rights holders have been careful to ensure that various divisional patent applications have been filed based on these earliest parent patent applications, allowing them to evolve and resurge as circumstances have changed in this field.

Broad suffered several revocations and limitations in opposition proceedings to some of their key patents because they were unable to prove that they met the formal requirements to keep their earliest priority dates in Europe. This meant key scientific articles published in early 2013 were citeable against these patents.

Appeals were filed but were suspended while the Enlarged Board of Appeal considered key questions around priority rights in Europe in G1/22. The decision in G1/22 established a presumption that a claim to priority was valid, by way of an implicit agreement on the transfer of the right to claim priority. This applies to any case where the subsequent applicant was not identical to the priority applicant apart from in "rare exceptional cases" in which it the presumption could be rebutted.

On recommencement of the appeals on these early Broad patents, it was found that they are now entitled to the earlier priority date, and the proceedings were remitted back to the Opposition Division. Hence, Broad's IP portfolio in Europe appears to have been restored to a position of strength.

However, this is subject to further change, because these early patents (EP 2 764 103, EP 2 784 162 and EP 2 896 697) will now go through opposition proceedings again and, no doubt, more appeal proceedings. As such, final decisions on these earliest patents are still years away. And it will take even longer for the EPO to decide the fate of Broad's plethora of divisional patents and other patent applications claiming priority to the organisation's earliest filings.

Likewise, CVC initially had very broad patents granted in Europe which were maintained unamended throughout opposition proceedings. Yet on 20 September 2024 CVC wrote to the EPO to request revocation of two of their own key early patents. In doing so, they cited procedural concerns based on previous conduct of the Board of Appeal in a case unrelated to CVC. This action followed an unfavourable preliminary opinion of the Board of Appeal in CVC's cases that indicated that they may not be entitled to priority and that some claims may lack novelty in view of a tracrRNA sequence disclosed in Deltcheva in 2011 due to how broadly the claims to sgRNA were defined.

The request for revocation prevents a final decision from being made on those earlier patents – a decision which would have repercussions for other patents and patent applications in the CVC portfolio that claim the earliest priority date. We can expect prosecution of further divisional patent applications attempting to cover IP rights lost on revocation of EP 2 800 811 and EP 3 401 400. Such that a final decision giving clarity over the strength of CVC's position in Europe could also be years away.

Similar rounds of oppositions, appeals and filing of further divisional patent applications have occurred for other parties too.

In the US, we are currently awaiting a decision from the US Court of Appeals for the Federal Circuit following CVC's appeal against the decision of the PTAB in Interference No. 106,115. The PTAB concluded that Broad invented CRISPR/Cas 9 able to cleave in eukaryotes earlier than CVC in that patent interference. The appeal hearing took place on 7 May 2024.

"Companies attempting to operate in the white spaces where there are no patent rights will encounter difficult challenges"

Moreover, this patent interference is not the only patent interference for CRISPR technology yet to be resolved: there are further patent interferences suspended pending the outcome of this appeal. These include two patent interferences in which Toolgen is facing off against Broad (Interference No. 106,126) and CVC (Interference No. 106,127) as well as patent interferences between Sigma Aldrich and Broad (Interference No. 106,133) and CVC (Interference No. 106,132).

Hence, as in Europe, it may be many years before we see a full resolution of the early CRISPR/Cas9 landscape for editing in eukaryotes in the US.

The CRISPR patent landscape and commercialisation

There are now over 17,000 patent families covering CRISPR related technology, according to a February 2024 estimate by SCBT-Centredoc. These cover all types of CRISPR systems, newer techniques and applications.

As with any freedom-to-operate assessment, it is easier to determine what third-party IP rights may impede commercialisation of a CRISPR product or method at a later stage in the R&D/commercialisation process when lead candidates have been determined, processes have been more concretely defined and it has become clearer which territories such products/processes may be produced, sold or utilised in.

From the outset, however, companies considering the use of CRISPR technology in their desired field should consider the benefits and drawbacks of using Type II CRISPR/Cas9 systems, which are better validated but have a more complex IP landscape, compared to the pros and cons of using:

- less validated alternative Cas enzymes which may have a less complex patent landscape and, in some instances, improved traits,
- older gene-editing techniques which have a clear licensing landscape, or
- new alternative systems purported to be outside the CRISPR landscape.

When considering using alternative systems, it is worth noting that purportedly alternative guide RNA systems can fall under the scope of CRISPR patents even if they have a low sequence identity to a particular Cas9. The percentage identity among Cas9 from different species can be very low. For example, the amino acid sequences of Cas9 from S. aureus only shares 17% of its identity with the amino acid sequence of Cas9 from S. pyogenes.

Furthermore, many of the patents in the field, while generally relating to CRISPR systems, use claim language which can extend beyond specific CRISPR systems, particularly in patent applications relating to methodologies and applications. As such, if a system is chosen primarily in an attempt to fall outside the CRISPR landscape, rather than for the effects seen with these new alternative systems, due diligence may be required to determine whether the new system actually falls outside the CRIPSR patent landscape.

Some companies may opt to use a combination of different systems in developing their products. This may have the advantage of helping to determine which systems may be the most beneficial for the desired outcome, but may further complicate the licensing situation. Not knowing from the outset which CRISPR systems will be utilised in the generation of lead candidates or products, and how they will be used, will make it more difficult to obtain the necessary licences at an early stage.

For commercial applications, where licences are likely to be required from more than one party, difficult decisions have to be made about when to license and from whom. This is particularly so where the costs of obtaining licences are not commensurate with the stage of a product's development. Multiple assessments are likely required along the commercialisation pathway.

Companies attempting to operate in the white spaces where there are no patent rights will encounter difficult challenges. Small white spaces may develop after 2033 and 2034 as some of the earliest patents in this field expire. Until then, however, commercial aspects of using CRISPR technology are likely to require licences from more than one party.

For those involved in CRISPR-related research, it is also important to be cautious when purchasing CRISPR research tools and reagents of any licence terms giving the research tool seller downstream rights to royalties on sales of products that are discovered or developed through use of such tools.

In areas outside of human therapeutics, surrogate licensing companies have been used to ease some of the complexities of seeking licences. In agriculture, most licences have been granted on

a non-exclusive basis, and even those organisations with exclusive licences, such as Corteva, have, in turn, granted various non-exclusive licences.

In human therapeutics, Vertex and CRISPR Therapeutics have recently gained FDA approval for their CRISPR gene therapy CASGEVY for the treatment of sickle cell disease and, thereafter, announced a non-exclusive patent sub-licence from Editas, which has exclusive rights to license the Broad's foundational CRISPR IP for use in human therapeutics.

This demonstrated that there is a path to commercialisation for CRISPR-Cas9 human therapeutics despite the ongoing patent disputes. But licences obtained at such a late stage of commercialisation often come at a greater cost than those negotiated at earlier stage. It is reported that Vertex is paying up to $100 million plus annual licensing fees.

Certainly, the fluid foundations of the early CRISPR patent landscape make it harder to understand what scope of protection is likely to be finally upheld for which parties in each of the territories of interest.

It is vital, therefore, to undertake multiple assessments of the CRISPR patent landscape at different stages along the commercialisation pathway. And it is particularly important to take an adaptable approach which can be altered as clarity in the earlier field emerges and which takes into account the ever-increasing number of patents in the CRISPR space. IAM

Catherine Coombes, Partner, HLK

"Organisations navigating this complex and fast-changing patent terrain need to be diligent from the outset but should also be willing to adapt their IP strategy throughout the product development process"

HOW LITIGATION, LICENSING AND COLLABORATION TRENDS IN THE MRNA PATENT LANDSCAPE ARE EVOLVING

Liz Cohen and Sophie Britton of Bristows investigate the complex web of IP rights in the mRNA field, and how this is impacting life sciences strategies

In recent years, the biotech industry has seen exponential growth and investment in messenger ribonucleic acid (mRNA) technology, which can be used not only for vaccines, but also other therapies such as regenerative medicine, treatment for genetic disease and in cancer immunotherapy.

Life sciences companies have long been competing for the market and looking for ways to innovate and unlock the transformational potential of mRNA technology, most notably demonstrated by the rapid development of the first mRNA-based COVID-19 vaccine in 2020.

However, the intellectual property landscape surrounding mRNA technology is complex and rapidly expanding, giving rise to a variety of partnership and licensing arrangements, the emergence of university spin-offs and staggering levels of fundraising and investment. Inevitably, it has also resulted in high profile and highly anticipated patent litigation cases.

A complex development landscape drives patent filings

The complexity of the technology involved in the development of synthetic mRNA platforms underlies the exponential increase in patent filings for mRNA and related innovation.

The two key strands that form the basis of mRNA technology are the delivery system and the coded mRNA, which expresses the desired encoded protein. However, several challenges to the successful development of effective mRNA vaccines have emerged, which has led to a web of technology being developed and protected in the field.

One challenge is that mRNA is itself very unstable and must be delivered to host cells without degrading. This involves crossing through the cell membranes, which can be difficult due to the size, instability and negative charge of mRNA. This challenge has led to the development of several delivery systems, such as lipids, polymers, protein derivatives and lipid nanoparticles (LNPs).

The delivery mechanism is of great importance to the efficiency of the therapy, allowing delivery to cells and protection against degradation. LNPs are the only delivery technology currently approved for use in mRNA vaccine technology and have been the primary focus of litigation in this field so far.

A second challenge is that the stability of mRNA can be improved by directly tailoring the structure of the mRNA molecule, for example using chemical modifications and optimising non-coding sequences. Finally, once successfully delivered to the host cells, the mRNA must then be correctly translated within the cell and the host cell must be able to express enough of the encoded antigens to lead to a therapeutic response, whilst importantly not triggering an adverse immune response. The incorporation of modified nucleosides, a 5' cap and longer poly(A)tails has led to improvements to overcome this.

Further innovation can be found in the development of innovative manufacturing techniques and formulations alongside the investment in mRNA sequence engineering and the delivery system.

Consequently, the scale of the patent portfolios presently in play poses a significant challenge from a freedom-to-operate perspective for any companies looking to enter the market and develop their own products.

It has been said that this can hinder start-ups and university spin-offs which lack the capacity or funding to complete a comprehensive freedom-to-operate analysis. This nature of the landscape also underlines the importance, for innovative companies looking to compete in this field, of investing to secure IP protection for as many components of their technology as possible.

Strategies for innovation and commercialisation

Given the complicated landscape and various strands of technology pertinent to this field, companies are having to carefully consider their strategy when looking to innovate, develop and commercialise mRNA technology, particularly if the aim is rapid development in response to a public health concern.

Perhaps inevitably given the increasing value and commercial importance of mRNA technology, there have been several high-profile patent litigation cases between the major players in this field.

Litigation in this field is primarily taking place in the US, the UK and Germany, generally involving the companies currently at the top of this field due to their involvement in development of the COVID-19 vaccines. As is typical, this national litigation is taking place against the backdrop of patent challenges at the USPTO and the European Patent Office.

In the UK, two first instance decisions have been handed down, with one Moderna patent being found valid and infringed, but the remaining patents in issue being found invalid. The litigation has also served to illustrate some of the strategies adopted and public policy decisions taking by companies to enter the market unheeded.

"Navigating overlapping patent rights with a view to licensing certain foundational technology can lead to high transactional costs"

The growth of the mRNA industry

The technology surrounding synthetic mRNA can be viewed as a platform, with a major advantage being the potential in speed of design and scalability. Once the genetic sequence of a protein or antigen is known, it is relatively fast and easy to synthesise mRNA that codes for that desired molecule, with the delivery system remaining broadly the same. As such, this technology is an attractive investment for companies looking to build a portfolio of products.

Reflecting this, the market is booming. The global mRNA vaccine and therapeutics market is currently valued at approximately $40 billion. This is an increase from $27 billion in 2020, with the market estimated to reach almost $70 billion by 2030.

North America is most prominent in the global mRNA and therapeutics market at present, with an ever-increasing availability of research funding alongside federal programmes for RNA-based therapeutics. Moderna and BioNTech have the most wide-ranging patent estates in relation to mRNA technology, with other key players including CureVac, GSK, Sanofi, CSL and Arcturus. And there is more to come, with the EPO reporting a steep increase in mRNA patent filings, including international patent applications, demonstrating multinational commercialisation strategies and the significant economic expectation in this field.

The potential of mRNA vaccines is emphasised by the number of viral targets for which patents have been filed, not only including coronavirus and influenza but also HIV, papillomavirus, pneumovirus and flavivirus, among others. It has also long been of interest in the treatment of cancer, with scientists using their knowledge from research and development of mRNA cancer vaccines to develop the COVID-19 vaccines. It has been reported that a global clinical trial for an experimental mRNA lung cancer therapy developed by BioNTech is underway, with the first UK patients receiving treatment at UCLH in early 2024.

Of note is the pledge that Moderna made in October 2020, that it would not enforce its COVID-19 related patents against companies developing further COVID-19 vaccines whilst the pandemic was ongoing.

Moderna updated its pledge in March 2022, committing never to enforce their patents for COVID-19 vaccines against companies manufacturing in prescribed low- and middle-income countries, and withdrawing from the commitment otherwise. Moderna then initiated proceedings against BioNTech and Pfizer in 2022, seeking a declaration that two of its European patents were infringed by Pfizer/BioNTech. In contrast to many patent litigation cases filed to date, Moderna did not initially seek an injunction but instead sought monetary compensation, emphasising that it did not wish to remove Pfizer/BioNTech's product from the market, but rather sought damages for sales made from when their patent pledge was modified.

"SEPs in the mRNA field may help to promote rapid and streamlined development of technology at a reasonable cost"

In July 2024, the first patent was found valid and infringed, but the second invalid for obviousness over the prior art and added matter, with permission to appeal granted in September 2024.

Notably, the EPO's decisions on these two patents have been in line with the UK so far. In parallel to the UK infringement/validity trial, a trial concerning the correct timeframe of the damages took place, with Moderna arguing that damages should be due from March 2022 (when it modified its pledge), and Pfizer/BioNTech arguing that the commitment instead only ended in May 2023. The judge agreed with Moderna, meaning damages from Pfizer/BioNTech from any infringements would be due from March 2022.

In Germany, the German Federal Patent Court nullified a Curevac process patent. In the UK, ahead of trial, CureVac accepted the invalidity of the process patent based on the present state of the law. The English High Court then found the remaining patents invalid for insufficiency (lack of plausibility).

The outcomes have not been favourable for CureVac thus far, demonstrating the difficulties in patenting such mRNA technology in

a way that is inventive, sufficient and not overly broad to the extent it impedes innovation in the field unfairly.

Further decisions on these patents are expected from the EPO in March 2025, and in the US following a trial in March.

Collaborations

Over the past few years, we have seen growth in multiple collaboration agreements allowing companies to combine their respective expertise and intellectual property, which is hoped will be a productive way to circumvent otherwise inevitable disputes, as well as a way to speed up the development of technology.

However, navigating the overlapping patent rights with a view to licensing certain foundational technology can lead to high transactional costs in terms of negotiating terms and creating the necessary contracts. Further, the upstream patent owners are likely to want to claim a share of the profit if their technology is used to produce a successful commercial product downstream, leading to higher prices for the consumer.

The most high-profile collaboration during the pandemic was between Pfizer and BioNTech which were very quick off the mark in 2020, successfully collaborating to jointly develop their COVID-19 vaccine, eventually sold under the Comirnaty brand. Off the back of this successful joint approach, the companies signed a new global collaboration agreement in 2022 to develop the first mRNA-based shingles vaccine.

Another lucrative collaboration can be seen between GSK and CureVac, which have been working together since 2020 under a collaboration agreement to develop mRNA vaccines for infectious disease. The collaboration was restructured into a new licensing agreement in 2024 reportedly worth approximately $1.4 billion, allowing GSK to take full control of developing mRNA vaccines.

