

# BIO TECH



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# Introduction



**Dr Robert Burrows**  
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Robert is a Partner in Bristows' Intellectual Property Department. He is very experienced in patent litigation matters in the UK, particularly for clients within the life sciences sector.

Many of the cases he has managed in recent years have required the coordination of parallel proceedings in multiple jurisdictions within Europe and elsewhere in the world in order to ensure that consistent and optimal arguments have been deployed in all jurisdictions.

The national and international cases with which he has been involved have required, inter alia, preparation for and attendance at preliminary injunction and main action proceedings in numerous countries within Europe and attendance at inspections of pharmaceutical manufacturing processes in India and Japan.

In addition to his litigation experience, Robert regularly assists clients with freedom to operate advice. Robert has a PhD in molecular genetics and has worked for a company specialising in DNA sequencing products.

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Welcome to the latest edition of Bristows' Biotech Review.

This publication is designed to provide an update on some of the key developments in this area over the last year.

Articles have been organised by legal practice area and include updates on the enforcement of second medical use claims, SPCs, regulatory data protection and the Nagoya Protocol.

With its introduction edging ever closer, we also provide our latest thoughts on the Unified Patent Court and its current status (about which more information can be found at [bristowsupc.com](http://bristowsupc.com)).

With many thanks for her time and willingness to assist, we close with a Q&A with Anne Lane of UCL Business.

As with all our publications, we welcome any feedback you might have and would be delighted to provide you with more detail on any of the articles featured in this Review.

# Patent litigation

## Our patent litigation practice

The majority of Bristows' IP lawyers have scientific and technology backgrounds, including physics, chemistry, biotechnology, electronics, engineering and material sciences. We actively recruit trainees who are First Class, and even PhD level, scientists from leading research institutions. This means that whatever the technology on which a client has built its business, Bristows will have someone with relevant background and experience.

## "Yes" to Tomatoes and Broccoli



**Nicholas Round**  
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**The Enlarged Board of Appeal has addressed the question of patentability of selectively bred or crossed plant products, but does its ruling really affect the law in individual countries?**

In March 2015, the Enlarged Board of Appeal (EBA) of the European Patent Office ruled on the effect of Article 53(b) of the European Patent Convention (EPC), which excludes from patentability "*plant or animal varieties or essentially biological processes for the production of plants or animals*", on the patentability of claims for tomato and broccoli plants (consolidated cases of "Tomato II" (G2/12) and "Broccoli II" (G2/13)).

The patents at issue contained method claims for a "*Method for breeding tomatoes having reduced water content*

*and product of the method*" (G2/12) and a "*Method for selective increase of the anticarcinogenic glucosinolates in Brassica species*" (G2/13). Both patents had been considered previously by the EBA which, in 2011, found that the method claims were excluded from patentability under Article 53(b) EPC because they concerned essentially biological processes for producing plants. Following those decisions the patentees had amended their patents by deleting the method claims and were seeking only to claim the products of the methods (i.e. tomato or broccoli plants).

The EBA therefore had to decide: "*Can the exclusion of essentially biological processes for the production of plants in Article 53(b) EPC have a negative effect on the allowability of a product claim directed to plants or plant material such as fruit?*" In a lengthy judgment the EBA concluded that the "*essentially biological processes*" exclusion in Article 53(b) was limited to process claims. It followed that product claims, and even product-by-process claims, were not excluded. Furthermore, it did not matter that the *only* method currently available for generating the products claimed was an essentially biological process.

In making its decision the EBA refused to consider wider economic, social and ethical arguments that were put forward in favour of exclusion from patentability (since such issues are for the legislators not the interpreters of legislation) and considered it important to maintain a distinction between patentability and scope of protection. It was pointed out that "*the protection conferred by the product claim encompasses the generation of the claimed product by means of an essentially biological process...*" (i.e. the scope of the patent protection effectively includes the process excluded from patentability). However, referring to G1/98, the EBA confirmed that scope of protection should not be taken into consideration when deciding such issues of patentability.

Hence it is now clear that, at least under the EPC, plant products produced by selective breeding, crossing or other essentially biological processes are, in principle, patentable. That is not to say that patents for such products will always be permitted across Europe. Although not excluded by the EPC, there are a number of EU member states, such as Germany, which exclude such patents as a matter of national law.

<sup>1</sup> [The same exclusion relating to essentially biological processes is also found in Article 4(1)(b) of the Biotech Directive 98/44/EC.

## Salt limitation leads to sweet and sour Court of Appeal judgment



**Dr Greg Bacon**  
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**Eli Lilly enjoyed initial success with regard to the Alimta (pemetrexed) litigation, where Actavis's innovative application for a DNI was denied. However, a subsequent trial on Actavis' new product could still change matters.**

The *Actavis v Eli Lilly* UK litigation concerning pemetrexed (sold by Eli Lilly under the brand Alimta®) relates to Actavis' innovative application to the English court for declarations of non-infringement (DNIs) of national designations of a European Patent in addition to the UK designation. On 25 June 2015, the Court of Appeal refused to grant the declarations sought by Actavis. This overturned the first instance decision in the Patents Court, which held that each of the UK, French, Italian and Spanish national designations of Eli Lilly's European patent were not infringed by the pharmaceutical products that Actavis intended to sell in each of those countries. The Court of Appeal agreed with the trial judge's conclusion that the patents were not directly infringed but overturned his decision on contributory infringement. The Court of Appeal's judgment, raises several points of wider interest, in particular in relation to claim construction, second medical use patent claims and the procedural requirements to seek DNIs of foreign patents before the English court.

### Claim construction

At first instance, the Patents Court had relied on the prosecution history as a guide to construction of the patent claim. During prosecution, the patentee had amended the wording of the claims sought in response to an office action from the European Patent Office that the claims previously sought were contrary to Article 123(2) of the European Patent

Convention. The Court of Appeal strongly disagreed that the prosecution history was useful and should be used in this manner on this occasion. Indeed, the judgment from the Court of Appeal suggests that if either party had contended that the prosecution history was inadmissible as a matter of law it is likely that the Court would have agreed.

In so finding, the Court noted that the person skilled in the art does not always read the prosecution history, particularly as it is often of limited value. Nor does reviewing the basis on which amendments have been made guard against potential abuse of the system (the reader will be familiar with the Angora cat analogy) unless an amendment during prosecution creates a kind of estoppel against arguing for wider claims, a proposition that the English courts have previously rejected. In this case, the Court of Appeal therefore declined to consider the prosecution history, albeit that the Court came to the same conclusion on scope of protection as the trial judge had.

### Second medical use claims

The relevant second medical use claims of the patent in suit were in both Swiss-type and EPC 2000 form. The Court of Appeal held that the claims were not directly infringed by Actavis' proposed products (which contained pemetrexed dipotassium), as the scope of protection was restricted to the claimed pemetrexed disodium salt and did not extend to other salts of pemetrexed. However, pemetrexed disodium salt was construed to extend to a solution of pemetrexed and sodium ions in a concentration of at least 2 to 1 in favour of sodium ions, on the basis that the person skilled in the art would not construe the claims as being limited to pemetrexed disodium salt in a solid pharmaceutical composition. As Actavis' products were indicated for use by injection after dissolution in saline, Eli Lilly argued that Actavis indirectly infringed by supplying means relating to an essential element of the invention. In reaching its conclusion on construction, the Court made a number of interesting findings.

First, the Court was of the view that as second medical use claims must involve



the step of manufacturing a medicament for treating a disease (otherwise they would be to a method of treatment), a formulation chemist would generally have to be part of the team that forms the person skilled in the art. Moreover, the Court held that a second medical use claim includes a requirement that the manufactured medicament is to some extent effective for treating the disease.

Second, in this case, the Court held that the dissolved lyophilisate could be the medicament referred to in a second medical use claim, and the manufacture of that medicament could take place by the physician.

Third, the Court said that the means supplied by the defendant did not have to constitute a free-standing feature or element of the claim but only means relating to an essential element. In this case, a means for releasing pemetrexed ions into the solution for injection related to an essential element of the invention, as it was the presence of pemetrexed ions in the solution which gave efficacy. It did not matter that the specific pemetrexed



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salts in the Actavis products were not an element or feature of the claim.

As Actavis had conceded that it intended for its products to be dissolved in saline, the Court held that it would infringe the UK patent. As it was common ground between the parties that there was no detectable difference in the laws of France, Italy and Spain regarding the approach to contributory infringement, the court therefore held that Actavis' products would also infringe the three non-UK patents in suit and thus refused to make any of the DNIs sought.

### Declarations of non-infringement of foreign patents

Whilst the Court of Appeal refused to grant the declarations sought on the basis that Actavis' products infringed the patents in suit under contributory infringement, the Court gave an *obiter* ruling on which country's procedural requirements an applicant must satisfy before commencing an action before the English courts to obtain a DNI. It was noted by the Court that English law

took the most relaxed attitude amongst the four relevant states of what a party must show before it can apply to the court for a DNI, and that Actavis had satisfied that requirement under the *lex fori*, i.e. English law. However, Eli Lilly had argued that an applicant should be required to satisfy the law of the national designation of the European patent, the *lex causae*.

In the Court's view, the rules at issue were conditions of admissibility of rights rather than rules concerning the substance or content of the parties' rights. Or in other words: "*They are all concerned with whether the court should hear a dispute about substance. They are not concerned directly with the substance itself*". Such rules would traditionally be considered, for private international law purposes, as procedural and not substantive and thus subject to the *lex fori* and not the *lex causae*.

Therefore, only if the exceptions in the Rome II Regulation applied should the Court not apply the *lex fori*. According to the Court,

none of the exceptions in the Regulation encompassed the rules for admissibility of a DNI. Therefore, had Actavis been entitled to the DNIs as a matter of patent construction/infringement, the Court would have granted them.

Prior to handing down judgment, Actavis also requested that the case be remitted for further trial in the Patents Court in relation to a proposed new product for reconstitution with dextrose rather than saline. The Court of Appeal has allowed this request to determine whether and to what extent there will be infringement in those circumstances if some persons administering the products reconstitute them in saline rather than dextrose. Therefore although the appeal judgment represents sweet success for Eli Lilly, the subsequent trial may sour the dish.

## Hospira v Genentech – take 3



**Katie Rooth**  
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### The latest update on this long-running dispute surrounding the patent protection for Herceptin.

On 24 June 2015 the High Court gave its latest decision in a dispute between Hospira and Genentech relating to patents for Herceptin. On this occasion Genentech's patent was to the use of the antibody, trastuzumab (the active ingredient in Herceptin) in combination with a taxane for the treatment of HER2-positive breast cancer. Taxanes are a class of chemotherapeutic agents which include paclitaxel and docetaxel.

The attacks on the validity of Genentech's patent were based on a single piece of prior art,

Before turning to the assessment of validity of the patent, Arnold J. made several observations on claim construction and infringement. He held, following the recent Court of Appeal decision in Warner-Lambert v Actavis, that

"for" in the claim meant that it must be known to, or reasonably foreseeable by, the manufacturer that trastuzumab would be intentionally administered in combination with a taxane for the relevant therapeutic purpose (i.e. for the treatment of HER-2 positive breast cancer). He also construed the claim as requiring that the combination of antibody and taxane be more effective than the taxane alone, as shown by an increased time to disease progression.

