WHAT PRACTITIONERS NEED TO KNOW ABOUT PATENT INVALIDITY AT THE FEDERAL CIRCUIT

Sterne Kessler's Michael Joffre, Anna G Phillips and David M Silversmith examine the strategic implications of recent Federal Circuit decisions on the validity of life science patents

Recent Federal Circuit decisions have made it easier than ever to invalidate patents in the life sciences space. It is therefore prudent for those involved in patent litigation to take account of the three main strategies that have been used to successfully challenge patent validity:

- patent eligibility under 35 USC (§101);
- written description under 35 USC (§112); and
- obviousness under 35 USC (§103).

In order to assess each strategy, it is key to analyse one recent Federal Circuit case where a patent challenger successfully invalidated a patent claim and one where the patent challenger was unsuccessful. These cases and strategies will undoubtedly have implications on life science patents moving forward.

Patent eligibility

The patent eligibility doctrine prevents an inventor from obtaining a patent on laws of nature, natural phenomena and abstract ideas. The rationale is that no individual should be able to prevent others from using such fundamental concepts, including when coming up with new innovations. Patent eligibility is now often a threshold issue in

litigation that may bar patentees from progressing to trial. Accused infringers frequently challenge whether a patent is valid under Section 101 at the motion-to-dismiss phase.

Two recent Federal Circuit cases on dietary supplements shed light on how to defend against or attack patents under Section 101.

In *ChromaDex Inc v Elysium Health Inc*, the Federal Circuit considered ChromaDex's patent claims on dietary supplements containing isolated nicotinamide riboside (NR) – a form of vitamin B3 present in cow's milk (59 F4th 1280, Federal Circuit 2023). When ingested, cells convert NR into the chemical NAD+, and NAD+ deficiencies can cause disease in both animals and humans. On summary judgment, the district court found ChromaDex's claims invalid under Section 101, finding that they were directed to a natural phenomenon.

On appeal, the Federal Circuit addressed whether the claims were directed to a product of nature or something more. The court concluded that the claimed isolated NR was not "markedly different" from non-isolated NR that is naturally present in milk. Indeed, ingesting milk increases NAD+ levels in animals. The act of isolating NR from its natural state does not confer patent eligibility. Accordingly, the court held that ChromaDex's claims were directed to a product of nature, which is prohibited under Section 101 jurisprudence. While ChromaDex argued that isolated NR had advantages over naturally occurring NR and milk, the court dismissed this argument for the simple reason that the asserted composition claims did not claim any of these advantages.

In contrast to *ChromaDex*, the patent owner in *Natural Alternatives International Inc v Creative Compounds LLC* did claim the differences between naturally occurring amino acids and those used in its dietary supplements, thereby defeating a Section 101 challenge (918 F3d 1338, Federal Circuit 2019). The patent owner, Natural Alternatives, had method and composition claims covering the use of a naturally occurring amino acid, beta-alanine, in a dietary supplement intended to increase the anaerobic working capacity of muscle. The district court ruled, on a motion to dismiss, that the claims were invalid.

The Federal Circuit reversed this decision. While the claims capitalised on a natural phenomenon – that combining beta-alanine with certain other amino acids results in increased anaerobic working capacity – the court nonetheless deemed these claims patent eligible. Many of the claims were for a method of treatment that required administering specific dosages in a particular dosage form to bring about a certain reaction that altered the patient's natural state. Moreover, there was a factual question as to whether providing the beta-alanine amino acid in a dietary supplement was a conventional, well-known method. When there are factual disputes about the conventionality of claims, usually these questions will be enough to survive a motion to dismiss challenging them under Section 101.

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Similar to the method claims, the composition claims required specific treatment formulations that incorporated the beta-alanine in specific amounts to "effectively increase [...] athletic performance". Thus, the court held that the claimed characteristics provided "significant utility" — namely, they described the use of beta-alanine in a way that resulted in specific results that could not be achieved by natural beta-alanine.

