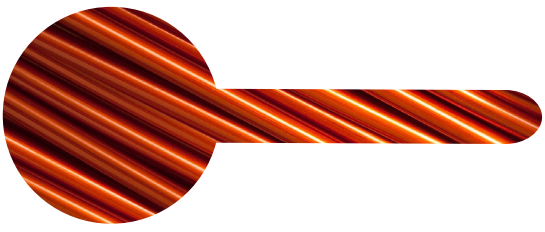
Biotech Review of the Year

Issue 10

10 years of Biotech Review



Bristows

“A decade later, many of the themes that we have been covering, such as innovation and regulatory change, remain as true today as when we first started this publication.”

Access our previous editions here

Dear readers,

Despite a turbulent 2022 marked by a significant decrease in general investment, the biotech industry continued to grow with more breakthrough therapies. Indeed, 2022 was marked by significant progress in the clinical and regulatory development of gene and cell therapies, a key driver in the innovation and growth of the biopharmaceutical sector.

Innovation in the biotech sector has been the subject of some of the highest profile litigation in 2022. With hundreds of millions of dollars in royalties at stake, one article in this edition examines the ongoing patent infringement litigation in the mRNA space. Other court cases are reported too, related to DNA sequencing by synthesis patents, trade marks and much more.

Change is a constant in our field, but this edition in particular reports on a number of important developments which have either taken place in the last year or are on the horizon. Perhaps the most anticipated change of all is the coming into force of the Unified Patent Court. After decades of preparations the new Court will be a reality in 2023 and so this edition features an extensive article dedicated to the UPC which includes recommendations on how to prepare for it in contracts and litigation strategy. From the new legislation applying to in vitro diagnostics to the revised EU Product Liability Directive and the new EU AI Liability Directive, there are plenty of important changes affecting the biotech sector that are unpicked by our contributors in this edition. With more and more discussions about ESG in boardroom meetings, we also report on new obligations at EU level in this growing space.

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On the investment and growth fronts, after a choppy year, the sector may still look ahead to 2023 with some optimism. As one article in this edition reports, interest in biotech remains strong even as investors adapt to changed market conditions. With growth comes an increased need for the best talent internationally. In view of the ongoing battle for talent, our article on global mobility will be an interesting read for any growing organisation.

As the use of AI in the life sciences sector proliferates, so does techbio and the need for specialist investors to support deep-tech and data-driven business models, as one article in this issue explains. Advances in AI are confirmed by Francesco Vazzana, Senior Director, Legal Counsel International at Alnylam and the subject of an interesting Q&A.

We are delighted to share with you insights from our lawyers who have been involved in the developments of the past 12 months. This year marks our 10th edition of the Biotech Review, a milestone we are particularly happy to share with you. A decade later, many of the themes that we have been covering, such as innovation and regulatory change, remain as true today as when we first started this publication. May the next 10 years be as exciting for the biotech sector as the last 10!

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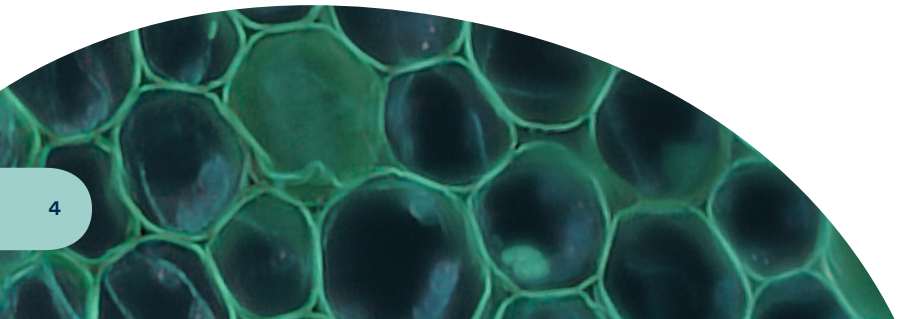


Innovation & case law

mRNA patent litigation...the new patent wars?

The world is a very different place to what it was back in 2020 when Moderna pledged not to enforce its mRNA patents during the pandemic.

Eden Winlow
Associate, Patent Litigation

The "updating" of that pledge in March 2022, limiting it to low-income countries, foreshadowed a new era in patent litigation. In this article we provide an overview of ongoing patent litigation relating to mRNA technology and discuss what the future might hold in this fertile new battleground for licensing disputes.

In Issue 9 of the Bristows Biotech Review of the Year, we took a closer look at mRNA, what it is and what it could potentially be used for. We discussed its transformational potential, not only as a vaccine platform but also for use as a therapy against genetic diseases, in cancer immunotherapy, and in regenerative medicine. This potential has led to staggering levels of growth and investment in mRNA companies. As expected, this has also led to companies jostling for position in the market.

Pfizer made $37.8bn in revenue from Covid vaccine sales alone in 2022, while Moderna made $18.4bn. This year, with hundreds of millions of dollars in royalties at stake, we examine the uglier and sometimes inevitable outcome of revolutionary technologies such as this - patent litigation.

mRNA technology

A detailed overview of mRNA technology can be found in a previous Bristows article here. However, in short, mRNA technology can essentially be viewed in two parts: (1) the delivery system and (2) the coded mRNA itself. The delivery system ensures the mRNA gets into the intended cells in the body effectively and safely. The most used delivery system is lipid nanoparticles (**LNPs**). The mRNA component corresponds to the specific genetic sequence of the protein or antigen you want the cells to produce. Broadly, patents protecting mRNA technology fall within one of these two categories.

IP landscape

As discussed in another previous article by Bristows, the web of intellectual property that protects mRNA technology is complex and overlaid by a large network of partnerships and licensing arrangements. However, there are a few key companies leading the way in the field, each with a market capitalisation in the multiple billion dollars. Moderna, BioNTech and CureVac are the largest of these and each have numerous mRNA products in their pipelines as well as large mRNA patent portfolios, valuable know-how and key patent licences and partnerships in place. Companies such as Arcturus and Translate Bio also have significant presences in the market, along with market capitalisations over a billion dollars and multiple products in their pipelines.

Early work on LNPs was carried out by Canadian biotech Arbutus Biopharma Corporation (**Arbutus**) in collaboration with the University of British Columbia. Several companies have since taken licences of LNP patents owned by Arbutus. In 2018, Arbutus spun out rights to its LNP technology (excluding rights to hepatitis B) into a company called Genevant Sciences GmBH (**Genevant**) as part of a joint venture with Roivant Sciences Ltd. The Arbutus patents have been the subject of some litigation, discussed below.

Moderna has been focused on the potential of mRNA since it was founded in 2010 and has invested heavily in delivery science. Moderna has indicated that it has an extensive portfolio of patents relating to its mRNA platform, including novel lipid components designed for optimal expression of both therapeutic and vaccine mRNAs. The Moderna patents have been the subject of some of the highest profile litigation in this space and Moderna's own Covid-19 vaccine is also accused of patent infringement.

BioNTech uses several delivery formulations for its products, including LNPs and its own proprietary lipoplex (lipid carriers) formulations for which it has several patent filings. Again reflecting the importance of delivery systems to the success of an mRNA product, BioNTech also has several active third-party partnerships focussed on this area, including a partnership with Genevant and a non-exclusive licence from Acuitas Therapeutics, Inc (**Acuitas**) for LNP formulations used in the Pfizer/BioNTech Covid-19 vaccine. BioNTech has also indicated it has a broad patent estate comprising over 100 patent families. BioNTech's patent estate includes patent filings directed to features of therapeutic mRNA structures, mRNA formulations (including its lipoplex formulations and lipid nanoparticles), mRNA manufacturing, and uses of mRNA therapeutics. Whilst BioNTech is not yet asserting its own patents, the Pfizer/BioNTech vaccine is accused of patent infringement.

CureVac is in the process of developing its own proprietary LNP system, however it currently relies on third party LNP delivery systems for its clinical assets. CureVac is also party to a Development and Option Agreement with Acuitas that provides CureVac with access to Acuitas' LNP technology and has entered into a development and option agreement with Arcturus Therapeutics (**Arcturus**) to access Arcturus' lipid-mediated delivery IP. CureVac similarly has a large patent portfolio relating to mRNA products. These include patents relating to CureVac's mRNA technology platform, its delivery system and its product candidates (which include oncology candidates and rabies vaccines). CureVac is actively asserting some of these patents already.

Unsurprisingly, almost all the ongoing patent litigation relates to these key players. The outcomes of these early battles could cement the parties as market leaders in the mRNA field. For the purpose of this article, we will therefore focus on these companies. However, this is by no means an exhaustive review and we expect more disputes focussed on mRNA to emerge in the future. Furthermore, there are ongoing invalidity proceedings in many jurisdictions, for example EPO oppositions, that we will not cover here.

Ongoing litigation

Arbutus and Genevant v Moderna

In the first major patent infringement lawsuit in the mRNA space, on 28 February 2022, Arbutus and Genevant filed a claim for patent infringement by Moderna in the US District Court of Delaware.

Arbutus alleges that Moderna infringes the claims of 6 US patents through sales of its Spikevax (Covid-19) vaccine and booster products. The patents relate to LNP technology, specifically lipid vesicles and nucleic acid-lipid particles. Moderna had previously sublicensed some of Arbutus' LNP delivery technology. However, following the limitation of these rights in 2018, Moderna

attempted to invalidate three of Arbutus' patents in proceedings before the USPTO's Patent Trial and Appeal Board (**PTAB**). These had mixed results and Moderna appealed the ruling on one patent that was later upheld by the Court of Appeals for the Federal Circuit, paving the way for the patent infringement claim by Arbutus and Genevant.

In further developments, Moderna countered with a motion to dismiss in May 2022, arguing that the US government should defend against the patent infringement because Moderna was simply providing vaccines under a federal contract. However, US District Judge Mitchell Goldberg was not convinced and dismissed the motion. Modena will therefore have to fight this battle on its own.

Alnylam v Moderna and Alnylam v Pfizer

Less than two weeks after the *Arbutus and Genevant* claim, on 17 March 2022, Alnylam Pharmaceuticals (**Alnylam**), an American biopharmaceutical company, also filed a claim against Moderna, and separately Pfizer, in the US District Court of Delaware. Alnylam alleges that both Moderna and Pfizer infringe its patent relating to LNP technology, specifically covering one of the four lipid components encapsulating the mRNA payload. Alnylam filed the claims on the same day the USPTO granted the patent in question.

On 12 July 2022, Alnylam added fuel to the fire and again separately sued Moderna and Pfizer for infringement of a second newly-granted patent, this time for the entire LNP and its method of production.

In both cases Alnylam is seeking royalties from the sales of vaccines and boosters, but no injunction.

CureVac v BioNTech

On 7 July 2022, CureVac filed a patent infringement claim against fellow German company BioNTech in the Dusseldorf Regional Court in Germany, alleging infringement of four CureVac patent claims concerning the features of the mRNA payload and lipid formulation used to make the BioNTech coronavirus vaccine.

CureVac said it has no intention to seek an injunction, but it does seek recognition and royalties from past and future sales. CureVac CEO Franz-Werner Haas stated "There's a piece of IP which we think has been used. That's OK. We're not against using it, especially in a pandemic... We just want to have this piece of contribution recognized."

If CureVac were to win, it is estimated by Berenberg Capital Markets, assuming $20bn of Pfizer and BioNTech's Covid-19 vaccine revenue could be in question, that there is a $500m "potential upside" for CureVac based on a royalty rate of 2% to 3% in an "optimistic scenario."

BioNTech maintains that its vaccines and boosters do not infringe the CureVac patents. In retaliation on 26 July 2022, BioNTech filed complaints in the US District Court of Massachusetts, seeking non-infringement judgments in relation to the equivalent US patents to those being asserted in the German case.

Moderna v Pfizer and BioNTech

In the most high-profile patent litigation case relating to mRNA, after more than a year of dominating the Covid-19 vaccine market between them, Moderna made patent infringement claims against Pfizer and BioNTech. After Moderna filed claims in August 2022 in the US and Germany, Pfizer and BioNTech countered with invalidity proceedings in the UK. Moderna alleges that Pfizer and BioNTech's vaccine infringes patents it holds.

Moderna is asserting patent rights filed between 2011 and 2016, relating to three elements of Pfizer/BioNTech vaccine:

- Use of lipid nanoparticles to encapsulate mRNA;
- Replacement of uracil with N1-methylpseudouridine in the vaccine mRNA; and
- Use of mRNA which codes for the SARS-CoV-2 spike (S) protein.

CEO Stéphane Bance said Moderna is seeking to "protect the innovative mRNA technology that we pioneered, invested billions of dollars into creating, and patented during the decade preceding the Covid-19 pandemic".

A company spokesperson for Pfizer stated that it is "surprised by the litigation given the Pfizer/BioNTech Covid-19 vaccine was based on BioNTech's proprietary mRNA technology and developed by both BioNTech and Pfizer" and will "vigorously defend against the allegations of the lawsuit."

Moderna is not seeking to remove the Pfizer/BioNTech vaccine from any market. It also is not targeting vaccine sales in lower income countries covered by the global COVAX initiative, instead focussing only on developed markets.

In recent developments in the US, Pfizer/BioNTech argue that their vaccine does not infringe the patents, that Moderna's patents are invalid, and that Moderna waived its rights to bring the claim when it pledged not to sue other Covid-19 vaccine producers during the pandemic.

Our take

It is important to note that none of the claimants in the above cases are seeking an injunction to remove vaccines from the market, in any jurisdiction. This is probably due to the very low chance of obtaining such an injunction owing to the public interest in allowing the vaccines to remain on the market. Furthermore, any claimant seeking an injunction would likely face significant public backlash. Therefore, the primary motivation in these cases is damages, normally calculated as a 'reasonable royalty' applied to infringing sales. With vaccine products having collectively achieved tens of billions of dollars in revenue in recent years, such damages awards could be quite significant.

All these cases are in their very early stages and anyone operating in the mRNA field should keep up to date with their outcomes. For example, if any of the early LNP patents are invalidated, other mRNA competitors could have more flexibility in the use of delivery formulations without having to take a licence. Alternatively, if patents survive validity challenges during litigation, then surviving patents would effectively be strengthened, having been battle-tested, and rights holders may be more likely to utilise them to force competitors to take a licence to the technology covered by those patents in the future.

As already mentioned, we expect many more disputes to arise in this area. It is expected that defendants in these cases will begin to weaponise and deploy their own patent portfolios in retaliation. These disputes may therefore take years to play out in full.

In conclusion, companies working in the mRNA space should monitor this ongoing litigation carefully and work with their IP lawyers to set appropriate strategies to traverse this complex space based on the outcomes.

DNA sequencing by synthesis patents held valid and infringed

On 17 December 2021, the Court of Appeal, with the leading judgment given by Lord Justice Arnold, handed down its decision in the appeal of the High Court's earlier decision in *Illumina v MGI*[1], dismissing MGI's appeal in its entirety and holding four of Illumina's patents in the field of DNA sequencing valid[2].

Chris Stubbs
Associate, Patent Litigation

The action had begun with Illumina's claim for patent infringement against MGI in relation to four of MGI's high throughput DNA sequencing systems including StandardMPS, CoolMPS and DNBSEQ E.

Background

The validity of four patents were in issue on appeal. There was no dispute as to infringement if the patents were valid. The patents can be conveniently split into two groups based on the technology claimed. The first group consisted of three patents, EP (UK) 1 530 578, EP (UK) 3 002 289 and EP (UK) 3 587 433, entitled either 'Modified Nucleotides for Polynucleotide Sequencing' or 'Modified Nucleotides' (Modified Nucleotide Patents), which claimed a technique for using a chemical group as a reverse chain terminator during DNA sequencing by synthesis.

Sequencing by synthesis is a high throughput DNA sequencing method that was designed to overcome the limitations of the well-known Sanger DNA sequencing method. Sanger DNA sequencing had been developed in the 1970s and formed the basis of DNA sequencing in the subsequent decades. The Modified Nucleotide Patents had arisen out of research into a form of DNA sequencing by synthesis using reversible chain terminators (RCTs). In Sanger DNA sequencing, the DNA template strand undergoing sequencing is presented with a mixture of the four nucleotides and one type of dideoxynucleotide (wherein the 3' hydroxyl group has been removed). The template DNA is synthesised by DNA polymerase up until the point at which a dideoxynucleotide is incorporated into the complementary strand, which due to the lack of the 3' hydroxyl group terminates synthesis. The output of Sanger DNA sequencing is thus a large number of DNA fragments of varying lengths. The DNA sequence is then determined using methods such as capillary gel electrophoresis. Sequencing by synthesis using RCTs differs in that the 3' hydroxyl group of each nucleotide is reversibly blocked. This means that following incorporation of a nucleotide the synthesis of the complementary strand is temporarily blocked, the nucleotide that has just been incorporated (which is also tagged with a fluorescent label) on the complementary strand is detected and identified, unblocked and then the synthesis process can continue with each new nucleotide being identified

1 [2021] EWHC 57 (Pat)
2 [2021] EWCA Civ 1924

in the same way. The Modified Nucleotide Patents claimed aspects of sequencing by synthesis using RCTs, in particular, modified nucleotides with a 3'-azidomethyl group.

The second group consisted of a sole patent, EP (UK) 2 021 415 (EP 415), that claimed a class of compounds including dyes and labelled compounds for use in the base detection stage of DNA sequencing by synthesis. Specifically, the claim in issue was to a nucleotide labelled with a compound formed of a cleavable linker and a fluorescent dye.

The four patents had been found valid and infringed at first instance. On appeal, the issues in dispute were: i) were the Modified Nucleotide Patents obvious over prior art named Zavgorodny; ii) were the Modified Nucleotide Patents entitled to the claimed priority as if not, it was agreed they would be obvious; and iii) was EP 415 obvious as a collocation of non-inventive features?

Obviousness of the Modified Nucleotide Patents

In addressing i), Arnold LJ held that the Modified Nucleotide Patents were not obvious over Zavgorodny. In particular, Arnold LJ held that the first instance judge was correct in deciding that the skilled team working on sequencing by synthesis would not approach Zavgorodny with a particular aim in mind. Although the skilled team would be aware of the concept of reversible chain termination at the priority date they would not approach Zavgorodny with the knowledge that there were problems with existing blocking groups that had prevented reversible chain termination from being successfully implemented. Therefore, the skilled team would not be interested in taking forward a new blocking group over existing ones. Zavgorodny also concerned synthetic chemistry and the use of nucleosides rather than nucleotides and was therefore in a different technical field from sequencing by synthesis. The skilled team would also not consider an azidomethyl blocking group as disclosed in Zavgorodny to be of greater interest than other blocking groups for use in sequencing by synthesis. A reference in Zavgorodny that azidomethyl groups could be removed "under very specific and mild conditions" had to be taken in context of the skilled team's mindset in approaching the prior art and would therefore not be a basis for further action. Finally, even if the skilled team considered azidomethyl as the blocking group they would have no reasonable expectation of success that it would be incorporated into the complementary strand of DNA and that it could then be removed to obtain a reasonable yield and at a reasonable speed.

Entitlement to priority of the Modified Nucleotide Patents

As for issue ii) on priority, Arnold LJ held that there was no squeeze between the priority attack and obviousness attack. MGI had alleged that if the Modified Nucleotide Patents were not obvious over Zavgorodny then they were not entitled to claim priority from the priority application. The allegation being that the priority application would have left the skilled team no better informed than Zavgorodny. Arnold LJ disagreed with MGI, holding that the priority application was an advance on Zavgorodny largely because Zavgorodny contained no indication that an azidomethyl blocking group should be used in sequencing by synthesis. The priority application made such a proposal, stating that nucleotides containing the group had been reversibly incorporated into the DNA complementary strand and also provided experimental conditions for the reversal step.