The attacks on the validity of Genentech's patent were based on a single piece of prior art, a paper describing a Phase III trial of trastuzumab in combination with different chemotherapeutic agents including paclitaxel. The paper did not disclose any results from the Phase III trial but did contain results from the earlier Phase I and II studies.

Arnold J. found in Genentech's favour on the issue of novelty and held that the prior art paper did not anticipate the claim. In so doing the judge noted that purpose limited claims can only be anticipated by (i) the disclosure of the invention or (ii) the disclosure of subject matter which, if performed, would inevitably result in the claimed invention.

Whilst arguments under the second of these two heads were the more persuasive in this instance, they did not invalidate the claim – given that the necessary mental element of the claim, i.e. the intention to administer the combination to increase efficacy in the treatment of breast cancer, was missing (as it was not known that this would be the effect before the results of the trial were available), it was not possible to anticipate the claim.

On the question of obviousness, Arnold J. held that the patent lacked inventive step. In coming to his decision, the Judge took into consideration a number of factors including motivation, the nature of the work and the effort involved, the alternative routes which could be pursued, and any perceived prejudices which would deter a skilled person. Even though the results of the Phase III trial were not disclosed in the prior art paper, Arnold J. found that on the basis of the positive results of the Phase II trials and the xenograft studies that were described, the skilled person would have had a reasonable expectation of success in the Phase III trial.

This is the third decision of the High Court in a dispute between Hospira and Genentech, where Hospira is seeking to revoke a number of secondary patents relating to Herceptin so it can launch its generic version of the drug; the basic patent and SPC for Herceptin have already expired. As a result these decisions, Hospira has now "cleared the way" of five of Genentech's Herceptin patents at first instance. At the time of writing this article the dispute is not yet over, as at least one of the cases is still subject to appeal proceedings.

## Painful conflict on the construction of Swiss-form claims and infringement by cross-label use



**Claire Phipps-Jones**  
Associate  
Bristows LLP

**In 2015, a series of pregabalin decisions addressed the debate around construction, infringement and relief issues related to second medical use patents and cross-label use. While the decisions have resulted in further debate, particularly around the analysis of indirect infringement, they also provide guidance on how originators and generics should engage with the NHS in the UK.**

The *Warner Lambert v Actavis* pregabalin cases have been before the UK Courts on no less than seven occasions since the beginning of 2015 and have had to deal with the thorny issue of the construction and infringement of second medical use patents containing claims in Swiss-form, i.e. "Use of drug X in the manufacture of a medicament for the treatment of disease Y". The cases have also dealt with potential infringement through "cross-label" use, i.e. where a medicament indicated solely for a non-infringing use is used for a different, patented indication and have touched on the question of the relief that would be available were such a patent to be held valid and infringed.

### Preliminary relief application

In January 2015, Warner-Lambert made an application to the Patents Court for interim relief in respect of Actavis' generic pregabalin medicine called Lecaent. Warner-Lambert held a patent with Swiss-form claims for the use of pregabalin in the treatment of pain and alleged direct and indirect infringement of that patent. At that time, approximately 50% of Warner-

Lambert's sales of its pregabalin medicine, Lyrica, was alleged to be used for the treatment of pain in the UK (although it should be noted that Pfizer subsequently contended that higher percentages of pregabalin were used for pain and at trial it was held that approximately 70% was so used). While Actavis' Lecaent was not authorised for pain and had a skinny label (i.e. the label did not identify that the product was indicated for the treatment of pain), Warner-Lambert asserted that some of the product was being prescribed, dispensed and used for the treatment of pain. The basis of this assertion was that doctors in the UK are encouraged by guidelines and the relevant prescribing software to prescribe drugs using the international non-proprietary name (pregabalin in this instance). Pharmacists, who often have no knowledge of the indication for which the product is to be used by the patient, are then financially incentivised to dispense the cheapest product available which will invariably be the generic product.

The interim relief requested by Warner Lambert was unique. It applied for a mandatory injunction forcing Actavis to:

- contractually oblige pharmacists and wholesalers to make reasonable endeavours not to dispense Lecaent for the treatment of pain;
- notify Warner Lambert of any supply to intermediaries;
- label its product as not being authorised for the treatment of pain; and
- send correspondence to NICE, all Clinical Commissioning Groups ("CCGs") and pharmacists supplied by Actavis noting that Lecaent was not to be used in the treatment of pain.

After three days of argument, in a decision dated 21 January 2015, the Court applied the *American Cyanamid* guidelines on interim injunctions and refused Warner Lambert's application. Applying the first limb of *American Cyanamid*, Arnold J. held that there was no serious issue to be tried on the issue



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of infringement, as the word “for” in the Swiss-form claim imported a requirement of subjective intention on the part of the manufacturer that the medicament was intended to be used for treating the specified condition, and Warner Lambert had failed to establish any sort of case in this respect. Arnold J. also suggested that there could be no claim to indirect infringement, as there would be no preparation/manufacture by a downstream wholesaler or pharmacist. It is quite clear that in considering construction, Arnold J. thought that the relevant process element of the claim was the manufacture or preparation of the medicament, as such a claim “is not aimed at, and does not touch the doctor”.

Considering the second limb of *American Cyanamid*, Arnold J. found that even if he was wrong and there was an arguable case of infringement, the balance of the risk of injustice favoured the refusal of the relief sought, principally because the relief sought could deter pharmacists from dispensing Lecaent for any indication, effectively excluding Actavis from the market for the non-patented indication.

### The application for NHS guidance

In his interim relief decision of 21 January, Arnold J. also commented that the best solution to the problem encountered by Warner-Lambert was for the NHS to issue guidance recommending that doctors should prescribe pregabalin by brand (i.e. “Lyrica”) for the treatment of pain and to prescribe pregabalin generically for other indications. Because pharmacists in the UK would be legally obliged to dispense the branded medicine to fulfil prescriptions written for the brand, if doctors adhered to the guidance, this ought to ensure that the generic medicine was not dispensed for the patented indication. The Judge also encouraged software providers to amend their electronic prescription systems to prompt doctors to prescribe branded pregabalin for pain. Arnold J. commented that “I consider that there is a reasonable prospect of NHS England issuing guidance in the near future but a lower prospect of software suppliers modifying their software quickly.”

No doubt spurred on, at least in part by the observations of the Judge,

Warner-Lambert immediately engaged in correspondence with NHS England asking it to issue guidance to CCGs. After some discussion, NHS England indicated that it would not oppose an Order that it must provide guidance, provided that certain conditions were met. The matter came before Arnold J. on 26 February, at which point he considered that the Court had jurisdiction to make the Order against an “innocent third party who is mixed up in the wrongdoing of others” and that the injunction was appropriate in all the circumstances as “the issuing of guidance by NHS England is the most efficacious, dissuasive and cheapest solution to the problem which confronts Warner-Lambert”. An order was granted requiring the NHS to issue guidance to the CCGs, who were then requested to issue further guidance to practitioners.

A cross-undertaking in damages was provided in favour of NHS England and those generic companies that applied for it as well as their group companies. Arnold J.’s willingness to order such an undertaking in favour of the generic companies was based on the possibility that the patent would later be held



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invalid, and also, even if the patent were held valid, the possibility that the guidance would have the effect of Lyrica being prescribed and dispensed at the expense of generic pregabalin for non-patented indications (referred to as "a chilling effect"). Finally, the Order made by Arnold J. made provision for additional guidance to be issued when the patent expired (or earlier in the event that the patent was revoked). The essence of the additional guidance was that practitioners should revert to their normal prescribing practices and that any software modifications should be reversed.

### Appeal of the PI

The Court of Appeal, (Floyd LJ giving the leading judgment) issued a unanimous decision on 28 May, upholding Arnold J.'s decision not to grant the interim injunction sought by Warner Lambert. This decision was based on the ground that Arnold J. had properly evaluated the evidence before him and reached a sensible conclusion on the balance of justice. There was therefore no basis to suggest that the Judge had exercised his discretion not to grant interim relief incorrectly. However, perhaps more significantly, the Court reached a different view on the correct approach to be taken to the construction of Swiss-form claims. In particular, the Court of Appeal held that the key issue is what the manufacturer knows (including constructive knowledge) or could reasonably foresee about the ultimate intentional end use of the product for the patented indication. In the appeal court's view, infringement would occur if the manufacturer knew or could reasonably foresee the ultimate intentional use for pain. The manufacturer did not necessarily need to have that specific intention or desire itself.

Also of note was the Court of Appeal's comment during an earlier strike out application that it was arguable that "putting the invention into effect" for the purposes of indirect infringement may occur when one person manufactured and another used the product for the patented indication. This certainly pointed towards the Court of Appeal considering a quite different approach to construction than that articulated by Arnold J. at first instance.

### The main action

Following a lengthy trial in July, the first instance decision in the main action was handed down on 10 September 2015. Despite finding that the main claims of the patent were invalid due to insufficiency, Arnold J. went on to consider the infringement position. He held that Actavis did not infringe the claims asserted against them and that Warner-Lambert was liable for having made groundless threats of infringement. Although appearing to disagree with the Court of Appeal's test of reasonable foreseeability, Arnold J. applied it and held that, on a number of dates in question, it was not reasonably foreseeable that Actavis' Lacaent medicine would have been intentionally administered for the treatment of pain. This was principally on the basis that the doctor would not know which company's pregabalin would be dispensed, and the pharmacist was unlikely to know the indication for which it was prescribed (and if it did, would dispense Lyrica for the treatment of pain as a result of the letters written to superintendant pharmacists by Actavis). This is particularly interesting, given Floyd LJ's observation during the preliminary relief appeal that *"the judge found that in these circumstances, it was foreseeable that a generic version of Lyrica with a skinny label will be dispensed for patients who have in fact been prescribed the drug for pain"*. An appeal is almost certainly inevitable and it is possible that the issues will eventually be considered by the Supreme Court such is their complexity and importance.

Arnold J. also refused to find indirect infringement, noting that he was "puzzled", "baffled" and did not understand the reasoning behind the Court of Appeal's decision to reverse his strike out decision. Returning to the theme of his decision on preliminary relief, the Judge also stressed that the answer to this problem should not be found in the patent system, but should lie in centralized and authoritative guidance instructing prescribers to prescribe by brand name where patents exist. He commented: *"In the present case, NHS England issued*

*guidance as a result of an order made by this Court [which] had two practical advantages. The first was that it provided a convenient forum to enable the interested parties to negotiate what was to be done, when and by whom. ... The second was that the procedure included the protection for the NHS and for the generic companies of a cross-undertaking in damages. ... Looking to the future, however, it does not seem to me to be in anyone's interests for these problems to be dealt with in the ad hoc manner in which they were addressed in this case. ... I consider that it behoves patentees who want their second medical use patents enforced to provide NHS England with all the information and assistance it requires to enable it to issue appropriate guidance as and when required. I also consider that it behoves generic companies who want their interests in obtaining untroubled access to lawful markets protected to cooperate with NHS England as well."*

### Concluding remarks

While Arnold J.'s initial subjective intent approach provides certainty for generic companies, it would be quite difficult without detailed disclosure for patentees to determine whether their patents had been infringed, even where significant sales were taking place for the patented indication. The more objective approach suggested by the Court of Appeal is more generous to originators and helps to prevent generic manufacturers turning a Nelsonian blind eye to the issues that are made of its products. There is no doubt that issues of construction, infringement and the relief to be granted are particularly thorny. The author wonders whether the indirect infringement analysis, which Floyd LJ began to dig into in the interim injunction judgment, provides the least worst (though still not perfect) solution. Ultimately, patent law is not the platform which will provide sufficient incentive for research-based companies and institutions to investigate potential new uses for existing drugs – a new IP right is needed. Until this time, originators and generics should follow Arnold J.'s guidance and engage at an early stage with stakeholders such as NHS England.