In 2022, it was reported that CSL Sequiris (a CSL subsidiary) entered into a global collaboration and licence agreement with Arcturus Therapeutics, granting CSL access to Arcturus' late-stage self-amplifying mRNA vaccine platform technology.

Further, in 2022, Merck entered into a collaborative agreement with Orna Therapeutics with the aim of discovering, developing and commercialising a new generation of mRNA technology programs, including vaccines, oncology and infectious diseases. The collaboration combines Orna's circular RNA technology with Merck's expertise in nucleic acid biology, clinical development and manufacturing.

In a further development Moderna are collaborating with OpenAI to advance mRNA medicine, a move that was announced in April 2024.

In lieu of collaboration, various companies have also decided to invest in sub-licences to certain technology, in order to make use of advanced but protected foundational technology. Notably, both Moderna and Pfizer/BioNTech sub-licensed technology from the University of Pennsylvania protecting nucleoside-modified mRNA. These patents were filed following the discovery that the incorporation of a naturally modified mRNA nucleoside, pseudorine, avoided the body's inflammatory and uncontrolled immune response to synthetic mRNA.

Nucleoside-modified mRNA has since been recognised as key to the high efficacy of the Moderna and Pfizer vaccines. Another example is Gritstone Bio's August 2023 agreement with Genevant Sciences, a leading nucleic acid delivery company with world-class platforms and a robust and expansive LNP patent portfolio. The agreement gives Gritstone a multi-year option for a non-exclusive licence for this LNP technology on a pathogen-by-pathogen basis to develop and commercialise self-amplifying RNA vaccines.

Although collaboration and licensing are in theory non-contentious strategies, it does not always go smoothly and disputes can arise in relation to, for example, breaches of contract and royalty payments.

Notably, BioNTech are currently involved in ongoing disputes in relation to a licensing agreement with the US National Institute of Health (NIH), over allegations from the NIH that BioNTech breached the terms of their agreement and owes the NIH royalties and other amounts on the sales of BioNTech's COVID-19 vaccine. There are also ongoing discussions between BioNTech and the University of Pennsylvania over royalty payments for the series of sublicences to mRNA patents discussed above.

Could SEPs solve licensing challenges?

In the wake of the COVID-19 pandemic, the success and potential of mRNA technology has become evident; mRNA vaccines can be developed quickly and can be very effective. However, the increasingly complicated patent landscape in this field is cause for concern for companies looking to develop their own mRNA vaccine technology.

Further, this technology is vital for healthcare and effectively (and quickly) treating or preventing disease. The availability of this technology is therefore a public health concern and the balance between respecting IP rights and allowing further technology to be

rapidly developed and commercialised, particularly in response to a public health emergency, is a high priority.

During the COVID-19 pandemic, a number of companies and institutions (including Moderna, AbbVie, the University of Oxford and the University of California Berkeley), which already held or were developing key mRNA technology made public commitments (ie, patent pledges) not to enforce their patents against other companies developing COVID-19 vaccines using their underlying technology. However, these commitments are not indefinite and can be withdrawn with a view to demanding licences to the necessary technology.

In revising its patent pledge in 2022, Moderna stated that it would consider a commercially reasonable licence for its technology going forward and, as discussed above, a number of companies have actively and voluntarily engaged in licensing deals for certain strands of foundational technology, to varying degrees of success. However, some companies may be hesitant to engage in such licensing deals, which require significant transactional cost.

An alternative solution to the current voluntary patent pledge dynamic could be the introduction of standard essential patents, to create a predictable and fair licensing model and facilitate the rapid development and commercialisation of life-saving mRNA vaccines.

The SEP model is, of course, well-known in the patent community, but mostly regarding standardised technology in the mobile phone and tech sectors. A SEP system in the mRNA field may help to promote rapid and streamlined development of technology at a reasonable cost, leading to better treatment for life-threatening disease and perhaps reducing side-effects or failed clinical trials due to non-standard technology being trialled to avoid patent infringement.

Whether or not this, or another alternative approach is successful, there is no doubt that the evolving world of mRNA technology is an exciting one to watch. IAM

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"SEPs in the mRNA field may help to promote rapid and streamlined development of technology at a reasonable cost"

BPCIA LITIGATION NOW: SHIFTING STRATEGIES IN US BIOSIMILAR DISPUTES

A first wave of litigation, characterised by a relatively conservative approach has been replaced with strategy that is both more aggressive and refined, writes Robert Cerwinski and Mike Cottler of Gemini Law, Bharati Nadkarni of Appropriate IP Services and Huiya Wu of Goodwin Procter

Though the United States' statute governing biosimilars, the Biologics Price, Competition & Innovation Act (commonly known as the BPCIA), was enacted in 2010, patent infringement litigation under the BPCIA's litigation resolution scheme did not begin in earnest until 2014.

That first wave of litigation, stretching from 2014 to 2020, involved older reference biologics such as filgrastim (Neupogen), pegfilgrastim (Neulasta), rituximab (Rituxan), trastuzumab (Herceptin), bevacizumab (Avastin), etanercept (Enbrel), infliximab (Remicade), and adalimumab (Humira) (although the last adalimumab litigation concluded in early 2022).

In this first wave, brand and biosimilar manufacturers, as well as the courts, learned some of the metes and bounds of the complex and often infuriatingly vague statute, and adopted a relatively conservative approach to testing infringement allegations and defences in court.

Most cases settled prior to a judgment of any kind on the merits, perhaps reflecting the industry's uncertainty about the risks and rewards of litigating cases under this complex new statute.

Since 2021, the US has been experiencing a second wave of biosimilar litigation, involving newer biologics such as ustekinumab (Stelara), natalizumab (Tysabri), ranibizumab (Lucentis), tocilizumab (Actemra), aflibercept (Eylea) and denosumab (Prolia/XGEVA).

This second wave has seen far more aggressive litigation, reflecting a refinement of tactics based on the lessons learned in the first wave, and with more at stake as each branded reference product attracts multiple biosimilar filers.

Below is a deeper dive into the lessons learned in these two waves of litigation.

What did we learn in the first wave?

In the first wave, commencing in 2014 and ending around 2020, litigants learned the ins-and-outs of the pre-suit exchange of patent and regulatory dossier information that became known as the "patent dance". Biosimilar companies learned how to safeguard the confidentiality of their dossiers and manufacturing processes beyond the bare-bones default confidentiality provisions in the statute. Both sides tested whether dancing was mandatory or not (it is, but the lack of a private right to enforce compliance with the dance means that, as a practical matter, biosimilar manufacturers can opt out to save the time and money it takes to dance when they deem it more efficient to do so).

The term "patent thicket" was coined to describe the vast estates of 30, 40, and even 80+ patents that brands had assembled to assert against biosimilar competitors. Biosimilar companies learned how to leverage *inter partes* review and post-grant review invalidity challenges at the Patent Trial and Appeal Board to winnow these thickets prior to district court litigation, and the circumstances under which a "one wave" or "two wave" litigation could make litigation more efficient (biosimilar litigants found little value to a "two wave" litigation, in which the parties first litigate a short list of key patents while leaving the others for a later day, except in cases involving AbbVie's unusually large patent estate for Humira, which consisted of 80+ patents).

Crucially, biosimilar companies learned key differences between the BPCIA and the Hatch-Waxman Act governing "small molecule" generic drugs, in particular the strategic advantages of there being no automatic 30-month stay of FDA approval blocking "at risk" launch, and the economic disadvantages of there being no first-to-file biosimilar exclusivity for the first biosimilar to tackle the brand's patent estate.

Further, litigants learned that pre-approval preliminary injunction proceedings could be key to settling litigation, with most litigations settling in the run-up to a preliminary injunction hearing, rather than the brand risking early biosimilar entry and the biosimilar risking being enjoined for the years it would take to obtain a judgment after trial.

Finally, few companies viewed the risk and cost of doing the extra clinical trial work needed to obtain an "interchangeable" designation from FDA as being worth it. In theory, an interchangeable designation allows for automatic substitution of the biosimilar for the brand product at the pharmacy level, akin to what happens with AB-rated generic drug substitution under the Hatch-Waxman Act. But few biosimilars had a clear enough understanding of the commercial benefits to risk the extra cost and regulatory uncertainty.

How has the second wave of biosimilar battles differed?

The second wave has seen the conservatism that was the hallmark of the first wave of litigation abandoned in many cases. Now it is very common for biosimilar manufacturers to seek approval in the first instance as interchangeables, to avoid being disadvantaged in the marketplace against other interchangeable biosimilars.

Patent thickets have grown larger and more prevalent, since the Humira patent estate demonstrated in the first wave of litigation the value of these thickets in driving favourable settlements with biosimilar manufacturers.

And while biosimilar manufacturers have continued to eschew a "two wave" patent litigation schedule in favour of one wave that moves as quickly as possible to resolve the inevitable preliminary injunction motion, litigants have been far more willing to litigate preliminary injunctions through a decision than to settle early. To date, most of those decisions have come out in favour of biosimilar challengers, with the multi-district litigation involving aflibercept being the lone example of an injunction being granted.

Inter partes reviews and post-grant reviews have become even more important, with some litigations, for example those involving tocilizumab, settling before BPCIA litigation even begins after the biosimilar obtained institution of multiple IPRs and/or favorable final determinations.

Finally, most district court cases happened in Delaware or New Jersey, which are among the most experienced in Hatch-Waxman litigation. But the aflibercept case has seen the Multi-District Litigation rules invoked to collect all biosimilar filers in West Virginia, a relative stranger to this kind of litigation, but a forum that Regeneron, the brand, viewed as favourable. This previewed the possibility of more forum shopping by brands.

Here are some of the more important lessons learned to date from this second wave of biosimilar litigation.

Patent thickets: here to stay

Patent thickets include various patents on everything from a dosing schedule, formulation, upstream process (USP), downstream process (DSP), purity/impurity profile, method of analysis, packaging, to an injection device. These thickets — once a target of government scrutiny in the US — are being used to stave off biosimilar competition by more than a few years.

These thickets are reflected in the FDA's "Purple Book". The Consolidated Appropriations Act, enacted on 27 December 2020, required the FDA to create a searchable, electronic database of biologics approvals and, by 25 June 2021, to update it with patent information provided by the reference product sponsor to a biosimilar applicant during the patent dance process.

The requirement to list patent information is forward looking; the FDA is not required to go back in time to list patent information that was exchanged before the enactment of the Act.

In practice, patents often get listed in the Purple Book, even before a complaint is filed. As of 13 September 2024, 13 biologics have been updated with patent information, resulting from patent dances ahead of litigation under the BPCIA. The Purple Book does not identify which patents may have been asserted against which biosimilar filer; it simply presents one list of all the patents identified by a reference product sponsor. A summary of the number of patents asserted in biosimilar matters is listed below.

Despite the trolling on patent thickets, they continue to be a mainstay in the US. In fact, very few brand companies have asserted fewer than 10 patents in litigation (only five out of the 13 products with patent lists in the Purple Book).

Table 1: A summary of the number of patents asserted in biosimilar matters

Brand name	Company	Product	Patents asserted
Eylea	Regeneron	Aflibercept	72
Lucentis	Genentech	Ranibizumab	11
Avastin	Genentech	Bevacizumab	22
Humira	AbbVie	Adalimumab	66
Neulasta	Amgen	Pegfilgrastim	01
Tysabri	Biogen	Natalizumab	32
Stelara	Janssen	Ustekinumab	06
Actemra	Genentech	Tocilizumab	35
Prolia & XGEVA	Amgen	Denosumab	47
Herceptin	Genentech	Trastuzumab	04
Rituxan	Genentech	Rituximab	15
Xolair	Genentech	Omalizumab	08

Source: Purple Book, last updated 13 September 2024

"The second wave has seen far more aggressive litigation, reflecting a refinement of tactics based on the lessons learned in the first wave, and with more at stake as each branded reference product attracts multiple biosimilar filers"

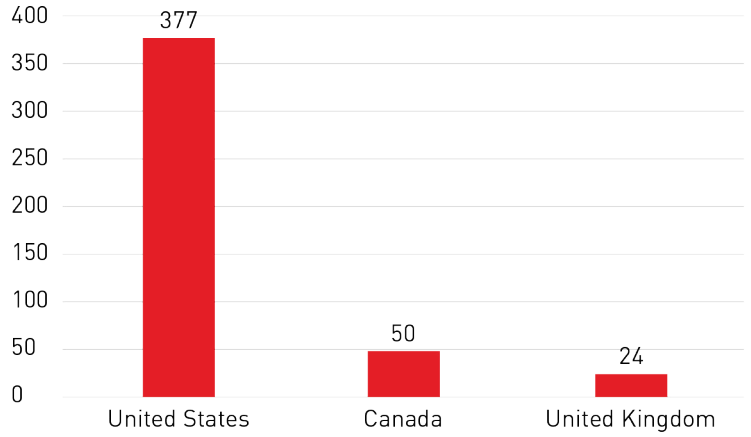
Regeneron recently asserted a total of 72 patents against various biosimilar filers to protect Eylea (aflibercept), which is six more than those asserted by AbbVie for protecting the Humira (adalimumab) franchise. This strategy has proven fruitful. Although a substantial number of Regeneron's method of use and formulation patents were invalidated in court, held unpatentable at the PTAB, or voluntarily disclaimed, Regeneron was still able to secure preliminary and permanent injunctions (all of which are now on appeal) based on one of its remaining formulation continuation patents.

While Purple Book-listed patents cover everything from cell line, cell culture medium, upstream and downstream processes, analysis, variants, formulation, method of use (including dose and regime), device and packaging, the majority of the asserted patents across all BPCIA cases seem to be directed to upstream processes and methods of analysis. It is also interesting to note that most of these process patents are not specific to any biologic product but are generic in nature. The patents on formulation, variants and devices, which are mostly specific to the product, are the next most commonly asserted types of patents.

The figure below, using information from Rachel Goode and Bernard Chao's "Biological patent thickets and delayed access to biosimilars, an American problem" published in the Journal of Law and the Biosciences, indicates the total number of patents asserted against 30 biosimilars, in various countries. Clearly, biosimilar litigation in US includes far more patents than its counterparts in Canada and the UK.

No surprises there, given the US is the largest market for these products.

Figure 1: The number of patents asserted against 30 biosimilars in various countries



Source: Rachel Goode and Bernard Chao "Biological patent thickets and delayed access to biosimilars, an American problem"

Preliminary injunctions: which way is the tide turning?

Most of the first wave of BPCIA litigations settled while injunction motions were pending. At-risk launches can carry risks for both sides: for the biosimilar, there is the risk that it could be enjoined for years until final judgment or that it could be subject to damages if it launches but later loses. For the patentee, there is the risk of an unfavourable decision that may open the market to multiple competitors earlier than planned.

The second wave of biosimilar litigation has seen an uptick in preliminary injunction proceedings, but settlements are less common. Because outcomes are somewhat mixed in this second wave, it is unclear if the tide is turning any particular way.

One PI case stands alone as having settled before the PI was resolved. Amgen filed suit in District of New Jersey against Sandoz regarding Sandoz's denosumab biosimilar product. The parties settled in April 2024 on the same day the court was set to issue its ruling.

Amgen's motion relied on three patents, a molecule patent expiring in February 2025, a process patent expiring in 2027, and another process patent expiring in the 2030s. Under the settlement agreement, Sandoz is free to launch at least as early as 31 May 2025.

Amgen is now litigating three other biosimilar manufacturers, Celltrion, Samsung Bioepis, and Fresenius, regarding the same molecule, and it remains to be seen how the outcome in the Sandoz case will shape these more recent ones.

All the other second wave preliminary injunction motions were fully resolved and limited to two venues: the District of Delaware and the Northern District of West Virginia.

The District of Delaware has yet to grant a preliminary injunction motion. In the first wave, it denied motions filed by Genentech concerning bevacizumab and trastuzumab, and that trend has continued.

