Rx IP - Court Decision

Federal Court finds Eli Lilly's tadalafil dosage form and process patents invalid.

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On September 10, 2020, Justice St-Louis of the Federal Court issued two decisions regarding infringement actions relating to Eli Lilly's **tadalafil** (**CIALIS**). The Court found Canadian Patent Nos. 2,371,684 (the 684 patent) and 2,492,540 (the 540 patent) invalid on the bases of anticipation and obviousness: *Eli Lilly v Mylan; Eli Lilly v Teva; Eli Lilly v Pharmascience and Riva; Eli Lilly v Apotex*, 2020 FC 816 and *Eli Lilly v Apotex*, 2020 FC 814.

The 684 Patent

The 684 patent relates to a unit dosage form of tadalafil and its use for the treatment of sexual dysfunction including erectile dysfunction (ED).

As previously reported, the Federal Court dismissed Lilly's application under the pre-amended *Patented Medicines (Notice of Compliance) Regulations*(*PMNOC Regulations*) against Mylan, finding Mylan's allegations of invalidity justified (2015 FC 125). As a preliminary issue, Justice St-Louis considered whether Lilly is estopped from re-litigating the findings in the 2015 NOC decision. Given the differences in evidence and legal positions, and developments in the law regarding the promise doctrine and file wrapper estoppel, she concluded that issue estoppel does not apply.

The 684 patent is not a selection patent

Lilly asserted that the 684 patent is a selection of Canadian Patent No. 2,226,784 (the 784 patent) as tadalafil is a subset of the compounds disclosed in the 784 patent to treat ED and the dosages claimed in the asserted claims (2 to 20 mg) are subsets of the dosage ranges set out in the 784 patent (0.2 to 400 mg). Lilly argued that the special advantage of the 684 patent lies in the "surprising efficacy at low doses with an improved side effects profile".

The Court rejected Lilly's arguments, concluding there is nothing in the specification or the claims to the effect that the advantage is peculiar to the claimed dosage range to the exclusion of any other unit dose or that a larger number of unselected doses do not possess the same advantage.

The 684 patent is anticipated by the 784 application

In construing the claims, the Court disagreed with Lilly that a "maximum daily dose" or a maximum of "one dose per day" should be read in the asserted use claims. The Court held that to introduce such limitations would be inconsistent with the plain meaning of the claims and Lilly's position during prosecution of the 684 patent as Lilly removed a maximum daily dose from the claim language to overcome the Examiner's objections.

As a result of the Court's construction of the asserted claims and the finding that the 684 patent is not a selection patent, the Court concluded that the essential elements of the asserted claims are all disclosed in the 784 application.

With respect to enablement, the Court concluded that the skilled person would be able to practice the invention and go from the 0.2-400 mg unit dose range disclosed in the 784 application to 2-20 mg claimed in the 684 patent, as dose selection is routine pharmaceutical work performed without undue burden.

The 684 patent is obvious

On the issue of obviousness, the parties diverged on the interpretation and application of the term "inventive concept". The Defendants focused on the "subject-matter defined by a claim" stated in section 28.3 of the *Patent Act*, which lies in the essential elements of the claims. In contrast, Lilly took the position that the "inventive concept" is not the subject-matter defined by a claim and includes, in this case, the surprising minimization of side effects as compared to sildenafil, even though these asserted advantages are not essential elements of the claims.

Justice St-Louis considered recent jurisprudence from the Federal Court of Appeal and concluded that the terms "the solution taught be the patent", "inventive concept", and "subject-matter defined by a claim" all mean the same thing and they relate to the essential elements of the claims, identified by claim construction. She emphasized that "a distinction must be made between the invention and what are alternatively called properties of the invention, benefits of the invention, or results of the invention." Where a viable inventive concept is present in the claims alone, there is no need to look to the disclosure for improved properties.

The Court agreed with the Defendants' articulation of the subject-matter defined by the claims, which "lies here in that the claimed dosages of tadalafil, orally administered, provide efficacy to treat male ED". The prior art already disclosed that oral administration of tadalafil can be effective at treating ED with a unit dose between 0.2 mg and 400 mg. Accordingly, the sole difference between the prior art and the subject-matter defined by the claims is the lower and narrower subset of dose range in the 684 patent. Upon considering expert evidence including that drug dosing is "routine work" with "minor possible variations", the Court concluded that the difference would have been obvious to a skilled person.