Arnold LJ also considered whether the priority application made it plausible that the claimed nucleotides in the Modified Nucleotide Patents had the claimed utility and therefore whether the Modified Nucleotide Patents were entitled to priority on that basis. Although MGI had not clearly run an implausibility argument, Arnold LJ agreed with the first instance judge that on the "unchallenged evidence"

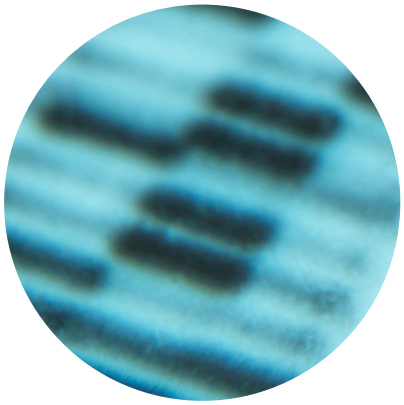
the priority document did make it plausible that the claimed compounds would work. The unchallenged evidence in issue was an example in the priority application showing one cycle of reversible chain blocking. The example made it plausible that an azidomethyl group would work and the Modified Nucleotide Patents just provided further support.

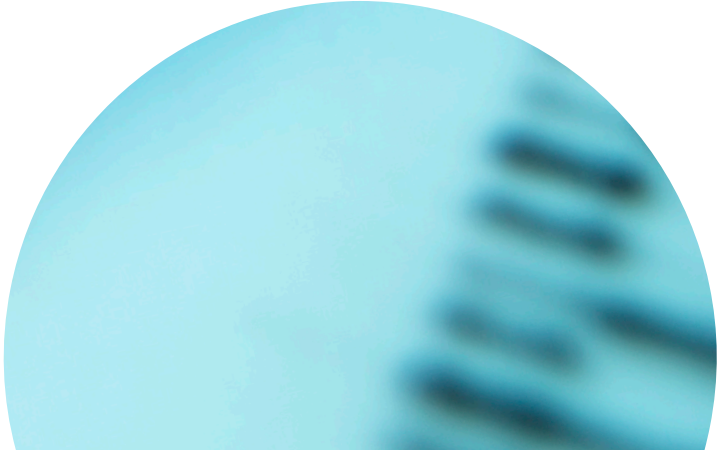
MGI's appeal in relation to the Modified Nucleotide Patents was therefore dismissed. Additionally, although Illumina's main case on priority was that the first instance judge's findings were correct, in the alternative it put forward an argument that plausibility was not required for priority as a matter of law. Although Arnold LJ did not need to decide this point, he noted that Illumina had not filed a respondent's notice raising its alternative argument and that it should have done so. The reason being that Civil Procedure Rule 52.13(2)(b) requires a respondent to file a respondent's notice if they wish to ask the appeal court to uphold the lower court for reasons different from or additional to those given by the lower court. Although on the facts of the case Arnold LJ said he would have given permission for a respondent's notice to be filed in any event, and ultimately the point did not need deciding, it had the potential to be a costly oversight.

EP 415 a collocation of non-inventive features?

On issue iii) on EP 415, Arnold LJ held that the class of compounds claimed in EP 415 were not a mere collocation of obvious features. MGI had alleged that the two elements of claim 1, the claimed linker and claimed dye, were two known obvious features that together achieved no synergistic effect or interacted in a non-obvious way. Although each of the features taken alone were obvious, EP 415 claimed a single invention (the whole compound) that made a technical contribution to the art that the prior art did not. Arnold LJ agreed with the findings of the first instance judge that a nucleotide with the claimed linker could interact adversely with the claimed dye and that the skilled team could not know whether this would occur without testing. EP 415 demonstrated that there was no adverse reaction and that the claimed compounds were useful for sequencing by synthesis. Showing that there was no adverse reaction was enough to render EP 415 inventive and therefore valid.

Nugee LJ and Warby LJ agreed with Arnold LJ's findings.





An inside job - how clinical reality can shape the medicines market

Is it possible that the confirmation of clinical discretion in product choice and a shift to personalised medicine could be helping to reshape the medicinal product economy?

Alex Denoon
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It's been clear since the NHSs' right to produce Avastin to treat macular degeneration was upheld by the Court of Appeal[1] (**Avastin decision**) that market rules do not restrict clinical practice. Once a product such as Avastin is placed on the market, it's up to practitioners whether or not to use it for the indication it was approved for. Indeed, the fact that there is already an authorised medicinal product for the target indication cannot fetter a clinical decision to use a different licensed product off label. Where, as in the *NHS Darlington case*[2], clinicians instruct a pharmacy to divide the licensed medicinal product into aliquot doses for use in treating individual patients for an off-label indication (e.g. WAMD), the person dividing doses into individual syringes (**Compounder**) will not be placing anything on the market, provided the compounder does not modify the authorised product.

The Avastin decision, which builds upon an earlier decision of the CJEU[3], is a signal indicator of the importance of clinical choice, but it's not the only one.

When the Advanced Therapy Medicinal Product (**ATMP**) Regulation emerged in 2007, many applauded its scheme for assisting SMEs. Others, however, argued that the incentives were misplaced. More important than encouraging small businesses, they claimed, was helping academics and clinicians.

At first blush, worrying about individual academics and clinicians makes no sense. But ATMPs are different. They require a denser dossier of manufacturing and clinical data than a biological medicinal product to stand a chance of receiving a marketing authorisation (**MA**). Very few small businesses can approach this level of funding. ATMPs tend to target rare diseases, a quality which, notwithstanding the possibility of securing orphan market exclusivity, rather blunts the financial appetite. But while businesses are chary about curing rare and supposedly incurable diseases, clinical academics are curious. They play a more significant role in

1 *R. (on the application of Bayer Plc) v NHS Darlington Clinical Commissioning Group, R. (on the application of Novartis Pharmaceuticals UK Ltd) v NHS Darlington Clinical Commissioning Group* [2020] EWCA Civ 449. The Supreme Court refused an application to appeal the decision

2 *R. (on the application of Bayer Plc) v NHS Darlington CCG, R. (on the application of Novartis Pharmaceuticals UK Ltd) v NHS Darlington CCG* [2018] EWHC 2465 (Admin)

3 Case C-535/11 (Apozyte)

developing and translating advanced gene and cell therapies than small businesses, so why wasn't the ATMP Regulation helping them?

Perhaps it is. Could the ATMP-specific "hospital use exemption" (**HE**)[4] provide a helping hand? The exemption applies where the cell or gene therapy product "is prepared on a non-routine basis according to specific quality standards, and used within the same Member State in a hospital under the exclusive professional responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient."
It's tailor-made for academic hospitals, isn't it?

In practice, academic hospitals in the EU and UK already have recourse to another exemption to the MA rule: one not restricted to fancy ATMPs, but available, in the right circumstances, to any medicinal product. The "specials exemption", which in the UK has been used in every instance where the HE might have been attempted. This excludes products supplied "to fulfil special needs" in response to a bona fide unsolicited order, where the product is "formulated in accordance with the specifications of an authorised health-care professional" for use by an individual patient under his direct personal responsibility. It's good enough, perhaps, and note the difference between "formulated in accordance with the specifications of an authorised health-care professional" and its more demanding HE equivalent: "prepared on a non-routine basis according to specific quality standards" and the associated manufacturing requirements. Who needs the hospital exemption? But not all Member States are quite so dismissive. Some, like Germany and Spain, consider the HE to be useful tool to encourage innovation.

In February 2021, Spain's regulator, Agencia Española del Medicamento y Productos Sanitarios (**AEMPS**), became the first medicines agency in Europe to formally authorise a complex ATMP under the HE[5]. ARI-0001 is a preparation of autologous CAR-T cells customised for the relief of relapsed/ refractory acute lymphoblastic leukaemia (**ALL**) in adults younger than 25. ALL is not only a rare disease[6], but a divided one, originating in either T or B cells. 85% of cases are B-ALL, for which the prognosis is poor despite breakthrough monoclonal antibody products. ARI-0001 was developed at Hospital Clínic de Barcelona. Preclinical and preliminary clinical data were obtained in an academic environment, which demonstrated robust and reproducible lentivirus and ARI-0001 cell production. The safety and efficacy of ARI-0001 were then assessed in a study conducted together with the paediatric hospital Sant Joan de Déu in Barcelona. To ensure compliance with strict manufacturing criteria, the CAR-T cell products are supplied to the hospital by a pharmaceutical company producing them under a manufacturing licence.

There are several striking aspects to AEMPS' scheme. First, there is the national regulatory framework to facilitate the HE. This not only complies strictly with the EU ATMP Regulation, but makes the exemption conditional upon satisfactory data on clinical efficacy and safety, and limits it to a three year "conditional licence".

4 Article 3(7) of the Medicinal Products Directive, inserted by the ATMP Regulation

5 AEMPS authorises Hospital Clínic's CAR-T ARI-0001 for patients with acute lymphoblastic leukaemia

6 1.28 in every 100,000 adults in Europe

The Spanish legislation also seems to consciously anticipate how emerging EU policy on "substances of human origin" (**SoHO**)[7] might help to overcome a key limitation of the HE: that patients in hospitals other than the one that developed an HE-ATMP may not access the product. The SoHO proposal aims "to provide representative technical expertise to the European decision-making organisations in the field of SoHO", essentially enabling a fluid and transparent environment for transferring SoHO technology and know-how. Could AEMPS use this as a lever to expand access to HE-ATMPs? It's certainly notable that the Spanish regulation describes the hospital developing an HE-ATMP as a "reference hospital"[8].

The clinicians who developed ARI-0001 clearly think Spain is on to something[9]. Even so, they consider that the "*the Spanish legislation is not agile enough to allow the development of new CAR-T therapies with the speed needed by patients with potentially life-threatening diseases for whom treatment alternatives are lacking*." Why? Because, primarily "*any change (either minimal or substantial) in the product is seen as a 'new product' in the eyes of the legislation, which means starting the development process (including generation of evidence) from scratch, with limited possibilities of bridging data between dossiers*." In other words, it's adopting the same standards as for ATMPs that are not exempt from having an MA. Given the autologous origin of the product, they ask why the approach shouldn't be less rigid where proposed improvements do not involve substantial changes of the core product. It would certainly remove a significant barrier to product improvement.

The second striking aspect of AEMPS approach is economic. It is reported that ARI-0001 costs a mere third of commercial CAR-T cell products available in Spain (although some have questioned the basis for calculation). Put another way, the prospects for a return on an ATMP investment have tripled, paradoxically, by not commercialising the product or following the conventional regulatory pathway (which is both demanding and expensive). The return on investment comes instead from the manufacturing and therapeutic delivery. So, should the HE now become the rule? When we contemplate that, since the inception of the ATMP Regulation 15 years ago, only 12 ATMP MAs have been granted in Europe of which only 8 have not been abandoned, we might well wonder.

7 The UK government has stated, sotto voce, that it will follow future EU SoHo regulation
8 Terapias avanzadas
9 *Bone Marrow Transplantation* (2022)

Re-packaging of parallel traded medicinal products

On 17 November 2022 the EU Court of Justice (CJEU) issued landmark decisions on the extent to which parallel traders are allowed to re-package branded medicinal products[1].

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Partner, Brands, Designs & Copyright

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The decisions clarify the situations when trade mark owners in certain circumstances may object to parallel traded medicinal products that have been re-packaged. The regulatory requirement for including an anti-tampering device does not mean re-packaging is necessary in every case. The presence of traces on the original packaging of the original anti-tampering device being removed does not warrant that re-packaging becomes necessary. It is only if the affected original packaging is met by consumer resistance (which needs evidence) then the re-packaging might be necessary.

Background

The parallel trade in issue occurs where original branded products are acquired in one country and imported into another without the permission of the brand owner. Typically parallel importers will often buy legitimate products in one country where the price is cheaper and then resell these in a different country for a higher price. In the UK and the EU due to the *exhaustion* principle, once the legitimate goods have been put on the marketplace with the brand owner's consent, the owner cannot ordinarily prevent the resale of original products on trade mark infringement grounds. However, it is possible for a trade mark owner to object but only if there are legitimate reasons to oppose the further marketing. Re-packaging by the parallel importer could fall into this category. Where the re-packaged products are medicinal products, the EU regulatory framework on the marketing of medicines also applies. In fact, to protect the public and ensure the safety of patients, a series of requirements were introduced under EU law which are relevant in the context of re-packaging of medicinal products. This article therefore discusses the grounds on which pharmaceutical companies may stop parallel importers from re-packaging medicines.

The disputes

These cases reached the CJEU through referrals from Courts in Denmark, Belgium and Germany. In all of these cases, the central issue was the extent to which parallel traded medicines could be re-packaged to meet the EU regulatory requirements for medicines without infringing the rights of the brand owner.

Notably, in *Novartis v Abacus*, Abacus argued that it was obliged under EU law to replace the packaging of Novartis' Votrient medicine with a new outer packaging in order to be able to market the product in Germany. The trade mark owner would not therefore be entitled to oppose that re-packaging on trade mark infringement grounds. Novartis disputed this by arguing that a new packaging was not

1 CJEU Judgments of 17 November 2022, *Novartis Pharma GmbH v Abacus Medicine A/S*, C 147/20 and *Bayer Intellectual Property*, C-204/20

necessary to comply with the requirements under EU law to prevent the entry of falsified medicinal products in the legal supply chain. These requirements could instead be complied with by affixing the unique identifier with an adhesive label and the placing of a new anti-tapering seal to cover the traces of opening after having included the new leaflet in German in the original packaging.

Abacus argued in response that, under the EU Falsified Medicines Directive[2] (the **FMD**) and Delegated Regulation[3] (the **DR**), products must have obligatory safety features such as an anti-tampering device on the external packaging. Suppliers of medicinal products are prohibited from selling products which show signs of tampering. As a result, Novartis' suggestion of re-sealing the packaging would not work as it would result in visible alterations to the original packaging. So, in Abacus' opinion, a new outer packaging was therefore necessary in order to comply with the FMD/DR.

The Court rulings

The CJEU decided that Novartis and Bayer were entitled to oppose the marketing by parallel traders of the re-packaged medicines on the basis of their registered trade marks. In essence, the re-packaging was unjustified in these cases as (a) the re-labelling of these products (including by affixing an adhesive label) and (b) replacement of the original anti-tampering device with an equivalent one would have been sufficient to satisfy FMD/DR requirements. The presence of traces on the packaging of having been opened as argued by Abacus is not, in itself, sufficient to justify re-packaging if the replacement anti-tampering device is "equivalent". Thus, re-packaging would not be necessary.

When deciding whether it was objectively necessary for the medicines to be re-packaged the CJEU considered its prior decision in *Boehringer Ingelheim*[4]. The re-labelling and re-packaging of medicinal products had been considered in that case where the CJEU ruled that if re-labelling is possible for the purposes of marketing the medicine in the country of importation then the replacement packaging is not necessary. If so, trade mark owners are entitled to oppose the re-packaging on the grounds that re-labelling is possible. In this context, the CJEU also emphasised that the re-packaging of medicinal products should aim at securing effective access to the market of importation. Securing a commercial advantage would not be considered "necessary" for market access and could no doubt be opposed by the trade mark owner.

However, it is important to note that if re-labelling alone hinders the effective access of that medicinal product in the country of importation the re-packaging would be a necessity. For example, if a significant portion of consumers showed strong resistance to the altered product then this could constitute an obstacle to effective access to that market. This, however, must be established on the evidence on a case-by-case basis.

The Court acknowledged that the replacement of the anti-tampering device with an equivalent one could potentially be met with consumer resistance, so it will need assessment on a case-by-case basis. The CJEU considered in this case that a parallel importer cannot rely on a general presumption of consumer resistance. Such resistance must be considered taking note of the specific circumstances.

Take-aways

- Trade mark owners can oppose the marketing of a parallel traded medicinal product which has been re-packaged provided such re-packaging was unnecessary to meet the EU regulatory requirements.
- For parallel traders, it is essential to perform an assessment of whether re-packaging is justified because it will be considered "a necessity" or whether re-labelling would be accepted. There would be room to argue that re-packaging is needed if, for example, consumers would meet the anti-tampering replacement with strong resistance.

2 Directive 2011/62/EU
3 Commission Delegated Regulation (EU) 2016/161
4 CJEU judgment of 26 April 2007, *Boehringer Ingelheim* and *Others*, C 348/04

Arrow declarations – is there a limit to their availability?

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"Is it proper for the courts of England and Wales to make a declaration solely for the purpose of influencing a decision by a foreign court on an issue governed by the law of the foreign court?" **This was in effect the question before both the Patents Court and the Court of Appeal last year in *Novartis v Teva & Ors*[1].**

Although the case concerned a small molecule medicinal product, the answer to this question is of broader interest in the life sciences field, as the circumstances under which *Arrow* relief is available is often a consideration for parties seeking to clear the way prior to launch, particularly in the biosimilars field.

An *Arrow* declaration is a declaration that a particular product, process or use would have been lacking in novelty or obvious as at the priority date of a patent application, in other words, a pre-grant declaration from the Court. The effect of such a declaration is that it gives the claimant in the *Arrow* proceedings a so-called Gillette defence[2] to any subsequent claim for infringement of any future patent rights relating to that product, process or use.

Background

On 25 February 2022, Teva issued proceedings against Novartis seeking *Arrow* declaratory relief. If granted, the relief sought by Teva would have deemed the use of a daily oral dose of 0.5 mg of fingolimod to treat relapsing-remitting multiple sclerosis (**RRMS**) obvious under English law as at 27 June 2006, the priority date of the Novartis patent application in issue – EP 2 959 894 (**EP 894**), directed to such use. Fingolimod is sold by Novartis in the UK for the treatment of RRMS under the brand name Gilenya®, primarily at the claimed daily oral dose of 0.5 mg. Regulatory exclusivity for Gilenya in the form of marketing protection expired in the UK and EU on 22 March 2022.

EP 894 was original rejected by the EPO's Examining Division (**ED**) in late 2020 but on 8 February 2022, the Technical Board of Appeal (**TBA**) allowed Novartis' appeal and issued a ruling directing the ED to grant the patent with the approved claim. EP 894 eventually granted on 12 October 2022.

1 *Novartis v Teva & Ors* [2022] EWCA Civ 775; EWHC 2779 (Ch) (Pat).
2 Named after a 1913 case, the defence operates where the alleged infringer can demonstrate that they work the prior art or an obvious variant, guaranteeing that the patentee cannot succeed in demonstrating that a later patent is both valid and infringed

Shortly after the TBA hearing, Teva issued its claim for *Arrow* declaratory relief. A week later (on 2 March 2022), Novartis issued infringement proceedings against a number of generics companies, including Teva, based on the EP 894 application and the threat by those companies to launch 0.5 mg generic fingolimod products in the UK for use in the claimed dosage regime. In addition to Teva, three of these companies also raised claims for *Arrow* declarations. Novartis also issued an application for interim injunctive relief, which was refused by Mr Justice Roth on 26 April 2022 on the basis of his finding that there would be no irreparable harm to Novartis should he refuse an interim injunction[3]. Permission to appeal this decision was ultimately refused on 25 May 2022. Although the interim injunction was refused, the generics companies were restrained from selling their fingolimod products pending determination of the application for interim relief, and the subsequent request for permission to appeal, in other words, from 22 March to 25 May 2022.