In the natalizumab matter filed by Biogen against Sandoz, Biogen's motion relied on three patents: two relating to diagnostic methods and

the other to cell culture media. Not only did the court find that Biogen was unlikely to prove infringement, it also found a lack of irreparable harm because the harm was "speculative and uncertain". Sources showed that the average sales price of a reference product generally did not change in the 12-18 months after an at-risk launch, and there was no nexus between the claimed inventions and commercial demand.

As to that last point, the court found it persuasive that Biogen did not identify as material the asserted patents until the PI motion was on file – reflecting that Biogen itself did not see value in those patents. Biogen's missteps proved costly; while the litigation remains pending, Sandoz launched its biosimilar in January 2024, within several months of receiving FDA approval.

In the eculizumab matter filed by Alexion against Samsung Bioepis, the court denied Alexion's PI motion based on two method of treatment patents after finding that Alexion had not established a likelihood of success with respect to validity.

Notably, as to one of the patents, the court concluded that Alexion was not likely to prevail solely because the PTAB had instituted Samsung's IPR against that patent – citing other district courts that had similarly found that institution of IPR by itself raised a substantial question of validity. Unlike Sandoz, however, Samsung did not launch at risk and instead recently settled with Alexion for an unknown settlement date.

The Northern District of West Virginia has now decided four preliminary injunction motions all concerning aflibercept and all relating to a single formulation patent; three of those injunctions – against Celltrion, Samsung Bioepis, and Formycon – were granted, and fourth – against Amgen – was denied.

The outcomes were different because, while Amgen found a way to design around the formulation patent, Celltrion, Samsung Bioepis and Formycon were forced to challenge the patent's validity. What makes the injunction orders interesting is the cases' procedural history. Mylan had already had a full trial on the same formulation patent before the same judge and lost on invalidity.

Although Celltrion, Samsung Bioepis and Formycon presented different defences and evidence, the prior trial may have given Regeneron a more favorable forum for its later preliminary injunctions. The outcome in the aflibercept cases stresses the importance of being a first mover in BPCIA to shape the district court's thinking and to find creative ways of designing around patents where possible.

How did the aflibercept cases end up in West Virginia?

Currently in the US, there are pending BPCIA litigations on the following three products: aflibercept (Eylea), denosumab (Prolia and XGEVA), and natalizumab (Tysabri). The most contentious involves aflibercept.

Regeneron has sued six biosimilar filers: Mylan (now Biocon), Celltrion, Samsung Bioepis, Formycon, Amgen, and Sandoz. All cases were either filed in the US District Court for the Northern District of West Virginia, or ended up there after referral from the Judicial Panel on Multidistrict Litigation. How did six biosimilar filers, five with little or no presence in West Virginia, all end up in such an uncommon district for patent litigation?

In TC Heartland v Kraft Foods Group Brands, the Supreme Court held that, for purposes of venue in patent-infringement litigation, a domestic US corporation "resides" only in the state where it is incorporated. In accordance with this decision, it makes sense that Regeneron sued Mylan, which is incorporated in the State of West Virgina, in the Northern District of West Virginia. TC Heartland's holding, however, does not explicitly encompass foreign corporations, so Regeneron argued that venue is proper against each of Celltrion, Samsung Bioepis and Formycon in any judicial district.

After an expedited trial in the Mylan case in June 2023 (and perhaps in anticipation of a favourable result), Regeneron decided to sue each of these three foreign corporations in the Northern District of West Virginia. Celltrion, Samsung Bioepis and Formycon each raised challenges to personal jurisdiction (which is different than venue),

"Patent thickets have grown larger and more prevalent, since the Humira patent estate demonstrated in the first wave of litigation the value of these thickets in driving favourable settlements with biosimilar manufacturers"

which the court has—for now—rejected, and which is up on appeal for review by the Federal Circuit.

But how did Amgen, a company headquartered in California and incorporated in Delaware, and Sandoz, a company incorporated in New Jersey and also incorporated in Delaware, also end up in the Northern District of West Virginia? The answer is multi-district litigation.

Pursuant to 28 U.S.C. §1407, related federal civil cases in different jurisdictions can be transferred to one judge for consolidated pretrial proceedings. Here, Amgen was initially sued in the US District Court for the Central District of California, but Regeneron moved to have the Amgen case transferred to Chief Judge Kleeh in the Northern District of West Virginia, arguing, among other things, that the defendants infringed a common set of thirteen US patents covering Regeneron's ophthalmic drug, Eylea.

The Judicial Panel on Multidistrict Litigation agreed with Regeneron, finding that the various aflibercept actions involve "common questions of fact and that centralization in the Northern District of West Virginia will serve the convenience of the parties and witnesses and promote the just and efficient conduct of the litigation". It granted Regeneron's motion to transfer the Amgen case to West Virginia over the defendants' objections that that were many non-overlapping patents, patent defences that are unique to each defendant, and different procedural postures of the cases. The panel also agreed that Sandoz should be joined with the other litigants too.

These aflibercept cases remind us that, unless you are the first biosimilar filer to be sued, it may be difficult to predict what court you end up in, and that venue in line with the holding of *TC Heartland* is not guaranteed, even if you are a domestic corporation.

Being first-to-file thus gives a (domestic) biosimilar company another advantage: venue in the judicial district where you reside. IAM

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"These aflibercept cases remind us that, unless you are the first biosimilar filer to be sued, it may be difficult to predict what court you end up in, and that venue in line with the holding of TC Heartland is not guaranteed, even if you are a domestic corporation"

CAPITALISING ON MEDICAL DEVICE IP OPPORTUNITIES IN A CHANGING ENVIRONMENT

Knobbe Martens Partners Philip Nelson, Sabing Lee and Irfan Lateef examine how medical device IP strategists can thrive despite technological and legal upheaval

Intellectual property managers in the medical device industry face a changing legal and business environment that can present significant challenges. Medical device inventors, such as physicians, engineers, and consultants, are frequently not employees and may be under restrictive obligations to others. Preferred patent strategies to protect medical technologies are complex, whereas IP budgets may be limited or company management may harbour false notions about IP value. Numerous patent lawsuits involving medical device patents are a reminder that patent infringement is always a concern, even for start-up companies. In this environment, how can an IP manager best protect the company's intellectual property position and address the latest trends in patent law and the medical device industry?

Know your inventors

Patent ownership in the United States begins with inventorship, requiring an IP manager to keep track of everyone involved in the inventive process. The prevalence of non-employee inventors involved in medical device development makes this an even greater challenge for the medical device IP manager.

Physicians are a common source for medical innovations—interfacing directly with patients—and thus well-positioned to assess unmet clinical needs. Physicians often collaborate with engineers or medical device companies to develop their inventions while maintaining their medical practices. Assignment obligations to healthcare institutions, universities, and other employers should be carefully scrutinised whenever a physician is involved in founding a company or is identified as an inventor. When physicians are asked to provide clinical input on a medical device, any ideas they generated could result in new inventions and raise ownership issues. IP managers should ensure that agreements assigning intellectual property rights to the company are executed and that these agreements do not impose obligations that conflict with prior existing obligations.

Medical device companies, especially early-stage companies, frequently hire consultants and independent contractors to provide design and engineering services, create prototypes, and perform testing. These services often merely validate a design, and thus do not provide inventive input. Often, the only agreements in place with consultants and independent contractors are nondisclosure agreements or purchase orders with limited terms and conditions. But inventions can arise spontaneously, and using a standard agreement without an IP assignment clause can spell trouble if a consultant conceives a significant improvement (for example, based on the company's confidential information), and the company has not yet acquired the rights.

Many skilled inventors are hired based on prior work experience, requiring IP managers to be mindful during job transitions. When hiring, companies should consider whether a former employee has surviving obligations, including restrictions on the use of the former employer's confidential information and requirements regarding assigning later-conceived inventions. Similarly, for departing employees, the company should confirm that employment agreements and exit procedures protect confidential information and should also remind departing employees of their ongoing obligations.

Special consideration should be given to the inclusion of any non-compete provisions, as the Federal Trade Commission has recently sought to ban such provisions completely. Courts may be reluctant to enforce the FTC ban; it is on hold, pending several appeals.

Assignment tip

In addition to obtaining standard or blanket invention assignment agreements, companies should require all inventors to sign patent-specific assignments whenever patent applications are filed for new technology. The earlier such rights are transferred, the better, especially where an inventor leaves or changes loyalties. Such assignments may include special provisions, such as a clause that restricts inventors from later challenging validity—a hedge likely warranted after the US Supreme Court's recent Minerva case narrowed the doctrine of assignor estoppel. Clauses restricting validity challenges may be included in a licence that returns royalties to an independent inventor.

Using patents to protect medical technology

Patents are vital for protecting medical device technology. According to the World Intellectual Property Organization IP Statistics Data Center, the number of US patent grants for medical technology has steadily risen over the last decade, from about 10,000 in 2010 to over 20,000 in 2020. While trade secret protection should still be considered for information and innovations a company can keep secret—for example, manufacturing methods and compositions that cannot be reverse engineered—most medical device innovations worthy of protection will eventually be commercialised or otherwise disclosed, subjecting them to imitation. For this reason, medical device companies pursue diverse patent portfolios with claims for multiple types of inventions. This may include claims directed to more traditional innovations such as implants, delivery tools and related methods, as well as innovations based on more recent technology trends, such as wearable devices, pre-operative and intra-operative surgical software, robotics, patient-specific devices and treatments, augmented and virtual reality, and use of AI.

File patent applications early and often

Most medical device innovations take years to reach commercialisation, and regulatory challenges before the FDA and around the world can

prolong the process. The medical device IP manager must navigate the timing of patent filings while considering clinical and commercial development.

Once a company learns of an invention, it should work quickly to describe and file a suitable patent application—potentially as a provisional patent application. Early-stage innovations can begin as a simple sketch, which the inventor can supplement with a short explanation of its significance and related clinical need. The inventor or company need not build a working embodiment or prototype; working with an experienced medical device patent attorney can help bring out the necessary details for patent filings, including how the invention is to be used in clinical practice and addresses an unmet need. Because the commercial product may still take years to develop, the initial utility patent application should cover the main functional concepts that address the unmet clinical need to remain relevant to future iterations. Design patents should be considered for protecting non-functional, ornamental aspects of the product.

Because medical device companies often work with non-employee inventors who haven't been trained on patent issues, it is good practice to remind inventors of the deadlines for further filings. Using the one-year deadline for conversion to a nonprovisional patent application can incentivise developments during the intervening year, with a series of provisional patent applications all building on the same initial disclosure. The ultimate application can collect all the options and embodiments. Inventors should also be reminded to file updated applications before any public disclosure, especially at medical conferences. Some companies disclose their ideas at conferences after the initial provisional application is filed, but any disclosure should not exceed the subject matter disclosed in the filed application. With every new public disclosure date, whether by the company or any inventor, the IP manager should consider if new filings are warranted.

Building a robust portfolio while managing expenses

As a company works through the stages of medical device development—for example, through prototyping, animal and human testing, and regulatory submission—the patent portfolio will grow. This is why many medical device companies have a large portfolio of patents covering various product iterations. IP managers must determine what protection to seek in each application, and how to manage costs.

What should companies claim in their nonprovisional filings? Medical device companies often seek apparatus claims first, covering aspects such as the structure of the device and the system for delivering it into the body. But "method of treatment" claims, where available, are sometimes preferred to seek a quicker allowance when the method itself is inventive. The United States is one of the few countries that allows method of treatment claims, directed to treating a patient using a medical device. Infringement of method of treatment claims is typically not pursued against the physician, but rather against the medical device manufacturer who "induces" infringement of the method claim steps, often by virtue of the "Instructions for Use" or "IFU." Because some medical devices are reusable and others are single use, IP managers should also consider claims directed to the device whose sales generate the most revenue, which may be a single-use, disposable device or component.

With the rise of drug-devices, pharmaceutical patent strategies and medical device patent strategies are merging to protect these hybrid products. Patent applications should include both Markush-style compound descriptions and detailed mechanical drawings, providing a great range of options for later patent procurement and enforcement.

IP budget limitations, especially for startup medical device companies, may make it challenging to simultaneously pursue all desired claim strategies. Company leadership, as well as the inventors, should understand that patent claims initially issued will not always protect all that is described in a patent application. Some medical device companies may choose to file a single comprehensive nonprovisional application that supports several types of claims, and file for different claims, one at a time. Obtaining a first patent may serve to protect one aspect of the invention, and may also help a startup company obtain financing, while subsequent continuation applications can include different claims. Serial prosecution allows companies to obtain additional protection for other innovations and to obtain more refined protection on aspects of the initial description that have become more valuable in hindsight. Other companies may file multiple parallel patents—often based on a single comprehensive disclosure—to quickly create a robust portfolio. Mixing these strategies is often the right approach.

Fee warning

In the past, medical device companies have often filed large patent applications describing more than one generation of their flagship technology, planning to use the serial continuation strategy described

above—and minimising up-front legal expense. However, in 2024, the United States Patent and Trademark Office announced it will significantly increase the fees it charges for continuation applications, adding a new $2,700 "surcharge" for continuations filed after six years from priority, and $4,000 for those filed after nine years (fees are reduced for small entities). These will begin January 19, 2025. Managers should consider filing parallel continuations if needed before that date, to avoid substantially increased fees—especially for older patent families. Because many medical device technologies can take more than six years to achieve commercialisation, IP managers in the future may want to track these six- and nine-year deadlines and file continuations to cover the latest embodiments before having to pay the surcharge.

Patent portfolio jumpstarts for medical device technologies

Medical device technologies at the USPTO are generally examined within Technology Center 3700 (TC 3700). The most recent statistics from the USPTO indicate that TC 3700 takes on average 19 months from filing to issue a first Office Action addressing whether the invention is new and novel. It takes about 28 months from filing to issue a final Office Action. Considering that many medical device patent applicants use provisional applications and file the nonprovisional application one year later, this means that it can take up to three-and-a-half years or more from initial filing to obtain a determination from the USPTO of whether a company's patent application is allowable.

For faster results in this medical-device specific Technology Center, companies should consider filing one or more "Track 1" applications, which require an additional fee, for faster examination. Patents can be issued in as little as six months using this option, and companies need only pay an additional fee of $4,200 for a large entity and $1,680 for a small entity to request prioritised, or Track 1 review.

Medical device applicants should also consider capitalising on inventor insight to help prosecution move forward. Managers should encourage the patent attorney to discuss claim strategy and office action responses with the inventors, even inviting them to participate in patent office interviews. For example, a physician inventor's description of problems solved and industry needs are often more persuasive to a patent examiner than purely legal arguments presented by patent attorneys. Patent examiners appreciate a glimpse into the clinical benefits, presented by doctors on the front lines. These interviews can add variety to an examiner's daily routine and are particularly well received for medical device inventions, where clinical benefits are so clear.

Trends in patent enforcement and defence

Patent litigation has changed significantly over the last decade for the medical device industry due to the prevalence of proceedings brought before the Patent Trial and Appeal Board. In the medical device industry, recent statistics indicate that about 56% of inter partes review petitions are instituted, meaning that a patent trial will proceed, 19% are denied institution, 9% are settled before institution, and the remaining petitions are dismissed on procedural grounds. Of the IPRs that are instituted, about 20% result in all claims being upheld, 19% result in at least one claim being upheld, and 61% result in all claims being held unpatentable.

Patent holders who enforce their patent through infringement litigation should be prepared for a fight at the PTAB. Potential infringers, even those not yet in a lawsuit, may want to start searching for prior art that can be used in an IPR challenge. Companies on both sides should know that while the PTAB has been more favourable to patent challenges than federal courts, a new proposed law (the PREVAIL act) could modify IPR procedures to the benefit of patent holders.