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### Idenix v Gilead: the increasing role of plausibility in the English courts



**Charlie French**  
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**As reported in Issue 2 of Biotech Review (How much information does a valid antibody patent need?), plausibility has found a more prominent place in the English courts in recent years, in particular in the context of obviousness and insufficiency. *Idenix v Gilead*<sup>2</sup> provides an illustration of the English courts' approach to claims covering broad classes of compounds and highlights the difficulties that can arise for patent holders.**

#### Background

The case concerns a patent claiming – by means of a Markush claim – various nucleoside pro-drugs for the treatment of *Flaviviridae* viral infections. Just hours after the patent granted, Idenix issued a claim for patent infringement, claiming that Gilead's sofosbuvir product (Sovaldi®) infringed the patent. Gilead denied infringement and counterclaimed for revocation.

The patent was held to be invalid for lack of novelty and inventive step, insufficiency and added matter. Although interesting issues of construction were raised, infringement was dealt with relatively briefly with Arnold J. concluding that, had the claims been valid, sofosbuvir would have infringed.

Arnold J.'s findings in relation to inventive step and sufficiency are likely to be of most interest to the biotechnology and pharmaceutical sectors, as they bring the issue of plausibility to the fore and suggest that it should be an increasingly important consideration for patentees.

#### Inventive step

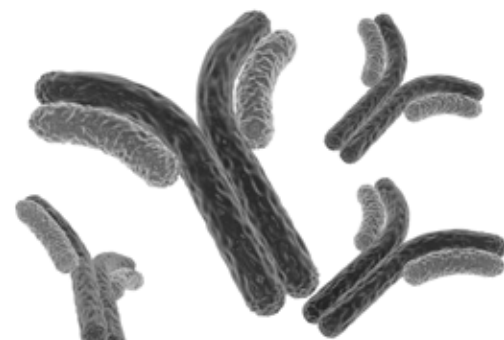
The Judge held that the patent was not inventive because it made no technical contribution to the art (*AgrEvo* obviousness). In forming this conclusion, he placed particular weight on the fact that it was common ground between the experts for Gilead and Idenix that the patent covered compounds for which anti-*Flaviviridae* activity would not have been considered plausible by the skilled team based on the disclosure of the patent.

Idenix proposed to amend the patent claims to remove the implausible compounds. However, Arnold J. found that the amendment did not go far enough to satisfy the plausibility threshold (and that it added matter) – the patent contained no experimental data or rationale to suggest that any of the claimed compounds may be effective, so the assertion that they were effective was mere speculation. The specification also added nothing to the common general knowledge as to which nucleoside analogues might exhibit anti-*Flaviviridae* activity. It was already known that certain nucleoside analogues could inhibit virus replication and it was therefore plausible based on the common general knowledge that untested nucleoside analogues *might* exhibit anti-*Flaviviridae* activity. Although Idenix had demonstrated that the compounds claimed were structurally related to known active compounds, this did not make it plausible that they *would* be effective against *Flaviviridae*, only that they were worth testing. Further, they were no more worth testing than any other nucleoside analogues. The patent merely invited the skilled team to carry out a screening programme and claimed any nucleoside that was found to be active.

The patent was therefore held invalid for lack of inventive step on the basis that the claims were not plausible. Arnold J. did not go on to apply the standard *Windsurfing/Pozzoli* test for inventive step.

#### Insufficiency

Plausibility was equally fundamental to Arnold J.'s assessment of insufficiency. Gilead claimed that the patent was



invalid for both classical insufficiency (failure to enable the patent to be performed without undue burden) and *Biogen* insufficiency (failure to enable the invention to be performed over the whole scope of the claim). Arnold J. applied the two-stage test articulated by him in *Eli Lilly v Janssen Alzheimer Immunotherapy*<sup>3</sup>: (i) determine whether the disclosure of the patent, read in light of the common general knowledge, makes it plausible that the invention will work across the scope of the claim; and (ii) if the disclosure does make it plausible, determine whether later evidence establishes that in fact the invention cannot be performed across the scope of the claim without undue burden. Applying his reasoning in relation to inventive step to part (i) of the test, he concluded that the patent did not make it plausible that the invention would work across the scope of the claims (as granted or as proposed to be amended) and was therefore insufficient.

For completeness, Arnold J. also considered part (ii) of the test. Neither the patent specification nor the common general knowledge enabled the skilled person to make the claimed compounds and there was evidence that Idenix had struggled for many years to make and isolate the claimed compounds before eventually succeeding through a combination of skill and luck. Even if the skilled person had been able to make the compounds, it was unclear whether such a compound would have anti-*Flaviviridae* activity. Accordingly, in addition to failing the plausibility threshold, the patent did not enable the skilled team to perform the invention without undue burden.

<sup>2</sup> [2014] EWHC 3916 (Pat).

<sup>3</sup> [2013] EWHC 1737 (Pat).

## Conclusion

The role of plausibility that emerges from *Idenix v Gilead* in light of other recent cases is an initial hurdle to be cleared before the conventional English law tests for inventive step and/or sufficiency are considered. If a patent does not clear this hurdle, it will be automatically invalid, whether for obviousness or insufficiency. The judgment suggests that patents claiming broad classes of substances will be vulnerable to attack in the English courts unless experimental data or detailed rationale to support effectiveness of the claimed substances across the full scope of the claims are provided in the specification. This is a particular issue for broad Markush-type claims but the reasoning applies equally to biological patents, for example broad antibody claims for which it may be difficult and expensive to perform experiments to demonstrate plausibility across the entire scope of the claim.

It appears that it will also be difficult for patentees to cure plausibility issues through claim amendment. In *Generics (UK) v Yeda & Teva*<sup>4</sup>, Floyd LJ noted that where certain products covered by a claim do not demonstrate the technical property that is said to be inventive, they must be excised from the claim by amendment. However, this proposal may be problematic in practice, since any amendment to remove products that do not plausibly make a technical contribution are likely to add matter. In *Idenix v Gilead*, the amendment was held to add matter since the skilled team would learn something new about the invention: that the new sub-class was effective against *Flaviviridae* (which was not the case for the broader class).

Applicants for pharmaceutical and biotechnical patents should bear in mind this emerging hurdle for patentability and consider whether the level of data and reasoning included in patent specifications is sufficient to support the claimed technical effect.

## Update on SPC cases



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**Four cases provide further guidance for anyone with an interest in SPCs. In brief:**

- **The SPC Regulation draws no distinction between active ingredients that are covalently bound to other active ingredients. What matters is whether the active ingredient produces a pharmacological, immunological or metabolic action of its own**
- **For an SPC to be granted it must be established that the active ingredients' own therapeutic effect is reflected in the marketing authorisation (MA) on which the SPC application is based**
- **The words "as such" have been clarified to an extent. A patentee cannot obtain a second SPC for a combination product in circumstances where: (i) he has already obtained an SPC for a mono product based on the same basic patent; and (ii) the product which is the subject of that mono SPC constitutes the sole-subject matter of the invention**
- **The scope of an SPC is not limited to the specific form of the active ingredient covered by the MA, but extends to other forms which are covered by the basic patent and which are therapeutically equivalent**
- **The date of the first authorisation to place the product on the market in the Community is the date when the decision granting the MA is notified to the applicant, rather**

**than the date when the decision granting the MA is adopted by the relevant authority.**

Despite the extensive number of references to the CJEU in recent years concerning the interpretation of Regulation 469/2009 (the "SPC Regulation"), it is indicative of the level of uncertainty that remains that since the publication of Bristows' last Biotech Review in November 2014, there have been three further decisions from the CJEU and one from the EFTA Court. With an increasing number of biologics coming off patent, the unresolved questions will be of particular concern to proprietors of the related SPCs and indeed those wishing to market biosimilars. This article considers each of these latest developments in turn.

### Case C-631/13: *Arne Forsgren v Österreichisches Patentamt ("Forsgren")*

First up, in January 2015, the CJEU rendered its decision in *Forsgren*, a referral from the Austrian Court concerning the interpretation of Article 1(b) and Articles 3(a) and (b) of the SPC Regulation.

In this case the applicant was the proprietor of a patent relating to Protein D – an IgD-binding protein of *Haemophilus influenza*. Protein D is covalently bound to other active ingredients in the vaccine Synflorix, which is indicated for the immunisation against the adverse effects of *Streptococcus pneumoniae* in children. Protein D is known to have two independent effects to those of the other active ingredients in Synflorix – firstly, as a vaccine against a middle ear inflammation caused by non-typable *Haemophilus influenza* bacteria and secondly, as an adjuvant to the substances effective against *pneumococci*.

The first question before the Court was whether an active ingredient, which is covalently bonded with other active ingredients within a medicinal product, but nevertheless maintains an effect of its own can be the subject of an SPC. The Court held that whether or not a

<sup>4</sup> [2013] EWCA Civ 925.



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substance could be considered an active ingredient for the purpose of the SPC Regulation depended entirely on whether it produced a pharmacological, immunological or metabolic action of its own. The SPC Regulation draws no distinction between active ingredients that are covalently bound to other active ingredients and as such the grant of an SPC could not be precluded on that ground alone.

The Court was then asked to answer the question of whether an active ingredient whose therapeutic effect is not reflected in a marketing authorisation ("MA") could be the subject of an SPC. The applicant submitted that Protein D was used in Synflorix not only because of its action as a carrier protein, but also on account of its capacity to confer protection against infections caused by *Haemophilus influenza*. However, the Court noted that the MA expressly stated that there was insufficient evidence that Synflorix provided such protection. Given that there was no trial or data concerning the purported therapeutic effects of Protein D in relation to *Haemophilus influenza* integrated into the MA, it could not be said that it accounted for any delay to the commercialisation of Synflorix. As such, the Court found that to grant an SPC in such circumstances would be contrary to the aim of the SPC Regulation.

Finally, and following some reformulation of the question, the Court considered whether a carrier protein conjugated to a vaccine could be regarded as a product for the purpose of the SPC Regulation (i.e. an active ingredient or combination of active ingredients). The Court rejected the Commission's submission that this question could be answered by reference to the CJEU's decision in *GSK* (Case C-210/13), distinguishing the present case on the basis that Protein D is used in Synflorix neither as an excipient nor an adjuvant. However, the Court noted that there was nothing in the SPC Regulation which explicitly answered the question. As such it was necessary to address the issue by reference to the purpose of the SPC Regulation i.e. the incentivisation of pharmaceutical research and the discovery of new

products. On that basis the Court found that a carrier protein could not be the subject of an SPC unless it was found to produce a pharmacological, immunological or metabolic action of its own. This would be for the referring Court to determine.

The Austrian Supreme Court gave its judgment following the reference in April 2015. It held that for an SPC to be granted it must be established that the active ingredients (in this case, the carrier protein's) own therapeutic effect is within the MA's indications, but it is not necessary for the active ingredient (the carrier protein) to be explicitly mentioned in the MA. Accordingly the Supreme Court referred the case back to the Patent Office.