On 10 August 2022, Novartis withdrew the UK designation of EP 894 whilst it was still pending as an application[4]. This meant that EP 894 would not grant in the UK. As a result, Novartis sought to discontinue the infringement proceedings and invited Teva and the other defendants to discontinue their claims to *Arrow* relief. Novartis indicated that it would not serve expert evidence and would not make any submissions on validity should a trial on the technical issues take place. On the same day that it de-designated the UK designation of EP 894, Novartis also notified the NHS that it was withdrawing from the proceedings.

Teva declined to withdraw its claim to *Arrow* relief, but successfully applied to amend the basis on which the claim was made[5], and a trial on the discretionary issues in respect of Teva's application for declaratory relief was held before Mrs Justice Bacon on 17-18 October 2022. If Teva were to be successful on the question of relief, a trial on obviousness would have been listed for a later date. In the meantime, Teva had served reports from two experts in support of their arguments on obviousness.

First instance decision

The previous case law on *Arrow* declarations held that in determining whether to exercise its discretionary power to grant such a declaration (in addition to the merits of the validity arguments), the court must take into account: (i) justice to the claimant; (ii) justice to the defendant; (iii) whether the declaration would serve a useful purpose; and (iv) whether there are any other special reasons why or why not the court should grant the declaration. Teva sought to argue that declaratory relief would serve a useful purpose for the following reasons:

1. Novartis' enforcement of EP 894 prior to grant, before later de-designating the UK designation, which in effect led to a short-term injunction until permission to appeal was determined, amounted to a special reason for the granting of the declaration, being a relevant factor in the assessment of useful purpose.
2. A declaration would alleviate alleged residual confusion about the status of generic fingolimod in the UK, in particular within the NHS.

3 [2022] EWHC 959 (Pat)
4 There was one pending divisional application in the same patent family, which was also withdrawn
5 [2022] EWHC 2366 (Pat)

3. The undertakings offered by Novartis regarding future patent rights were allegedly insufficient to provide certainty to Teva and third parties regarding possible future patent rights which might impact upon sales of generic fingolimod in the UK.
4. A reasoned judgment on obviousness would be taken into account by the courts in other jurisdictions, where Novartis may also be seeking to enforce EP 894, in particular the courts in Germany.
5. A reasoned judgment on obviousness would help to protect Teva's supply chains for generic fingolimod to the UK, including transit through confidential "Country A".
6. A reasoned judgment would assist in settlement discussions between the parties across Europe.

In respect of the first reason, the judge held that the actions of Novartis alone could not support the grant of an *Arrow* declaration where there was otherwise no useful purpose, and therefore had to be considered as part of the other factors relied on by Teva. As to the second ground, uncertainty in the UK, the judge noted that there was no evidence before her that a declaration from the court would make any difference to the NHS' procurement policy or its understanding of the situation. Nor was there any evidence, as there had been in the earlier *Fujifilm v AbbVie case*[6], of any commercial uncertainty perpetuated by Novartis' actions in the litigation. On the third issue of undertakings, by the time of judgment the judge was satisfied that the undertakings being offered by Novartis were not ambiguous or lacking in clarity such as to create or perpetuate uncertainty on the market.

The tenor of the judgment was therefore in relation to the question of "spin-off" value abroad, including in relation to the supply chain to the UK. The parties had served expert evidence on German law as to the value of a judgment from the English court in German infringement proceedings, including applications there for a preliminary injunction. In essence, the evidence on German law was that an English declaratory judgment would be of interest to and taken into account by a German court in deciding whether to grant preliminary injunctive relief in Germany. Teva also argued that a validity decision would have benefit in other EPC member states even if the court did not have expert evidence before it from any additional jurisdictions. Ultimately the judge held that the fundamental problem with Teva's main argument on spin-off value was that the existing (first instance) case law established that if the only or predominant purpose of the declaration sought is to use it for a foreign court, the court will look carefully at the justification for the declaration. In such a case, a declaration is only likely to be granted in unusual cases where there is a compelling justification for doing so.

In assessing the supply chain argument, the judge accepted that based on the evidence before her a declaration may well have an impact on Teva's supply chain in so far as it is taken into account in Country A through which Teva transhipps its generic fingolimod products. The question was whether that was enough to grant a declaration where the sole or predominant purpose is for its use abroad. She did not think that it was. Given the prevalence of international supply chains, decisions of foreign courts will often have an indirect impact on supply routes to the UK. However, that did not change the fact that the purpose of the declaration sought here was to use it abroad in Country A and other countries, rather than to obtain or enforce any right in the UK. The judge therefore did not consider that there were particular unusual circumstances in the case to provide a compelling justification for the grant of the relief sought. Nor did Novartis' conduct in the UK case tip the balance in favour of granting a declaration where the conduct could not be said to have resulted in any continuing uncertainty on the UK market.

6 [2017] EWHC 395 (Pat)

In passing, the judge also dismissed the argument regarding promotion of settlement. Although unchallenged evidence had been adduced to the effect that a reasoned judgment in the UK would not assist settlement in other jurisdictions, the judge in any event held that promotion of settlement would not have been a sufficiently compelling reason to grant a declaration in this case.

Overall, the judge endorsed the judgment of Mr Justice Birss (as he then was) in the earlier case of *Pfizer v Roche*[7], who had come to much the same conclusion.

Teva's appeal

On application to the Court of Appeal, permission to appeal was granted by Lord Justice Arnold, and the hearing took place on an expedited basis on 28 November 2022, in light of parallel preliminary injunction proceedings in Germany under EP 894 that were listed to be heard on 16 December 2022. Having heard the arguments of both sides, the Court of Appeal indicated at the end of the hearing that Teva's appeal was dismissed and that written reasons would follow. The reasoned judgment was handed down on 8 December 2022.

Teva argued on appeal that the first instance judge had erred in principle in failing to ask whether (i) the declaration sought would serve a useful purpose; and (ii) whether there were any reasons for or against the grant of a declaration, and that the judge had further erred in asking whether there was a "very compelling justification" for granting the declaration.

Giving the leading judgment (with which Nugee LJ and Sir Christopher Floyd agreed), Arnold LJ stated that Bacon J had been correct to find that, once it was shown that a declaration was not required in order to dispel uncertainty in the UK market, it followed that the only purpose which could be served by a declaration was to assist the courts of other countries.

Arnold LJ concluded that assisting a foreign court to decide an issue under its own law is not a legitimate reason for the grant of declaratory relief, and that it is not the function of the Patents Court to provide advisory opinions to foreign courts seised of issues which fall to be determined in accordance with their own laws. Arnold LJ added that the fact that the grant of an injunction in another country would affect the supply of Teva's product in the UK is simply a knock-on consequence of the courts of that country applying their own law within their territory.

Impact of ruling

This ruling is important in terms of further clarifying the circumstances in which *Arrow* relief can be obtained from the court, including guidance from the higher Court of Appeal which can be binding on the first instance courts.

Arnold LJ clarified that "spin off" value does not justify the diversion of significant resources to trying purely academic questions in the UK. If anything, the Court of Appeal adopted a stricter approach than the judge at first instance, who had at least held open that the court might grant a declaration solely for spin-off value to one or more foreign courts in compelling circumstances. The decision of the Court of Appeal does not appear to leave open that possibility. Notably, Arnold LJ indicated that comity requires restraint on the part of the English courts, not jurisdictional imperialism, otherwise the English courts would be enabling forum shopping.

If there are no remaining relevant IP rights covering the UK and no commercial uncertainty in this country, this ruling makes clear that it will be very challenging for parties to persuade a court to grant such relief.

7 [2019] EWHC 1520 (Pat)

Legislative & regulatory change

Unified Patent Court: state of play and what biotech companies can do to prepare now

The Unified Patent Court (UPC), an important new patent litigation system in Europe that will sit alongside existing national patent litigation in jurisdictions including the UK, will soon become a reality.

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This article provides an overview of the latest information, including key dates and updates on participating states, judges and divisions. We also outline the decisions that need to be made and implemented now by biotech companies in relation to patent portfolio management, litigation strategy and existing and future contracts in preparation for the UPC opening its doors later this year.

What is the UPC?

As many readers will be aware, the UPC is a new international court that is (finally!) due to open its doors later this year. In participating states, the UPC will have jurisdiction over disputes relating to the infringement and validity of patents granted by the European Patent Office (**EPO**) - both classic European patents and the new unitary patents that will become available when the UPC comes into force. However, during a transitional period of at least 7 years after the UPC begins, classic European patents may be opted out of the UPC system, with opt out becoming possible from the beginning of a sunrise period that will commence three months before the UPC comes into effect otherwise, both the UPC and national courts will have jurisdiction over these patents.

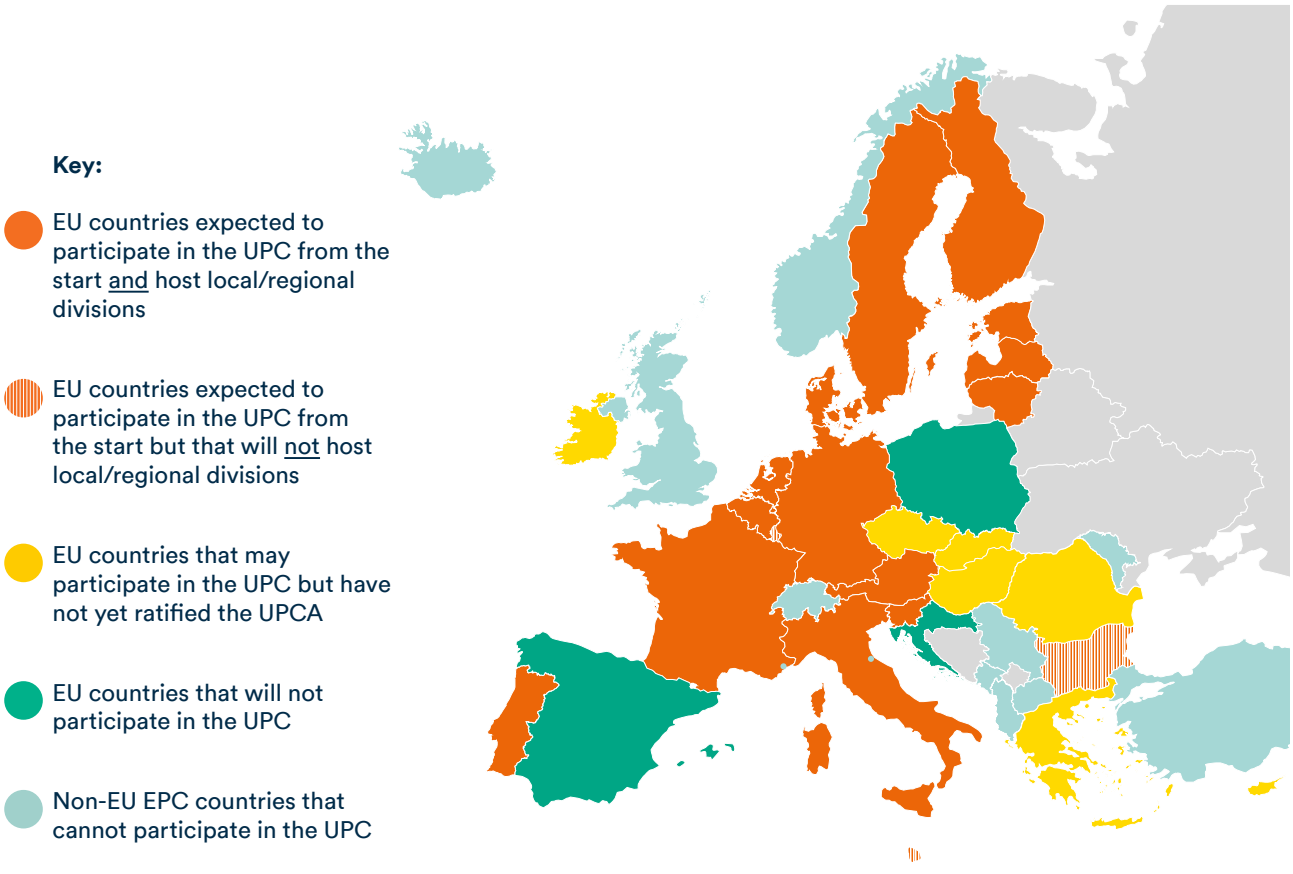
When will the UPC open its doors?

The start of the UPC was further postponed at the end of last year and the UPC roadmap at the time of writing foresees the sunrise period commencing on 1 March 2023 and the UPC opening its doors on 1 June 2023. Although this is only the latest in a number of delays, the postponement is said to be solely to give users of the UPC's case management system (**CMS**) additional time to obtain the secure authentication systems required to interact with the CMS. No further postponements are therefore anticipated by the authorities, unless this or further issues relating to the CMS remain unresolved. The start date of the EPO's transitional measures, which relate to the new unitary patent, was 1 January 2023. Steps that can be taken from 1 January 2023 and 1 March 2023 to prepare for the UPC are set out below (**What should biotech companies be doing to prepare now?**).

Which countries are participating in the UPC?

Not all European Patent Convention (**EPC**) states will participate in the UPC. Only those EPC states that (1) are EU Member States and (2) have signed and ratified the UPC Agreement (**UPCA**) may participate. At the time of writing:

- 17 EU Member States will participate in the UPC from the start: Austria, Belgium, Bulgaria, Denmark, Estonia, Finland, France, Germany, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Portugal, Slovenia and Sweden. Germany has not yet ratified the UPCA but has passed the legislation enabling it to ratify; Germany's ratification instrument will be deposited with the EU Council to trigger the commencement of the sunrise period. The other 16 countries have already ratified the UPCA.
- 7 EU Member States have signed but have not yet ratified the UPCA: Cyprus, Czech Republic, Greece, Hungary, Ireland, Romania and Slovakia. The UPC will not have jurisdiction in these countries prior to ratification and unitary patents granted before the respective ratification of the country in question will have no effect in that country. Ireland's ratification of the UPCA has been delayed by the need for a referendum to approve the associated amendment to its Constitution, however the Irish Government reaffirmed its commitment to participate last year and the referendum is expected to be held in 2023 or 2024.
- 3 EU Member States have not signed the UPCA and will not participate in the UPC: Croatia, Poland and Spain.
- A number of EPC states that are outside the EU will also not participate in the UPC, e.g. Albania, Iceland, Macedonia, Montenegro, Norway, Serbia, Switzerland, Turkey and the UK.



Where will the courts be located?

The UPC will be made up of a Court of First Instance, a Court of Appeal (which will hear appeals from the Court of First Instance) and a Registry (which will be responsible for administration of proceedings). The Court of Justice for the European Union will also have limited jurisdiction to hear questions on EU law referred to it by the Court of First Instance or Court of Appeal.

The Court of First Instance, made up of a Central Division and several local/regional divisions, will be spread across several locations (see below), whereas the Court of Appeal and the Registry will be located in Luxembourg.

Central Division of the Court of First Instance

The three seats of the Central Division were originally due to be in London (human necessities, chemistry and metallurgy, including pharmaceutical and biotech cases), Munich (mechanical engineering) and Paris (all other patent classifications). However, since the UK confirmed that it would no longer participate in the UPC post-Brexit, a new Central Division seat with responsibility for pharmaceutical and biotech cases has not been confirmed. The Italian Government has proposed Milan as the replacement for London but we understand that the final locations and responsibilities of the seats of the Central Division remain politically sensitive and may not be confirmed until the start date of the UPC.

Local and regional divisions of the Court of First Instance

Local divisions have been confirmed in Vienna, Brussels, Copenhagen, Helsinki, Paris, Düsseldorf, Hamburg, Mannheim, Munich, Milan, Lisbon, Ljubljana and The Hague and a Nordic-Baltic regional division based primarily in Stockholm will hear cases from Sweden, Estonia, Latvia and Lithuania. Three of the countries that will participate in the UPC from day 1 (Bulgaria, Luxembourg and Malta) will not host a local or regional division. However, additional local divisions may be added as further countries join the UPC, for example the Irish Government has announced that it will host a local division if it joins.

Who will the judges be?

The UPC Administrative Committee announced the appointment of 34 legally qualified judges (seven of whom have been appointed to the Court of Appeal) and 51 technically qualified judges in October 2022. The full list of judges is available from the UPC website: www.unified-patent-court.org.

Of the appointed judges, drawn from 13 of the 17 states that will participate in the UPC from the start, only five will be full time: the President of the Court of First Instance (Florence Butin), the President of the Court of Appeal (Klaus Grabinski) and three other Court of First Instance judges in the Presidium. All other judges will at least initially be part time.

The technically qualified judges who have been appointed are listed according to specific fields of technology. Eight judges have been appointed in the field of Biotechnology: Arwed Andreas Burrichter (Germany), Eric Enderlin (France), Rainer Friedrich (Germany), Paolo Gerli (Italy), Krister Karlsson (Finland), András Kupecz (the Netherlands), Roman Maksymiw (Germany) and Cornelis Schüller (the Netherlands). Of these, six are patent attorneys in private practice and one is an in-house patent attorney. It will therefore be interesting to see how potential conflicts of interest are managed given that these judges will continue in their private practice and industry roles while acting as judges part time.

What should biotech companies be doing to prepare now?

A number of decisions need to be made and implemented in the immediate run up to the UPC start date on 1 June 2023.

Opt outs

For patentees wanting to keep their patents and supplementary protection certificates (**SPCs**) out of the UPC during its early days, European patents and SPCs should be opted out during the sunrise period (from 1 March 2023) to avoid any day 1 challenges within the UPC. In this case, not only existing European patents should be opted out but also any expired European patents for which corresponding SPCs have been granted or for which future damages claims are contemplated.

Opt-out applications should be submitted via the online UPC CMS and must be made in respect of all states for which a European patent has been granted or that have been designated in the application (this includes EPC states that are not participating in the UPC, such as Spain and the UK, although the legal basis for requiring a proprietor to opt out European patents in non-UPC countries remains dubious). For co-owned patents, the agreement of all proprietors is required for opt out to be effective so discussions with co-owners should be held as soon as possible if this has not been done already. See below (**Contracts**) for further information on the steps to be taken for co-owned patents. Determination of the true proprietor of each designation of a European patent should also be completed, as the opt out needs to be filed by the true proprietor rather than the party registered as proprietor on the various national patent office registers (if different).

In order to access the CMS, a Client Authentication Certificate (which must be on a physical device such as a smart card or USB stick) and an Electronic Signature Certificate will need to be obtained. A list of providers that have claimed they meet the required technical standards for certification is available from the UPC website, including a number of providers that provide online rather than in-person identification. The certificates are specific to individual users so patentees wishing to opt patents out should consider carefully which individuals in their organisation will be responsible for opt outs and therefore need to obtain certification. Although the provider of the Client Authentication Certificate and Electronic Signature Certificate will need to be located within the EU, some will provide these to non-EU residents.

Any European patents that are not opted out before 1 June 2023 will automatically be subject to the jurisdiction of the UPC. However, such patents may be opted out at a later date if no action has been brought before the UPC in relation to that patent or associated SPC in the meantime. An opt out can also be subsequently withdrawn (once) so long as no action has been brought before a national court in relation to that patent or associated SPC prior to filing the withdrawal.