"Most medical device innovations take years to reach commercialisation, and regulatory challenges before the FDA and around the world can prolong the process. The medical device IP manager must navigate the timing of patent filings while considering clinical and commercial development"

Section 101 attacks on medical device inventions

The internet of medical things is spawning many inventions as devices become more sophisticated and networked. But recent patent cases may cause networked or algorithm-reliant devices to fall under a disfavoured tier of patent applications. If a patent relates to software or medical diagnostics, it could be vulnerable to attack for being an "abstract idea", and hence unpatentable under 35 U.S.C. § 101. The Supreme Court decision in *Alice* spawned a series of cases striking down issued patents, many in the medical diagnostic or software domains, for being directed to "abstract ideas". As medical devices become increasing software-dependent, their patent strategies can be upended by allegations that algorithms somehow render their device too "abstract" for patenting. Even patent applications that claim devices have been rejected by patent examiners on § 101 grounds, for example, where the claim is for a device using a processor making determinations using a basic sensor.

If a company finds itself facing § 101 rejections, or if its patent strategy is based heavily on software or diagnostics, IP managers should carefully craft initial claims based on the relevant case law. IP managers should also stay abreast of actual and potential changes in the law, including a new proposed law (PERA) that would restore patent eligibility to certain inventions. Under this proposed law, processes that cannot be "practically performed" without the use of a machine (including a computer) would generally be eligible for patent coverage.

Litigation trends and assertion of physician-created inventions

Medical device patent litigation remains active, with ongoing cases across several sectors, including cardiovascular, orthopedic, and wearable technologies. Litigation in the medical device industry also extends beyond disputes between commercial stage companies. Prolific physician innovators, for example in the spine industry, are known to build large patent portfolios, using many of the prosecution patent strategies described above, to obtain claims that they enforce against smaller companies to derive licensing revenue. Many doctors ask law firms to enforce the patents on a contingency, where a percentage of any damages (or royalties) would be divided between the law firm and the doctor/inventor. In such cases, the inventor may agree to be available as a witness or consultant for legal proceedings, without having to fund the litigation. Medical device companies who conduct patent searching should include physician-owned patents in their search strategy to locate potential risks. IAM

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PATENTING PERSONALISED MEDICINE – ONE SIZE DOES NOT FIT ALL

Sterne Kessler's Paul Calvo points out IP pitfalls of personalised medicine innovation – and how to sidestep them

The rise of personalised medicine is creating new opportunities for life-changing life sciences innovation. The development of new diagnostic and computational techniques for identifying and analysing biomarkers – such as particular generic features – is enabling the creation of drugs designed to treat smaller, more specific patient populations.

However, there are significant pitfalls that need to be avoided when seeking patent protection for the diagnostic approaches often involved in personalising medicines and major potential obstacles to enforcing related IP rights. Fortunately, there are tactics that can be used to secure strong protection of personalised medicine-related innovations.

Global considerations

Different countries have different perspectives on the patentability of personalised medicine therapies. For example, the US focuses heavily on subject matter eligibility of personalised medicine therapies, while other jurisdictions, such as Europe, focus more heavily on novelty and inventive step analyses. This begs the question, is the way to skirt the issues associated with personalised medicine to have creative exercises in claim drafting?

Some jurisdictions, such as China, do not allow methods of diagnosis claims or methods of treatment claims all together. However, careful drafting of the claims, such as using Swiss-type claims which are allowed in China, may facilitate patentability of personalised medicine approaches in these types of jurisdictions. In addition, patent applicants in China should consider drafting two

sets of claims: one set directed to the manufacture of a diagnostic kit, and the other set directed to a manufacture of a medicament for the treatment of a disease. Having two sets of claims provides more protection because personalised medicine therapy often involves multiple steps that are performed by different parties (eg, a diagnostics test performed by a laboratory and the prescription of a drug by a physician). An example of Swiss type claims directed to a personalised medicine therapy is as follows:

[Diagnosis Swiss-type Claim]: Use of a biomarker Z detection reagent in the manufacture of a or determining the efficacy of substance X therapy for Y disease.

[Treatment Swiss-type Claim]: Use of Substance X in the manufacture of a medicament for the treatment of Disease Y, wherein Disease Y is [a specific subgroup].

Some other jurisdictions, such as Japan and Europe, prohibit patents on inventions directed to methods of diagnosing and treating humans. In jurisdictions such as these, drafting the claims as medical use claims or Swiss-type claims may likewise allow for patentability of personalised medicine therapies.

The specific requirements of each patent office should be carefully considered when drafting claims to protect personalised medicine therapies. Differences in patentable subject matter across jurisdictions may require pursuing several different claim formats to cover these therapies.

Subject matter eligibility

In the US, there are significant potential barriers to obtaining patents for personalised medicines. It has been well established since the Supreme Court's *Mayo v Prometheus* decision in 2012 that claims reciting a correlation between a metabolite and the likelihood of a patient to respond to a drug is not patentable without "more".

Similarly, the Federal Circuit's *Myriad Genetics* ruling of the same years established that screening for cancer-predisposing mutations with no further non-mental steps is ineligible for patent protection because these acts are mental processes without "more".

However, a glimmer of hope for patent applicants came about when the Federal Circuit decided *Vanda Pharmaceuticals Inc. v West-Ward Pharmaceuticals* (2018) in favour of the patentee. The claims in *Vanda* were directed to methods of treating patients with iloperidone comprising a determining step and an administrating step of the drug. A comparison of a representative claim from *Vanda* and *Mayo* is shown below:

Both the *Vanda* and *Mayo* claims are broadly directed to a patient's ability to metabolise a drug. However, in *Vanda* the Federal Circuit distinguished *Mayo* stating that the claims in *Mayo* recited a natural relationship, while the claims in *Vanda* provided an application of that relationship. In *Mayo*, the majority observed that the claims were not directed to a novel method of treatment, but rather a diagnostic method based on the "relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm."

Vanda	Mayo
A method for treating a patient with iloperidone, wherein the patient is suffering from schizophrenia, the method comprising the steps of: determining whether the patient is a CYP2D6 poor metaboliser by: obtaining or having obtained a biological sample from the patient; and performing or having performed a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metaboliser genotype; and if the patient has a CYP2D6 poor metaboliser genotype, then internally administering iloperidone to the patient in an amount of 12 mg/day or less, and if the patient does not have a CYP2D6 poor metaboliser genotype, then internally administering iloperidone to the patient in an amount that is greater than 12 mg/day, up to 24 mg/day, wherein a risk of QTc prolongation for a patient having a CYP2D6 poor metaboliser genotype is lower following the internal administration of 12 mg/day or less than it would be if the iloperidone were administered in an amount of greater than 12 mg/day, up to 24 mg/day.	A method of optimising therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising: (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and (b) determining the level of 6-thioguanine or 6-methyl mercaptopurine in said subject having said immune-mediated gastrointestinal disorder, wherein the level of 6-thioguanine less than about 230 pmol per 8×108 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and wherein the level of 6-thioguanine greater than about 400 pmol per 8×108 red blood cells or a level of 6-methyl mercaptopurine greater than about 7000 pmol per 8x108 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

Conversely, the majority stated that the claims in *Vanda* are "directed to a method of using iloperidone to treat schizophrenia". The *Vanda*

court explained: "At bottom, the claims here are directed to a specific method of treatment for specific patients using a specific compound at specific doses to achieve a specific outcome. . . They recite more than the natural relationship between CYP2D6 metaboliser genotype and the risk of QTc prolongation. Instead, they recite a method of treating patients based on this relationship that makes iloperidone safer by lowering the risk of QTc prolongation."

Therefore, a key takeaway from the *Vanda* decision is to draft claims to include methods of treatment (ie, a therapeutic component with a specific drug) to increase the probability that an administration step will confer subject matter eligibility through a physical act and not merely mental processes.

USPTO guidance on subject matter eligibility

As an outcome of the *Alice*/*Mayo* set of cases, the USPTO provided a two-step approach for determining whether the subject matter of a claim is patent eligible:

Step 1: Is the claim to a process, machine, manufacture or composition of matter? If NO, the claim is not eligible subject matter. If YES, proceed to Step 2A.

Step 2A: Is the claim directed to "a judicial exception", i.e. a law of nature, a natural phenomenon, a product of nature or an abstract idea? If NO: the claim qualifies as eligible subject matter. If YES: proceed to Step 2B. Step 2A is a 2-pronged test. The test of whether the claim is directed to a judicial exception asks whether the claim recites a judicial exception (Prong 1) and whether the claim also does not recite additional elements that integrate the judicial exception into a practical application (Prong 2). If the answer to both is YES, then the claim relates to a judicial exception. commercial importance.

Step 2B: Does the claim recite additional elements that amount to significantly more than the judicial exception? If NO, the claim is not eligible subject matter. If YES, the claim qualifies as eligible subject matter. While Step 2A, Prong 1, and Step 2B are quite similar Step 2B includes a consideration of whether the additional elements in the claim are "significant", in the sense that they are more than well-understood, routine, or conventional. A claim will be found to be ineligible at Step 2B if the additional elements are found to be insignificant.

In July 2024, the USPTO issued a guidance update on patent subject matter eligibility to address innovation in critical and emerging technologies, including artificial intelligence. Example 49 of the guidance is directed to a personalised medicine approach to a method of treatment. Specifically, the method comprises the steps of (1) using an AI model to calculate a risk score to identify patients at risk of a particular disease, and (2) treating these patients with an appropriate (non-specific) treatment. The exemplary claims are shown below:

[Claim 1]: A post-surgical fibrosis treatment method comprising:

(a) collecting and genotyping a sample from a glaucoma patient to provide a genotype dataset;

(b) identifying the glaucoma patient as at high risk of post-implantation inflammation (PI) based on a weighted polygenic risk score that is generated from informative single-nucleotide polymorphisms (SNPs) in the genotype dataset by an ezAI model that uses multiplication to weight corresponding alleles in the dataset by their effect sizes and addition to sum the weighted values to provide the score; and

(c) administering an appropriate treatment to the glaucoma patient at high risk of PI after microstent implant surgery.

[Claim 2]: The method of claim 1, wherein the appropriate treatment is Compound X eye drops.

According to the Guidance, claim 1 includes elements in addition to the abstract idea of the AI model. These additional elements include collecting and genotyping patient samples, and administering an appropriate treatment to the patient. However, these steps are insignificant extra-solution activities that amount to mere data gathering or, in the case of the treatment step, lack specificity and thus are not meaningful constraints. Therefore, claim 1 is directed to a judicial exception and is patent ineligible.

Claim 2, which incorporates all of the limitations of claim 1, however is considered patent eligible because it recites administration of a specific new compound for the treatment of a specific disease. Therefore, determining patient risk of PI after microstent implant surgery and administering Compound X eye drops to glaucoma patients at high risk of PI is a specific treatment that amounts to a "significant" element for patent eligibility. Thus, the addition of a

"significant element" (ie, administering new Compound X) removes the claim as a whole from the judicial exception into a practical application.

Therefore, inclusion of an administration step of a specific treatment may support an argument for subject matter eligibility, but it may introduce other deleterious issues.

Divided infringement

While *Vanda* provided some degree of hope with respect to subject matter eligibility, it did not fully address patentee fears with respect to the enforceability of these claims.

Personalised medicine often requires method steps that are performed by more than one unrelated party. This can lead to divided infringement, which occurs when multiple actors collectively perform all the steps of a method claim such that no one party directly infringes a patent under 35 U.S.C. § 271(a). Direct infringement, "occurs where all steps of a claimed method are performed by or attributable to a single entity", according to the Federal Circuit's Akamai Technologies v Limelight Networks decision (2015).

This often poses enforcement difficulties because an entity can only be held responsible for others' performance of infringing steps in two circumstances: "(1) where that entity directs or controls others' performance, and (2) where the actors form a joint enterprise."

A two-part test for determining when a party is directing or controlling another's actions was articulated by the Federal Circuit in *Akamai*. Specifically, a party can be found to be directing or controlling others' performance when: (1) the party "conditions participation in an activity or receipt of a benefit" upon performance of a step or steps of a patented method, and (2) the party "establishes the manner or timing of that performance."

More recently, the Federal Circuit broadened the two-step divided infringement test from *Akamai* to cover contractual relationships and discussed how to apply the "conditions" test, in Travel Sentry v Tropp (2017).

In *Travel Sentry*, the claims at issue were directed to a method of improving airline luggage inspection by a luggage screening entity by using locks for luggage that could be opened either by the owner entering a combination or by a screening agency using a master key. The claimed method comprised steps of: (1) making available a combination lock for consumers, a key lock for the luggage screening entity and an identification structure known to the luggage screening entity, (2) marketing the lock such that the consumers would know that the lock can be opened by the luggage screening entity, (3) informing the luggage screening entity that there would be an identification structure, and if necessary, (4) having the luggage screening entity act pursuant to an agreement to use their provided master key to open locks.

In applying the first *Akamai* prong, the Federal Circuit found that the Transportation Security Administration realised a tangible "benefit" by using Travel Sentry's technology to identify, open, and inspect checked baggage. The court also relied on TSA's representation that it would undertake "good faith efforts" which could amount to a sufficient "condition" to receive a benefit. Therefore, the court found divided infringement.

Alternatively, to avoid divided infringement scenarios altogether, method claims can be pursued where only the administration step is the active step. For example, a hypothetical claim would read:

A method of inhibiting tumor growth in a patient, comprising: administering to the patient a therapeutically effective amount of an ANTIGEN X inhibitor; wherein the patient is predicted to respond to treatment with the ANTIGEN X inhibitor based upon ANTIGEN X expression in a sample of the patient's tumor.

By drafting claims to have a single administration step or multiple steps that would clearly be attributable to the same actor, divided infringement issues can be avoided while maintaining subject matter eligibility.

"While Vanda provided some degree of hope with respect to subject matter eligibility, it did not fully address patentee fears with respect to the enforceability of these claims"

Other factors

Lack of novelty and obviousness can also be considerable hurdles for applicants attempting to protect new personalised medicine approaches that use known therapeutics. Since these products are known in the art, it can be difficult to protect specific usages that rely on a particular biomarker or dosing regimen.

According to Nova One Advisor, the global personalised medicine market was $530.11B in 2023, calculated to be $574.11B in 2024, and is expected to reach $1,176.66B by 2033. The increasing focus on personalised therapeutics like CAR-T and gene therapy will no doubt also help drive the market as companies focus on protecting platforms and platform processes to ensure freedom-to-operate and identify potential licensing opportunities. IAM

Paul Calvo, Director, Sterne, Kessler, Goldstein & Fox

"By drafting claims to have a single administration step or multiple steps that would clearly be attributable to the same actor, divided infringement issues can be avoided while maintaining subject matter eligibility"

THE CONVERGENCE OF TECH AND LIFE SCIENCES IP STRATEGIES

There has traditionally been a sharp divergence between IP strategies in the life sciences and high-tech sectors. While this remains true to a significant extent, the rise of digital healthcare and the growing role of artificial intelligence in the biopharma sector is creating large areas of innovation where the two sectors overlap and where IP strategists from both sides of the old divide must work together and learn from each other.

The articles in this section how examine companies are seeking to protect inventions in the overlap between tech and the life sciences and how the rise of digital healthcare is creating a new demand for hybrid teams. They also explore how this trend is giving rise to new forms of IP monetisation, including by non-practicing entities, which are beginning to enter the biopharma space for the first time. IAM

DIGITAL HEALTH DISRUPTION: HOW AI IS SHAPING IP STRATEGIES

Patent experts from across the HGF team explore what the rise of AI and digital healthcare means for life sciences IP strategies – from the composition of IP teams and portfolio management to IP licensing and monetisation

Digital healthcare – the use of software for diagnostics, treatment and more fundamental research leading to medical breakthroughs – is everywhere. Such is the transformational impact of computation in the life sciences that 2024 saw a significant high point in the field: the Nobel Prize for Chemistry being won by Sir Demis Hassabis and Dr John Jumper (both of DeepMind) and Professor David Baker (University of Washington and co-founder of various biotech companies).