### **Case C-577/13: Actavis v Boehringer Ingelheim ("Actavis")**

Next up, in March 2015, was the CJEU's decision in *Actavis*, which concerned the interpretation of Article 3(a) of the SPC Regulation i.e. whether the product was protected by a basic patent in force. Boehringer Ingelheim ("B.I.") had obtained an SPC for telmisartan, the active ingredient in the medicinal product Micardis. Having obtained an MA for telmisartan in combination with hydrochlorothiazide (HCTZ) (MicardisPlus), B.I. applied for an SPC for telmisartan + HCTZ. The UK Intellectual Property Office (UKIPO) informed B.I. that Article 3 of the SPC Regulation was not fulfilled; the combination had to be clearly claimed in order for it to be regarded as "protected" for the purpose of Article 3(a). At the suggestion of the UKIPO, B.I. requested that its application be suspended pending the amendment of its patent to include an express claim to telmisartan + HCTZ. Under UK patent law, a patent amendment is deemed to take effect from the date of the grant of the patent. The UKIPO allowed the postponement, B.I. obtained the amendment such that the patent contained an express claim to telmisartan + HCTZ, and the UKIPO subsequently granted the SPC. Actavis sought to invalidate the SPC and the High Court subsequently referred a number of questions to the CJEU.

A key issue to be determined was the interpretation of the definition of basic patent in Article 1(c) and in particular the words "as such". B.I. contended that the fact that telmisartan + HCTZ was specified in the claims (as amended) was sufficient for it be considered protected "as such". Actavis argued that the expression meant that only the product which is the true subject matter of the invention should be regarded as protected "as such". The CJEU favoured Actavis' interpretation finding that a patentee cannot obtain a second SPC for a combination product in circumstances where (i) he has already obtained an SPC for a mono product based on the same basic patent; and (ii) the product which is the subject of that mono SPC constitutes the sole-subject matter of the invention. The CJEU considered that HCTZ did not constitute the subject-matter of the invention and therefore the SPC for telmisartan + HCTZ should not be granted. Having determined that B.I. was not entitled to an SPC for telmisartan + HCTZ in any event, the CJEU declined to answer the questions relating to whether or not it was permissible for B.I. to obtain an SPC on the basis of an amended patent that would not have qualified for an SPC at the date of the SPC application and the corresponding questions relating to what the duration of such an SPC should be.

### **Case E-16/14: Pharmaq v Intervet ("Pharmaq")**

In April 2015, the focus switched to the EFTA Court, a supra-national court with jurisdiction over Norway, Iceland and Liechtenstein, states which are not members of the EU but are party to the EEA. Judgments of the EFTA Court are not binding on the CJEU or EU Member States but can be persuasive in the absence of alternative authority. *Pharmaq* was a referral from the Norwegian Courts for guidance in relation to Articles 2, 3 and 4 of EU Regulation No 1768/92 which contains essentially identical provisions to those in the SPC Regulation. The case concerned vaccines for viral pancreatic disease in salmon. From 2003 to 2011, Pharmaq supplied its vaccine in Norway pursuant to a special approval



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exemption, which allowed the product to be supplied prior to having obtained an MA. A provisional MA was granted in the UK in 2005. Full MAs were granted in Norway and the UK in 2011. The Court was asked to determine whether the special approval exemption amounted to “placing a product on the market” for the purpose of Article 2 of the SPC Regulation. Furthermore, the Court was asked to determine whether an MA granted according to Article 26(3) of the Veterinary Medicines Directive could constitute the first MA for the purpose of Articles 3(b) and (d) of the SPC Regulation.

The EFTA Court held that an MA granted pursuant to Title III of the Veterinary Medicines Directive could fulfil the requirements of Articles 3(b) and (d). This would include authorisations granted in exceptional circumstances pursuant to Article 26(3). However, the Court noted that the strictly limited, provisional permission to supply vaccines in the event of serious epizootic disease under Article 8 of the Veterinary Medicinal Code does not require the same safety and efficacy testing, nor does it entitle the producer to market the product, but only to supply it to the extent necessary to combat the disease in question. The Court therefore held that such permission does not constitute an MA and will generally not constitute placing the product on the market for the purposes of the SPC Regulation. It therefore appears that the provisional use of an unauthorised vaccine in the face of an outbreak of disease would not usually disqualify the product from subsequently obtaining an SPC, thus alleviating some concerns that patent holders might lose the entitlement to an SPC if they were to make their unauthorised product available in response to an epizootic crisis.

Perhaps of more relevance to the biopharmaceutical industry were the questions relating to the scope of the SPC. Pharmaq’s SPC purported to cover not only the specific strain of the virus that was covered in its MA, but also other strains covered by its basic patent, thereby bringing

Intervet’s vaccine within the scope of Pharmaq’s SPC. Pharmaq argued that the principles set out in *Farmitalia*, which concerned an SPC for a chemical entity, should apply equally to biologics, given that the SPC Regulation draws no such distinction. As such, Pharmaq argued that the scope of an SPC is not limited to the specific form of the active ingredient covered by the MA, but also other forms which are covered by the basic patent and which are therapeutically equivalent. The Court agreed and, as a result, Pharmaq was entitled to prevent Intervet from marketing its vaccine, provided that it was adjudged to contain the same active ingredient (irrespective of form) with a therapeutic effect that falls within the indications for which Pharmaq’s MA had been granted. These issues were a matter of fact to be determined by the national courts.

### Case C-471/14: *Seattle Genetics Inc*

In a very recent decision, published in October 2015, the CJEU held that Article 13(1) of the SPC Regulation (which concerns the duration of an SPC) must be interpreted as meaning that the date of the first authorisation to place the product on the market in the Community is the date when the decision granting the MA is notified to the applicant (rather than the date when the decision granting the MA is adopted by the relevant authority). Whilst this decision only adds around two to five days to the length of an SPC, it is likely to provide significant commercial value to SPC holders who typically obtain peak sales of their innovative products towards the end of any patent term.

### Biosimilar applicants in the US are not obliged to dance



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In July 2015, the United States Court of Appeals for the Federal Circuit issued

its first decision on biosimilars (i.e. generic versions of biologic drugs) in a dispute between Amgen and Sandoz concerning the interpretation of the 2009 Biologics Price Competition and Innovation Act (“BPCIA”).

The BPCIA provides, for the first time in the United States, an abridged process for FDA approval for biosimilars. It contains complicated patent negotiation provisions that have come to be termed the “patent dance”, prescribing how the parties (i.e. the originator and the biosimilar applicant) decide which patents will be litigated during the time prior to FDA approval of the biosimilar. This dance begins with the biosimilar applicant providing the originator with a copy of its FDA application (including a description of its manufacturing process). The Act also contains a provision requiring a biosimilar applicant to provide the originator 180-day notice of the first commercial marketing of the biosimilar.

The case concerned the first biosimilar approved by the FDA, Sandoz’s filgrastim product Zarxio (a glycoprotein indicated for the treatment of neutropenia), marketed by Amgen under the brand name Neupogen. Sandoz decided not to share its manufacturing information with Amgen, and provided its 180-day commercial marketing notice before obtaining FDA approval for Zarxio. Amgen sued Sandoz, arguing that the BPCIA does not allow biosimilar applicants to opt out of the patent dance, or to provide the 180-day commercial marketing notice prior to obtaining FDA approval. The case was first heard by the District Court for the Northern District of California. It found in Sandoz’ favour on both issues, holding that the patent negotiation provisions were not mandatory, and that the 180-day notice could be provided before FDA approval was obtained. Amgen appealed to the Federal Court, which concurred with the decision of the District Court that the dance-off was optional, but held that the 180-day notice was mandatory and could not precede FDA approval of the biosimilar.

## Progress towards the UPC – an update



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**It is now more or less certain that the UPC will open for business in Q1 2017. There are no remaining legal hurdles in its way; only four more countries need to ratify; and the number of practical steps requiring completion means the work of the Preparatory Committee is nearly at an end. Alan Johnson explains more.**

As we have commented in previous issues, the relevant European authorities have in the past been very optimistic about the date when the UPC will come into effect. However, the date which is now being talked about by the UPC Preparatory Committee - the start of 2017 - seems much more realistic. Importantly, since our last issue, the final legal hurdle in the way of the system starting has been removed: the CJEU ruled last May that the so-called "second Spanish challenge" to the legality of the system failed, and all that now remains are a limited number of further ratifications of the UPC agreement and completion of some practical details.

The progress which has been made over the last year includes a significant number of further ratifications bringing the total to nine. This includes one (France) of three mandatory ratification countries (the others are the UK and Germany), and eight others. There are clear signals coming out of another four non-mandatory ratification countries (notably including Italy) that they will ratify relatively soon, meaning that by summer 2016 the required threshold of ten non-mandatory countries should have been reached. The UK has committed itself to completing the ratification process also by summer 2016, including stating that this will be unaffected by the promised EU in/out referendum. Some



may have regarded this as inevitably causing a further delay, but not only is the UK Government proceeding with UPC preparations regardless, but even an "out" vote before UPC start-up may well not derail the process, with the real possibility of proceeding anyway, and exiting from the UPC system along with other EU withdrawal steps.

This, then, leaves only Germany with some question marks over it. Rumours have abounded for two years or more that Germany has been dragging its feet for at least two reasons. First, because of dissatisfaction with its share of the central division (something which is impossible to change as it is written into the agreement), and second because it will end up providing much of the financing in the opening years of the court. Nonetheless, it is still believed that Germany will ratify within about six months.

This is not to say, however, that the start of the UPC will come into force in an uncontrolled way as soon as the last ratification occurs. Rather the start date depends on the timing of the *deposit* of the last instrument of ratification, and hence the relevant country can control the start date. Therefore, it is expected that one or more likely both of the UK and Germany will withhold the event which actually triggers the countdown. But given present expectations on ratifications, it is perfectly possible that the UK and Germany could both deposit their instruments of ratification in September or October 2016, such that

the system would indeed be ready to start by January or February 2017.

Ratification (or indeed readiness to ratify) will also trigger another very significant event, that is a new transitional / provisional UPC authority, to replace the UPC Preparatory Committee and established pursuant to an agreement signed in October 2015. This authority will be able to enter into contracts, notably with employees including judges, as well as to take over the IT system which is currently being organised by the UK government. Current expectations are that this authority should come into existence about September.

Creation of a provisional authority is a particularly significant matter for industry. As most patent owners will be aware, one of the most important aspects of the UPC is that it will, upon opening of the court, have jurisdiction over all *existing* European patents<sup>5</sup>. However, in recognition of the fact that this new system was not one which patentees "signed up to" when applying for their patents in the first place, a transitional arrangement has been agreed under which patent owners are able to opt their patents out of the new system so that national courts continue to have exclusive jurisdiction over disputes concerning these patents. Hence, the plan for the provisional authority includes that it will permit opt-outs to be registered in a "sunrise" period. Whilst it will still be possible (absent UPC proceedings) to opt out after the

<sup>5</sup> In as far as contracting states to the UPC are designated by those patents (as surely all but a very few will be).

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sunrise period, the possibility of opting out from about September 2016 brings sharply into focus the need to consider corporate policies on opting out now. Without going into the detail, even if a patent owner is a supporter of the UPC and may very well wish to enforce its patents in that forum, there are still good reasons why such patents might be opted out. This is because it will also be possible<sup>6</sup> to withdraw that opt-out, and having the opt-out in place until the patentee is ready to sue removes from potential defendants the option of applying to the UPC for central revocation.