Unitary patents

Patentees also need to decide whether to request that current European patent applications are granted as unitary patents. Unlike classic European patents (which become a bundle of separate national rights on grant needing validation (where appropriate) and maintenance in each country), the new unitary patent will be a single patent that covers all participating UPC states at the time of grant and may not be opted out of the UPC. A single annual renewal fee will be payable. Assuming no additional countries ratify the UPCA before 1 June 2023, any unitary patents granted on that date will cover the 17 countries coloured orange on the map on the previous page.

For patentees who wish to obtain unitary patents, the EPO introduced two transitional measures on 1 January 2023:

1. An applicant for a European patent that has reached the final phase of the grant procedure, i.e. for which a communication of intention to grant under Rule 71(3) EPC has been despatched, may file an early request for unitary effect before the start of the UPC so that a patent will have immediate unitary effect on grant, potentially even on day 1 of the UPC depending on timing.
2. An applicant for a European patent coming to grant shortly before the UPC start date may request that the issue of the decision to grant a European patent be delayed until the start date so they do not miss the opportunity to obtain a unitary patent, which is only available for patents that grant on or after the UPC start date. In this case, the applicant will have one month from the start date to request unitary effect.

Litigation strategy

Clearly preparation for the UPC does not end with opt outs and requests for unitary patents.

For patents that are intended to be enforced within the UPC (European patents that are not opted out or unitary patents), decisions need to be taken as to where each patent should be enforced as there will often be a choice between a number of local, regional and central divisions under Article 33 UPCA. Factors relevant to this decision will include, for example, the likely approach of each division to bifurcation of validity and infringement proceedings, preliminary and final relief (including the security required for a preliminary injunction) and expert evidence, as well as the speed of judgment and quality of judicial decisions. Although many of these factors should become harmonised between divisions over time, there are expected to be national variations in procedure based on individual judges' prior experience in the early years, so it is worth considering existing differences in national patent litigation in Europe and selecting a division based on the appointed judges.

Biotech companies should also be keeping a close eye on their competitors' patents. For any European patents that are not opted out, 1 June 2023 could be the time to bring a central revocation action and take the opportunity to try to invalidate the patent in 17 jurisdictions at once. On the flip side, companies should be prepared to defend against any infringement actions brought by patentees within the UPC, where they will not have any choice over the division.

The UPC system is front-loaded and requires the case to be set out in detail from the beginning, including legal arguments, facts and evidence. A full defence must be filed by the defendant within three months of service of the claim, which does not leave long to put together a legal team, complete a statement of case and expert reports in an untested system. Further, any preliminary objection (such as a challenge to the jurisdiction of the UPC or the competence of the division selected by the claimant) must be lodged by the defendant within one month of service of the claim. For defendants who wish to delay proceedings within the UPC, there are likely to be a number of procedural challenges that could be made in the early days as judges and users of the system grapple with the rules, particularly some of the more opaque rules on jurisdiction. Given the short timeframes, it is worth biotech companies having some arguments up their sleeves now and potentially preparing draft written submissions that may be deployed quickly in the case of an early UPC challenge.

UPC litigation strategies should not be limited to consideration of the UPC itself. Since only 17 countries will participate in the UPC from the start and certain major European patent jurisdictions including the UK will never take part, there is ample scope for parallel litigation in the UPC and other European jurisdictions

and a well-planned litigation strategy can make good use of the different systems. Given the fairly rigid fast-track procedure envisaged in the Rules of Procedure for the UPC, it is at present difficult to see how the UPC will be able to cater to some of the more complex litigation solutions available from national courts and, in light of the delays expected from procedural challenges in the UPC's early days, a speedy reasoned judgment from a jurisdiction like the UK is likely to be extremely valuable. Pre-emptive strikes by filing national patent proceedings in participating UPC states before the UPC start date should also be considered where there is a concern that a competitor may have plans to file a central UPC action, in order to limit the jurisdiction of the UPC under the lis pendens rules of the Brussels Regulation.

Contracts

In order to formulate and implement a UPC strategy, patent owners and licensees should consider the terms of existing contracts and should also consider including UPC and unitary patent specific wording in future agreements.

- Opt-out decision making

Given the importance of a decision on whether or not to opt out a European patent and the consequences of that decision (the risk of central revocation in particular), it is important that parties ascertain who is entitled to decide whether to opt out. Under the UPCA an opt-out can only be exercised by the owner of the European patent. This means licensees will be reliant on the patent proprietor to opt out, even if contractually the licensee has control over the decision. Some agreements may address the UPC expressly, whereas others will not. If an agreement does not expressly address the UPC, determining who controls an opt-out decision will be a matter of interpretation of the relevant agreement. As an opt-out decision is a matter of jurisdiction relating to enforcement and defence of the patent, the enforcement and defence provisions, rather than prosecution provisions, are likely to be relevant.

If a European patent is jointly owned, an opt-out must be filed by all joint owners. This means that co-owners will need to agree on and implement an opt-out strategy. Parties should therefore examine the terms of any co-ownership agreement to determine whether it dictates how such decisions should be made, which party (if any) has control over opt-out decisions and whether there is a process for resolving disputes in the event of a disagreement.

The risk of central revocation of a European patent will be of particular concern to licensors as royalties will often be tied to validity of the licensed patents. Central revocation could therefore lead to a significant reduction or loss of royalty payments.

- Filing new patents in Europe

As outlined above, the unitary patent provides an additional option for patent applicants in Europe. Where an invention is the product of collaborative development, or a licence includes a European patent application, parties should consider who can decide whether to apply for a unitary patent, or to request that the licensed European patent application is granted with unitary effect. This decision will lie with the party that has the right to control patent prosecution. Parties will need to consider similar issues to those outlined above in relation to opt-out decisions. While in some cases it may be more cost effective to apply for a unitary patent rather than national patents (although this will depend on many factors), the risk of central revocation is still likely to be a concern for both licensors and licensees.

- Future agreements

Parties negotiating licence and collaboration agreements should agree a strategy for dealing with European patents. Parties should consider who will have control over opt-out decisions,

under which circumstances an opt-out can be withdrawn and whether to agree a default opt-out position. If control over those decisions can be exercised by the licensee (or one of the co-owners) that party should consider ensuring the licensor (or its fellow co-owner) is obliged to comply with its decision and not opt out or withdraw an opt-out without the licensee's consent.

Parties should also consider now whether they need to alter their stance on control of patent prosecution in light of the new unitary patent. Licensors may in the future wish to include express provisions requiring a licensee with control of prosecution to seek the licensor's approval or input on decisions as to whether or not a licensed European patent application is granted as a unitary patent. Licensees may also wish to require some level of cooperation on decisions whether to seek a unitary patent. Exclusive licensees in particular may wish to require their preferred approach to be followed, particularly if the licensor is controlling the patent prosecution, and step-in rights if the licensor decides to let a unitary patent lapse at a later date.

Finally, parties may also wish to consider the input they have into the formalities of the application process. In particular, depending on where co-owners are resident or have a place of business, the governing law of a co-owned unitary patent as an item of property may differ depending on which co-owner is listed first as applicant. An administrative decision can therefore have important ramifications (although ultimately, provided that law allows the parties to regulate their respective rights by contract, co-owners are best advised to vary the default legal position anyway so that the arrangements are more suitably tailored to reflect their wishes).

2022: a big year for R&D tax relief

2022 was a turbulent time for tax reform. We witnessed Kwasi Kwarteng's drastic tax cutting event, in which he abolished the additional rate of income tax and cancelled the planned corporation tax increase. This so-called 'mini-budget' was promptly followed by reversals and U-turns, culminating in Jeremy Hunt's Autumn Statement on 17 November which aimed to stabilise financial markets. Needless to say, it has been a rollercoaster of a year for tax payers across all sectors.

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For life sciences companies, the alterations to the UK's R&D tax regime will be of particular interest. Rishi Sunak had already announced significant changes to the regime in the 2021 Autumn Statement so it came as a surprise to tax advisors and tax payers alike when further substantial modifications were announced in November 2022. We hope this summary helps you prepare for the changes ahead.

Progress on the changes announced in the Autumn Statement 2021

The following changes will be included in the Finance Bill 2023, expected to become law in Spring 2023:

1. Territoriality restriction

A territoriality restriction for sub-contracted R&D claims will come into force for accounting periods beginning on or after 1 April 2023. The aim of this measure is to 'refocus' the UK's R&D tax reliefs towards activity that actually takes place in the UK. Understandably, many concerns were voiced following this announcement. In particular, those in the life sciences sector were concerned about the effect this would have on clinical trials taking place outside the UK. Under the existing rules, supporting this overseas activity with the UK tax relief had enabled UK-based life sciences companies to develop life changing medicines and therapies, whilst also attracting investment on an international level.

After successful lobbying, an exemption to the territoriality restriction has been introduced based on a "wholly unreasonable" test. This means that the restriction will not apply in situations where it is wholly unreasonable to expect the activity to be carried out in the UK. Helpfully for life sciences companies, HMRC's new guidance published on 20 December 2022 specifically notes that the following are both factors that should be taken into account when determining whether the exemption is available:

i. medical factors, such as incidence of a disease or availability of volunteers to trial a new medicine or treatment; and

ii. the requirements and decisions of regulatory bodies (e.g. if testing of a medicine must be done according to a method agreed by a regulatory body and that body decides that activity must take place in a particular country, or imposes requirements that make that necessary).

This means that sub-contracted R&D activity taking place outside the UK as a consequence of either of the above can still qualify for UK R&D relief.

It should be noted that the cost and availability of workers are specifically excluded as relevant factors, so claiming R&D relief will not be possible where a trial is carried out abroad simply in order to keep costs down or use a particular workforce.

Evidence of scenarios that meet the 'wholly unreasonable' test will need to be provided by claimants, but HMRC have suggested that it will be sufficient for tax payers to self-assess, rather than obtaining third party reports.

As at the time of writing, there is no clear guidance on whether HMRC consider it 'wholly unreasonable' to break a pre-existing legal commitment to complete R&D activity overseas such that any existing arrangements that continue past 1 April 2023 can continue to qualify for relief.

2. Cloud computing and data

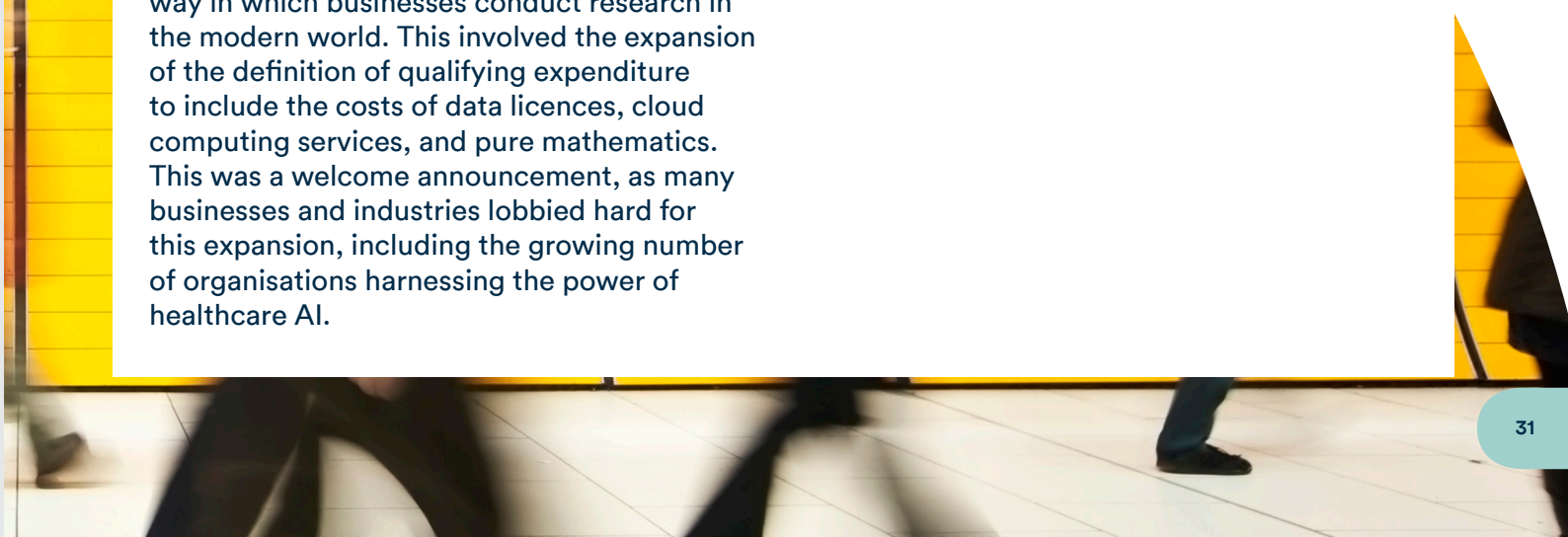
Another change announced in 2021 was an attempt to ensure that R&D relief reflects the way in which businesses conduct research in the modern world. This involved the expansion of the definition of qualifying expenditure to include the costs of data licences, cloud computing services, and pure mathematics. This was a welcome announcement, as many businesses and industries lobbied hard for this expansion, including the growing number of organisations harnessing the power of healthcare AI.

Practical tips for CRO Agreements

1. CRO Agreements should be clear **where** R&D activity will take place (and ideally **why** it will take place there).
2. Where costs will be incurred partly in relation to UK based activity and partly on overseas activity, the agreement should clearly split out those costs.
3. Evidence of specialist resources, expertise, patient populations or facilities and any bespoke regulatory environment requiring research or trial activity to take place in a specific jurisdiction should be collected and kept on file.

3. Combatting abuse

Further changes were announced to combat abuse of the R&D tax system, including a requirement for all claims to be made digitally and to include a breakdown of costs across the qualifying categories. Claims will also need to be endorsed by a named senior officer of the company and will need to include details of any agents advising on the claim. In addition to these new requirements, an advance notice will need to be made to HMRC before making a claim, although there will be an exemption from this for companies who have made recent claims within the previous three accounting periods.



Changes announced in the Autumn Statement 2022

These changes were focused on the rates of the reliefs available under both the small or medium sized companies (**SMEs**) regime and the Research and Development Expenditure Credit (**RDEC**) scheme (the latter being primarily aimed at larger companies, although it can be useful to SMEs in certain scenarios).

Under the existing SME regime, where the necessary conditions are met, R&D relief is available to SMEs in the form of an effective 230% deduction on qualifying expenditure. It is then up to the SME to choose whether to utilise those losses or surrender the losses in return for a cash repayment (currently capped at 14.5% of the losses that would otherwise be available). There is also a cap by reference to the company's PAYE and NICs liabilities, which was introduced in 2021. In the Autumn Statement 2022, the Government announced plans to reduce the SME tax credit additional tax deductions rate from 130% to 86% (reducing the effective deduction to 186%) as well as plans to reduce the rate for SME R&D cash claims from 14.5% to 10%. This latter reduction is a particularly key change for many loss making companies who rely heavily on the repayable credit to support their cash flow needs.

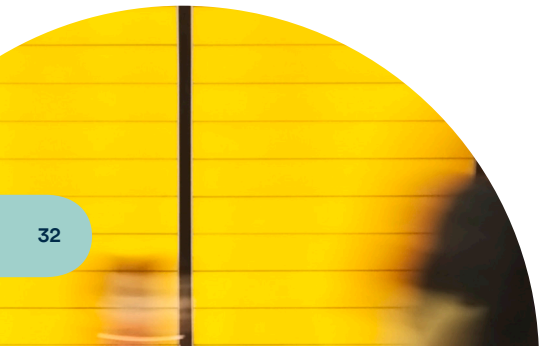
The changes to the SME system are clearly very disappointing. Many have expressed concerns as to the effect the reductions will have on the attractiveness of the UK to start and grow a life sciences business, and the potential movement of jobs to the US and the rest of Europe as a result. The purpose of these rate changes remains unclear. Jeremy Hunt stated in his speech that the changes were aimed at combatting reports of abuse and fraud; however, it is difficult to identify a clear 'avoidance' rationale for the changes, particularly as the effectiveness of the anti-abuse measures announced in 2021 (which will come into force in April 2023) has not yet been tested.

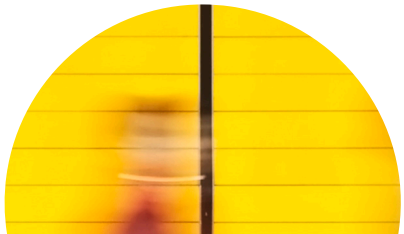
By contrast, there was better news on the RDEC scheme which should please large pharmaceutical and life sciences companies in the UK undertaking (or planning to undertake) significant R&D activity. The headline rate of the credit will increase from 13% to 20% for qualifying R&D expenditure incurred on or after 1 April 2023. This taxable credit may be used to offset liability to UK corporation tax or claimed as a cash payment. This change was made with a view to "rebalancing the reliefs" as between large companies and SMEs.

These measures have been included in the Autumn Finance Bill 2022.

Potential reform in 2023

And if the 2021 and 2022 announcements weren't enough, the Government has also announced that it will consult on the potential implementation of a new R&D system. The idea is that this would be a single system rather than two separate systems for SMEs and RDEC – a concept which was considered in the Government's 2021 consultation but not taken any further (until now). It remains to be seen how a single scheme would work, and the impact that it would have on the life sciences sector, but we are expecting further details to be published in Spring 2023.





Updates to EU and UK competition authority guidance – why the biopharma sector should sit up and take note

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Competition authority guidance can make a critical difference for companies seeking to navigate the competition rules in their commercial agreements.

Not only do the various guidance documents (which run to many hundreds of pages in aggregate) provide helpful insights as to how the authorities believe the rules should apply in particular commercial contexts, they also provide a degree of control over how the authorities are permitted to exercise their enforcement powers. In our experience as external counsel, following the available guidelines on topics such as technology transfer/licensing agreements or R&D agreements is critical, and often of greater importance than seeking to fit agreements mechanically within the scope of relevant block exemptions.[1]

Against that backdrop, it is worth taking note of the recent and current EU and UK reviews of some of the guidance that is particularly relevant to the biopharma sector. Three sets of guidance are currently under consultation by the UK's Competition and Markets Authority (**CMA**) and/or the European Commission:

Horizontal Guidelines and RDBE:

1. **CMA**: Consultation complete and new RDBE now in force; Guidelines not yet published
2. **Commission**: RDBE and Guidelines due to be adopted by June 2023

Technology Transfer Guidelines and TTBE:

1. **CMA**: Consultation starting in spring 2023 to decide whether to introduce UK version
2. **Commission**: Longer term consultation expected prior to expiry of current TTBE in April 2023

Notice on Relevant Market:

1. **CMA**: No news on any consultation
2. **Commission**: Draft replacement published; consultation concluded in January 2023

1 Block exemptions automatically exempt particular categories of agreements from the competition rules if certain conditions are satisfied

We comment on each of these below.

Horizontal Guidelines and R&D Block Exemption

The UK R&D Block Exemption Order was introduced in December 2022.[2] Following feedback, the CMA sought to bring additional clarity to the definitions used in the block exemption, but has otherwise largely maintained the status quo regarding the key terms of the prior EU block exemption and the related guidance.