The Nobel Prize was awarded to this brilliant trio based on their groundbreaking advances in fundamental research core to the drug discovery pipeline. Specifically, these advances were:

- the elucidation of the 3D structures of proteins in AlphaFold; and
- the design of new proteins with new capabilities in Rosetta, allowing the in-silico prediction of the likely behaviours of these complex biological molecules.

Now, these fundamental computational techniques will become part of the diagnostics and treatment of diseases everywhere, providing powerful tools for identifying promising treatments and unravelling biological mechanisms in a way which was previously impossible. As Dr John Jumper said in his call after receiving the Nobel prize news:

"We could draw a straight line from what we do to people being healthy because of what we learn about biology in the cell."

This is what the revolution of computational biology promises.

Businesses that will benefit include big pharma, with computational biology feeding into making their drug discovery pipelines more efficient in terms of:

- finding targets for a disease;
- designing new molecules to hit targets; and
- designing clinical trials more effectively.

Meanwhile, there are smaller biotech companies based around AI-based drug-discovery platform tech, as well as diagnostic companies basing diagnosis not only on any one biomarker but on a complex pattern (for example, in radiology images or from DNA sequencing) in a patient sample that AI can efficiently pick out. Lastly, there are companies supplying software to aid powerful innovations in early blue-sky research, for example ThermoFisher and Illumina.

The changing IP team skillset

So how can businesses navigate this emerging cross-over space between software and life sciences from an IP perspective? It starts with the IP team these companies will need, where the use of AI and/or other mathematics plays a key role in their research and commercial offering.

Before the more widespread use of AI, it used to be that life sciences companies naturally would work with a life sciences IP team. This team would likely have specialists in molecular biology, pharmaceutical chemistry and other 'wet' technology. However, given the integration of software and AI (often as a key part of the innovation) across pharma and biotech companies in general, IP teams both in-house and those providing private practice support increasingly have a bioinformatics specialist in the mix.

Cross-disciplinary teams provide the best support for these digital health companies. Such teams ideally have not only life sciences and software patent attorneys, but people with experience bridging these traditional technology groups who understand both sides, to grasp the important details of how the biology and the mathematics/software mix to output the new and clever results. Attorneys with mixed technological backgrounds are often best placed to cover this middle ground – for example, computational biologists, or electronics and software attorneys with a post-grad in biophysics or the like.

Going further, a trade secret solicitor – whether in-house or external – working in tandem with the patent team can provide a complementary skill set of increasing importance in this space. There has certainly been a resurgence in interest in trade secrets in recent times. There are a number of reasons for this, including that:

- the increase in AI means there is great value in data (such as training data used to train the AI model and the resulting weighting factors) which is not in itself patentable; and
- US law, specifically the inconsistent application of Section 101 to mathematics and software based inventions including AI during US patent examination, has shifted the dial, making companies more willing to use a mixture of patents and trade secrets to cover their tech (although new AI regulatory requirements may shift this back again to patents depending on how much detail regulatory authorities require companies to disclose about their AI tools).

Finally, when considering how to put the optimal IP team together, as mentioned above, US law has particular idiosyncrasies that need to be accounted for in patent applications for AI, ideally at the drafting stage. At the EPO there are also particular considerations to take into account for AI-based patent applications. This is because the EPO examine these applications differently from standard life sciences applications: AI-based applications are examined using the legal tests for computer and mathematics-based applications.

It is therefore important when your IP team are drafting, to keep both the particular US and EP laws relating to software in mind. For important applications, cross-checking the priority ideally, or at least the PCT draft, with an experienced attorney on the opposite side of the Atlantic is recommended to be best prepared for the extra hurdles these applications have to overcome compared with traditional 'wet' life science applications.

What about portfolio management and litigation in this cross-over space?

So now the IP team is in place, we turn to portfolio management.

There is not currently the stream of oppositions around patents relating to drug discovery pipelines between the big pharma companies, in contrast to what is often seen around small molecule patent portfolios. This could be because litigation may not be the main reason behind current software-focused patent filings, but

rather publication and ensuring no-one else can obtain a patent for a particular step in the pipeline.

That said, if there is discovery of a vital platform technology which is AI-based, this is where patent litigation could begin. It brings to mind other fundamental platform technologies, for example phage display, where there was extensive litigation due to the field-changing nature of the way it could identify effective antibodies.

Therefore, the shift to litigation could yet come for large pharma in the AI space (or for smaller AI-drug discovery innovators). Patents being granted for the application of AI and software in the life sciences are exponentially increasing, meaning an increase in EPO oppositions in this space is likely on its way. We are already seeing this in the crowded T-cell therapy space. As these cases go through the EPO, from opposition to the EPO Board of Appeal, the case law in this space will develop and will be important to follow.

Why a multi-faceted approach to IP matters

From smaller AI biotech companies, there can be the view that "we are patenting the end drugs, where the money is, and we will keep our drug discovery pipeline secret". However, small biotech companies will often have an exit strategy in mind, and therefore need investment or buy-out.

Although the patent protection for the end small molecules or other active molecules is where revenue is generated in the short term, the longevity of the company is based on the innovative software platform. If a competitor can use the same platform (because keeping it secret does not stop a competitor independently arriving at your clever platform) then justifying longevity to investors could be more difficult than if there was patent protection in place for the core steps that result in the end drugs.

Furthermore, there are many research collaborations already under way between big pharma and AI-drug discovery companies. Having patent protection for your unique selling point, for example in designing new APIs, will make you more attractive to big pharma.

A multi-faceted IP approach then, of patented core steps to generate/run the AI model, as well as patents directed to the end drugs generated, will provide good protection for your business model if a drug discovery company. Trade secret protection for the training data and weights to run the model, to prevent handing useful information to a competitor, enhances that protection.

Although the patent application should describe how to assemble the AI training data which provides the inventive result (with more detail needed if this training data is the key novel and inventive aspect over the prior art), it is generally not necessary to publish the actual data values or the weighting factors used in the AI model. Keeping this specific information secret can hinder your competitors getting to your specific best model and working out potentially how to design around it – delaying and frustrating your competitor's offering in the market.

For companies involved in providing software to aid early blue-sky research, the software could provide a key selling tool for the wet science machine/kit. For example, if we look at the DNA sequencing field, many companies now sell increasingly sophisticated sequencing adaptors. But how are we to differentiate between them? The provision of specialist AI software to process DNA sequencing data could be a key selling point for the wet kits.

The same could be said for machinery such as mass spectrometers: clever software could help sway a buyer to your mass spectrometry machine over another, making research into such software, and protection for such software, commercially useful.

So again, as for smaller biotech companies, an IP strategy could include a mix of patents for the end product and for software, but this time software is offered to accompany those end products. The same holds true for AI-based diagnostic software accompanying a medical device. In terms of patent prosecution strategy, in the US, keeping continuations pending and using appeals during prosecution can be useful tactics in view of the inconsistent application of Section 101.
It will also be important to monitor more closely the patents in your portfolio for the AI/software protection side of things: software-focused patents may become redundant more quickly than the patents in your portfolio for your small molecules/machines/sequencing adaptors.

It could be that the software protection has done its job and held off competitors for a useful time, but then the field moves on to something else. Therefore, a portfolio review when patent renewal fees are due

"IP teams increasingly need to have a bioinformatics specialist in the mix"

"As AI continues to transform healthcare, the opportunities for businesses in this evolving landscape are both vast and exciting, and having suitable IP protection and IP strategies in place will be key to capitalising in this emerging multidisciplinary technological space"

(to ask the question of whether the patent is still doing its job) is useful to control costs and to continue to sculpt your overall IP protection into something as useful as possible.

If we turn to options in Europe, the powerful discovery tools available under the Unitary Patent Court will help proving infringement if the patent protection contains a feature that is not evident from the AI software itself (eg, some aspect of the way the AI has been trained). Speed of the UPC is also attractive in the fast-paced tech space, to bring an infringement or invalidity action, or obtain a preliminary injunction, while the patent is still relevant. The sweeping breadth of the UPC (covering at least 18 different countries) is another useful feature given the global footprint that digital healthcare potentially has.

This brings us lastly to licensing, which is often interesting in this field given that the technology can be used across a wide variety of fields. An example we have seen is secure encryption of DNA sequencing data being licensed well outside the life sciences field. Therefore, keeping your company open to further non-traditional revenue streams could prove useful for smaller biotechs.

Keeping pace with change

The increase in digital application seems to herald a change in how healthcare is provided. IP teams and strategies need to keep pace with this change. The increasingly interdisciplinary nature of life sciences and software calls for specialised, cross-functional IP teams that can navigate the complexities of protecting innovative AI-driven platforms. With the potential for rapid advancements in this field, a strategic mix of patents and trade secrets can help to ensure a competitive advantage and long-term success.

As AI continues to transform healthcare, the opportunities for businesses in this evolving landscape are both vast and exciting, and having suitable IP protection and IP strategies in place will be key to capitalising in this emerging multidisciplinary technological space. IAM

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DATA AS A VALUABLE INTANGIBLE ASSET IN THE PHARMACEUTICALS INDUSTRY

Life sciences companies now need to look beyond patents to protect their innovations as usable healthcare data becomes a valuable intangible asset in its own right, writes IAM Deputy Editor Adam Houldsworth

Life sciences IP value creation is being disrupted and reshaped by the rapid development and application of AI to drug R&D processes.

This technological change is enabling pharma businesses to generate more high-value patent-protected inventions, although in the longer term it may undermine the patentability of some otherwise valuable innovations.

The rise of AI is also increasing the need for life sciences companies to look beyond patents to protect their innovations. And it is turning usable healthcare data into a valuable intangible asset in its own right – and one whose monetisation raises new and distinctive strategic challenges.

Moreover, this trend is also creating new needs for hybrid subject matter knowledge among both in-house and private practice IP professionals.

AI drug development revolution

AI technologies have become integral to life sciences R&D over the past few years, and are now being used by the vast majority of large pharmaceutical companies to help discover, design and develop new drugs, as well as to design clinical trials and create personalised medicines.

Much of this work is being done in partnership with specialist

AI healthcare companies, which have struck a slew of high-value agreements with traditional pharma businesses in recent years. Exscientia, for example, has formed lucrative R&D partnerships with Sanofi, Bristol-Myers Squibb, Bayer and Sumitomo Dainippon Pharma among others. Recursion signed a drug development deal worth up to $12 billion with Roche in 2021. And Owkin has nine-figure deals with Sanofi and Bristol-Myers Squibb, as well as agreements with Servier, Genmab, Johnson & Johnson and Amgen.

Many other healthcare AI businesses such Benevolent AI, InstaDeep, Healx, DeepMatter, Insilico Medicine, Insitro, AI Vivo, Gero, Gatehouse, Kairntech, Atomwise and OpenAI have all formed drug development partnerships with pharma innovators.

New healthcare AI companies are cropping up all the time. In recent months, AI company Xaira Therapeutics emerged from stealth mode with over $1 billion in funding already in its pocket.

Some 'AI-native' companies, such as Nimbus Therapeutics, are developing their own innovative drugs in-house and progressing them in to clinical trials.

Conversely, many well-established pharmaceutical players are developing, or have developed, their own proprietary AI technologies. AstraZeneca, for example, owns JARVIS, and Illumina owns PrimateAI and SpliceAI, while Amgen has an AI tool called ATOMIC.

Other traditional pharma companies have bought in AI drug development technologies. At the beginning of 2023, for instance, BioNTech paid £362 million – plus up to £200 million in milestone payments – to acquire InstaDeep.

"AI is not simply creating new challenges for those managing traditional intangible assets like patents – it is giving rise to a new intangible asset, which presents its own strategic opportunities and challenges"

And the convergences being brought about by AI are further underscored by the fact that Big Tech players like Google have also produced healthcare AI technologies.

These patterns of technology use, development, ownership and collaboration are having a major impact on the creation of new therapies. Seventy-five AI-discovered molecules have entered clinical trials since 2015, according to Dr Dave Latshaw, CEO of BioPhy and former AI drug development lead at Johnson & Johnson. This represents an astonishing compound annual growth rate of over 60%.

Fifty additional novel therapies could be produced over the next decade as the result of AI and machine learning, according to Morgan Stanley. Amgen estimates that by 2030 AI will have shaved two years off the typical decade-or-more that it currently takes a pharma company to develop a new drug product.

More high-value patents

These developments are generating new opportunities for the creation of valuable IP, for the protection and monetisation of both healthcare-related high-tech inventions and of drugs that have been developed with the assistance of AI.

Morgan Stanley estimates that the 50 extra novel therapies that will be developed over the next 10 years as the result of AI translates into an economic opportunity exceeding $50 billion. Given that innovative drugs often depend on a small number of IP rights for their market exclusivity, the commercial importance of the patents protecting AI-generated drugs will be extremely high.

Perhaps the best illustration of this to-date is the $4 billion-plus sale of an AI-discovered drug by Nimbus Therapeutics to Takeda Pharmaceuticals in early 2023. The deal – one of the most valuable single-asset transactions in the history of the life sciences – related to NDI-034858, a late clinical-stage drug for the treatment of moderate-to-severe plaque psoriasis. The drug was developed by Nimbus, which has never owned its own laboratory and which uses computational chemistry, machine learning and other cutting-edge technologies to identify promising drug candidates. Takeda agreed to pay up to $2 billion in potential future milestones, on top of the $4 billion it handed over upfront.

Meanwhile, healthcare-related AI technologies (and other digital healthcare inventions) have been the subject of a fast-growing number of patent applications. A 2021 study by Mewburn Ellis, for

example, showed that the patenting of computer-implemented healthcare inventions had risen rapidly in the previous few years, especially in areas such as computational chemistry, bioinformatic, computer-assisted diagnosis and medical image analysis.

The large amounts of investment being attracted by healthcare AI companies and the high value of the deals being struck by those companies with (often several) traditional pharmaceutical companies, means that many of these new life sciences-related high-tech patents are/will be worth a lot of money.

New patterns of value creation, new IP teams

Interestingly, the Mewburn Ellis study highlighted that key owners of computer-implemented healthcare invention patents include life sciences specialists like Roche and Illumina, as well as tech companies like IBM, Sony and Philips. This type of convergence likely also applies more specifically to the patent landscape for AI drug-development tools.

One result of this is that the IP portfolios of many traditional large pharma companies contain an increasingly large number of high-tech patents. As such, those businesses – which are habituated to an exclusivity-first model of IP strategy – will have to consider whether to emulate specialist AI businesses and to monetise their high-tech tools by striking deals with other life sciences innovators working in different areas of drug development.

In-house IP teams at these companies will also have to adapt to include a wider range of scientific expertise, including hybrid expertise at the intersect of computing, data sciences, chemistry and biology. This also applies to IP departments at the myriad specialist healthcare AI entities working in this field, as well as to the teams at private practice firms hoping to attract the business of these companies.

Patentability challenges?

Despite bringing about these new opportunities, the rise of AI could create new conditions that make it more difficult for life sciences companies to obtain valid patents for their otherwise-valuable inventions; although it is not yet clear how serious a threat this is.

This possibility is reflected in the USPTO's April 2024 call for comments regarding the impact of AI on patentability determinations. This invites the patent community to submit responses on the possibility that AI may impact patentability by changing the volume and nature of prior art, and/or by altering conceptions of the person having ordinary skill in the art.

Some have argued that AI may create a flood of new prior art making it harder to patent future drug-related innovation – a development that would have severe consequences for the biopharma commercial model. It has also been suggested, more specifically, that organisations may even use AI to publish prior art defensively to prevent companies from obtaining patent protection over certain molecules.

Others have pushed back against this narrative. The IP Owners' Association, in its recent response to the call for comments, for example, has pointed out that in many cases AI-generated disclosures would not be considered "publicly accessible" – as is required to qualify as prior art. And much of it will be "non-enabled, inoperative and irrelevant", the IPO stated.

The use of AI tools may "enhance a PHOSITA's level of skill", the IPO stated, however, although this will continue to be analysed on a case-by-case basis.