The difference between *ChromaDex* and *Natural Alternatives* comes down to the fact that the patent owner in *Natural Alternatives* claimed specific treatment formulations and dosages that were used to elicit certain results that could not be achieved with the naturally occurring product by itself. In other words, claims that are susceptible to patent eligibility attacks likely do not transform the law or product of nature into a useful application.

Written description

Another trend in attacking the validity of life science patents has been to question whether the patent's written disclosure sufficiently describes the full scope of the invention. In the life sciences space, this issue often arises when claims are written to cover a broad genus, such as a genus of compounds, enzymes or amino acids.

When a patent claims a genus, the accompanying written description must either describe the invention literally or contain so-called 'blaze marks' sufficient to guide a skilled artisan to the claimed invention. Specifically, this means that the patent disclosure should provide at least a few representative examples that fall within the claimed genus or describe structural features common to the genus with enough precision that a skilled artisan can visualise or recognise its members. A broad outline of the genus is insufficient to meet the requirements of Section 112.

Regents of the University of Minnesota v Gilead Sciences Inc is one example where the written description of the patent failed to literally describe or sufficiently provide blaze marks to outline the bounds of the claimed genus (61 F4th 1350, Federal Circuit 2023). The patentee claimed a genus of chemical compounds — prodrugs of nucleoside derivatives that prevent viruses or cancerous tumours from reproducing. The PTAB found that the patent was not entitled to an earlier-filed application's filing date because the application's written disclosure did not support the claims. As a result, the PTAB found that the patent was anticipated.

The Federal Circuit agreed. It held that instead of providing blaze marks indicating the bounds of the claimed genus, the written disclosure "recite[d] a compendium of common organic chemical functional groups, yielding a laundry list disclosure of different moieties for every possible chain or functional group". Such a broad disclosure failed to clarify how many compounds fell within the genus. The recitation of structural features of the genus were, in the court's determination, too varied to be sufficiently common to its members. As a result, the written description did not support the claims.

A good example of using at least one sufficient blaze mark is *Pharmacyclics LLC v Alvogen* (2021-2270, 2022 WL 16943006, Federal Circuit, 15 November 2022). At a bench trial, the accused infringer argued that the claims were invalid for lack of written description, but the district court ruled that they were valid.

On appeal, the Federal Circuit affirmed, asserting that the patent's written description adequately supported a method-of-treatment claim. The claim covered the use of a genus of BTK inhibitors in treating relapsed or refractory mantle cell lymphoma (R/R MCL). Alvogen argued that the claim lacked written description for failing to describe the inventor's preferred BTK inhibitor. The court disagreed because the specification provided sufficient blaze marks to guide a skilled person to the appropriate BTK compound, ibrutinib, that treats R/R MCL in accordance with the claim requirements. The written disclosure specifically identified ibrutinib by name and was the only BTK inhibitor identified for the treatment of R/R MCL. The claim also required a specific dose of the inhibitor to treat the condition. This too, was sufficiently supported by the written disclosure because the claimed dose was provided in the specification, including in an example describing a clinical trial protocol for the treatment of R/R MCL using a BTK inhibitor.

The bottom line is that when a patent broadly claims a genus, it is imperative to pay attention to any potential blaze marks or examples that could define the genus' bounds. If, like in *Regents*, the disclosure provides varied options or a list of possibilities, the claim is at risk of lacking sufficient written description. On the other hand, while the disclosure in *Pharmacyclics* provided an example of a claimed genus sufficient to survive a written description challenge, the risk in providing only one example is that the court may limit the invention to only that example.

Obviousness

Patents must claim a non-obvious invention, meaning that people in the relevant field would not find it to be a readily apparent extension of the knowledge already available. To that end, when multiple publications dated before the invention disclose elements of the claimed invention, the patent may be found invalid as obvious. In such instances, the inquiry is whether:

- the combination of publications disclose the invention;
- a skilled artisan in the field would be motivated to combine the publications' teachings; and
- the skilled artisan would have a reasonable expectation of success in making the invention based on the publications' teachings.