The 2010 EU R&D Block Exemption was also due to expire at the end of 2022. However, the EU consultation was delayed following substantial feedback raising significant concerns about the treatment of innovation markets. In its draft published for consultation,[3] the European Commission proposed that where parties compete in innovation, three or more competing R&D efforts that are "comparable" must exist before the block exemption will apply. The proposed change was perhaps influenced by a number of merger decisions in relation to pipeline products in the pharma sector, where divestments were required where the number of independent competitors was reduced to fewer than three. However, this appears misguided in this context: requirements to divest in cases such as *GSK/Novartis* and *Hospira/Pfizer* related to pipeline products rather than early-stage R&D. In those cases the contemplated acquisitions clearly would have resulted in a reduction in the number of independent products; R&D collaborations by contrast are intended to *increase* innovation.

As well as the (not insignificant) practical problem of identifying such other R&D efforts, it is far from obvious that R&D intended to lead to a first-in-class product is likely to restrict competition, such that agreements leading to such R&D should be excluded from the scope of the relevant block exemption.

At the time of writing, it remains to be seen whether the EU will take account of the feedback from business and law firms on this issue.

Technology Transfer Guidelines and Block Exemption

The EU Technology Transfer Block Exemption (**TTBE**) and accompanying guidelines provide a framework for assessing the compliance of technology licensing agreements with EU competition law.

The CMA has brought forward a planned consultation on this issue in advance of the expiry of the EU TTBE, given the UK government's policy of replacing EU legislation. The CMA is planning to consult on whether to retain a UK version and if so whether to diverge materially from the EU version.

Our expectation is that, as with previous consultations on UK versions of EU block exemptions, the UK will implement a UK Technology Transfer Block Exemption Order (**TTBEO**) with some accompanying guidance. The timing of the UK consultation in advance of the expiry of the EU TTBE means that the CMA has an opportunity to take the policy lead in this area.

The CMA is, however, well aware of the risks of divergence for the UK economy.[4] Many licences will cover the whole of Europe, including the UK, so losing regulatory alignment would result in added complexity and increase the compliance burden. For this reason, we anticipate that the CMA will enact a TTBEO which closely resembles the EU TTBE, subject to necessary changes to make it UK-specific. However, the CMA may give itself the opportunity for a further review after the new EU TTBE has come into force (rather similarly, the new UK Verticals Block Exemption Order has a relatively short period of validity, having been introduced last year and expiring in 2028, before the EU equivalent).

2 The Competition Act 1998 (Research and Development Agreements Block Exemption) Order 2022

3 Public consultation on the draft revised Horizontal Block Exemption Regulations and Horizontal Guidelines

4 See, for example, comments recently made in relation to a review of the Liner Shipping Block Exemption, paragraphs 4.18-4.19

That being said, there are a number of issues that may come up in both the UK and EU consultations. Below we identify three that we think are particularly interesting:

1. No-challenge clauses (again)

Looking back to the consultation on the 2013-14 review of the EU TTBE, a flashpoint in the consultation concerned the EU's plan to remove all protection for no-challenge clauses, including previously permissible 'terminate-on-challenge' provisions (i.e. clauses allowing a licensor to terminate the licence if the licensee challenges the validity of the licensed IP).

Significant representations were received on this issue from the biotech industry, which had a concern about well-funded licensees using this change in the rules to increase challenges to the licensed IP before commercialisation, with potentially significant implications for the viability of licensing programmes. The European Commission subsequently backtracked, and allowed such provisions to continue to benefit from the block exemption but only where included in exclusive licences. However, the guidance made clear that the protection was dependent on market share thresholds being met. That leaves licensors potentially exposed where the product based on their technology opens up a new market, and the parties' market shares grow beyond the thresholds in the TTBE. Considerations arising from the Notice on the Definition of the Relevant Market (also under consultation – see below) may also be relevant here. This issue may therefore come under the spotlight once again.

2. Long-term licensing obligations

Not strictly a new issue, but one that seems to come up with increasing frequency in recent years. Licence agreements in the pharma sector often involve royalties being payable long after patent expiry. In many cases that can be a sensible way to structure compensation given the time it can take to commercialise a new pharma product. However, where licences go further and have no, or no effective, ability for licensees to terminate (for example, where a combined patent and know-how licence is granted and the licensee needs continued access to the know-how), licensees can be locked in to payments that bear no resemblance to the value of the licensed rights.

The current EU Guidelines take a permissive approach to post-expiry royalties, which is arguably not fully in line with recent case law of the Court of Justice (notably Case C-567/14 *Genentech v Hoechst*). Additional guidance on assessing the appropriateness of such post-expiry royalties and related restrictions would be welcome.

3. Platform technologies

Licensing programmes for therapies based on technologies such as CAR-T or RNA are increasingly operated as a form of platform, with the core technology being made available for a multitude of potential applications. Relevant markets (and thus market shares) are often particularly difficult to assess in this context, given that licensees may retain considerable flexibility to make exploratory use of the licensed technologies, with no certainty as to the nature of final products. Tailored guidance on acceptable licensing practices in this area would likely be of benefit to the industry.

Notice on Definition of the Relevant Market

The final relevant consultation concerns the EU Notice on the Definition of the Relevant Market. The Notice serves a different purpose to the block exemptions and guidelines referenced above. Rather than providing guidance on specific types of agreement, the Notice has relevance across antitrust and merger control, providing an explanation of how the European Commission assesses relevant markets and competitive constraints.

As such, it is relevant whenever parties need to assess their market shares (as under most block exemptions), and is also critical to the assessment of whether a company is dominant and subject to a 'special responsibility' not to distort competition.

To a large extent, the general principles set out in the draft revised Notice[5] are unchanged compared to the current version, which has been in place for nearly 25 years. Market definition is a "tool" for defining the boundaries of competition between firms and its main purpose is to identify "immediate competitive constraints" in a systematic way. Identifying the extent to which customers can switch easily to readily available substitute products (demand substitution) remains at the core of that process.

However, there are three important differences of emphasis in the draft revised Notice.

- First, it downplays the centrality of competition on price and, consequently, the SSNIP (small but significant non-transitory increase in price) test as the sole or main measure of competitive constraints. Other parameters of competition, such as quality, sustainability, security or privacy, are all relevant to the question of market definition.
- Second, market definition in relation to innovation and tech is a significant theme in the revised Notice. The need to take account of the "specific factors" in industries characterised by frequent and significant investments in R&D is recognised. The revised Notice emphasises that while innovation is a "key parameter of competition", the results are inherently "largely uncertain". As a result, it seems that the Commission will cast its net widely to factor in all potential outcomes.
- Third, and most critically for the biopharma sector, the draft Notice gives increasing recognition to the potential for markets to change over time. Where technological progress leads to "structural market transitions" that affect the general dynamics of demand and supply, the Commission may adopt a "forward-looking assessment". In a pharma context, the Commission specifically notes that this may lead to widening the market to include pipeline products (potentially broadening the class of agreements that will be deemed to be between competitors) or narrowing the market to a single molecule where the entry of a generic alternative is imminent (in line with the CJEU's recent ruling in Case C-307/17, *Generics UK*). If adopted in the final version, this latter point confirms that – particularly for patentees facing near-term loss of exclusivity – narrow market definitions are increasingly likely. That obviously has very significant implications for the risk of competition authority investigations under abuse of dominance rules – some current examples of which are discussed elsewhere in this publication.

It is notable that the initial EU request for stakeholder input on the TTBE elicited only 12 responses, none of which have a focus on the biopharma sector.[6] While keeping on top of all of the ongoing consultations is a significant challenge, particularly for companies active in both the UK and the EU, the investment may pay off in terms of identifying potential future risks and shaping the discussion around sector-specific issues.

5 Competition: Commission seeks feedback on draft revised Market Definition Notice

6 EU competition rules on technology transfer agreements – evaluation

Proposal for a Regulation for substances of human origin

In last year's edition of the Biotech Review, we speculated as to the likely changes to the EU legislation governing the quality and safety of human blood, tissues and cells (BTC).

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Since that article, the European Commission has published a detailed proposal for a Regulation on standards of quality and safety for substances of human origin (**SoHO**) intended for human application (the Proposal) which will repeal the twin Directives currently in force[1]. In this follow-up piece, we take a detailed look at the Proposal and the key changes it will bring to SoHO regulation in Europe. We also look at what is happening in Great Britain (**GB**).

Legislation

The Proposal was adopted by the European Commission in July 2022 and is currently being discussed by the European Council and the European Parliament. Once the final text is agreed and adopted, it will come into force with a two-year transition period for most provisions and a three-year transition period for a few specific provisions.

The Proposal is the culmination of a project that has been ongoing for several years. In 2019 the European Commission conducted an evaluation that identified several gaps and shortcomings in the existing legislation on quality and safety of BTC. The twin Directives on BTC have been in force for nearly 20 years and the European Commission concluded on the basis of a public and stakeholder consultation that they no longer address the scientific and technical state of the art. The introduction of a new EU Regulation to repeal and replace the old Directives continues the recent life sciences legislative trend in the EU of favouring Regulations (which have direct effect) over Directives (which require Member State implementation). Indeed, this approach takes on the views expressed as a result of the consultation that a common EU Regulation would avoid the diverging national interpretations and implementations that can arise under Directives. At present, these deviating approaches result in unequal levels of safety and quality and in barriers to the exchange of BTC across the EU, barriers that were exacerbated by the pandemic.

1 Directives 2002/98/EC and 2004/23/EC

Key changes

Scope

The proposed Regulation covers all substances of human origin, except for solid organs for transplantation, which will remain regulated by the existing Directive. The old Directives regulated BTC only, so the scope of regulation is being both expanded and consolidated.

SoHO encompasses not only BTC, but also substances invoking similar safety and quality concerns, such as human breast milk and microbiota, which are currently unregulated. In addition, other SoHO that may be applied to patients in the future will automatically fall within the scope of the proposed Regulation.

Standards

SoHO must be prepared and treated according to specific standards to ensure safety. High-level standards on SoHO will be written into the proposed Regulation. These standards will protect recipients of SoHO and will be extended to protect both offspring born from medically assisted reproduction and donors of SoHO. The proposed Regulation will provide for a hierarchy of rules for the implementation of standards to facilitate efficient and responsive uptake of the most up-to-date guidelines.

Scientific expert bodies

At present, industry consensus is that the technical standards set by the existing BTC Directives lag behind innovation. The consultation established strong industry support for SoHO safety and quality standards to be set jointly, with technical guidelines written into the legislation but developed and updated by nominated expert bodies.

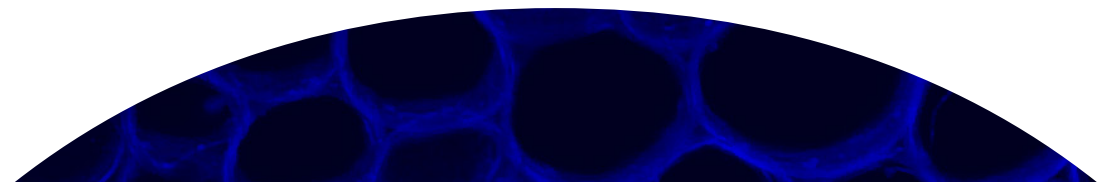
The new approach will involve standards being set by the European Commission, with some written into the text of the proposed Regulation and others set by implementing acts, and nominated expert bodies such as the European Directorate for the Quality of Medicines & HealthCare and the European Centre for Disease Prevention and Control. In the absence of a technical guideline from an expert body it will also be acceptable for establishments to set their own technical methods, taking into account international standards, evidence and risks.

Registration

All entities conducting activities that will affect the safety and quality of SoHO will be required to register, either with a national SoHO competent authority or with a central EU SoHO platform. The new platform is intended to reduce administrative burdens on national authorities and the European Commission by facilitating the secure transfer of information (such as safety data and alerts) between those authorities and the Commission.

Reporting

The 2019 evaluation identified vulnerability to interruptions in supply of some BTC as a key shortcoming of the existing legislation. The EU is highly dependent on importing BTC from third countries, especially the US. The current legislation does not contain concrete measures to protect or increase supply of BTC, and this has not been proven adequate to protect against the risk of shortages or sudden supply disruptions. To address this, the proposed Regulation will introduce increased reporting requirements for SoHO entities, including the reporting of annual activity data, to allow Member States to implement measures to improve donation collection rates when needed. Entities working with critical SoHO (SoHO for which an insufficient supply will result in serious harm or risk of harm to patients) will be required to alert the relevant competent authority in the case of a sudden fall in supply and must also put in place emergency plans for such situations.



Oversight

One of the fundamental revisions that the proposed Regulation introduces is to both strengthen and harmonise oversight with a view to facilitating better exchange of SoHOs between Member States and improved access for patients.

The proposed Regulation achieves this goal through the introduction of common measures on oversight and the joint regulation model described above. The common oversight measures include new and more-efficient practices such as joint inspections, risk-based oversight approaches such as risk-based inspections, and EU level support such as EU auditing of oversight systems and training courses for competent authority personnel.

The package of common oversight measures aims to increase mutual trust and facilitate collaboration between Member States.

Position in the UK

In September 2022, the Department for Health and Social Care (**DHSC**) published a policy paper on the proposed regulation. The paper considers the impact of this regulatory change on Northern Ireland (**NI**), as when it is introduced the Regulation will apply in NI. DHSC acknowledge that the intention of the proposed Regulation is to increase the safety, quality, innovation and supply of SoHO within the EU, and therefore the Regulation is likely to have a positive effect in NI. However, the paper also discusses the consequences of regulatory divergence between NI and GB, which could include supply chain disruption since NI is reliant on importing SoHO from GB.

It seems clear from the paper that the UK government wishes to harmonise some aspects of the UK framework with that of the proposed EU Regulation. Remarkably, given the nature of government Brexit rhetoric, the paper stresses the importance of maintaining minimum standards with the EU to allow the movement of NI and EU SoHO into GB. DHSC expects to conduct a targeted stakeholder consultation (but not a public consultation) to inform policy decisions. Overall, this paper suggests that overarching harmonisation between the UK and EU life sciences regulatory frameworks may be a theme that will continue.

Conclusion

Finally, it is interesting to consider some of the potential points of revision that were consulted on but did not make it into the proposed Regulation, especially the borderline between the BTC framework and other regulatory frameworks. This area proved particularly contentious during the consultation and the explanatory memorandum to the proposed Regulation states that the Proposal will: (a) reinforce cooperation among the other adjacent regulatory frameworks; and (b) feed into the ongoing and separate evaluation and revision of the pharmaceutical legal framework.

The explanatory memorandum suggests that the issue of regulatory delineation between the BTC sector and the pharmaceutical sector will be considered as part of this wider legislative review as "*the delineating criteria are set by definitions in the pharmaceutical framework and are not altered by this proposal*."

The wider life sciences industry eagerly awaits the much-anticipated outcome of the review of European pharmaceutical legislation, which is now due to be published in the first half of 2023. With almost every aspect of pharmaceutical regulation currently under review, it will be fascinating to see whether there is appetite to alter the definitions affecting this delineation. However, we cannot but welcome the new Regulation, which will hopefully bring a much needed harmonisation and will bring the legislation in line with the state of the art.

Anticipating the revised EU Product Liability Directive and the new EU Artificial Intelligence Liability Directive

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It has been a busy few years for legislative developments in life sciences in the EU. We have seen the introduction of landmark new pieces of legislation, such as the Medical Device Regulation,[1] the In Vitro Diagnostic Medical Device Regulation,[2] and the Clinical Trials Regulation.[3]

We have had proposals for cutting edge new legislation, such as the Artificial Intelligence Regulation and the European Health Data Space Regulation, which break new ground in terms of the technologies they address and the problems they aim to solve. A consultation has also been conducted regarding major revisions to the general pharmaceutical law legislation, which has yet to result in a legislative proposal. The Orphan and Paediatric Regulations are also under review.

To add to that list, the European Commission has announced two significant new legislative proposals. These are the proposal for a revised Product Liability Directive (**Revised PLD**) and the proposal for an Artificial Intelligence Liability Directive (**AILD**).

The Revised PLD and the AILD will not be blockbuster pieces of legislation along the lines of the GDPR or the Medical Device Regulation. They do not establish lengthy regulatory codes for companies to get to grips with. However, the Revised PLD will nonetheless introduce new rules on liability which will impact economic operators across product supply chains, and both the Revised PLD and the AILD will make some noteworthy changes to litigation procedure in EU Member States. Life sciences companies ought to be aware of these changes - especially those with products which incorporate software or AI as a significant component.

1 Regulation (EU) 2017/745 on medical devices
2 Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices
3 Regulation (EU) 536/2014 on clinical trials on medicinal products for human use

Revised PLD

The Revised PLD will replace the existing Product Liability Directive,[4] in existence since 1985. The Revised PLD preserves the basic principle of strict liability for defective products which cause harm to consumers, which is the core of the 1985 Product Liability Directive, but it makes a number of key changes which are intended to bring product liability "into the digital age."

The following are some highlights:

- Standalone software and AI systems will be expressly considered "products" for the first time, allowing claimants to obtain compensation under the Revised PLD if such systems are defective and cause them harm;
- "Harm" for which a claimant can obtain compensation will include medically recognised psychological harm and the loss or corruption of electronic data (where it is not used exclusively for professional purposes);
- A product will be considered "defective" if the manufacturer has not designed and maintained it to a sufficiently high cybersecurity standard. A product incorporating software will also become "defective" if the manufacturer fails to release necessary cybersecurity updates;
- The list of entities which could be liable for defective products under the Revised PLD will expand significantly. In addition to manufacturers of defective products, importers and distributors can sometimes be liable for defective products under the 1985 Product Liability Directive. The Revised PLD will also place authorised representatives,[5] fulfilment service providers (**FSPs**) and even online platforms which facilitate transactions between traders and consumers in the firing line in certain circumstances.

As well as increasing the scope of product liability by expanding the definitions of "product", "harm" and "defective", and adding to the list of potential defendants to a defective product liability claim, the Revised PLD will also make changes to procedural law to make it easier for consumers to bring claims in certain circumstances.

Under the 1985 Product Liability Directive, consumers injured by a defective product must bring a claim within a limitation period of 10 years from the product being put into circulation. Under the Revised PLD, if consumers are unable to commence proceedings within 10 years because of the latency of the personal injury caused by the defective product, the limitation period will be extended to 15 years. It can be quite common for personal injuries caused by defective life sciences products to be latent – such as where an implantable medical device gradually leaches a hazardous substance into the body or where a medicinal product has a long term adverse effect on internal organs such as the liver – so life sciences companies should regard this change as a potentially significant increase in their product liability exposure.

As well as extending limitation periods, EU Member State courts will have the power to order disclosure of information in the context of defective product liability litigation. To litigators with experience before the English courts, this will not sound like a radical development, but comprehensive disclosure of relevant documentary evidence is not a routine part of litigation in many EU Member States. Generally, parties are only obliged to disclose the evidence they intend to rely on, and parties can then apply to the court for an order requiring the other party to disclosure further specific documents. The Revised PLD is phrased such that claimants in defective product litigation may be able to obtain disclosure of all "relevant" evidence relating to the litigation, which is much closer to the English procedural approach in civil litigation.

4 Council Directive 85/374/EEC on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products

5 Article 11(5) Medical Device Regulation already makes authorised representatives liable for defective medical devices, but it has never been clear how exactly this provision is intended to work

In order to remedy perceived expertise and resource imbalances between consumer claimants and economic operator defendants, the Revised PLD will also shift the burden of proof onto the economic operator defendant in certain circumstances. Specifically, a product will be presumed to be defective where:

- The defendant has failed to comply with an order for disclosure made under the Revised PLD;
- The defendant has failed to comply with requirements under mandatory product safety laws which are intended to protect against the kind of harm which the claimant alleges they have suffered; or
- The allegedly defective product has obviously malfunctioned under normal conditions of use.