Litigation and opt-out strategy is a very complex matter and needs careful consideration. It should therefore be at the top of the agenda for consideration over the next six months. As part of this, discussions with co-proprietors and licensees may also be necessary, and in the case of licensed-in patents, similar discussions will be necessary with the patent owners.

### What else is new in the last year?

Perhaps the major development which will be of interest to patentees is the announcement of the renewal fees for unitary patents. Unitary patent protection will be available to any applicant at the EPO whose patent comes up to grant after the UPC comes into existence, unless the application is itself very old. It has been announced that the renewal fees will be set at the equivalent of national validations in UK, France, Germany and the Netherlands: a so-called "True TOP4" solution. This will mean that for many companies in the bio-pharma sector, if considering only the issue of initial cost of protection, unitary patent protection will be more attractive than the conventional route. Of course there are other considerations. There is a price to be paid in terms of lack of flexibility since in subsequent years it will not be possible to "prune" the portfolio and save renewal fees. There is also uncertainty over the future of SPCs for unitary patents. And the main drawback (if it is regarded as such) of the unitary patent approach is that there is no possibility of opting such

patents out of the UPC jurisdiction. Consequently patent owners would be committing themselves to an untested court system by going for unitary protection. However, it is very much to be hoped that within at least a very few years, the UPC will have an established track record and hence the decision as to whether to elect for unitary protection can be made in a more informed manner.

### Conclusion

It is now only a matter of precisely when the UPC will open for business – whether it is January, February or March 2017. Not even the UK's in/out EU referendum seems to stand in the way. Business simply cannot afford to delay their own UPC preparations a moment longer.

## Gene patenting in Australia – *D'Arcy v Myriad Genetics* [2015] HCA 35



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### Alex May assesses the recent *Myriad* decision in Australia and the potential ramifications for gene patenting in Europe.

Australia's highest court has unanimously decided that isolated nucleotide sequences derived from human nucleic acids are not patentable in Australia. The judgment therefore excludes certain cDNA sequences from patentability because, although synthetic, they are derived from human RNA. It therefore goes further than its US equivalent, the 2013 decision of the Supreme Court of the United States in *Association for Molecular Pathology v Myriad Genetics*, in which it was held that isolated human DNA is not patentable whereas cDNA is patentable. Neither judgment is in line with the legal position in Europe – set out in the Biotech Directive of 1998 – that isolated or synthetic nucleic acids are in principle

patentable. This article describes how the High Court of Australia reached its 7 October 2015 decision and reflects on the legal position in Europe.

Only three of the claims of *Myriad*'s Australian patent were in issue: those which claimed an isolated nucleic acid coding for a BRCA1 polypeptide having one or more of the mutations or polymorphisms identified in the patent. *Myriad* had discovered that these mutations and polymorphisms were indicative of a predisposition to breast cancer and ovarian cancer. The other 27 claims, which relate to possible applications of that discovery (a probe, vectors, the preparation and use of polypeptides, and methods of diagnosis), were unchallenged.

Miss *D'Arcy*'s case was that the three claims did not meet the requirement in Australia for an "invention", archaically defined in the legislation as "the sole working or making of any manner of new manufacture". The more usual grounds of invalidity – anticipation, obviousness and lack of usefulness – were not raised at any stage in the proceedings. Instead, the need for a 'manner of new manufacture' was pursued, which is an Australian alternative to the requirement in Europe for something more than a "simple discovery", or in the US, to the 'law of nature' exception. Claims in *Myriad*'s US patent to isolated human DNA were held invalid under this exception.

The first instance and appeal courts in Australia had concluded (applying case law dating from 1959) that isolated nucleotide sequences, whether or not synthetic, were products consisting of an "artificially-created state of affairs of economic significance" and therefore patentable inventions. In reaching this conclusion, the appeal court had focused on the differences in structure and function between naturally-occurring nucleic acids and those isolated by human intervention, including the separation of nucleic acids from associated proteins and their consequent inability to generate mRNA or polypeptides through transcription or translation.

<sup>6</sup> Although not if national litigation has been started in the interim.

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The judgment of the High Court is particularly critical of the appeal court's focus in that regard, which caused it to make a different determination than the US Supreme Court, whose judgment preceded it. That Court had observed that Myriad's claims to isolated human DNA *"were simply not expressed in terms of chemical composition, nor do they rely in any way on the chemical changes that result from isolation of a particular section of DNA"*. The appeal court's contrary finding, that chemical changes occurring on the isolation of nucleic acids were *"of critical importance"*, was considered *"misplaced"*, and its characterisation of the claims as to a class of chemical compounds was *"superficial"* and one which *"elevates form over substance"*. In the High Court's view, the claimed invention could be better characterised as chemical compounds embodying and conveying genetic information, where the existence of that information is an essential element of the invention, and the particular nucleic acid molecule which carries it is just the medium.

Moreover, whether the genetic information codes for a polypeptide with the mutations or polymorphisms identified in the patent depends only on the DNA sequence of the person from whom the molecule was isolated. This sequence is not made by human action; it is only discerned in that way. The High Court therefore concluded that the claims lay on the boundaries of what established case law considers a manner of new manufacture.

The judgment takes issue with the breadth of the claims to isolated

nucleic acids per se, which extended beyond Myriad's discovery that certain mutations and polymorphisms are indicative of susceptibility to cancer. Rather, they claimed a monopoly over any isolated nucleotide sequence which on examination is found to contain the mutations or polymorphisms identified in the patent, even though such sequences are naturally occurring. This would be the case regardless of whether the examination actually related to the BRCA1 gene, because the claims encompassed an unquantifiable class of isolated DNA fragments of indeterminate length, potentially including vast stretches of sequence surrounding the BRCA1 gene. Further, it would not be apparent that an isolated DNA fragment fell within the claims unless and until its BRCA1 gene was sequenced and found to contain the mutations or polymorphisms specified in the patent.

Accordingly, the High Court shared the concerns of Miss D'Arcy. In practice, the claims in issue could prevent the isolation and testing of DNA even if the clinician or researcher was doing so for a purpose unrelated to Myriad's discovery. There was a real risk that this *"chilling effect of the claims would lead to the creation of an exorbitant and unwarranted de facto monopoly"* on all methods of isolating or testing DNA fragments that might contain the BRCA1 gene. The Court therefore reasoned that to extend the concept of manner of new manufacture to encompass the claims was not an extension appropriate for judicial determination. Rather, it was a matter of public policy which should be left for the legislature to decide

(notwithstanding that the legislature had on more than one occasion tried and failed to pass laws explicitly excluding genetic information from patentability).

On 15 December 2015, IP Australia published the Patent Office's "Examination Practice following the High Court decision in *D'Arcy v Myriad Genetics Inc.*"

As a result of the Australian and US Myriad judgments, patent claims to isolated nucleic acids are not valid in the US or Australia, and claims to isolated cDNA sequences which merely replicate the genetic information of a naturally occurring organism are not valid in Australia. The European Patent Office has held claims in these terms to be valid, one example being the 2002 case T 0272/95 (Relaxin/Howard Florey Institute). Moreover, the European Biotech Directive provides that, although the simple discovery of one of the elements of the human body (including a gene sequence) is not patentable, an element isolated from the human body (including a gene sequence) may be patentable even if its structure is identical to that of a natural element. Accordingly, in Europe, isolated nucleic acids are patentable provided the other requirements for patentability are met, namely that the isolated nucleic acid is novel and inventive in comparison with the prior art, and that its industrial application is disclosed in the patent specification.

Myriad's European patent claims to isolated human BRCA1 and BRCA2 sequences never made it to court in Europe. Those claims were revoked in EPO oppositions due to lack of novelty or inventiveness over earlier published DNA sequences. This illustrates the practical difficulty in Europe of defending the validity of claims to isolated nucleic acids; as a result of the Human Genome Project and other research efforts, much of the sequence of the human genome is already in the public domain. Perhaps this makes it less likely that courts in Europe will ever have to consider the validity of a claim which represents an allegedly exorbitant and unwarranted de facto monopoly over the isolation or testing of nucleic acids that might contain the relevant gene.



# Regulatory

## Our regulatory practice

Our regulatory practice serves the most heavily regulated industries globally, including leading pharmaceutical and biotechnology companies and major manufacturers of medical devices and chemical products. Our team has a wide variety of backgrounds, including the fields of bioscience, neuroscience and reproductive medicine in the clinical setting.

## Regulation data protection for Biologics: EU vs US



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**What data protection is provided for bio/pharmaceutical companies for products in development and how does this compare between the USA and Europe? Grant Strachan explains below.**

The biologics industry has grown at a significant rate and recent studies indicate that over 900 biotechnology medicines for over 100 diseases are in clinical development. However, biological medicinal products are complex and challenging to manufacture and are subject to stringent regulatory requirements before they can be placed on the market. Indeed, bio/pharmaceutical companies have to conduct rigorous pre-clinical and clinical trials ('scientific data') in order to demonstrate the quality, safety and efficacy of the medicinal product

they are seeking to commercialise. It is estimated that it costs in the region of \$1.2 billion to bring a biological medicinal product to the market.

In recognition of the significant investment required by the bio/pharmaceutical companies to generate the necessary scientific data, legislation provides that the scientific data would be protected for a specific period of time during which no applicant would be able to refer to it in support of its own application. This period is referred to as regulatory data protection (RDP) (also referred to as 'data exclusivity' in the US) and is a unique unregistered intellectual property right that benefits companies operating in the bio/pharmaceutical sector.

This article briefly compares the contrasting regulatory approaches towards the protection afforded to biological medicinal products between the EU and US and also assesses the implications of the widely anticipated Trans-Pacific Partnership Agreement.

### What are biologics and biosimilars?

In contrast to small traditional molecules which are typically manufactured by

chemical synthesis, biologics are complex, large-molecule medicines derived from living organisms. Biologics are already being used to treat medical conditions such as cancer and diabetes and may hold the key to unlocking new cures for disease.

Unlike pharmaceutical products, whereby generic medicines are an exact chemical copy of the original, biosimilars can never be exactly the same as the innovative biologic due to inherent differences in the way the products are manufactured. Because they are larger and structurally more complex than traditional 'small molecule' drugs, the development and manufacture costs are considerably greater. For example, in the US, the cancer drug Avastin can cost over \$500,000 per patient per year and the rheumatoid arthritis drug Remicade can cost up to \$2,500 per injection.

As explained below, a biological medicinal product may benefit from a fixed period of RDP which cohabits with other potential IP rights. When the RDP period expires, other companies can apply for a marketing authorisation for their own product by relying upon



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the scientific data of the innovator product under certain conditions and independently of the existence of other IP rights (such as patent protection). In the case of traditional chemical molecules this is known as a 'generic' or an 'abridged' application'. In the instance when the originator product is a biological medicinal product, the procedure is known as a 'biosimilar' application.<sup>7</sup>

### RDP for biologics – EU v US

#### (i) The EU framework

The importance of RDP has been internationally recognised in the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement which entered into force in 1995 and is part of the legal system of the World Trade Organisation. It obligates Contracting Parties to the Agreement to implement protective mechanisms against unfair commercial use of the data submitted by originator companies as a pre-requisite to obtaining marketing approval of pharmaceutical products.<sup>8</sup>

As for any medicinal product authorised in the EU, a biological medicinal product must meet the requirements for the demonstration of quality, safety, and efficacy. A biological medicinal product authorised in accordance with Article 8(3) of Directive 2001/83/EC may serve as a reference medicinal product for the purpose of abridged applications brought by other companies. The data supporting the application will benefit from an eight-year period of RDP running from the date of authorisation in the EEA/EU during which other companies may not use that product as a reference product. In addition, the product will benefit from an additional two-year period of marketing protection. A further one-year period of marketing protection (covering the full dossier) may become available if, within the first eight years from the date of authorisation in the EEA/EU, the MA holder obtains an authorisation for one or more new therapeutic indications. This is known as the '8+2+1 formula'. In practical terms, biosimilar applicants can apply for the marketing authorisation after the 8-year

period of RDP, but they cannot enter the market until marketing protection expires (i.e. 2 or 3 years later). Therefore the EU regulatory framework provides an identical term of RDP for both biologics and traditional chemical molecules.