The IPO also suggested that AI tool use could become a factor in enablement analyses – analyses that are often at the heart of high-value pharma patent disputes. "Whether access to a particular AI tool reduced the amount of experimentation needed to make and use an invention to an amount that no longer reached the level of undue experimentation is a factor that could be considered in a non-enablement analysis," it commented.

Other forms of IP protection to become more important

However, IP value creation and protection is not merely about patents. In fact, AI inventors – whether in the healthcare space or any other industry – often lean heavily on non-patent IP rights, especially trade secrets and copyright.

This is reflected in a recent SEC filing from major AI drug innovator Exscientia, which states: "The software code underlying our technology platform is generally protected through trade secret laws rather than through patent law. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research

organisations, contract manufacturers, consultants, advisors, collaborators and other third parties."

Therefore, the rise of AI in the life sciences and elsewhere is making trade secrets and proprietary information more valuable – and having a strategy to protect them more important.

Data is the new oil

In order to play a useful role in drug discovery, trial design, diagnostics and precision medicine, AI must be trained using relevant, high-quality scientific, clinical and/or healthcare data. As such the growing importance and use of AI is creating a greater demand for these types of data, which have become a potentially lucrative form of intangible asset in their own right.

Sourcing, using and monetising this data can be difficult, however. This is because privacy and data restriction rules limit the use of healthcare information – especially under the General Data Protection Regulation – and because such data is highly dispersed and siloed across large numbers of separate organisations. Healthcare data is also sometimes poorly organised and curated.

Several organisations are seeking ways to overcome these difficulties and are attempting to license data for use in healthcare-related AI.

One such company is the aforementioned Owkin, which employs a 'federated learning' approach that allows it to train its own AI models using decentralised data from many different hospitals and research institutes without ever gathering that data in a single place. As well as drawing information from the InstitutCurie, Institut Universitaire du Cancer de Toulouse and the Gustave Roussy Cancer Campus Grand Paris, Owkin has access to data collected by the MELLODDY project, which draws together information from many public and private research institutes.

This allows Owkin to overcome patient privacy restrictions in place in the European Union – a point that was cited by Sanofi's R&D chief John Reid when the two companies entered into a $270 million agreement in 2021. "Because of the more onerous state of privacy issues in Europe, very few groups that are trying to play in this space of real-world evidence and machine learning applied to clinical data have really been able to access European data," he stated, praising Owkin's approach. The two companies expanded their collaboration in March 2024. As noted above, Owkin has secured deals with a slew of other pharma innovators.

Another interesting player in the healthcare data space is Truveta, a company which facilitates the use of data from US healthcare providers for use in the training of AI and machine learning algorithms. In turn, its AI and machine learning technologies interpret and curate that data. It launched in 2021 with 14 healthcare providers onboard but now boasts 30 participating healthcare organisations and draws data from 800 hospitals and 20,000 clinics.

Truveta has secured investment from Microsoft and has announced partnerships with Pfizer and Boston Scientific, as well as Harvard University and data-analytics company Panalgo. Recently, it launched what it claims to be largest and most complete mother-child electronic health record dataset in the world.

In a similar vein, Datavant – a subsidiary of Roivant – also has platform that facilitates the 'secure and compliant' sharing and analysis of US clinical data with life sciences companies, government agencies and healthcare providers. Its network consists of 70,000 hospitals and clinics and 70% of the top 100 largest health systems. Among its most recent moves is a partnership with Promptly Health, which provides real-world data access in Europe. Its annual revenue now stands at $750 million.

In contrast, however, some data-owning organisations have provided their data directly to the market. One example of this is the Mayo Clinic, which started its own Clinical Data Analytic Platform to collect and monetise its medical records. Since its launch in 2020, this platform has grown to include data from other institutions such as Hospital Israelita Alvert Einstein, Sheba Medical Center, Mercy, and University Health Network (Canada).

As such, AI is not simply creating new challenges for those managing traditional intangible assets like patents – it is giving rise to a new intangible asset, which presents its own strategic opportunities and challenges. IAM

Adam Houldsworth, Deputy Editor, IAM

KOREAN NPE'S MOVE INTO BIOTECH SHOWS IMPACT OF TECH CONVERGENCE ON LIFE SCIENCES IP STRATEGIES

There is an increasingly porous boundary between the life sciences and high-tech industries, which creates new opportunities for IP owners, writes IAM Deputy Editor, Adam Houldsworth

A subsidiary of Korean patent assertion entity Intellectual Discovery recently became the first non-practicing entity to assert a biotech patent at the Unified Patent Court – a move it is considering following up with legal actions elsewhere. Indeed, GXD-Bio has since told IAM that it plans to source further biotech-related patents and it predicts a "paradigm shift" towards the life sciences among NPEs.

This is the latest indication of how the growing use of high-tech innovations in the healthcare sector is not only changing the patent strategies of life sciences companies, but also creating new opportunities for IP owners to monetise their inventions in new verticals and for tech-based patent professionals to apply their skills in new fields.

Best known for asserting patents in the cellular connectivity and video codec spaces, Intellectual Discovery – a former government-supported sovereign patent fund from Korea – has established a presence on the biotech patent landscape with GXD-Bio. This is "a bio-IP monetisation company that collaborates with the government,

university hospitals, and biotech companies, based on Korea's world-class medical system", according to Dongsuk Bae, CEO of both GXD-Bio and Intellectual Discovery.

"Korea is expanding its presence in the global market with leading biotech companies such as Samsung Biologics, Celltrion, and SK Biopharm," Bae tells IAM. "In light of this, government investment in the domestic biotech industry is expected to increase, and the biotech sector is forecasted to grow further, centred around the top 10 medical schools, advanced IT engineering schools, and biomedical engineering schools."

GXD first came to public attention when it filed a UPC lawsuit, accusing Myriad Genetics and Eurobio Scientific's genomic test EndoPredict of infringing European patent 3 346 403. This patent – originally obtained by two Korean biotech companies, Abion and Gencurix, covers a method for analysing gene expression data to identify endogenous reference genes.

The asserted patent bridges the gap between high-technology (which has accounted for the vast majority of NPE suits historically) and pharma/biotech, where very few NPEs have operated in the past. In fact, according to Clarivate, there was just one biotech-related NPE assertion in the EU between 2012 and 2023. Meanwhile, there were 281 cases in the digital communication sector, 202 in telecommunications and 200 in computer technology.

The '403 patent is by no means the only healthcare-tech patent to have emerged recently, however. In fact, there is a surge in data-driven and computer-assisted healthcare patents – a surge which is being driven by the increased application of high technologies for diagnostics, patient-monitoring and the personalisation of patient treatment, as well as the use of artificial intelligence and machine learning for drug development and clinical trial design.

"Therefore," Bae tells IAM, "while most NPEs have been focused primarily on the IT sector until now, it is anticipated that a paradigm shift will occur within the NPE industry towards bioengineering and AI biotech in the future." Bae has previously said that Intellectual Discovery is ramping up its enforcement efforts in an attempt to become one of the world's top three IP monetisation players, appears to have big plans for GXD.

"GXD-Bio is focusing on sourcing bio-related patents in the Korean market through the end of this year," he explains. "Starting in 2025, the company plans to expand its patent sourcing activities globally, targeting the U.S. and European markets."

So other healthcare companies will likely be approached for licensing discussions by GXD and – if Bae's forecasts are correct – other NPEs in the future.

But this is by no means the only IP implication of the tech-healthcare convergence. This process has radically increased the number of tech patents owned by pharma/biotech companies (Hoffman La Roche, Illumina and Grail are leading owners of bioinformatics patents, for example, while AstraZeneca and Amgen own innovative AI tools) and healthcare patents owned by tech companies (Philips, IBM and Sony are major players in the computer-aided therapy and monitoring IP landscape).

It has also created a new ecosystem of healthcare AI companies – such as Benevolent AI, InstaDeep, Healx, DeepMatter, Insilico Medicine, Insitro, AI Vivo, Gero, Gatehouse, Kairntech, Atomwise and OpenAI – which have built valuable IP portfolios of their own. IAM

Adam Houldsworth, Deputy Editor, IAM

TECTONIC SHIFTS IN THE LEGAL AND REGULATORY LANDSCAPE

Legal, regulatory and policy environments shape IP strategy in all industry and technology sectors. Nowhere is this truer than in the life sciences industries where regulatory intervention is especially pronounced and policy debates particularly heated. Pharma and biotech innovators are currently adapting to significant shifts in the legal environments, and face the prospect of imminent regulatory and policy interventions.

The articles in this section explore the likely impact on IP strategy of a slew of healthcare-related regulatory changes set to take effect in Europe. They also examine how pharma and biotech companies have used – and have been affected by – the Unified Patent Court, which has transformed Europe's patent litigation landscape over the past 18 months.

The articles also include an interview with the IP boss at one of the US's most innovative biopharma research institute, the Dana-Farber Cancer insitutes. As well as sharing wider leadership and strategy advice, Steven Caltrider expresses concern about the recent direction of case law in the country and about the potential for current policy proposals to negatively impact America's most inventive healthcare organisations. IAM

THE UPC: A NEW ROCKET DOCKET FOR LIFE SCIENCES PATENT LITIGATION

Despite expectations that life sciences patentees would avoid the Unified Patent Court, the new court has already made its mark on healthcare-related patent strategies, while pharma and medical device cases are helping to shape UPC case law, argue Paul England and Anja Lunze of Taylor Wessing

The UPC is over 18 months old and it has had an impressive start, in particular in the field of life sciences. Contrary to initial predictions that big pharma would rather stay away from the UPC, the UPC is surprisingly busy not only with medical devices but also pharma and biotech cases. Several prominent multijurisdictional life sciences IP disputes now have an important UPC component.

This means that the case law of the UPC will be significantly shaped by the life sciences industry and not only – as initially anticipated – by IT and FRAND cases. It also means that the UPC is already having a significant impact on enforcement strategies in the industry.

One major impact of the new system on the life sciences patent landscape has been through the creation of unitary patents, which became possible to obtain from granted European Patent applications granted by the EPO after 1 June 2023, including those for which grant had been delayed or requested early. The 18 countries that are covered by these new unitary rights include the large German, French, Italian and Dutch markets. These are populated by some 300 million people, nearly equal to the US.

By the end of October 2024, 20% of the over 38,000 Unitary Patents that had been registered since the start of the system relate to subject

matter including medical technology pharmaceuticals, biotechnology, food technology and analysis of biological materials subject matter.

Life sciences subject matter is therefore comparable to telecoms, electronics and computing in terms of numbers of unitary patents granted. Given that these rights can only be asserted at the UPC, this figure shows that many life sciences innovators have already factored the new system into their strategies.

The number of infringement cases and standalone revocation cases is representative in this respect. Here, the UPC's statistics for these show that patent subject matter which has a first IPC class of A and C – which includes pharmaceuticals, biologics and medical devices – account for 27% of infringement suits. Of the standalone revocation cases, the figure is over 50%.

UPC decisions so far

One of the first questions potential users of the UPC want to know is what the patentee success rates are. Some caution is needed here as well, because the win rates do not reflect the complexity of the decision making involved and the different facts and issues raised. However, on the relatively few cases decided so far on the merits and for preliminary injunctions, the general win rate of patent holders across all subject matters is approximately one third of cases. For life sciences subject matter it is more balanced.

As regards enforcement strategies, however, it should be noted that only a limited number of actual legal issues has been decided by the court so far. Many questions of substantive law with regard to infringement and validity, have not been decided yet.

Moreover, several issues of particular interest to life sciences innovators have yet to be clarified by the UPC: how to deal with pre-expiry offers, how to construe the Bolar exemption (in particular with regard to supply of the API from third parties), how to deal with the interplay between patent law ruled by UPC law on the one hand and EU and national regulatory law on the other hand, in particular when a product has no marketing authorisation in all UPC Member States, how to calculate damages, how to deal with off-label use of second medical use patents, as well as major topics such as whether a so-called "plausibility" requirement will be applied in the UPC, how obviousness will be examined in detail and the application of a doctrine of equivalents.

There have been some notable life sciences decisions, such as the case concerning the detection of analytes in a cell or tissue sample in the Local Division Munich (10x Genomics v NanoString, UPC CFI 2/2023, 19 September 2023) which, although later overturned on the merits, sets out the UPC's general approach to preliminary injunctions. And in the same case, the Court of Appeal (UPC_CoA_335/2023, 26 February 2024) outlined the important basics of validity law.

With the lack of case law on many of the above areas, however, the success rates can only give limited guidance for future cases. It is to be expected that the UPC will quickly fill out the open questions provided that suitable cases are brought before the UPC.

The high-level view can also mask to some extent important differences between life sciences sectors -in particular, between medical devices on the one hand, and generics and biosimilars on the other.

Medical devices

A characteristic of patent litigation over medical devices – for example, heart valves, stents and monitoring devices – is that it is usually between parties who develop and manufacture devices in their own right and own their own patent portfolios. Many devices are complex and multi-featured in their structure and function, and as a result they can be covered by very large portfolios of patents, including divisionals. Furthermore, because the features of medical devices tend to evolve with time, new patents are continually being prosecuted and granted.

These characteristics have consequences for patent litigation, particularly at the UPC.

Firstly: because devices are often multi-featured and protected by more than one patent, the prospect of any one patent being revoked carries a lower strategic and commercial risk than it does in the field of small molecule pharmaceuticals. This has allowed patentees a freer hand with regard to risk and to keep European patents in the UPC system and in many cases to convert them to unitary patents.

Secondly: the lower risk associated with instances of revocation means that patentees have more freedom to exploit the powerful enforcement possibilities made possible by the UPC, namely by obtaining an injunction in up to 18 countries in one action. Again, the larger number of patents available may allow for opposing manufacturers to attempt the enforcement of several patents in the UPC.

Thirdly: the number of local divisions (and the one regional division) in the UPC also lends itself to the enforcement of multiple patents, thereby favouring medical device IP owners. Although these divisions have shown a degree of consistency in their procedural approach so far, this provides potential forum options for the claimant where particular features of procedure have developed that are perceived to be useful. For example, the Nordic-Baltic division allows the examination of experts. The different branches of the court may also adopt different approaches to the concept of "unreasonable delay" in preliminary injunctions. And possibly, in the future, they may develop different track records in decision making for and against patentees.

Finally, the speed of the court, which aims to make decisions on the merits within 12 months of the start of proceedings and whose early decisions have outpaced most national proceedings, is attractive to patent owners in the medical device sector. This is because medical devices commonly have a developing pipeline of new patents and divisionals, reflecting advances in the functioning of the protected product itself. In other words, when new patents are granted they can potentially be enforced at timescales commensurate with changes to the products in suit.

Not all of these aspects of the UPC are particular to medical devices as a class of subject matter, but they do provide options and advantages to litigating these patents that will not be found in any one national court alone.

Generics and biosimilars

Patent strategies are somewhat different in the small molecule and biologic drug space, where products tend to be protected by relatively few patents and product development timelines are longer. But the speed of the UPC and the breadth of its jurisdiction are attractive to patentees in this sector too, despite the greater dangers associated with centralised revocation.

Indeed, there have already been several infringement and preliminary injunction cases filed at the UPC, including by Alexion Pharmaceuticals, Amgen, Novartis, Genentech, GlaxoSmithKline and Sanofi. And these disputes have already produced a small number of significant decisions.

One of the factors that will determine the UPC's attractiveness for drug patent owners is the willingness with which it grants preliminary injunctions. As such, the criteria that the UPC will apply for granting preliminary injunctions, particularly in the life sciences field, have been under close monitoring since the court's inception. It is interesting to note that, so far, generics and biosimilars have not been treated unfavourably by the court as is sometimes done in national preliminary injunction litigations. This might also be due to the fact there has not yet been a classical launch at risk case in the UPC so far.