It will also be rebuttably presumed that the product was defective, and/or that its defectiveness caused the harm to the claimant, where the court considers that it would be excessively difficult for the claimant to prove either of these assertions. First the claimant will have to succeed in showing that: (a) the product contributed to the harm; and (b) it is likely that the product is defective and/or that its defectiveness caused the harm in question.

AILD

Even more so than the Revised PLD, the AILD is brief. Its core operative parts cover scarcely more than two sides of A4 paper. However, it will introduce some quite striking changes to procedural law in EU Member States in relation to non-contractual fault-based claims concerning damage caused by AI systems.

That phrase "fault-based claims" deserves exploration. The Revised PLD (and the existing 1985 Product Liability Directive) create liability in relation to defective products which is not dependent on the defendant being at fault. The AILD will not apply to such claims. The AILD will create procedural rights for claimants in the context of claims where it is asserted that the defendant was at fault in the use or production of an AI system – either deliberately or negligently causing harm.

The purpose of the AILD is to make it easier to bring fault-based claims in respect of harm caused by AI systems, where the complexity and opacity of such systems would make it difficult for claimants to discharge the evidential burden. In effect, the AILD will confer two new procedural rights on claimants harmed by the use of AI systems. Interestingly, where the Revised PLD prescribes the kind of harm which is recoverable under it, the AILD does not. Seemingly, claimants can rely on the rights created by the AILD in relation to non-contractual fault-based claims for any kind of harm, including damage to business property and perhaps even pure economic loss caused by relying on the recommendations of an AI system.

The first procedural right created by the AILD is the right to seek pre-action and/or third party disclosure of relevant evidence from the "providers" and/or the "users" of "high risk" AI systems which are said to have caused harm to the claimant. This can include disclosure of the logs automatically generated by the AI system which will have to be kept under the proposed Artificial Intelligence Regulation. The terms "provider", "user" and "high risk" will also have the meaning conferred on them by the proposed Artificial Intelligence Regulation.

If the "provider" or "user" of a high risk AI system is the defendant in a fault-based action and fails to comply with a disclosure order made under the AILD, there will be a rebuttable presumption that the defendant did not comply with its duty of care to the claimant.

The second procedural right created by the AILD echoes aspects of the Revised PLD: a reversal of the burden of proof consisting of a rebuttable presumption that the defendant's (actual or presumed) failure to comply with its duty of care to the claimant caused the harm which the claimant alleges. This rebuttable presumption will arise where the following criteria are met:

- The claimant has established, or it has been presumed, that the defendant did not comply with a duty of care to the claimant which is directly intended to protect against the harm which has occurred;
- It is reasonably likely in the circumstances that the non-compliance has influenced the output of the AI system or its failure to produce an output; and
- The output of the AI system, or its failure to produce an output, has caused harm to the claimant.

Where the AI system which is said to have caused harm is a "high risk" AI system within the meaning of the Artificial Intelligence Regulation, non-compliance with the requirements of the Artificial Intelligence Regulation will be considered a failure to comply with a "duty of care" to the claimant for the purposes of the presumption.

Where the AI system which is said to have caused harm is not a "high risk" AI system within the meaning of the Artificial Intelligence Regulation, then the presumption will only apply where the national court considers that it would be "excessively difficult" for the claimant to prove that the defendant's wrongful acts or omissions were the cause of the harm suffered.

Takeaways

Evidently, the EU has lost none of its enthusiasm for piling on multitudinous new legislation in response to changes in the European economy. There is a lot coming down the pipeline for life sciences companies to stay on top of. For the time being, the Revised PLD and the AILD are only legislative proposals, and they may undergo further changes.

The Revised PLD is an evolution rather than a revolution in the field of product liability. Nonetheless, it will bring some changes of which life sciences companies should be aware. Life sciences companies should be aware that they will be exposed to potential product liability claims for a significantly longer period of time where the damage caused by a defective product is latent. Life sciences companies should also consider their own potential liability as distributors of original equipment manufacturer (**OEM**) products. For instance, pharma companies which distribute OEM software medical devices intended for use with their medicinal products should be aware of their potential liability.

Where the Revised PLD is evolutionary rather than revolutionary, the AILD is genuinely new, but in many ways it is simply a liability-related adjunct to the much more ambitious Artificial Intelligence Regulation (although narrow sections of the AILD do apply to AI systems outside the scope of the Artificial Intelligence Regulation). Much more would need saying to fully explore the proposed scope of the Artificial Intelligence Regulation, but a brief internet search or a perusal of previous Bristows publications will explain quite how broad that scope is. Any business which will be affected by the Artificial Intelligence Regulation should have the AILD on its radar. In particular, businesses should be prepared for applications for disclosure under the AILD, even where they are not a party to the litigation. They should also be aware that non-compliance with the Artificial Intelligence Regulation will increase their potential exposure to non-contractual fault-based liability claims, due to the rebuttable presumption mechanism created by the AILD.

Living with IVDR – 6 months on from the date of application

The last few years in EU medical devices regulation have been characterised by endless new developments, drama and delays. The Medical Device Regulation (MDR) has played a significant role in this, but it is only half the story.

Xisca Borrás
Partner, Regulatory

Jamie Hatzel
Associate, Regulatory

Roughly six months on from the date of application of the In Vitro Diagnostic Medical Device Regulation (**IVDR**) on 26 May 2022, now is a good time to take stock of how the IVDR has gone so far and where we are going next.

Notified Bodies

It is impossible to talk about the transition to the IVDR without talking about Notified Bodies. As the entities responsible for certifying that IVDs comply with the requirements of the IVDR, they are the gate through which almost every IVD must pass in order to be placed on the market in the EU. That includes existing IVDs certified under the old regulatory framework which require re-certification under the IVDR.

The fraction of IVDs which required certification by a Notified Body under the old EU regulatory framework was miniscule. Unless the IVD was intended for diagnosis of a short list of medical conditions, it could be placed on the market following a self-assessment by the manufacturer. Nonetheless, a manufacturer requiring the services of a Notified Body had more than a dozen to choose between.

Under the IVDR, that has all changed. Medtech Europe estimates that 70% of existing IVDs now require certification by a Notified Body for the first time. Based on another Medtech Europe estimate, Notified Body workload under the IVDR has increased by 700%. At the same time, there are currently only 8 Notified Bodies designated under the IVDR. This has created a bottleneck which is preventing manufacturers from coming into compliance with the IVDR before the transition periods start to run out on 26 May 2025.

These figures from the European Commission's recent update note give some sense of the scale of the problem: as of 22 October 2022, Notified Bodies had received 822 applications for certification of an IVD, yet had granted only 268 certificates; meanwhile, 1,551 existing IVDs require recertification before 26 May 2025. Due to the nature of the IVDR's staggered transition periods, hundreds of IVDs will require recertification every year until 26 May 2028.

IVDR Notified Body capacity is growing, but slowly. On average, one new Notified Body is designated every 4-5 months. An 8th Notified Body for IVDR was designated on 23 December 2022, but this is not expected to transform certification capacity.

Issues with certification capacity are not limited to the IVDR. The same problem exists under the MDR, though it is perhaps more acute under the IVDR due to the sheer scale on which IVDs require Notified Body certification for the first time. As a result, the European medtech and pharmaceutical industries – including Medtech Europe, SNITEM, BVMed, EFPIA, the European Cancer Patient Coalition and lately the Heads of Medicines Agencies Group – have long called for urgent action to tackle the risk that patient-critical devices will be forced off the market.

Having long resisted legislative intervention, the European Commission has now conceded that action is needed. Its recent update note proposes legislation to significantly extend the transition periods under the MDR and keep device certificates granted under the old regulatory framework from expiring. Surprisingly, the Commission does not seem to be proposing any similar action for the IVDR. Its proposals are limited to removing the sell off period under the IVDR, which will only mean that manufacturers will not have to undertake a recall of IVDs certified under the old framework which have not made it into the hands of end users by a certain date.

We will see whether any further changes to IVDR are reflected in the draft legislation which we expect from the Commission in early 2023.

Economic operators

The IVDR has increased the regulatory burden for IVDs in almost every way. We have already touched on the huge increase in IVDs requiring conformity assessment by a Notified Body. More clinical data is also required to demonstrate conformity with the IVDR's requirements. It is now the norm to obtain clinical data on IVDs from clinical studies on human subjects (known as "*performance studies*"), where before this was the exception. Manufacturers are effectively required to operate a Quality Management System (**QMS**) which complies with ISO 13485:2016. There are strict device traceability and labelling requirements, and much more detailed post-market surveillance obligations. The list goes on.

However, the major regulatory change which we have seen catch biotech companies out this year is the introduction of the "economic operator" concept. Under the previous regulatory framework, it was essentially only the manufacturer that had any regulatory responsibilities. A manufacturer might include provisions in its distribution agreements requiring distributors to aid it with regulatory activities such as complaints handling and recalls, but it was the manufacturer who had ultimate responsibility.

Under the IVDR, importers and distributors now have regulatory responsibilities of their own: primarily to verify that the IVDs which they distribute are in compliance with the IVDR. They have obligations to inform the manufacturer of complaints and of suspected non-compliance and are required to cooperate with corrective action (such as recalls). They are also required to keep documentation relating to the IVDs which they distribute and to provide it to the regulator upon request. Importers also have some further obligations specific to their role, including an obligation to include their company details on the label of the IVDs which they supply.

The reason that we have seen this new construct catch biotech companies out is that a company does not become an importer or a distributor as a result of being appointed by the manufacturer or by anyone else. A company becomes an importer if it *places on the market* in the EU an IVD from a third country.[1] A company becomes a distributor if it *makes available* an IVD on the EU market.[2] Essentially, a company which supplies IVDs will perform a regulated role under the IVDR.

It is quite easy for a biotech company to accidentally fall foul of this. For instance, it may distribute an OEM IVD alongside its medicinal product range. This can get complicated where an OEM IVD is co-packed together with a medicinal product, especially if the IVD is mentioned in the marketing authorisation, because it is then not so simple for the company to simply stop distributing the IVD if it doesn't want the regulatory burden. There are other new complexities relating to distance selling of IVDs as well. Companies now need to tread a little more carefully when dealing with IVDs.

Clinical trials and companion diagnostics

Historically, performance studies on uncertified IVDs did not require any significant regulatory approval under EU law. It was generally enough to compile some documentation and to obtain research ethics committee (**REC**) approval in accordance with national law. Not so under the IVDR. There are now complex rules which regulate how performance studies should be conducted and which establish various regulatory pathways for the authorisation of different types of performance study.

Obviously these changes are significant for companies which develop IVDs. However, they are also significant for companies which are in the business of developing medicinal products and which use uncertified IVDs in the course of conducting clinical trials.

The most common scenarios in which an uncertified IVD might be used in a clinical trial are:

1. where the uncertified IVD is a companion diagnostic and is undergoing a performance study in parallel with a clinical trial of an investigational medicinal product (IMP) in order to gather clinical data on both the IMP and the IVD; and
2. where the uncertified IVD is being used to gather data for the purposes of the clinical trial, e.g. for endpoints analysis or for clinical trial subject management purposes. In these circumstances the manufacturer often does not want to gather clinical data relating to the IVD and simply wants to use it as a research tool.

Where an IVD is intended to be used as a companion diagnostic, the IVDR anticipates the conduct of parallel clinical studies: a clinical trial of the IMP and a performance study of the companion diagnostic IVD. The European Commission's electronic systems for management of performance studies are intended to be interoperable with the electronic systems for management of clinical trials in respect of performance studies involving companion diagnostics.[3] The European Commission also has the power to adopt implementing acts addressing how Member States should conduct coordinated assessments of concurrent applications for the conduct of a clinical trial and a performance study of a companion diagnostic IVD, although that power has not yet been used.[4]

1 *Placing on the market* means the first making available of a device on the EU market
2 *Making available* means any supply of a device for distribution, consumption or use on the Union market in the course of a commercial activity
3 Article 69(2) IVDR
4 Article 74(7) IVDR

In practice, it is not easy to set up and run parallel clinical studies involving an IMP and a companion diagnostic IVD. The IVDR's requirements have not been harmonised with the Clinical Trials Regulation (**CTR**).[5] There is certainly no "safe harbour", in which compliance with either the CTR or IVDR creates a presumption of compliance with the other legislation. One simply has to conduct two notionally separate clinical studies in parallel, which involves two sets of study documentation, two separate protocols, two separate sets of study endpoints, two separate adverse event reporting requirements, and in some EU jurisdictions, dealing with two separate regulatory bodies.

The IVDR also does not leave room for research use of uncertified IVDs in a clinical trial, even where clinical data on the IVD is not being gathered for certification purposes. On the face of the legislation, it is unlawful to use an uncertified IVD in a clinical study unless the IVD is also being investigated under a performance study or, very exceptionally, the IVD qualifies an "in-house device" which is exempt from certification. There is no formal Research Use Only exception to certification. As a result, sponsors essentially cannot use an IVD in a clinical trial unless it has been certified, or it is exempt from certification (which is rare), or it is being investigated as part of a parallel performance study (which is complex, as explained above).

The MDCG 2022-10 guidance on the interface between the CTR and the IVDR opens a small exception to this rule. According to this guidance, a device which is not used for a "medical purpose" does not meet the definition of an IVD under the IVDR, and so does not need to be certified in order to be used in a clinical trial. A device is generally not used for a "medical purpose" where it is not used for the medical management of clinical trial subjects: use of a device to select and allocate patients in the clinical trial is a medical purpose; use of a device for endpoints data analysis is not.

This guidance is helpful and generally considered authoritative, but the exception it creates is narrow. The lack of a broad statutory Research Use Only exception encourages biotech companies to run wholly artificial performance studies (which will never generate useful clinical data) simply to ensure regulatory compliance when using an as-yet uncertified IVD in conjunction with a clinical trial.

5 Regulation (EU) 536/2014 on clinical trials on medicinal products for human use

Q&A: what does 2023 hold?

The industry view

To hear first hand from the sector, we caught up with Francesco Vazzana at biotechnology company Alnylam. Alnylam focuses on the discovery, development and commercialisation of RNA interference therapeutics for genetically defined diseases.

Francesco Vazzana
Senior Director,
Legal Counsel International
Alnylam

What were the main issues you dealt with in 2022 that will impact the next 12 months?

In 2022, the availability of vaccines gradually allowed a less restrictive management of the pandemic and a return to in person interactions. The increased presence of technology in our lives and the social and technical learnings of the past two years caused the proliferation and expansion of “hybrid” settings. This might accelerate decentralization in many areas and reduce (not necessarily increase) people’s and resources’ mobility. It will take time to fully understand what this entails for clinical trials, drugs commercialization, patients' access to healthcare, talent acquisition and management and so on. There will be opportunities to be seized and challenges to be addressed.

What biotech trends do you expect for 2023 and how are they going to affect your work?

In its acute phase, as many have observed, the pandemic significantly accelerated an evolution in the way drugs are discovered, developed, manufactured, approved and commercialized. Rapid and potentially long-lasting changes will continue to happen as new problems become more prominent and acute: for instance, as the US Inflation Reduction Act is showing, inflation containment policies are now shaping not only market access practices but even drug development.

What are the main industry challenges faced by the biotech industry at the moment?

Inflation resulting from the pandemic and geopolitical instability; the measures put in place to tame it; the risk of economic recession: all point to the topic of sustainability. Sustainability of national health systems and sustainability of the industry's innovation engine. Austerity measures across Europe seem often inevitable but might impact innovation and, ultimately, patients' access to treatment, causing health inequity. Identifying long term solutions and addressing transparently the inevitable trade-offs is a key challenge but also represents a great opportunity, considering the interdependencies of our social and economic systems.

Biotech companies can be proactive on the front of patient access too. Alnylam, for instance, has proposed value-based agreements (**VBAs**) in several negotiations with European payers and is now pioneering novel approaches to the payer dialogue. We have developed a new value-based negotiation framework (**VBNF**) to support better communication between companies and authorities, to increase the creativity and flexibility governing access decisions and speed up the time to reimbursement.

What scientific/technical biotech developments do you expect will take centre stage in the next 5-10 years?

Considering their potential and versatility, platform technologies like those based on RNA and DNA will take more and more centre stage in the next 5-10 years. Since genetically validated targets allow for more rapid and effective discovery and development, these technologies often have an intrinsic advantage compared to alternatives.

What changes do you see happening in your field in the next 5-10 years?

I believe that genetics and AI will radically transform the life sciences sector and hope we will see many breakthroughs happening at the intersection of these two areas of research. I am not a scientist but imagine that 5-10 years from now it will be impossible to conceive diagnostics, drug discovery and development, as well as manufacturing, in isolation from genetics and AI.

How is the biotech industry embracing AI?

Despite being still at an early stage, AI already seems to have endless applications in the industry. Besides diagnostics and drug development, AI comes to play whenever data analysis is particularly complex and necessary for a given decision - which is practically always, in our world. AI is already impacting the clinical practice, market access procedures and marketing, to the point that the concept doesn't seem sectorial or esoteric anymore. Rather, as chat bots start integrating or even replacing search engines, AI will become mainstream.

Under the antitrust spotlight: (mis)use of patents in the pharma sector

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Pharma remains an enforcement priority for competition authorities across Europe. The last year has seen a fresh wave of enforcement action in the sector, along with a new focus on dominant conduct comprising alleged misuse of the patent system and disparagement campaigns against rival drug products.

The investigations – only one of which has yet reached the stage of an infringement decision – test the boundaries of when competition law may intervene in relation to the exercise of patent rights.

While the outcomes of most of the cases remain uncertain, pharma companies – who may find themselves in a dominant position in the period prior to patent expiry – would be well advised to consider patent filing and enforcement strategies through the lens of competition law, to ensure that they do not fall foul of antitrust rules.

European Commission investigations

In October 2022 the European Commission (**EC**) issued a Statement of Objections against Teva, alleging that the company breached EU competition rules on abuse of dominance by engaging in practices aimed at delaying generic competition to its blockbuster multiple sclerosis treatment, Copaxone. In the EC's preliminary view, Teva's approach to filing and in some cases subsequently withdrawing divisional patents on Copaxone "artificially extended" its patent protection after the expiry of the original basic patent, thereby (it is claimed) forcing its generic rivals to file new patent challenges each time, with the result that their access to market was delayed. Although filing and enforcement of divisional patents is commonplace in the pharma sector, and although a divisional patent can never extend the period of patent protection beyond that of the original right, the EC considers that Teva's strategy "*artificially prolongs legal uncertainty to the benefit of the patent holder, and can effectively block or delay entry of generic or generic-like medicines*".[1] The EC has also alleged that Teva implemented a disparagement campaign targeted at healthcare professionals, which it says created doubts about the safety and efficacy of a rival generic medicine and its therapeutic equivalence to Copaxone.