If so, the patent claim may be found obvious.

More and more, the Federal Circuit is putting emphasis on the motivation to combine and reasonable success requirements of the obviousness inquiry. In *Best Medical International Inc v Elekta Inc*, the PTAB found that the patent claims at issue were obvious (46 F4th 1346, 1349, Federal Circuit 2022).

On appeal, the Federal Circuit focused on whether there was a motivation to combine the teachings of two publications, Carol and Viggars, that together would reasonably result in the claimed invention. The court affirmed the PTAB's finding that there was a motivation to combine, rendering the claims obvious.

The patent claimed a method to calculate an optimal radiation beam arrangement to treat tumours while minimising radiation to other parts of the patient. Carol disclosed a radiation treatment programme, while Viggars described a computer program that evaluated whether a planned dose of radiation would be clinically acceptable. After determining that both publications disclosed every element of the claims, the court considered whether a skilled artisan would have reason to combine them. Viggars stated that its evaluation program could be used to decide whether a particular treatment programme was acceptable, which was reason enough for the court to believe that there would be motivation to combine it with Carol's treatment optimisation programme. Moreover, Viggars stated that its treatment evaluation program had already been successfully integrated with a commercial treatment planning system, demonstrating a reasonable expectation that it was possible to successfully integrate the teachings of the two references.

By contrast, the Federal Circuit's ruling in *Mylan Pharmaceuticals Inc v Merck Sharp & Dohme Corp* shows how a lack of motivation to combine with a reasonable expectation of success can result in a finding that the patent is not obvious (50 F4th 147, 156, Federal Circuit 2022). The patent was directed to a salt of sitagliptin, which is a compound used to treat Type 2 diabetes. Sitagliptin belongs to a class of enzyme inhibitors known as DP-IV inhibitors. Claim 3 of the patent recited a specific form of the sitagliptin salt, and Claim 4 recited a monohydrate form of sitagliptin salt. The PTAB held that the claims were not obvious in light of the prior art.

On appeal, Mylan argued that the patent claims would have been obvious over three publications: Edmondson, Brittain and Bastin. Edmondson discussed certain DP-IV inhibitors useful in the treatment of Type 2 diabetes and disclosed a genus of DP-IV inhibitors and 33 species in that genus, including sitagliptin; Brittain described the pharmaceutical importance and prevalence of crystalline hydrates of pharmaceutical compounds and Bastin disclosed salt selection and optimisation procedures during the development of pharmaceutical compounds.

In discussing Claim 3, the court upheld the PTAB's finding that there was no motivation to combine Edmondson and Bastin to make the sitagliptin salt. First, the court noted that Edmondson's broad disclosure of DHP-IV inhibitors encompassed millions of potential compounds and salts. The court reasoned that this disclosure did not provide any motivation to make sitagliptin salt or any reasonable expectation that one could do so, "particularly in an unpredictable activity like salt formation".

Similarly, for Claim 4, the court held that there was no motivation to combine Edmondson, Bastin and Brittain with any reasonable expectation of success. The evidence showed that a skilled artisan would have avoided hydrates because of numerous downsides. Further, an expert testified that hydrate formation could not be predicted with any degree of certainty, so there would be no reasonable expectation of success.

Best Medical and *Mylan* show that the court is conducting a more extensive analysis of the motivation to combine and reasonable expectation of success inquiries in any obviousness analysis. Therefore, it is insufficient for patent challengers to simply point to the references and assert that there was motivation to combine them and that there was a reasonable expectation of success from doing so, particularly in unpredictable areas such as the life sciences.

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These recent cases bring renewed emphasis on considering patentability, written description and obviousness in challenging and defending patents in the life sciences. They demonstrate that the Federal Circuit has no problem invalidating patent claims that fail to meet each legal test. It is therefore wise for both challengers and defenders to keep them in mind throughout litigation. IAM

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