Nevertheless, the Local Division Hamburg in *Amgen v Alexion*, which concerned a biosimilar, (UPC_CFI_124/2024, 26 June, 2024) carefully weighed up the criteria that are necessary to consider a patent as a sufficiently secure basis for granting a preliminary injunction. The court found that the defendant bears the burden of presentation and proof for facts concerning the lack of validity of the patent.

Amgen v Alexion demonstrates that when addressing invalidity arguments the court will first consider whether the patent is or has already been under attack, be it in EPO opposition proceedings or a national or UPC revocation action. Furthermore, while the UPC has to form its own view on the validity of a patent, because it can only undertake a summary assessment in preliminary injunction proceedings, it has, in a second step, to consider whether – if there is a parallel opposition – there is sufficient likelihood that the EPO will revoke the patent

The Local Division Hamburg also dealt with the important circumstances in which third-party observations had been filed during prosecution. In German preliminary injunction proceedings, the courts generally assume that the validity of a patent has been "sufficiently secured" if due to the filing of third-party observations the prosecution could be considered as "inter partes" proceedings. In this case, however, the third-party observation mostly dealt with formal aspects of the original patent application but not with the arguments that had been central to the defendants' case at the UPC. Therefore, the Hamburg Court made clear, it it could not blindly follow the grant decision.

Imminent infringement and distribution network

Amgen v Alexion is not the only case in the biosimilars sector. In a second case, the Local Division Düsseldorf in Novartis and Genentech vs. Celltrion (UPC_CFI_165/2024, 6 September, 2024), decided on the

requirements for establishing imminent infringement and on how to deal with a distribution network.

According to the Düsseldorf division, imminent infringement requires that the potential infringer has already set the stage for the infringement to occur – the infringement is only a matter of starting the action for which preparations have been fully completed. These circumstances must, as always, be assessed on a case-by-case basis and very much depend on a thoroughly prepared and argued request by the applicant, supported by evidence.

As regards companies that are members of a group and play a key role in a distribution network for the infringing product – such as a sole manufacturer or a European sales and marketing hub – the Local Division Düsseldorf made it clear that they may also be considered as infringers although they are located outside the Contracting Member States, provided that they supply their products to other members of the group located in the Contracting Member States and these companies distribute these products on the European market, including at least one Contracting Member State where the patent-in-suit is valid.

Prospects for the UPC as a life sciences venue

Even though these two decisions both went against the patent owners, they, like the other early decisions of the UPC, are well-reasoned and balanced. The UPC has, so far, carefully weighed the arguments of the parties and handed down clearly argued and comprehensible decisions. In combination with the speed of the decisions in the first 18 months of the UPC, the quality of the decisions is impressive. As such, sooner or later, the UPC will become the new rocket docket for life sciences industry patent litigation. IAM

Paul England, Senior Counsel – Knowledge, Taylor Wessing
Anja Lunze, Partner, Taylor Wessing

"Contrary to initial predictions that big pharma would rather stay away from the UPC, the UPC is surprisingly busy, not only with medical devices but also pharma and biotech cases"

MARCH-IN RIGHTS AND SECTION 112 CASE LAW THREATEN EARLY-STAGE LIFE SCIENCES INNOVATION, SAYS DANA-FARBER IP LEADER

Effective leadership underpins success in all IP endeavors, but it is hard to define and measure. In this wide-ranging conversation, Dechert's Katherine Helm and Steven Caltrider of the Dana-Farber Cancer Institute discuss how to optimise team management and reflect on some of the challenges facing life science IP professionals

"To bring your 'A-game' over time, you simply must take the time to sharpen the saw"

Leadership in IP is crucial when assessing policy goals and engaging in the everyday practice of patent litigation. Katherine Helm, intellectual property and litigation partner at Dechert, and Steven Caltrider, chief IP counsel at the Dana-Farber Cancer Institute, have been at the forefront of life sciences patent practice both defensively and offensively, as well as in related policy work. In a fireside chat, Helm and Caltrider reflect on the ingredients for successful leadership and explore some of the pressing issues facing IP professionals in the life sciences space.

Katherine Helm: What do you consider to be the most significant new challenges/opportunities for life science IP leaders?

Steven Caltrider: Perhaps as a sign of the turbulent times, there are a host of challenges and/or opportunities for life science IP leaders. Top of mind for me is the draft guidance proposed by the National Institute of Standards and Technology, which would permit so-called march-in rights for patents, which are procured from federally funded research, based on price considerations of the product claimed by the patent. Ostensibly, the guidance is to lower pharmaceutical drug prices. While I seriously doubt this guidance will have any meaningful effect on drug prices, I'm nearly certain it will have serious unintended consequences on non-profit research institutions, such as the Dana-Farber Cancer Institute.

Unlike the pharmaceutical industry where 15-20% or more of sales revenue is invested into research, non-profit research is funded through three primary sources: private grants and donations, federally funded grants and royalties from existing IP licenses. There is no sales revenue in the non-profit sector to invest in research. At Dana-Farber, federal grants represent roughly 50% of research spending. The challenge is that virtually none of the life-saving research at Dana-Farber will reach patients without a commercial partner. In view of the guidance, David Kappos and others have described that companies will avoid patents "contaminated" by federal funding. I agree. The exceptional and perhaps desperate company to supplement its research pipeline will do so at deep discounts, given the limited market. The non-profit research sector stagnated prior to Bayh Dole. It is likely to do so again under the NIST guidance.

The second issue is the remarkable opportunity of artificial intelligence. Its impact is already evident in research, and in the diagnosis and care of patients. The AI revolution is just beginning. The challenges as an IP leader are two-fold. First, will policies, including IP policy, develop to facilitate or dampen this revolution? And second, how will AI impact the practice of law? I'm actively engaged on both challenges.

The final issue that is top of mind is the issue of claim scope following the US Supreme Court's ruling in *Amgen v Sanofi*. The patent system is not working if meaningful patent protection is only available to applied research – that is, research generally conducted in the for-profit sector where the future commercial product is the target of the research and therefore central to the patent claims. Such a system would fail to deliver the promise for early stage, discovery research, which is often the research that represents the breakthrough in thinking and therefore sets the foundation from which a commercial product becomes possible. How should the patent system handle early discovery-based innovation?

Fortunately, this problem is not new. It dates to at least Samuel Morse's invention of the telegraph and has spurred cases such as *Holland Furniture and Halliburton Oil*. Section 112(f) or 112(6), as it was then known, was promulgated to provide the fair scope of protection to advance such basic research. The challenge from my perspective is how will the law develop to apply 112(f) in the life sciences, and perhaps as importantly how will the scope of equivalents be applied. The courts' near hostility to equivalents in the 1990s, an era that some commentators called the doctrine of 'near death', is a body of law that should be re-visited. If you are going to restrict the scope of claims under Section 112 then there must be robust equivalents under 112(f) and the doctrine of equivalents, to sweep-in those clearly exploiting (rather than building upon and improving) early-stage discoveries.

KH: What are the notable recent or future challenges impacting pharma IP strategy?

SC: Some in the industry have viewed IP with an attitude that 'more is better'. They posit that it is simply a math exercise where the more patents that cover a drug, which statistically only has about a 40% to 60% chance of being upheld depending on the forum, the greater the overall probability of success. Respectfully, I disagree.

First, at least the last time I studied this issue in detail, the data shows no correlation between success in maintaining exclusivity for a drug product and the number of patents in the portfolio protecting the product. One or two good patents often carry the day. Second, a patent system that tolerates such a strategy is unsustainable because it is unaffordable for many. Big companies with generous IP budgets can afford this investment, but start-ups and small players cannot. Such a skew is not good for an IP system and its core mission to advance innovation. Often it is the small player willing to think boldly or out-of-the-box that changes the paradigm. Finally, it is bad for the patent system overall. The IP system works effectively when the public, the courts and competitors have confidence that the patents issued are reliable and durable. This confidence is undermined by practices that

some policymakers characterise as gaming the patent system through patent thickets. The proposed reforms to counter this gaming now threaten the life science industry and even the IP system more broadly.

KH: So how should this be addressed?

SC: The best way to deal with this problem is to address the root causes. First, we need to improve the reliability and durability, ie, the quality, of patents. An issued patent should have a much better than roughly a coin flip chance of being sustained if challenged. The system also works most efficiently and effectively when patentability is correctly decided during examination. A fresh look at examination and how examiners and applicants can work together is needed. Judge-made doctrines – inequitable conduct and to lesser extent prosecution history estoppel – drive applicants to defensive prosecution tactics where applicants cite references having little relevance to the claims and are fearful to engage the examiner productively to identify patentable subject matter. *Ex parte* prosecution would be much more effective when the drivers of defensive prosecution tactics are eliminated. Of course, the opportunity to leverage technology and collaboration amongst patent offices on search presents unprecedented opportunity to improve examination. With thoughtful changes in law and practice, significant improvement in quality is achievable. Much greater confidence in the reliability and durability of the patent right will obviate the need to play the odds that more patents are better.

Secondly, a patent applicant should have flexibility in how an invention is claimed, and if an invention meets the rigorous statutory standards of patentability, there should be no issue with a commercial product embodying more than one invention (or even many more inventions). However, an applicant is not necessarily entitled to more than one patent for a single invention. The near exponential growth in the number of patents per invention – largely the basis of so-called patent thickets – is due to continuation practice. With the forementioned changes to inequitable conduct and an expanded flexibility in how an invention is claimed, including post-issuance, one could envision a 'one and done' patent system where an applicant is entitled to a patent to protect an invention.

Pharmaceutical IP strategies that some characterise as gaming the system with patent thickets and evergreening are in the crosshairs of policymakers. To date, the solutions proposed by policymakers will weaken the patent system – the proven engine of innovation, economic prosperity, and advances in human health. The better future is to reform the system to fix the underlying root causes. At that time, the pharmaceutical patent strategy – like all other industries – will be to issue a quality patent for each invention made from discovery through product development. No thickets, no games – just the transparency and certainty needed for the advancement of the arts.

Leadership excellence

KH: What do you consider to be the most significant new challenges/opportunities for life science IP leaders?

SC: For a short period of time, I worked with, and led, a team that seemed to agree with everything I did or said. You might think this is the panacea of leadership – a team uniformly aligned in its mission, goals, objectives, tactics, and strategy. I was mortified. Were team members afraid to speak up? Were they checked-out? Were we falling into groupthink? I quickly realised that such a team would be destined to mediocrity without change. While we were diverse in all the outward measures, we lacked diversity of thought.

While a task can be completed with excellence by a monolithic team, long-term and sustained excellence cannot. To challenge yourself and the team to evolve and change – to up your game continually – you must have a team where members think differently, work with different styles and are willing to assume the role of 'devil's advocate'.

KH: How did you overcome that challenge?

SC: To change the dynamic, I recruited an internal colleague to join the team. She was a terrific addition for a few reasons – she was an excellent lawyer, we rarely saw an issue in the same way, and perhaps most importantly she was more than willing to share her view. I also turned to my senior staff and asked them critique or stress

test ideas and to play devil's advocate when reviewing an issue or while in the deliberative stages.

Ultimately, this team accomplished great things. Most of that success is attributable to the team members, each of whom was excellent; however, I still believe we would have been on a different path had we not recognised the critical need for diversity of thought.

KH: How did you become a leader?

SC: This is a great question, and to be honest I'm not sure. I've been in leadership roles, initially in academic roles and sports and subsequently professionally and in my community, for as long as I can remember. I became a leader answering the call that still drives me today.

First, if I see a problem I am willing to step-up and help solve it. In fact, I've had to teach myself, just because I can do something, does not mean that I should. I've learned that you cannot solve for everything, and you will accomplish less trying to do so.

Second, my parents instilled in me a sense that if you do something then you should do it the right way. In my early years this led to me to be a leader largely by example. I would step up (ie, volunteer) to take on a project and others joined me. In my later years, I realised that others may be, and likely are, better at something and my role as leader is to match the task at hand with the person most capable of doing it the right way.

Finally, I became a leader as a calling to serve others. I find it rewarding. I get as much professional joy in scoring an assist as I am scoring a goal. Or more broadly, putting the right players on the field to do great things. I believe any success I have had as a leader really starts with this premise.

KH: Everyone I know, who knows you, marvels at how you 'do it all'. How do you maintain that energy, from waking up to going to sleep at night? I know we share a love for athletics.

SC: Yes - my day starts early with a good workout. My first choice is a 20-30 mile ride, whether outdoors or on the trainer. My off-cycling days are roughly a mile swim or run, which I only do often enough so that it does not hurt when traveling without time or access to a bike or pool. I also find time during the workout to pray the rosary to keep me grounded. This routine is essential to clear my head and focus my thoughts on the day.

I then start the workday checking any overnight messages for anything urgent or high priority. I will spend an hour or so answering emails, but I refuse to make email my highest priority of the day. While there is upside in doing so – people who send you emails appreciate the responsiveness – I found doing so led me down the path of mediocrity. Email can be all consuming. I struggled to find time to be strategic, to add value coaching or mentoring, to think or draft, or to step back to see the bigger picture. It pulled me into the minutia of too many issues that candidly really do not matter to patients.

Much of my current workday is spent in meetings. However, like email, meetings can be somewhat counterproductive to excellence. I once had a mentor, who was an executive vice president for the research organisation that my team supported, share that my role on the team was to not watch others work. This was not a lesson on speaking up but a lesson on time management. He wanted me to be fully engaged on the team but gave me permission to not attend meetings that kept me from higher priorities, especially those with more than one lawyer attending. I practice this lesson today. If someone on my team is attending a meeting and more than capable to handle the issues on the agenda, I defer and decline the meeting with appropriate communication.

My day generally concludes with any evening business calls, community service, or children's sporting events followed by a wind down period watching the news or sports before a generally early bedtime. I am a believer that proper sleep and exercise are the keys to clear thinking and high execution. I guard my early morning and evening with this in mind.

"I'm nearly certain [the use of march-in rights] will have serious unintended consequences on non-profit researchinstitutions, such as the Dana-Farber Cancer Institute"

KH: What's a leadership lesson that is worth repeating?

SC: My mother used to say that you cannot judge a book by its cover. I'm not sure that she meant it as a leadership lesson, but I'm reminded of this nearly every day. The message is a message of inclusiveness – and particularly the need to listen sincerely to understand the unique perspectives of everyone as an individual. This comes up with my team, business colleagues, partners of the Institute, and those on the other side of a negotiation or litigation. In each instance, I've learned that listening to understand – without assumptions of intent, motive, or a personal or industry stereotype – is critical to success. When you work with people, and more particularly as a leader, and can see the potential of people as unique individuals, you can do great things.

KH: What's one book that has had a profound impact on your leadership so far? Can you briefly tell the story of how that book impacted your leadership?

SC: *The 7 Habits of Highly Effective People* by Stephen Covey is a simple read that resonated with me. I deploy two of the habits regularly on my teams. Habit three: 'put first things first'. This sets out a grid with the axis as 'urgent/not urgent' and 'important/not important' as a tool to identify priorities. I identify tasks as 'important/not urgent' or 'important/urgent' to set expectations on timing for answers.

I also found habit seven ('sharpen the saw') as helpful. Particularly in the early- and mid- stages of my career, it is too easy to take on projects or issues and too hard to say 'no'. You are eager to please and want to impress your management with your 'can do' attitude. There are several problems with this, but the aspect of this relevant to habit seven is that you sacrifice your development and well-being. You lose sight of the importance of eating, exercise and sleep. Professional success is dependent upon continuous learning. To bring you're 'A-game' over time, you simply must take the time to sharpen the saw – to commit to develop yourself and serve others. It will make you a better lawyer and leader.

KH: If you could only give one piece of advice to a young leader, what would it be?

SC: Dream big, be patient and pivot as needed as you go. Greatness in your chosen profession is generally the result of perseverance and diligence. It does not happen overnight, and it is hard work. It also is rarely a straight line. Dreaming big sets high goals and will set the mindset to take initiative and action. Being patient is a reminder that leadership is a calling to serve others that is perfected over time, and pivoting as you go reflects the reality that even well-laid plans will evolve over time. Doors will open, and doors will close. It is part of learning and development.