1 Antitrust: Commission sends Statement of Objections to Teva over misuse of the patent system and disparagement of rival multiple sclerosis medicine

The Teva investigation is the first time the EC has pursued a company for its divisional patent filing and enforcement strategies. The issue is not completely new. In its Pharmaceutical Sector Inquiry Final Report of 2009, the EC commented on the proliferation of divisional patent applications and noted that in some cases "*divisionals seemingly serve to prevent or delay generic entry. While this, during the period of exclusivity, is generally in line with the underlying objectives of patent systems, it may in certain cases only be aimed at excluding competition and not at safeguarding a viable commercial development of own innovation*".[2] However, it remains controversial to suggest that the use of divisional patents – which are used across sectors and do not result in any extension of the scope or period of protection compared to the original patent from which the divisional was carved out – can amount to an infringement of competition law. It remains to be seen how the EC seeks to distinguish between legitimate and illegitimate conduct in this area.

In June 2022, the EC announced that it had opened an investigation to assess whether Vifor Pharma had restricted competition by disparaging its closest competitor in the market for intravenous iron deficiency treatments. The EC is concerned that Vifor may have pursued a misleading communication campaign, primarily targeting healthcare professionals, which may have unduly hindered uptake of Monofer, a competing iron deficiency drug produced by the Danish company Pharmacosmos. Announcing the investigation, Executive Vice-President Margrethe Vestager stated: "*Competition in the pharmaceutical sector is important. It provides access to affordable and innovative medicines to patients. The dissemination of misleading information regarding the safety of Pharmacosmos' iron deficiency treatment, Monofer, may have delayed its uptake. This would ultimately harm patients by stifling competition from an innovative medicine.*"[3]

This is the first time that the EC has opened an antitrust investigation based solely on a disparagement theory of harm. However, there have been a number of cases before the French Competition Authority in which promotional campaigns by companies including Schering Plough (Subutex), Sanofi-Aventis (Plavix) and Janssen-Cilag (Durogesic) have been found to amount to an abuse of a dominant position due to their effects on the penetration of generic products following patent expiry. The decision in the last of these cases (Durogesic) was upheld by the French Supreme Court in July 2022.

The Vifor case is noteworthy as it concerns rival originator products: previous investigations have tended to focus on competition between originators and generics. The case therefore has the potential to clarify the extent to which the EC's framework of assessment will differ in situations where generic competition is not at stake. Regardless of the outcome, the case is an important reminder that competition law may apply to promotional statements made by pharmaceutical companies. This is something that companies should consider alongside their compliance with regulatory rules on the promotion of medicines.

Enforcement action in Switzerland and Spain

In September 2022 the Swiss Competition Commission (**COMCO**) opened an investigation to assess whether Novartis had sought to protect its blockbuster psoriasis drug, Cosentyx, from competition by using patents that it had acquired from Genentech to initiate litigation against its competitors, including Eli Lilly (**Lilly**).

2 See para 523 of the report: Pharmaceutical Sector Inquiry

3 Antitrust: Commission opens investigation into possible anticompetitive disparagement by Vifor Pharma of iron medicine

According to a statement issued by COMCO, the investigation is focusing on "*whether the alleged behaviour constitutes the use of a so-called blocking patent, which might amount to an unlawful abuse of an allegedly dominant position*".[4] Writing in his personal capacity, the President of COMCO, Professor Andreas Heinemann, previously criticised so-called 'blocking patents' in a 2019 article:

> "*Blocking strategies do not aim at all at protecting one's own inventions, but their purpose is to block competing products. It is inherent to blocking patents that they are not exploited for creating something new but to prevent the development of new products and processes by competitors.*"[5]

As things stand, however, there is no case law on so-called blocking patents, as defined by Professor Heinemann, in either Switzerland or the EU. There are many legitimate reasons why companies file patents that do not directly protect existing intended innovation, and the patents are not granted or withheld based on the use that the patentee intends to make of them. Novartis has now also in any event discontinued its litigation against Lilly.[6] It remains to be seen whether COMCO and the EC (which has opened a parallel preliminary investigation) will discontinue their investigations in the light of this development.

In October 2022, the Spanish competition authority (**CNMC**) fined Merck Sharp and Dohme (**MSD**) just under €39 million for abusing its dominant position in the market for contraceptive rings.[7] MSD owns patents protecting its Nuvaring product and in 2017 it sought an ex parte interim injunction from the Spanish courts to prevent the manufacture and sale of a competing contraceptive ring developed by Insud Pharma. The CNMC found that in applying for the interim injunction, MSD had "*deployed a strategy of deception by withholding relevant factual and technical information from the court*", and that this lack of transparency was a "*determining factor*" in obtaining the injunction. According to the CNMC, "*the purpose of MSD's legal actions was not to enforce its patent rights*", but rather "*to suppress competition from the new market entrant for as long as possible*".

There are parallels between the MSD case and the landmark case on misuse of the patent system, *AstraZeneca*. In 2005 the EC found that AstraZeneca had abused its dominant position by persuading various patent authorities to grant it supplementary protection certificates, extending the period of patent protection, on the basis of misleading information. In upholding the EC's decision, the Court of Justice (**CJEU**) stated:

> "*AZ's consistent and linear conduct [...], which was characterised by the notification to the patent offices of highly misleading representations and by a manifest lack of transparency, [...] and by which AZ deliberately attempted to mislead the patent offices and judicial authorities in order to keep for as long as possible its monopoly on the PPI market, fell outside the scope of competition on the merits*."[8]

Where should the line be drawn?

As alluded to in the above extract from the CJEU's *AstraZeneca* judgment, dominant firms are entitled to compete with their rivals 'on the merits' – and they may maintain or even increase their market share by doing so. The CJEU observed in *Intel* that "*not every exclusionary effect is necessarily detrimental to competition. Competition on the merits may, by definition, lead to the departure*

4 COMCO : Investigation on use of patents
5 Andreas Heinemann, 'Blocking Patents and the Process of Innovation' (March 2019)
6 According to Lilly's quarterly financial report for Q3 2022, Novartis and Lilly reached a settlement in October 2022 to resolve their patent-related disputes
7 https://www.cnmc.es/sites/default/files/editor_contenidos/Notas%20de%20prensa/2022/20221025_NP_Sancionador_Merck_eng.pdf
8 Case C-457/10 P, *AstraZeneca v Commission*, ECLI:EU:C:2012:770, para 93

from the market or the marginalisation of competitors that are less efficient and so less attractive to consumers from the point of view of, among other things, price, choice, quality or innovation".[9]

At the same time, however, dominant firms have a 'special responsibility' not to allow their conduct to impair 'genuine, undistorted competition'. This special responsibility may deprive a dominant firm of the right to engage in conduct that would be unobjectionable if adopted by a non-dominant company. In the recent case of *Servizio Elettrico Nazionale*, the CJEU held that in order to establish an exclusionary practice as abusive, a competition authority must show two things: first, that the practice is capable of producing exclusionary effects (i.e. that it is capable of making it more difficult for competitors to enter or remain on the market); and second, that the practice relies on "*the use of means other than those which come within the scope of competition on the merits*".[10]

In practice, the concept of competition on the merits can be hard to pin down – particularly in an IP context. In his *Opinion in Servizio Elettrico Nazionale*, Advocate General Rantos observed that when applying Article 102 TFEU to exclusionary practices, competition on the merits generally refers to "*a competitive situation in which consumers benefit from lower prices, better quality and a wider choice of new or improved goods and services*".[11] Whilst this formulation is attractively simple, it is questionable whether it adequately caters for scenarios in which dominant firms enforce their IP rights – which inherently serve to block competition – against parties which may be infringing those rights. How does one distinguish between abusive and non-abusive enforcement in such situations? Cases such as *ITT Promedia* and *Protégé International* suggest that actions based on the assertion of valid rights or claims will only be found to be vexatious and thus abusive in exceptional circumstances. These cases suggest that other factors – such as evidence of bad faith or the existence of a strategy aimed solely at harassing competitors – are relevant to the analysis.

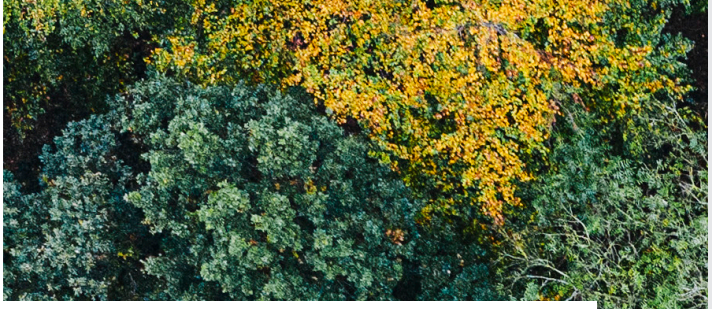
The way in which the pending cases discussed above develop has the potential to shed further light on the dividing line between competition on the merits and its converse in an IP context. If the competition authorities pursue the cases to final decisions, that is likely to result in appeals which will need to consider the distinction between legitimate IP strategies (which are necessarily exclusionary in nature) and an abusive restriction of competition. The role that courts play in assertions of IP and the seeking of injunctions will also be a relevant point of distinction from the *AstraZeneca* line of case law, in which applications for SPCs were made to patent offices which have limited discretion or budget to conduct factual investigations.

In the meantime, the ongoing investigations illustrate the breadth of pharma sector practices that competition authorities are willing to investigate and their appetite (and public budget) for doing so. They also provide an important reminder that whilst the competition rules do not call into question the existence of IP rights, the *exercise* of such rights is not immune from antitrust scrutiny.

9 Case C 413/14 P, *Intel v Commission*, ECLI:EU:C:2017:632, para 134. See also Case T-321/05, *AstraZeneca v Commission*, EU:T:2010:266, para 804: "*[...] the preparation by an undertaking, even in a dominant position, of a strategy whose object it is to minimise the erosion of its sales and to enable it to deal with competition from generic products is legitimate and is part of the normal competitive process, provided that the conduct envisaged does not depart from practices coming within the scope of competition on the merits [...].*"

10 Case C-377/20 *Servizio Elettrico Nazionale SpA v Autorità Garante della Concorrenza e del Mercato*, ECLI:EU:C:2022:379, para 61

11 Case C-377/20 *Servizio Elettrico Nazionale SpA v Autorità Garante della Concorrenza e del Mercato*, Opinion of Advocate General Rantos dated 9 December 2021, ECLI:EU:C:2021:998, para 63



The present and future of SESG for biopharmaceutical companies

Xisca Borrás
Partner, Regulatory

Ralph Giles
Associate, Commercial IP/IT

Taking effect from 5 January 2023, the European Council has signed the Corporate Sustainability Reporting Directive (the CSRD) into law, meaning that certain companies will be subject to new reporting requirements on sustainability, environmental, social and governance (SESG) matters in the coming years.

The intention is to make businesses with a presence in the EU more accountable by requiring publication of transparent information about how they impact the environment and society around them. The CSRD will replace the Non-Financial Reporting Directive (**NFRD**), with a significant expansion of the depth and breadth of the reporting requirements to ensure that companies report reliable and comparable sustainability information.

It is expected that almost 50,000 companies will be subject to the CSRD, as opposed to the approximately 11,000 companies that fell within the remit of the NFRD[1], which is a relatively small number given the total amount of companies established in the EU. Nevertheless, it is likely that a larger number of biotech companies will fall within the scope of the CSRD going forward.

The new reporting requirements will be phased in over the next 5-6 years, starting on 1 January 2024 (depending on the size of the company), and require large companies and listed SMEs to gather data and publish such information (in the subsequent financial year) in the form of a Sustainability Report (as part of their Management Report). The CSRD stipulates that the Sustainability Report is to include information that is forward-looking and retrospective, qualitative and quantitative, and based on conclusive scientific evidence, where appropriate.

The CSRD is just another reason why internal SESG corporate compliance initiatives are becoming much more important and arising much more frequently in boardroom discussions, as businesses try to effectively manage related legal and reputational risks.

1 Sustainable Finance and EU Taxonomy: Commission takes further steps to channel money towards sustainable activities

Reporting standards for the biotech sector

The technical advisory body involved in supporting the implementation of the CSRD (the European Financial Reporting Advisory Group, **EFRAG**) has published the first set of European Sustainability Reporting Standards, which describe four SESG reporting areas: i) governance structures; ii) corporate sustainability strategy; iii) impact, opportunities and risk management; and iv) other assessment-related information and targets.

Each reporting area is divided across three layers of disclosure, which are referred to as "*sector-agnostic*" (to apply to all companies subject to the CSRD), "*company-specific*" and "*sector-specific*" categories, with the sector-specific disclosure requirements currently under development. In the summer of 2022, EFRAG sought expertise from the pharma, biotech and medical devices industries to develop sector specific standards, and so it seems highly likely that these sectors will be caught.

In addition, there are also a number of standards that can be voluntarily supported by businesses. For example, in the pharmaceutical industry, the Pharmaceutical Supply Chain Initiative has published the PSCI Principles, which set out what it thinks should be the industry's standards relating to human rights, ethics, labour, health and safety, environment and related management systems.

The importance of sector-specific SESG reporting requirements is vital to reach a more consistent approach for reporting SESG data, making it easier to draw fair and effective comparisons. The current lack of a standardised and generally recognised measurement system is perhaps the biggest threat to effective SESG disclosures. No wonder, then, that current SESG reporting among many biotech companies is limited.

Environmental factors

The environment and climate change are currently two of the biggest focuses for investors, and sectors such as the oil and gas industries, the (fast) fashion industry or the agriculture sector are at particular high risk. However, the biotech industry cannot put environmental and climate change initiatives on the back burner, even if it is at a less high risk relative to other sectors.

One of the key factors that particularly affects the biotech and pharmaceutical industries is the impact of manufacturing operations, including up the supply chain. Companies should start thinking about how they can measure their emissions and put structures in place to collate that information, which will allow them to assess their direct impact on the environment as an organisation, as well as engaging with its key suppliers and customers to measure emissions they create indirectly throughout the value chain. This should allow companies to identify any obvious areas that are causing a disproportionate environmental impact, report effectively and take steps to address the issue.

Social concerns and governance

The pandemic highlighted the socio-economic damage that can result when there is limited access or affordability restrictions of medicines. Companies in the biotech and pharmaceutical industries are generally being encouraged to engage with each other and public authorities and consider how to address this issue.

Under the CSRD, companies will also be required to reflect internally on their workforce and ensure that they are monitoring diversity and inclusion statistics, including equal pay and human rights – for example tackling modern slavery in its business and through its supply chains. SESG corporate governance will be most successful when it involves all groups within the company so as to identify any institutional changes that need to be made to a company's culture or ethics.

Looking beyond the EU, in the summer of 2021, the US Securities and Exchange Commission approved Nasdaq's proposal to amend its listing standards to encourage greater board diversity and to require board diversity disclosures for Nasdaq-listed companies. Subject to transition periods and limited exceptions, Nasdaq-listed companies are required to publicly disclose board-level diversity statistics on an annual basis using a standardised matrix template. They also have to have a minimum of two diverse board members, or explain why they do not have them.

With young talent becoming more sensitive to SESG and more likely to consider seeking employment at a company with good SESG credentials, the biotech industry is not badly positioned when it comes to social and diversity reporting. Some studies[2] suggest that biotech companies are currently better at disclosing data related to social factors than information related to corporate governance initiatives for the benefit of the environment. This is probably due to greater availability of some of the social metric data.

Why is SESG monitoring and compliance important?

The trickiest part of SESG for biotech companies is, without a doubt, the pricing of therapies and medicines, given its potential to detrimentally affect the organisation's SESG performance. This is particularly so as pricing sustainably has become central to the social debate and healthcare policymakers, especially after the pandemic.

The impact that biopharmaceutical companies can have on society is of the highest relevance, given the potential to save lives. With public perception of the biopharmaceutical industry at its highest as a result of the industry's reaction to the pandemic, demands around SESG will only become more challenging and complex for the biotech sector in the coming years.

2 Biotech's ESG Crossroads

Investment & growth

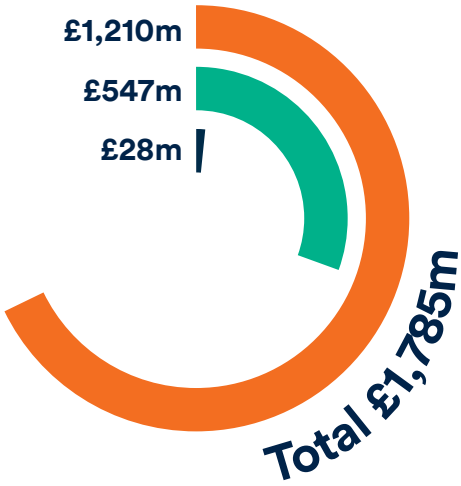
The future of biotech: the stats

£1.8 billion

raised by UK biotech in 2022, down from **£4.5bn in 2021**

2022 figures at a glance:

- Venture capital
- All other public financing
- IPO



Finance raised by UK-based biotech companies:

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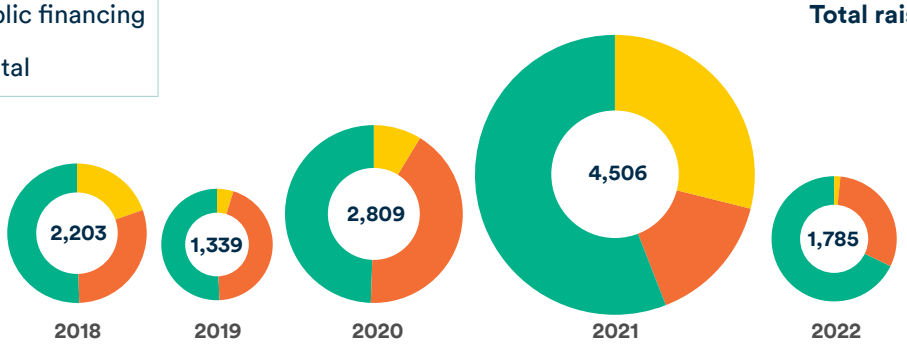


Source: https://biotechfinance.org/wp-content/uploads/2023/01/BIA-UK-biotech-financing-202230.01.2023.pdf

TechBio investment scene: two tribes go to war?

Traditionally, technology and life sciences investors have been decidedly different beasts: the former targeting investments that turn a profit quickly, whilst the latter – long the preserve of specialists – are well versed in the patience required by longer development times and higher regulatory hurdles.

Marek Petecki
Partner, Corporate & Tax

Claire Smith
Partner, Commercial IP/IT

This demarcation is blurring now, with thanks, in part, to the growth of TechBio companies and the proliferation of AI within the life sciences sector. Indeed, investors from both tribes are slowly, but surely, starting to bridge the divide to become investors in life sciences tech – but currently there is only a relatively small (albeit growing) pool of investors that truly specialise in the TechBio space.

The rise of AI

It is clear that AI is making big waves in the life sciences industry. AI is being deployed in a wide variety of healthcare settings, including in diagnostics and also throughout all stages of the lifecycle of a medicine. For example, the speed and volume of data that AI can consume and the impressive analytics of some AI tools can significantly shorten traditional drug discovery lead times - and when designing a clinical trial, AI can radically improve the chances of selecting the right patients who will respond to the treatment - with the potential to make a big impact on cost savings and the timelines for medicine approvals. Having said this, at the moment, the costs of drug discovery are ironically going up in part due to the level of investment that is being made in adopting these new tools.

Big strides have been made right across the globe. Medicines that have been developed with the use of AI have been reaching the clinic in the last 3 years. In 2020, UK's Exscientia made history when it announced the first AI-designed medicine to enter a clinical trial, for an established protein target. Various other companies have since followed suit, including

Utah's Recursion Pharmaceuticals and San Francisco's Verge Genomics. Most notably, Insilico Medicine (headquartered in Hong Kong) took the next big leap, when in 2021 it began what is believed to be the first clinical trial for a medicine that has been developed wholly by AI. In a statement made by its chief scientific officer, the company said "*we believe this is a significant milestone in the history of AI-powered drug discovery because to our knowledge the drug candidate is the first ever AI-discovered novel molecule based on an AI-discovered novel target*".