#### (ii) The US framework

By contrast, in the US, traditional chemical molecules are afforded a period of five years of protection whereas biologics enjoy twelve years. The twelve year data exclusivity period for biologics was established in the Affordable Care Act following intense debate, and has continued to attract criticism. It is argued that in light of the huge costs and resource associated with bringing biological products to market, a twelve year term is justified in order to stimulate continued investment and innovation.

### Scope of protection – general considerations

In addition to the different approaches to RDP/data exclusivity, the global alignment of standards for biologics and biosimilars encompass numerous challenges, such as: marketing authorisation requirements; nomenclature; substitution and interchangeability; and product labelling. An examination of these issues is not within the scope of this article. In both the EU and US, during the term of RDP/data exclusivity, a regulatory authority cannot approve a biosimilar application that relies on the data submitted as part of the original biologic application.

In the EU, it should be noted that the scope of RDP does not prevent a third party (i.e. a company unrelated to the originator company) from submitting its own full stand-alone application with all the necessary scientific data in support of its own product and obtaining an independent period of RDP for the data it has generated.

### The Trans-Pacific Partnership (TPP)

The period of protection afforded to biologics in the US has come under scrutiny and is a major policy issue in the Trans-Pacific Partnership (TPP)

negotiations. The TPP is a proposed free trade agreement being negotiated among the United States and eleven countries across the Asia-Pacific and Latin American regions.<sup>9</sup> Most countries party to the TPP negotiations offer biologics a similar level of data exclusivity as non-biologic medicinal products. The US is the only country in the TPP negotiations that offers greater RDP for biologics. The TPP negotiations have been ongoing for nearly five years and may be concluded in the near term, although several challenging issues remain unresolved. The issue of data exclusivity is likely the most sensitive for negotiating parties and may require political-level decisions to reach final agreement. Under current proposals from the Obama Administration, participating countries would be required to match the US term of twelve years data exclusivity.

The TPP has vast economic implications and it is predicted that once the agreement is finalised it will impact up to one-third of world trade and roughly forty percent of global gross domestic product.<sup>10</sup> It remains to be seen whether participating countries will embrace the merits of additional data exclusivity for biologics, namely that of stimulating continued investment and innovation and thereby creating a harmonised standard across TPP participating countries.

### Conclusion

The protection afforded to the scientific data supporting an application for a marketing authorisation is essential to bio/pharmaceutical companies. The US have acknowledged the significant additional costs incurred by bio/pharmaceutical companies in bringing a biological medicinal product to the market as compared to traditional chemical entities which is reflected by a longer period of RDP of 12 years (as opposed to 5 years for traditional molecules). Therefore, one may be wondering whether the period of RDP provided by the EU system is fit for its purpose (i.e. does it provide an appropriate level of protection to which the biopharmaceutical industry should be entitled to?).

<sup>7</sup> The follow-on compound is referred to as a 'similar biological' or 'biosimilar' in the EU and as a 'follow-on biological' in the US.

<sup>8</sup> Article 39(3) Trade-Related Aspects of Intellectual Property Rights (TRIPS). The TRIPS Agreement is Annex 1C of the Marrakesh Agreement Establishing the World Trade Organization (WTO), signed in Marrakesh, Morocco on 15 April 1994.

<sup>9</sup> The participating countries include: Australia, Brunei, Canada, Chile, Japan, Malaysia, Mexico, New Zealand, Peru, Singapore, and Vietnam.

<sup>10</sup> [www.brookings.edu/blogs/health360/posts/2015/05/19-trans-pacific-partnership-prescription-drugs](http://www.brookings.edu/blogs/health360/posts/2015/05/19-trans-pacific-partnership-prescription-drugs)

# Competition



## Our competition practice

Our lawyers are recognised as experts in both national and EU competition law, with a long track record of representing clients before the competition authorities and courts in Brussels, Luxembourg and the UK. Drawing on the firm's wider IP and technical expertise, we advise on everything from current licensing policy through to dealing with competition investigations and the latest changes in competition law.

## Protecting innovation in the life sciences – a new focus for merger control?



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**Last year's upturn in merger and acquisition activity in the life sciences sector has led to some interesting developments in EU merger control<sup>11</sup>. One particular trend of note for those in the biotech sector is the European Commission's renewed focus on the competitive impact of proposed deals on pipeline products and innovation incentives, as discussed below.**

The Commission's recent approval of the multi-billion euro deal between Novartis

AG (Novartis) and GlaxoSmithKline plc (GSK) marked a development in the Commission's approach. The three-part inter-conditional transaction which completed in March 2015 involved the creation of a consumer healthcare joint venture, under the sole control of GSK; the acquisition of Novartis' non-influenza vaccine business by GSK; and the acquisition of GSK's oncology business by Novartis.

All parts of the Novartis-GSK deal were approved by the Commission in January 2015, subject to certain conditions<sup>12</sup>. It was the sale of GSK's oncology business, however, which saw the Commission focus heavily on the effect on early stage pipeline products, not just the more developed drugs in the companies' portfolios. The Commission was concerned that the sale of the oncology business could lead to a reduction in competition and innovation for several cancer treatments.

First, in the Commission's opinion, the deal as notified would have led to a reduction in the number of companies developing and marketing products used for the treatment of skin cancer,

leading to a duopoly between the merged entity and Roche. In reaching this conclusion, the Commission distinguished between targeted cancer therapies (such as those held by both of the merging companies) and other immuno- or chemotherapies.

Although no final decision on market definition was reached, the Commission maintained its approach of considering competitive impacts on narrowly-defined markets by considering monotherapies and combination treatments for the same cancers to fall into separate markets. The Commission reasoned that the trend towards the use of combination treatments for certain cancers means that such treatments were to be considered as complimentary to monotherapies, rather than competing with them.

The stage of product development was also relevant to this analysis. For example, the merging parties' combination skin cancer treatments were at a similar phase of development, with both companies having potentially ground-breaking therapies in Phase III clinical trials. These products were found to be in competition, along with a

## Competition

close-to-market combination treatment developed by Roche. Competition in this market, however, was found not to be constrained by similar products at earlier stages of development. Given its competitive analysis, the Commission concluded that the transaction was likely to lead to the abandonment of Novartis's pipeline products resulting in lessening of competition in the market.

The Commission's approach demonstrates a willingness to intervene where innovation may be stifled, and represents something of a departure.

Second, the Commission queried the long term impact on innovation and on the development of future markets. The principal active ingredients of the same skin cancer treatments were also being developed by the merging parties for the treatment of other cancers. For the treatment of ovarian cancer, where both companies had therapies in Phase III clinical trials, a traditional analysis of the sources of potential and actual competition to the products under development was carried out. For the treatment of other cancers, where both companies had therapies in Phase I and II clinical trials, the Commission instead considered the companies competing clinical research programmes which it defined as those with *"R&D efforts aimed at developing substitutable products and having similar timing"*.

The market investigation indicated that GSK and Novartis had two of the three research programmes based on the relevant principal active ingredients. The Commission was therefore concerned that bringing the research programmes together under sole ownership would lead to the abandonment of one of the programmes, resulting in a lessening of competition in future product markets and higher prices for patients and healthcare systems. Even if there remained some incentive for the acquirer (Novartis) to develop the

programmes in parallel, the Commission had a concern that investment in late-stage clinical trials (which are typically carried out to differentiate treatments from competing products on the market) would be reduced. This would result in a reduction in the variety of treatments available to patients, for example in terms of tolerability and safety profile.

The Commission concluded that, despite the uncertainty faced by pipeline products at early stages of clinical trials, the transaction would lead to a lessening of competition. In particular, there would be reduced incentives for research programmes to be run in parallel, leading either to the abandonment or at least a significant reduction in current R&D efforts.

To ease these concerns and to *"protect innovation"* the Commission approved the transaction subject to the commitments pledged by Novartis, namely the divestiture of two Novartis cancer treatments which were in early stages of development. In particular, Novartis returned rights to one cancer drug to its owner Array BioPharma Inc. and divested another drug to the same company. The Commission's approach demonstrates a willingness to intervene where innovation may be stifled, and represents something of a departure from past practices – traditionally, only divestitures of products already on the market or at a later stage of development have been required.

The development in the Commission's approach can also be noted in its approval of the acquisition of Shire Inc by AbbVie Inc. (the deal had been notified for merger clearance, even though it ultimately fell through). In this decision, the lack of overlapping pipeline products was explicitly cited as part of the reason for its approval.

The Commission's Director General for mergers, Carles Esteve Mosso, is reported as having acknowledged this shift, stating that the Commission would be ready to intervene where it can see the *"impact of how a merger affects an investigation [in the] earlier stages"* of drug development<sup>13</sup>. This is

not a wholesale change in policy, and it should not necessarily be expected that the Commission will always need to look at early stage pipeline products.

That said, we can expect to see more focus on products in clinical trials and on innovation incentives in future merger investigations by the Commission. Parties contemplating transactions in this area should consider possible overlaps in pipeline products at an early stage in order to plan an effective merger clearance strategy.

<sup>11</sup> See for example the Commission's decisions in Novartis/GSK (M7275 and 7276), Mylan/Abbott Laboratories (M7379), Zimmer Holdings/Biomet (M7265), Becton Dickinson and Company/CareFusion (M7459) and Actavis/Allergan (M7480).

<sup>12</sup> Case M.7276 – GlaxoSmithKline/ Novartis Vaccines Business (Excl. Influenza)/ Novartis Consumer Health Business; Case M.7275 – Novartis/ GlaxoSmithKline Oncology Business.

<sup>13</sup> Speaking at the Sixth Annual Chicago Forum on International Antitrust Issues. Information based on a report of the event provided by Mex.

# Commercial

## Our commercial practice

Consistently ranked among the world's top IP firms, Bristows has a wealth of experience in handling a wide range of deals involving intellectual property rights. Our clients range from multinational household names to small startups, and they seek our advice on protecting and extracting value from their most valuable assets – their inventions and ideas, their brands, their reputation, their secrets and their designs.

## UK approves three person babies



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**Dr Sahar Shepperd**  
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This was the headline on many of the front pages and news broadcasts at the beginning of 2015. A phrase that, when read on its own, suggests an almost unethical scenario.

The reality is that the UK took a bold and much appreciated step to prevent the inheritance of deadly genetic diseases by passing the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (the "Regulations"), which came into force on 29 October 2015.