KH: What is one meaningful story that comes to mind from your time as a leader to date?

SC: As I reflect on my career, the 'aha' moment was when I learned to trust others to do great things. I mean really trust – an empowering trust. Good people want to do well. They want to do the right thing the right way. My role as leader is to facilitate their success. With less experienced staff, facilitating includes coaching and mentoring on the details – teaching while providing autonomy to learn from what goes well and not so well. With experienced staff, it is setting expectations or objectives, identifying what success looks like, serving as a sounding board or otherwise helping as needed. And then generally getting out of the way. With both, it is about empowering people and helping them do great things. I had always thought of leadership as a vocation of service, but until I committed to an empowering trust reflecting this service, I may have been closer to a micromanager than effective leader. IAM

Katherine A Helm, IP Litigation Partner, Dechert
Steven P Caltrider, Chief IP Counsel, Dana-Farber Cancer Institute

HOW CHANGES TO EU PHARMACEUTICAL REGULATORY LAW ARE SET TO IMPACT IP STRATEGY

Ella Green, Richard Newell and David Holland of Carpmaels & Ransford reflect on how changes to the rules on clinical trials, orphan drug exclusivity and SPCs will require a pivot in IP strategies

Pharmaceutical regulatory and IP law in Europe is undergoing significant change, with three notable reforms currently at different stages:

- Reforms to clinical trials, which have been implemented since 2022, with revised transparency rules since 2024.
- Reforms to regulatory and orphan exclusivity, which are working their way through EU legislative bodies.
- Reforms to supplementary protection certificates (SPCs), which are further away on the horizon.

All three have, or are set to, impact on IP strategy – particularly when preparing for authorisation of a medicine in Europe.

Clinical trials and public transparency rules under the EU-CTR

The EU recently reformed its Clinical Trials Regulation (EU-CTR) legislation, overhauling the way in which clinical trials are run and reported in Europe. From 31 January 2025, the legislation will come into in force for all ongoing clinical trials in EU member states (replacing the former EU Clinical Trials Directive).

Probably the most relevant aspect from an IP perspective are the

revised rules on increased public transparency, which require greater (and earlier) disclosure to the public.

When the new EU-CTR was first implemented in January 2022, there was an initial period during which all documents submitted to the European Medicines Agency (EMA) were made publicly available, by default and almost instantly after submission, with only limited exceptions for confidentiality on request. User feedback was that this system was controversial and confusing, and led to a further revision. The current rules on transparency came into force on 18 June 2024.

Under the current system, documents are categorised depending on the phase of trial and the public interest in the document, with only the documents falling into the 'most interest' category now being published.

Certain documents can be redacted – trial sponsors are encouraged to submit two versions (redacted and unredacted) – and certain documents will not be published at any stage, for example, the investigational brochure, summaries of interim results, and assessment reports.

The main categories and timings of publication are summarised in table one, and apply to trials submitted after 18 June 2024. Many existing trials which were ongoing before this date (referred to as historical trials) are also affected, but older and ongoing publications are governed by more complex transitional provisions.

Clinical trial reforms are also set to impact IP, with clinical trial related disclosures emanating from European trials likely to become earlier, more detailed and more problematic prior art against patent applications.

By way of background, some patents filed at later stages face clinical-trial related disclosures as prior art. Examples include publicly

"Close coordination between in-house regulatory teams and IP counsel will become increasingly important for optimising patent filing strategies"

Table 1: Trial categories and publication schedule under the EU-CTR

Trial category	Document	Timing of publication
Phase 0 and Phase I trials in paediatric populations Part of Category 1	Protocol, synopsis, and patient-facing documents, if available	When the final summary of results is submitted
	Final summary of results, with a layperson summary	Upon submission
	SmPC	Never
	Informed consent form and patient information sheet	
	Recruitment arrangements	
Phase 0 and Phase I trials in adult populations Part of Category 1	Protocol, synopsis and patient-facing documents, if available	30 months after the end of the trial in the EU/EEA
	Final summary of results, with a layperson summary	30 months after the end of the trial in the EU/EEA
	SmPC	Never
	Informed consent form and patient information sheet	
	Recruitment arrangements	
Phase I/ II integrated trials, Phase III/ IV integrated trials, and Phase II, Phase III, and Phase IV trials Category 2 and 3	Protocol, synopsis, and patient-facing documents, if available	When the decision to allow the trial in a Member State is issued
	SmPC	
	Informed consent form and patient information sheet	
	Recruitment arrangements	
	Final summary of results, with a layperson summary	Upon submission

available protocols and accompanying press releases. Common scenarios are third parties arguing that documents or medicaments were distributed without confidentiality or that some of the public disclosures confirming the existence of an investigation, despite lacking results, invalidate medical use claims. Some patents have been revoked over non-confidential disclosures, for example, the informed consent form distributed to patients revealing, in a non-confidential manner, a dosage regimen claimed in a patent.

The potency of the public-facing prior art (eg, the protocol) varies case-by-case, although a general trend in European Patent Office case law is that a document merely confirming that a therapeutic use is being investigated does not destroy novelty of a claim to the relevant (second medical) use – but establishing inventive step is challenging. For example, on the one hand, case T 1437/21 stated that "the approval of a clinical trial does therefore not, by way of a heuristic, imply an expected positive outcome of the treatment". By contrast, case T 1941/21 from earlier this year stated that "clinical trials are usually initiated on the basis of encouraging results from preclinical experiments", and so "the announcement of a phase II clinical trial protocol for a particular therapeutic agent and a disease may provide the skilled person with a reasonable expectation of success".

The new transparency regime under the EU-CTR may remove some counter arguments against such prior art, for example the argument that certain documents (eg, patient consent forms) are confidential – patient consent forms may be published on the register – or that certain documents (eg, protocols) are not conclusive on therapeutic effects, since more detailed synopses may be published on the register.

One impact of the EU-CTR may therefore be on patent filing strategy, namely increased pressure to file certain patent applications before clinical trial related disclosures emerge, even at a stage when supporting data for patent filings is more limited (in this respect, recent decision G2/21 may be timely relief, since it may lower the supporting data requirements).

Close coordination between in-house regulatory teams and IP counsel will become increasingly important for optimising patent filing strategies without missing opportunities.

Vigilance will also be required at the stage of redacting commercially confidential information too, if the information might be relevant to patentable inventions (for example, formulation detail or a dosage regime) and the redactions are aimed at avoiding prejudice to future patent applications. The European Medicines Agency's guidance acknowledges that "patentable matter" may be justification for a redaction, although it also suggests that heavy-handed redactions such as entire pages or entire sections of a protocol document would not usually be acceptable; only specific sentences, words, and figures should be redacted.

Innovators may nevertheless welcome the more predictable predetermined timeline of publications under the revised transparency regime and be reassured by the fact that certain categories of documents (for example, the investigational brochure) will not be published at all under the new rules.

It remains to be seen whether the new regime will affect overall clinical trial and approval timelines, but any acceleration or slowing of approval dates in Europe will have impacts on IP strategy via regulatory exclusivity periods and SPC terms too – as we discuss below.

Changes to regulatory exclusivity periods and orphan drug exclusivity periods

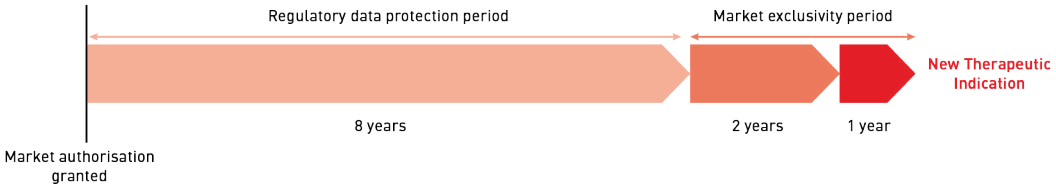
The next reform in the pipeline from the EU is likely to be in relation to regulatory data protection, since modifications to the existing exclusivity periods and incentive schemes have been approved by the European Parliament. Draft legislation is currently working its way through the further legislative steps.

Under the current system, marketing authorisation (MA) holders in Europe benefit from an '8+2+1' exclusivity regime system extending up to 11 years:

- eight years of data protection, during which generic, hybrid or biosimilar MA applications cannot refer to the data from the innovator's dossier;
- two years of market exclusivity, during which generic, hybrid or biosimilar medicines cannot be sold, and in some cases;
- one additional year of market exclusivity if a new indication bringing significant clinical benefit in comparison with existing therapies is approved within eight years of the original approval.

Under the proposed reforms, the basic period of data protection will be shortened by six months from eight to seven-and-a-half years. The reduction can, however, be offset by newly introduced incentives which will allow MA holders to extend the data protection up to a maximum of eight-and-a-half years. For example, extensions will be available for products meeting a high unmet medical need, new active substances that have undergone a comparative trial against the best-known drug for the

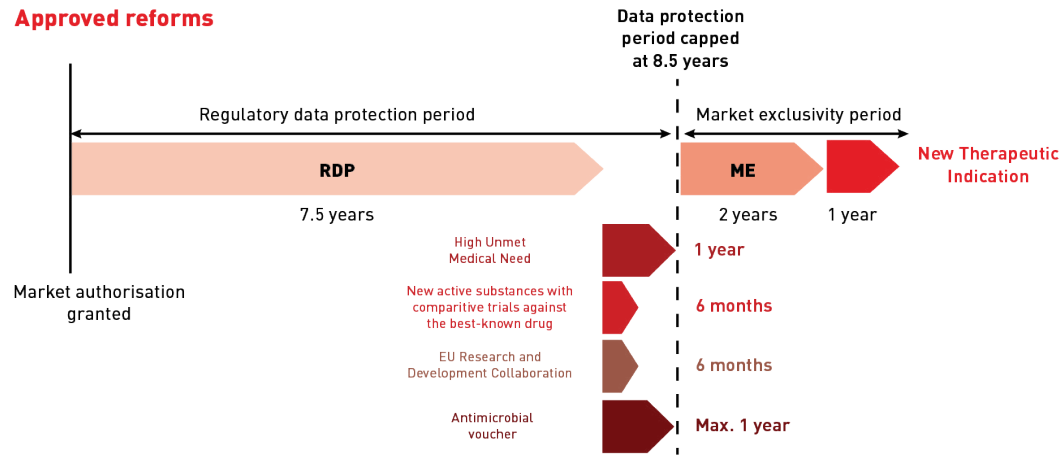
Figure one: Summary of regulatory exclusivity periods under the current system



disease, or products where there was significant R&D that took place in the EU and in collaboration with EU research entities. An extension will also be available by using a new antimicrobial reward voucher, but as these are limited in number, this will be rare in practice.

The exclusivity periods for orphan drugs are also being reformed. Orphan drugs currently benefit from ten years of marketing exclusivity, during which the regulatory authorities cannot accept or grant an MA application for a similar medicinal product intended for the same therapeutic indication. A two-year extension is available where all results from a completed paediatric investigation plan are submitted to the regulatory authorities.

Figure two: Summary of (expected) regulatory exclusivity periods under the new system



This orphan exclusivity period typically runs in parallel with the 8+2+1 exclusivity periods mentioned above. Orphan exclusivity is specific to an orphan indication, and where one active is approved for two different orphan indications the innovator benefits from two independent periods of orphan exclusivity.

Under the proposed reforms, orphan drugs will be stratified into three categories, each benefitting from different periods of exclusivity:

- standard protection (nine years);
- products meeting a high unmet medical need (11 years);
- products with a well-established use (four years).

Two extensions of one year will be available where a new indication is approved for the drug, but only for products in either the standard orphan market exclusivity or high unmet medical need categories.

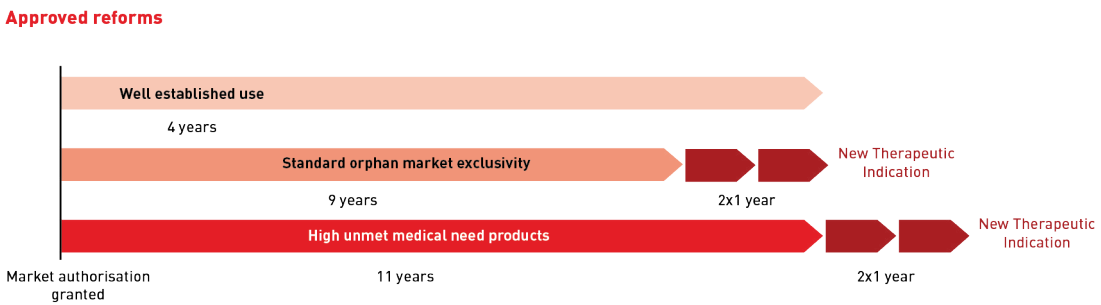
This represents a significant reduction in protection for drugs that have multiple orphan indications. For example, at present an orphan drug that receives authorisation for a second indication five years after the first indication will receive a new 10 (or 12) year period of orphan exclusivity (in relation to the second indication) starting from the date that second indication is approved. In the same scenario under the new system the innovator may receive only one extra year of protection instead.

In terms of impact on IP, many carefully planned timelines defining loss of exclusivity dates will need to be reconsidered once the new regime enters into force. There is often a detailed and complex interplay between regulatory exclusivity periods, patent expiry dates (20 years from filing), sometimes involving a number of patents, SPC expiry dates (15 years from marketing authorisation, capped at five years from patent term) and paediatric extensions (adding two years to orphan market exclusivity or six months to an SPC).

Planning IP strategy can thus be a delicate exercise, and reform may rock the boat, especially when conducting diligence on early-stage assets given the likely change in projected loss of exclusivity dates.

Complexity in IP strategy planning may also be complicated by the unpredictable nature of the regulatory exclusivity periods. Under the new system, there will now be a range, since the minimum regulatory exclusivity periods for drugs (both non-orphan and

Figure three: Summary of (expected) orphan drug exclusivity periods under the new system



orphan) will be slightly reduced, while the maximum periods will be slightly increased. It may also be difficult for innovators to say in advance whetherextensions may be available in the future, and which category a new orphan drug therapeutic might fall into.

When assessing loss of exclusivity timelines (important for due diligence, divisional planning, national validation decisions, SPC planning, etc) it will be important to bear in mind the new timelines. A few months of variation could have a significant impact in some cases, for example, if regulatory exclusivity periods expire before or after a concurrent IP right.

One further impact may be the stimulation of further R&D, in order to meet the new incentives, which could give rise to new discoveries and new patent filing opportunities

Supplementary protection certificates

The SPC reform is probably farther away from realisation, but is firmly on the horizon. The EU Supplementary Protection Certificate legislation was approved by the European Parliament in February 2024.

Briefly, the legislation seeks to introduce a centralised examination procedure for SPCs in the EU, and to introduce a new unitary SPC, in parallel to the Unitary Patent system. The proposals envisage that the European Union Intellectual Property Office will centrally examine SPC applications that rely upon a European patent and a centralised marketing authorisation granted by the EMA, rather than SPCs being individually examined by national patent offices. Noteworthy changes on SPC validity include explicit prohibitions on 'economically linked' parties from obtaining multiple SPCs for the same product, and attempts to codify some (but not all) CJEU decisions on the working of Article 3 into the recitals.

It is hoped that these reforms will reduce the administrative burden, and hence the time and costs associated with filing SPCs across Europe. However, it seems most of that potential upside will happen only when innovators are happy to use unitary patents as the basis for unitary SPCs.

But several uncertainties remain in the current proposals, such as the lack of transitional provisions, the requirement for applicants to obtain consent if a marketing authorisation holder differs from the patent holder, and a controversial pre-grant opposition procedure which arguably has the potential for causing undue, or even abusive, delays. Discussions are ongoing as to the specifics of the proposals, for instance which institution should be responsible for examining and refusing SPC applications, and the forum for invalidity hearings.

Innovators considering SPC filing strategy should already consider the potential impact of the new system coming into force. IAM

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