The birth of TechBio

With the direction of travel clear, the sector has been seeking a way to best acknowledge and accommodate the increasing prevalence of this new technology – and so we come to TechBio.

Whilst it is still hard to be precise about the exact nature of TechBios, they can be defined in comparison to their more traditional pharmaceutical cousins, BioTechs. As the name suggests, TechBios place an increased emphasis on the use of cutting-edge deep-tech and data-driven business models, and are likely to position themselves one step further removed from the eventual product. It is a subtle difference, but not one without precedent. A similar distinction happened in finance not too long ago, between FinTechs and TechFins. As Helen Panzarino of Imperial College Business School summarised, "*FinTech companies' core business is financial services…TechFin companies, in contrast, are technology companies that are leveraging their existing technologies, data, brands, customer bases or other assets to broaden their product offerings into financial services*."

Bridging investment appetites

So why must investor profiles evolve with the emergence of TechBios? The embrace of AI and deep-tech has not come without its challenges from an investment perspective. Whilst astonishing amounts of capital have been pouring into the TechBio space, most of the funds have been confined to investments in a few, select companies in headline-grabbing deals. When it comes down to it, the two traditional types of investors in tech and life sciences tend to have fundamentally different outlooks and risk appetites.

Life sciences investors are typically seeking an asset (a promising medicine candidate), backed up by credible scientific data. They understand the capital, time and regulation-intensive processes it takes to bring medicine to market. They also understand the inherent risks of the sector – most significantly, that being in it for the long haul might not even pay off.

In contrast, the tech investors are used to business models which focus on speed and innovating traditional ways of working - or which "*move fast and break things*", to use a famous Mark Zuckerberg saying. Compared to a new medicine, a tech platform can be up and running swiftly, often with relatively little capital cost. Unlike a drug too, its evolution can come over time, whilst on the market. Nor – at least traditionally - have tech businesses been beholden to strict regulations around safety, efficacy and quality. Perhaps because of this, tech investors have less patience than life sciences investors when looking to get a return on their investment.

With increased emphasis on tech and the speed of development in this space, TechBios are bringing the two different attitudes into sharp relief. Yet we need more specialist investors to sit in this middle ground and understand the needs of this type of company. These include the need to have the right multidisciplinary team at the helm of the business and, crucially, for the company to strike the right balance between building a strong platform as well as having a number of promising therapeutic assets (either those of its own, or those generated in a collaboration). An investment approach that involves drip-feeding capital and which is dependent on having a clinical medicine candidate with little regard for the value of the platform and other non-therapeutic assets is unlikely to be a recipe for a TechBio's success. Nevertheless, with all the hype that is currently surrounding AI, there is a weight of expectation that AI-enabled drug discovery will yield results at breakneck speeds. If a TechBio company has not been able to discover and validate a medicine target or a candidate within short order, investors will see it as a particularly risky venture.

Venture Capital activity shows that understanding of this sub-sector is growing and some specialist investors are emerging. But, as of yet, the pool is limited, and certainly in the UK/Europe. We need more. Building a TechBio business model can be harder than most, given the various uses their technology can be applied to. These businesses need experienced guidance to find the right use cases, and to de-risk and scale up. Key ingredients for a TechBio's success include having diversity in its business models. Lessons learned from genomics companies that boomed in the dot-com era and then crashed, indicate that, for the long-term survival of a TechBio, it will need a healthy mix of strategic collaborations whilst also keeping one eye firmly on its own pipeline, and not just the pipelines of its pharma partners.

Only one point to score?

The lines are blurring, as sector borrows from sector to push forward. Interestingly, just as life sciences is borrowing from tech, so tech is borrowing from life sciences. Increasingly, the tech giants of the world are transforming their AI initiatives into something that would be more familiar to pharmaceutical-style demonstrations of value, creating wet labs for their testing (e.g. as seen with Isomorphic Labs, set up by Google's parent, Alphabet).

There is wealth of opportunity there for investors, in the middle ground. It will come with time, but the traditional investors in the UK/Europe are not pivoting fast enough to keep apace with TechBio. The US investment community is betting heavily on TechBio and perhaps lessons are to be learned from across the pond. Almost twenty years ago, Frankie Goes to Hollywood sang "*when two tribes go to war, a point is all that you can score*". Is it time to drop the two tribes and focus on creating a more sophisticated community of investors to support TechBio?

Event highlights:

Here's what you might have missed

Panel discussion: Technology in Women's Health

Wednesday 18 January 2023

Bristows recently hosted a panel discussion on the evolving role of technology in women's health.

Our industry-leading panellists shared what motivated them to join the sector, the gender gap in healthcare data and the investment challenges for companies in this space, amongst other things.

Find out more about this event on the event page here

Meet the speakers:

Dr Helen O'Neill
Founder and CEO, Hertility

Dr Sioned Jones
Co-founder and COO, BoobyBiome

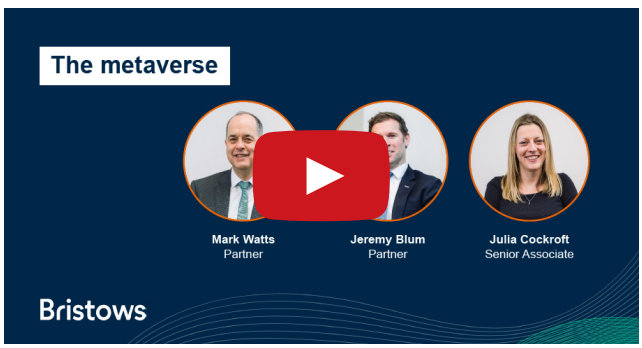
Barbara Domayne-Hayman
KQ Labs Chair and Entrepreneur-in-Residence, The Francis Crick Institute

Bristows Tech Summit

Thursday 26 November 2022

Always with an eye to the future, Bristows' leading tech experts tackled the most important legal and commercial issues that the technology industry is currently facing.

You can now watch videos of the presentations on the **Bristows website**, or by clicking the videos below.



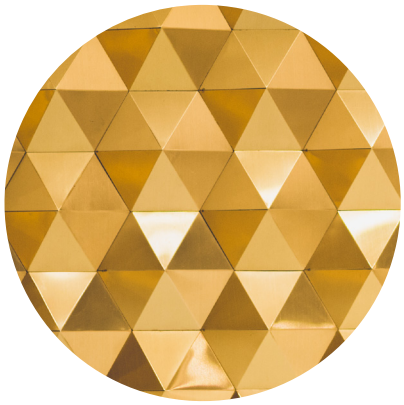
Global mobility in the war for talent

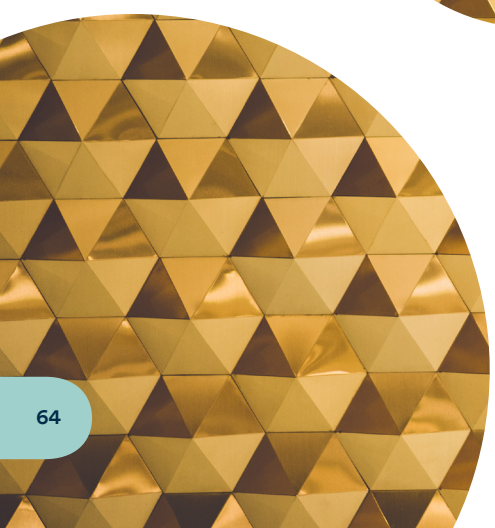
Securing and managing talent has long been a strategic priority for organisations. The last decade has been characterised by a shortage of talent, and securing and retaining the right people continues to be a critical issue for employers.

Gareth Wadley
Partner, Employment

Lizzie Field
Of Counsel, Employment

There is a particular shortage of, and fierce competition for, the highly specialist skills required within the biotech sector especially digital and artificial intelligence. More than ever, employers cannot rely on local markets and need to look internationally to find the right talent. Changes in ways of working, and the expectations of employees, has resulted in non-standard employment arrangements and an increased focus on embracing a truly global and mobile workforce.





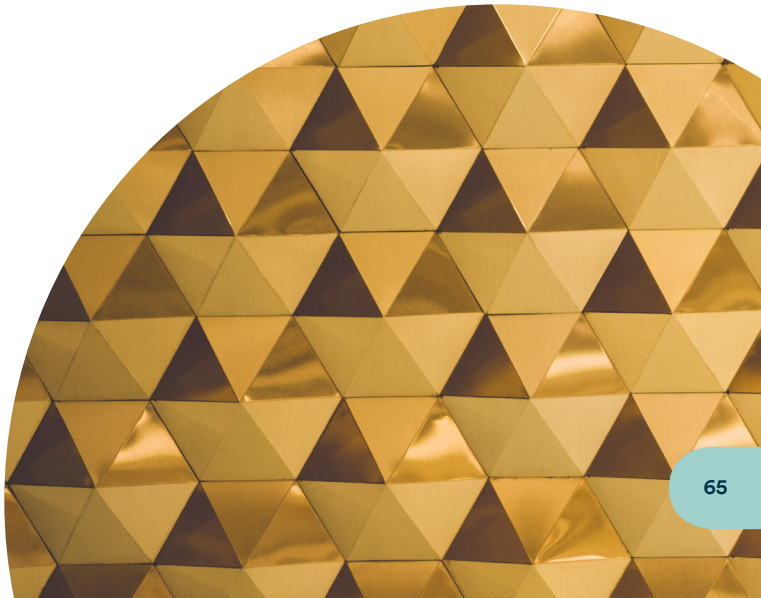
Since the pandemic, remote working and flexible working have become the norm. During the pandemic, employers were forced to embrace remote working such that work has now become something employees do rather than a place to which they go. Many employees have also re-evaluated their priorities and are determined to achieve a work-life balance and the best quality of life for them and their families. The pandemic lockdowns proved that remote working is an effective way of working and with advances in technology and communications it is simpler than ever for employers to adopt a globally agile work culture. Since the lifting of travel restrictions, there is a renewed appetite for business travel and many candidates are more determined than ever to experience life overseas and the opportunity to gain additional experience through international assignments. Travel opportunities, global assignments and flexible working patterns have re-emerged as valuable tools for both attracting and retaining talent. Taking into account increasing demands from candidates who know their worth within this highly competitive market, commuter contracts, hybrid working and flexible working patterns are also on the rise. Equally, other non-remuneration benefits such as leave policies and training and

development programmes as well as diversity and ESG credentials are proving important tools to attract and retain individuals who have a tendency to place as much value on the culture of the organisation as on traditional remuneration packages.

Advances in technology mean it is now quick and easy for organisations to identify and access talent anywhere in the world. As always, where it is critical for an individual to be based in the UK, an overseas candidate may relocate, but more than ever before there is an increase in global remote working. Globally remote executives are an increasing trend with organisations moving the job to the location of the right talent rather than moving the talent to the location of the job. Whilst it is not always possible for particular roles to be carried out wholly remotely, due to the requirements of the role or regulatory considerations, there is an increased willingness, and a need, for organisations to reassess and be more flexible when determining from where staff must work. It is no longer viable to expect the best candidate to come to you.

Remote working certainly has a number of benefits for employers, not least because it means they are truly able to recruit the best individual for a role without geographical restrictions and can access a larger pool of candidates including those who would not ordinarily consider the opportunity if they had to relocate. Where employees live in a different country, there may actually be a cost saving for the employer due to the cost of living, local market/salary benchmarks and the level of social security taxes. Further, remote working means that expansion of operations and the workforce is not constrained by physical premises and growth of the business and/or entry into a new market can often be achieved more quickly. International candidates also mean a more diverse workforce. From an employee's perspective, remote working reduces commuting time and geographical limitations are removed. Candidates can fulfil their career ambitions without having to relocate or move their families, and in turn, the careers of partners and schooling of children can continue without disruption.

Whilst looking overseas to hire talent has benefits and is undoubtedly attractive, recruitment of individuals from outside an employer's home country always requires specific consideration of HR and tax issues. Essential considerations include how and where the individual will be paid, the employment status of the individual (it is illusory and deceptive to think a consultancy arrangement is the obvious solution!), whether they can be paid from the "home" payroll, whether a company branch or subsidiary is required in the jurisdiction, whether there will be access to a pension scheme or other benefits and also whether the organisation needs to withhold tax and/or social security. The answers to these questions will always depend on the specific facts of each case, including the countries involved and what the individual will actually be doing for the organisation. There is seldom a common, quick answer and appropriate legal advice must be sought at the outset to ensure compliance with all relevant rules and in order to avoid future difficulties. Getting it wrong is costly especially since issues may not emerge for some time. There is also the risk of fines and sanction from authorities with serious repercussions for the organisation and also the individual.



Matters are further complicated where the candidate is not a national of the country in which they will be working or where they will undertake a global role which requires them to work in multiple jurisdictions. A paramount consideration must be the ability to obtain the appropriate right to work. Since Brexit, EEA and Swiss nationals require authorisation to work in the UK and UK nationals are now subject to the immigration rules of each continental European country. Whilst visa free travel is still permitted between the EU and UK, there are restrictions on what an individual may do and they are rarely permitted to work. From an immigration perspective, planning in advance and appropriate expert support is essential to ensure successful navigation of complex rules and processes and that appropriate permissions can be obtained within any specific timeframe.

Of course, securing talent is only the first step. Organisations also need to work to retain talent, recognition of which has given rise to the concept of so called “re-recruitment”, that is applying the same tools and strategies of external recruitment to existing talent. An open mind and willingness to offer existing staff the opportunity to take on new responsibilities and to move within the organisation, both in terms of role and location, is particularly valuable to mitigate the risks of losing talent to competitors.

In the face of the various pressures within the biotech sector and the tech industry as a whole, biotech companies need to be open to adopting a global agile working strategy and use all the tools at their disposal to give them the competitive edge.

Visit profile

Meet Gareth Wadley...

Gareth Wadley is the new head of Bristows’ employment team. Gareth advises innovative, multinational organisations on their business-critical employment matters. He has a particular focus on immigration and global mobility, supporting tech and life sciences businesses on issues related to the recruitment, retention and relocation of international talent, and with the design and implementation of their global people strategies.

Reasons to be optimistic in 2023

The global economy, according to the head of the International Monetary Fund, is like "a ship in choppy waters". And though there may be disagreement about the precise size of the waves buffeting the economy, it is clear that for many sectors the last few months have been anything but plain sailing.

David Horner
Partner, Corporate & Tax

Nick Cross
Senior Associate, Corporate & Tax

Indeed, according to KPMG, in Q3 2022 the number of global VC deals fell to the lowest level in five years, whilst global VC investment dropped below $100bn.

Perhaps inevitably, the economic headwinds are also being felt by the UK's biotech market. The latter half of 2022 has not only seen a fall in the amount of capital raised – UK VC investment decreasing by 11% between Q2 and Q3, according to the UK BioIndustry Association – but a drop in the number of such deals, too. Meanwhile, private equity's appetite for M&A deals has been diminished by a cocktail of inflation and increased interest rates. The chilling effect of falling stock markets – particularly NASDAQ, which has tended to be the market of choice for UK biotechs – has served as an impediment to IPOs as well as preventing listed companies from raising additional capital.

But, even amidst the concerns of a recession, the sector can look ahead to 2023 with some optimism. Interest in biotech remains strong even as investors adapt to changed market conditions. The result is that whilst raising money on public markets has certainly become more difficult, the latter stages of 2022 have seen a number of investors continuing to deploy substantial amounts of funding into an array of privately-held life sciences companies. Indeed, several big institutions – banks and PE houses, for instance – have established funds to make varying types of investments in the life sciences sector, whilst a number of smaller venture funds have likewise sprung into being. One such example of the former is J.P. Morgan Asset Management's Life Sciences Private Capital team, launched in November 2022, which looks set to start deploying venture and growth capital in 2023. Elsewhere, Blackstone Life Sciences announced the close of its royalty and structured credit-focused Life Sciences Yield Fund at $1.6bn in April 2022, the largest first-time fund of its nature. Overall investment may have dipped, but, as the new funds demonstrate, wellsprings of capital do still exist for life sciences innovators.

Meanwhile, when it comes to mergers and acquisitions, the UK saw a flurry of higher-value acquisitions by large US-based life sciences companies in late 2022, a trend that may well continue into 2023. Here, the acquisition of DJS Antibodies by AbbVie for around $225m is emblematic. At the same time, a healthy flow of deals in the secondaries market – a hallmark of 2021 that saw private equity funds sell life sciences assets to each other – could provide something of an ongoing tonic to depressed valuations. For all the choppy waters, then, the sector may yet weather the storm in 2023.

After all, the fundamentals remain strong. The UK has retained its allure as a biotech hub, with the Government publicly committed to making the country a life sciences superpower. The Golden Triangle – the universities of Oxford, Cambridge and London – remains a source of strength: a report by Beahurst in 2022 found that Oxford alone had produced 90 spin-out companies across multiple sectors. Evidently, UK spin-outs continue to be regarded with interested eyes.

What's more, Covid-19-inspired interest in life sciences – not least therapeutics – has yet to dissipate. Gene therapy, for instance, remains a real source of investor interest, whilst AI-based drug discovery is not only grabbing headlines, but, as is explored elsewhere in this issue, investors' attention, too.

As we look to 2023, we can do so with the confidence that investors are not turning their backs on life sciences. They remain poised to spend – albeit on different terms and using different structures as might have been the case had it not been for the current economic climate. The waters of 2023 may look choppy, but for the life sciences sector, they remain navigable.

Meet the editors

Gregory Bacon

Partner, Patent litigation

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Greg is a contentious IP specialist whose advice extends across all industries, with a particular focus on patent litigation in the life sciences sector. This has included coordination of parallel litigation in a number of cross-border IP projects. He also advises on wider issues relevant to the life sciences sector.

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Xisca specialises in all aspects of EU and UK regulatory law in the biopharmaceutical sector, with a special focus on medicinal products for human use. She brings a strong business approach to her legal advice, which she developed while she was an in-house lawyer at a leading innovative biopharmaceutical company.

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Hugo is an associate in the life sciences regulatory department advising on contentious and non-contentious regulatory matters in the EU and the UK. Hugo joined Bristows as a trainee solicitor in September 2019 and as part of his training contract gained experience in a range of practice areas, including transactional intellectual property, patent litigation, data protection, brands and real estate.

About Bristows

Bristows has one of the most highly-regarded multi-disciplinary life science legal practices in the world.

We have a true cross-disciplinary team in this space encompassing our renowned IP, regulatory, competition, transactional, dispute resolution, IT and data protection teams. The strength of each individual practice complements the others to provide a fully integrated and comprehensive service.

Our life sciences specialists - many with backgrounds in biology, chemistry, biochemistry, genetics and neuroscience - work with leading clients across the private, public and academic sectors.

We pride ourselves on the breadth of our client base in the sector and actively seek to advise clients from the different key participants making up the life sciences eco-system. As such we act for global pharma, specialist investors, growing biotech and medtech companies, universities and research institutes, specialist service providers and government funded bodies. Our clients also include tech companies now entering the sector as convergence takes hold.

We believe that these different perspectives help us to best advise our clients and give us true expertise in relation to the sector and where it is heading.

Meet the co-heads of the life sciences interest group

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