Mitochondrial diseases, inherited from the mother, affect at least 1 in 200 children in the UK, with 1 in 6500

developing serious mitochondrial disorders. The effects can be devastating, with symptoms that can include heart problems, diabetes, loss of movement, weak muscles and sometimes death. Mitochondria are the 'power houses' inside our cells – small structures that generate energy to fuel our bodies. They contain a very small amount of DNA which controls mitochondrial function and which is separate from DNA in the nucleus of a cell, the DNA which determines our physical characteristics and personalities. It is genetic faults in the mitochondrial DNA which cause mitochondrial disease.

Two new mitochondrial donation techniques have been developed to prevent a mother from passing mitochondrial DNA disease to her child. Currently these techniques can only be used in research and the Regulations now pave the way for the technique to be used in IVF. The nucleus is removed from an egg that contains faulty mitochondria and is placed into a donor egg with healthy mitochondria (the donor egg has had its nucleus removed). The child will have the same combination of nuclear DNA from both

parents as it would otherwise have done and is far from the 'three person baby' that some of the headlines suggest. In fact, the mitochondrial DNA that the baby will have from the donor is only 0.1% of the total DNA in the cell.

The Human Fertilisation and Embryology Authority ("HFEA") convened an expert review panel which conducted three separate reviews, none of which found any evidence suggesting the techniques would be unsafe when used in a clinical setting. Practitioners will have to obtain a licence from the HFEA to use the techniques in patients, and it will be up to the HFEA to assess which clinics should be allowed to offer mitochondrial donation – something that will be followed in the coming months and years with interest.





## Commercial

## Protecting biological resources – implementation of the Nagoya Protocol in Europe



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**With the EU Regulation 511/2014 related to the Nagoya Convention in force, companies working with nature-based ingredients (the food and feed industry, the pharmaceutical and cosmetics industry, and more) must review and adapt their relevant practices and policies to ensure they are Regulation-ready.**

There is no doubt that the world's diverse biological resources are vital for social and economic development. Accordingly, players in the pharmaceutical market are no strangers to conducting nature-based research and including in their products active ingredients derived from living organisms, such as rare plants and microorganisms, in some instances originating from remote parts of the world. With the growing commitment to sustainable development and the need to safeguard the interests of communities that provide such biological resources or contribute traditional knowledge about them, attempts have been made to give these communities (often located in developing countries) the authority to control access to these resources. In return, the communities receive a share of the rewards reaped by the organisations (often based in developed countries) that are developing and commercialising these unique biological assets.

The International Convention on Biological Diversity (the "Convention") was adopted

in 1992 to provide a legal framework for access to genetic resources and for sharing any benefits (monetary or otherwise) arising from the utilisation of such resources with the providing states. The follow-on Nagoya Protocol (the "Protocol") was adopted on 29 October 2010 by the signatories to the Convention in an attempt to clarify the Convention and facilitate its implementation into signatories' national law.

The European Union and its Member States are parties to the Convention. The EU Regulation No. 511/2014 (the "Regulation"), which entered into effect on 12 October 2014, brings EU law in line with the framework agreed at Nagoya. Given its potentially far-reaching impact on research (academic or otherwise), some breathing space was provided, such that some of the Regulation's key provisions did not apply until one year after it came into force.

### (i) Rationale

The objective of these legal instruments is: (i) to ensure the conservation of biological diversity and the sustainable use of its components by giving the countries providing genetic resources and any traditional knowledge associated with such genetic resources (also referred to as 'associated traditional knowledge' ("ATK")) control over access; and (ii) to ensure that the providers receive fair and equitable compensation or benefit if genetic resources are exploited, particularly on a commercial basis. The Convention refers to this exploitation as "utilisation" of the genetic resources, and the Protocol and Regulation define "utilisation" as "to conduct research and development on the genetic and/or biochemical composition of genetic resources".

### (ii) Scope

The Regulation applies to "genetic resources" which it defines as "genetic material of actual or potential value". "Genetic material" is "any material of plant, animal, microbial or other origin containing functional units of heredity". ATK is defined as the "traditional knowledge held by an indigenous or local community that is relevant for the

utilisation of genetic resources and that is as such described in the mutually agreed terms applying to the utilisation of genetic resources". (Although somewhat helpful, this still does not explain what 'traditional knowledge' is).

Excluded from the Regulation's scope are human genetic resources and genetic resources obtained from beyond national jurisdictions (e.g. the high seas). The Regulation also makes it clear that, in a manner similar to the Protocol, the Regulation does not apply to genetic resources, where access is governed by other international instruments. For example, it does not apply to the sharing of influenza viruses of human pandemic potential and access to vaccines for such strains, as this is governed by the pandemic influenza preparedness framework (PIP Framework).

### (iii) Core Obligations of Users of Genetic Resources/ATK

The Regulation obliges users (natural or legal persons) of the genetic resources and/or the ATK ("Users") to exercise due diligence to ascertain that the genetic resources and any ATK are being accessed in accordance with applicable legislation or regulatory requirements, and that benefits are fairly shared upon mutually agreed terms. This due diligence obligation applies to all Users irrespective of size. Notable Users would be the food and feed industry, the pharmaceutical and cosmetics industry, and academic researchers.

In order to comply with this obligation, Users are required to seek and keep (for 20 years) (and to require any subsequent Users to seek and keep) an internationally recognised certificate of compliance. Where such certificate is not available, Users must seek and keep:

1. the date and place of access to genetic resources or any ATK;
2. the description of utilised genetic resources or any ATK;
3. the source from which the genetic resources or any ATK were obtained;





4. the presence or absence of rights and obligations regarding access and benefiting sharing;
5. access permits, where applicable; and
6. any additional terms, if any that were agreed between the User and the provider of the genetic resources and/or the ATK.

The Regulation recognises that there may be some uncertainty amongst Users as to the exact measures required to comply with this obligation and, therefore, provides for associations of Users to submit their notions of what constitutes best practice for consideration by the Commission. It also encourages Users to be guided by such accepted best practices.

#### (iv) Monitoring Compliance by Users

Users' compliance will, in the first instance, be monitored by competent authorities appointed by Member States.

At identified points in the chain of activities which constitute "utilisation", a User of the genetic resource/ATK is required to declare to the relevant competent authority that it has exercised due diligence and to also provide supporting evidence. Suitable points of declaration identified in the recitals to the Regulation include when Users receive research funds and at the final stage of development of the product (which the Regulation envisages to be before requesting marketing approval).

The final stage of development of a product may differ substantially depending on the market sector and, so, there is room for the Commission to use its implementing powers, as and when needed, to identify a final stage of development in a particular sector.

In addition to the absolute declarations on the part of the User, the appointed national competent authority can also carry out checks (including on the spot checks) to verify User compliance. The frequency of such checks is presently unclear, but Member States are required to ensure that the checks are

proportionate and dissuasive.

#### (v) Enforcement

Users who fail to comply with the requirements imposed by the Regulation will face penalties which are set by Member States. The Regulation envisages that these penalties should be effective, proportionate and dissuasive. In the UK, civil and criminal sanctions for non-compliance with the Regulation are set out in the Nagoya Protocol (Compliance) Regulations 2015 (SI 2015/821). Civil penalties include being issued with a compliance notice, a stop notice or a variable fine. Guidance regarding the use of these civil sanctions will be published in due course. Criminal offences comprise failure to comply with such notices, obstructing inspectors or failure to retain the information listed at (iii) above. Criminal penalties include fines from £5,000 up to an unlimited amount and imprisonment of between three months' to two years depending on the particular offence. Compliance will be enforced by the National Measurement and Regulation Office. It will be interesting to note the approach it takes.

#### (vi) Comment

According to a review by the Department for Environment, Food and Rural Affairs, the volume of use of genetic resources and ATK amongst the main affected UK sectors is up to 90,000 transactions per year in the largest organisation<sup>14</sup>. Although most companies working with nature-based ingredients already have ethical sourcing practices in place, in light of the relatively low-profile with which the Regulation came into force, it would be prudent for such companies to now review and adapt their relevant practices and policies to ensure they are Regulation-ready.

Unsurprisingly, the Regulation is not without its controversy and has been criticised as being excessively burdensome and bureaucratic with a possible knock-on chilling effect on innovation. The main objection raised by different organisations is that, in practice, compliance with the Regulation's due

diligence requirements is onerous as a company may be working with a significant number of genetic resources at any one time. Keeping a document trail, particularly of every line of plant used in a breeding program, for example, may be practically impossible. For example, German and Dutch associations of plant breeders sought annulment of the Regulation before the Court of Justice of the EU (Cases T-559/14 and T-560/14, respectively), albeit both challenges were ruled inadmissible.

There is some respite; the Regulation will not have retrospective effect and the provisions dealing with the obligations of Users (Article 4), the monitoring of User compliance (Article 7) and checks on User compliance only took effect on 12 October 2015.

Additionally, the Regulation attempts to alleviate administrative and compliance requirements by providing a framework for the establishment of a Commission-run, internet-based register of collections of genetic resources. A register would arguably lower the risk of the supply or use of genetic resources where evidence of legal access is inconclusive or lacking. According to the recitals to the Regulation, Users that obtain a genetic resource from a collection included in the register will be considered to have exercised sufficient due diligence. Such a collection of genetic resources will be particularly useful for those conducting nature-based research on a smaller scale such as universities and small and medium-sized enterprises.

Given its vast scope and far-reaching impact, we expect a fair amount of interest and commentary on the Regulation from Users and industry organisations across Europe over the coming months.

<sup>14</sup> See: [http://randd.defra.gov.uk/Document.aspx?Document=10322\\_WC1016\\_Non-technicalsummary.pdf](http://randd.defra.gov.uk/Document.aspx?Document=10322_WC1016_Non-technicalsummary.pdf)

## Commercial

## Nanorobotics



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**Nanorobotics, the category of machines or robots whose components are at or close to the scale of a nanometre, is an emerging technology in the field of medical-use robotics with a potentially huge impact.**

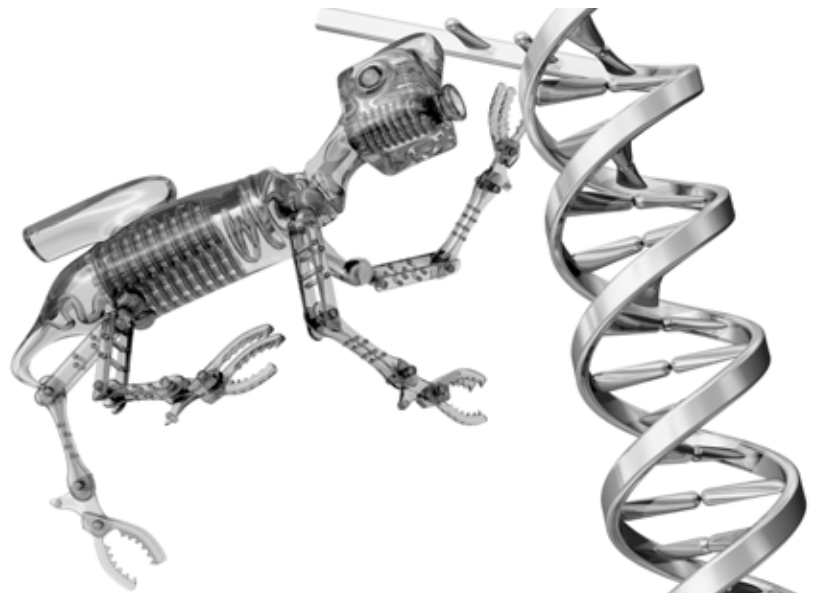
Nanorobots may be deployed across a range of disciplines, but their first useful applications are likely to be in medicine: tiny biological machines which identify and destroy cancerous cells, molecular machines for drug delivery, and devices sent into the body to carry out targeted surgery are a few examples. They are also likely to play an important role in wider genomics and brain-mapping initiatives. Given their microscopic size, potential medical applications involve large numbers of nanorobots working together to perform tasks.