Conclusion

In view of the above, the Court held that the asserted claims are invalid for both anticipation and obviousness. Had the asserted claims been valid, the Court would have found that they would be infringed by each of the Defendants' tadalafil tablet products. Accordingly, Lilly's infringement actions against all four Defendants were dismissed.

The 540 Patent

The 540 patent relates to a commercial manufacturing process to synthesize tadalafil and focuses on the synthesis of a key intermediate compound, a *cis*-diastereomer. The synthesis of this key intermediate is achieved by an improved Pictet-Spengler reaction, in which the desired *cis*-diastereomer is insoluble at reflux temperature or lower while the undesired *trans*-diastereomer is soluble, resulting in concomitant crystallization and separation of the desired *cis*-diastereomer.

Validity

With respect to **anticipation**, the Court found that the essential elements of claims 1, 3 and 4 are disclosed and enabled by an example process in Canadian Patent Application No. 2,412,594 (the 594 application). The main dispute between the parties was whether the suspension resulting from the prior art process indicates that the desired *cis*-diastereomer crystallized. The Court found in favor of Apotex and rejected Lilly's argument that Apotex is required to conduct an experiment to determine the nature of the suspension as part of the disclosure analysis.

On **obviousness**, the Court found that the subject-matter defined by the claims is discernable from the essential elements of the claims as construed and accepted Apotex's articulation of the inventive concept. Contrary to Lilly's assertions, the Court found that the 540 patent "claims particular means to achieve the results, not the desirable results themselves". Upon considering expert evidence, the Court concluded that routine solvent screening would have led to the invention. All of the asserted claims were found invalid for obviousness.

With respect to **utility**, Apotex argued that if the Court fails to correct an error in one of the asserted claims, that claim would be invalid. However, the Court found that the error would not render the claim inoperable, as the skilled person would understand the claim to bear a mistake and be able to make tadalafil by following the sequence of actions.

Finally, claims 1, 3-4, and 7-10 are not invalid on the ground of **overbreadth**. The Court cautioned that "the doctrine of overbreadth should not be applied in the manner suggested by Apotex, akin to the promise doctrine".

Infringement

Lilly asserted that the four processes which Apotex currently employs to make tadalafil infringe claims 1, 3-4, 7-10 and 12 of the 540 patent. The Court found one of the four processes would infringe, if the claims were valid.

The Court's infringement analysis turned on claim construction, regulatory exemption, and burden of proof.

As a preliminary matter, Lilly relied on the statutory presumption as set out in section 55.1 of the *Patent Act* and the common law presumption enunciated in *Hoffmann-La Roche Ltd v Apotex Inc* (1983 CarswellOnt 871 (ONSC), aff'd 1984 CarswellOnt 1197 (ONCA)) to argue that Apotex bears the burden to prove infringement. The Court declined to apply either presumption, and concluded that the evidentiary burden remains Lilly's.

In construing the asserted claims, the Court held that Lilly is precluded from arguing that a specific claim element is non-essential, as it was labelled as "required" during prosecution to avoid an obviousness finding by the Examiner. In addition, Lilly sought to apply the doctrine of equivalents and took the position that variants known at the date of publication should be added as essential elements of the claims. The Court disagreed, finding that "the patentee intended strict compliance with the primary meaning to be an essential requirement of the invention".

Given the Court's construction of the asserted claims, one process was found to infringe claims 1, 3 and 4, and a second process was found to be not infringing.

With respect to Apotex's third process, the Court was satisfied that the evidence from Apotex's fact witness confirmed that all the material manufactured using the process was for regulatory purposes and was therefore exempt under section 55.2 of the *Patent Act*.

With respect to the fourth process, Lilly's expert confirmed non-infringement of the process as outlined in Apotex's batch record; however, Lilly asserted that the process described therein was "fabricated". Given the Court's ruling that the common law presumption does not apply, the Court held that Lilly had not met the burden to establish infringement.

Conclusion

In view of the above, the Court declared that claims 1, 3 and 4 of the 540 patent are invalid for anticipation and all asserted claims are invalid for obviousness. Lilly's infringement action against Apotex was dismissed.

Eli Lilly may appeal both decisions as of right.

Should you have any questions, please do not hesitate to contact a member of the Pharmaceutical Litigation group.

The preceding is intended as a timely update on Canadian intellectual property and technology law. The content is informational only and does not constitute legal or professional advice. To obtain such advice, please communicate with our offices directly.

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