Although still in the research and development phase, there is sufficient enthusiasm and investment across the public and private sectors to suggest nanorobotics will represent an important development in medical evolution.

### Regulation and Ethics

A key issue regarding most emerging technologies is how they will be regulated. Will existing law and regulation suffice or do we require new product or sector-specific regulation? The approach thus far appears to have been to control nanorobotics under existing regulation. This approach presents several issues.

The US regulates nanotechnology by reference to size and delivery method, so nanotech acting through chemical means is regulated as drugs while those acting by physical means are regulated as devices. In the EU, nanomedicines are considered within existing guidelines, either as a medicinal product or a medical device (although in 2014 the EU Commission published guidance on the assessment of



potential risks posed by nanotechnologies used in medical devices). However, as the technology becomes more complex, and single forms of nanotech comprise both physical and chemical elements, it may be unclear which regulations apply.

To the extent nanorobots are products, manufacturers may be strictly liable.

The question of whether any particular application is a drug or a device has implications not only for how its use is controlled, but for how the application is released into the market (generally drugs undergo slower, more expensive testing than devices, and regulatory pathways for devices are simpler than for drugs).

It is likely that nanomedicines, as specialised delivery systems for active pharmaceutical ingredients, would be classified as medicinal products. However, nanorobots of the future would likely be very different and may not include a biologically active chemical. As such, we should not rule out their being regulated as medical devices in future

or even new regulations being created to deal with them. Guidance may also need to be issued.

### Liability

A sound regulatory framework would mitigate the risks associated with nanorobotics. However, regulation will never completely remove that risk and, as in other areas of medicine, things inevitably go wrong. A key area of debate is the liability of the various players given it may not be clear who or what caused the harm. To the extent nanorobots are products, manufacturers may be strictly liable under existing product liability law. Implementers and administrators of the technologies (such as clinicians) may be liable in negligence. The preferred approach is to mitigate liability/litigation risk by ensuring the health risks are understood prior to use of the technology and, where harm does occur, to have strong remedies available.

The incentive for producers to avoid negative effects is clear, and it is not uncommon for scandals involving medical products to have a chilling effect or result in a moratorium on their use. Parallels can be drawn between the current state of nanorobotic technologies and previous technologies that became widely adopted before health risks were detected, such as asbestos, the health

# Tax

risks in which only came to light (or in some cases were deliberately held back) once significant damage had been caused. The nanorobotics industry should learn from this and ensure safety is not sacrificed for innovation or time-to-market.

## Intellectual Property

As primarily functional objects, the main IP right of interest in nanorobots is patents. As the technology becomes more widely used, questions of interoperability and standard essentiality may arise. Access to the IP rights in this technology may need to be made widely available to ensure users are not 'locked' into a particular manufacturer's system and that competing producers are able to benefit. Parallels can be drawn with existing standard essential patents in the medical and technology spheres and which in many cases must be licensed to third parties on fair and reasonable terms. Further, it is likely that nanorobots will fall foul of the European exception to patentability for methods of treatment, diagnosis or surgery (but will still be protectable both as pure products and as products for methods of treatment, diagnosis or surgery). Any dilution of the extent of IP protection available to nanorobotics is likely to be a significant factor in the assessment of the value of the IP in this technology, and therefore the technology itself.

## Conclusion

As we've seen, nanorobotics involves the injection of robotic systems into the body. While invasive devices have long been a part of medicine, one of the possibly unique aspects of this technology is the extent of that invasion. It is therefore clear that nanorobotics gives rise to important legal, ethical and social questions that will probably not be fully resolved before it becomes commonplace. The key for manufacturers will be to understand, manage and mitigate the risks while maintaining the incentives needed for a viable business model. The key for regulators will be to keep up with the pace of take-up in this area and to strike the appropriate balance between regulation and encouraging innovation, since both are required to deliver the advances promised by nanorobotics.



### Our tax practice

Our tax experts enable clients from multi-nationals to start-ups to minimise tax exposure and do business while complying with the UK's maze-like tax system. We offer advice on the full range of tax issues affecting corporates, including VAT, stamp duties and other specialist areas. Core areas of expertise include helping clients, both UK based and overseas to structure corporate and commercial transactions.

## Tax developments in 2015



**Samuel Rippon**  
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Bristows LLP

**Tax continues to be in the news both in the UK and elsewhere and the recurring themes are avoidance, evasion, so-called sweetheart deals and international tax structures.**

In the past, the apparent focus of the UK government has been to cut tax rates (now 20% in the UK, the lowest it has ever been and significantly lower than many other major EU jurisdictions), to increase tax reliefs (such as R&D reliefs, now in the form of the research and development expenditure credit (RDEC)) and encourage investment (e.g. through the increased annual investment allowance for capital allowances). However, recently there has been a shift towards more aggressive means of reducing alleged tax avoidance and the introduction of methods to encourage people to pay a 'fair' amount of tax. One of these has been the OECD's BEPS (Base Erosion and Profit Shifting) project, which counts among its activities a project to look at

whether redefining some international tax definitions might bring the jurisdiction in which tax is paid more in line with the jurisdiction in which the related economic transactions take place.

The UK has taken a more significant (and extreme) step by introducing a new tax – the Diverted Profits Tax (DPT) with effect from 1 April 2015. This tax is intended to apply to the types of companies that engaged in the much talked about 'double Irish' structure, but, as is always the case with broad sledge-hammer measures, it carries the risk of a much wider impact. Life sciences businesses and patent rich companies should always explore options for maximising tax benefits (such as patent box), but this tax might have unpleasant hidden surprises.

The effect of the DPT is that the profits that have been 'diverted' from the UK using contrived arrangements to a jurisdiction with a low(er) rate of tax are actually taxed in the UK at 25%. The Treasury is of the view that there is not (and, seemingly, that there should not be) any possibility of relief against double taxation in respect of DPT (i.e. where both the UK and an overseas jurisdiction tax the same profits). There are limited exemptions to the DPT, but the most significant is that it does not apply where the company which has

## Q&amp;A with Anne Lane

## Q&amp;A

'diverted' profits (when taken together with its associated companies) is (or are) small or medium sized enterprises. The reason that this could be of particular concern to companies in the life sciences sector is that the draft guidance on the DPT published by the Treasury in March 2015 contains two examples which specifically mention IP holding companies. IP holding structures are common in both the pharmaceutical and medical devices sectors, in addition to countless other situations where a lot of value is derived from originating IP (whether patents, design rights or trade marks).

Both examples in the guidance involve IP holding companies established outside the UK (in a low tax jurisdiction) licensing that IP back to the UK. However, the first example combines this with R&D activities being carried out in the low tax jurisdiction and IP being licensed to other companies in the group (outside the UK). In the second example the IP holding company only provides IP protection and management activities in relation to the IP and takes the associated risk of ownership. The guidance concludes that the first example is a non-offensive arrangement to which the DPT does not apply. But, the second example is alleged to give rise to profits being diverted from the UK to the low tax jurisdiction and is a situation (assuming that the other relevant conditions are met) where the DPT would apply to tax those 'diverted' profits in the UK. This second example is not an uncommon situation and therefore some very careful thought needs to be given to any such structures before putting them in place.

At this stage we don't have a clear idea how much grey area there is between the two examples set out above and therefore where HMRC draws a line between the profits that have been 'diverted' using contrived arrangements and those that have not. However, the current draft guidance suggests that no businesses are immune from the reach of DPT and there are risks for companies outside the original target sector of international technology companies.



**Anne Lane**  
Executive Director  
UCLB

**Anne Lane is Executive Director of UCLB, acts as Director and interim CEO on several of UCLB's spinout companies and oversees the company's licensing activity. Anne is also on the committee for the Intellectual Property Lawyers Organisation (TIPLIO). She has a PhD in medicine from UCL and an Executive MBA from Molson Business School, Montreal. After conducting research at UCL and Harvard Medical School, Anne worked for RTP Pharma Inc in Montreal, out-licensing and preparing valuations of the company's portfolio for public listing. Anne joined UCL Ventures in 2000 and acted as consultant for the National Transfer Centre in the US.**

All views and opinions expressed in this article are personal to Anne Lane and do not necessarily reflect those of UCLB.

**Q How long have you worked at UCLB for?**

**A** I have worked for UCLB since 2006, but have worked in technology transfer at UCL since 2000.

**Q What does your role at UCLB involve?**

**A** I oversee the two technology transfer groups (life and physical sciences) and legal team. I am also a board director.

**Q What have been the highlights of your current role?**

**A** Having a key input into the strategic development of UCLB and also technology transfer within UCL itself. Also seeing some of the excellent research at UCL having a real impact, both in the UK and internationally.

**Q What challenges do Technology Transfer companies face?**

**A** Limited budgets, access to investment funds, maintaining strong and healthy relationships with the academic research base, and the universities they serve.

**Q What is the most difficult thing about your job?**

**A** Communicating between industry and academia – a TTO is always in the middle!

**Q What changes do you see happening in the Life Sciences space in the next 5-10 years?**

**A** Much more development in the areas of gene therapies and personalised medicine.

**Q What advice would you give to a novice in your sector?**

**A** Try and talk to someone who has had both a good experience and a bad experience with a TTO, so you can see what works and what doesn't. Don't be afraid to ask questions and ask for advice.


**Q Do/did you have one or many mentors? Or do you mentor anyone?**

**A** Nothing official, but I do try and ask advice from people both in industry and academia whose opinion I respect.



# Quick facts

about our life sciences practice



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

Our clients range from multinational pharmaceutical and biotech companies and medical device manufacturers to universities, SMEs and technology start-ups, private equity and venture capital investors.

Our clients come to us for advice on a wide spectrum of IP issues including patents, trade marks and licensing, freedom to operate opinions, collaborations, mergers and acquisitions, financings and the coordination of disputes in multiple jurisdictions.

The Bristows' life sciences team is among the largest in Europe comprising 20 partners and 47 associates, many with backgrounds in chemistry, biochemistry, engineering, genetics and neurosciences as well as law. They include some of the UK's leading practitioners in this sector.

# Editorial team



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**Liz Cohen**

Partner

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Liz specialises in intellectual property matters with a particular focus on patent litigation. She has over 14 years experience of representing clients in patent matters in the English Courts and has also represented clients in the UKIPO and EPO. Liz's background in Natural Sciences provides her with an excellent understanding of the technical and commercial issues facing the life sciences sector in particular.



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**Dr Robert Burrows**

Partner

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Robert advises on patent and other IP litigation matters in the UK, particularly for clients within the life sciences sector. Many of the cases he has managed in recent years have required the coordination of parallel proceedings in multiple jurisdictions within Europe and elsewhere in the world.



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**Dr Laura von Hertzen**

Associate

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Laura specialises in intellectual property dispute resolution, with an emphasis on patents. Laura advises across all industries, with a focus in the life sciences sector. Her extensive scientific background provides her with a valuable understanding of the technical issues that can underlie intellectual property matters, particularly in the pharmaceutical and biotechnology fields.

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