Federal Court of Appeal | Cour d'appel fédérale

Date: 20230602

Dockets: A-234-20
A-236-20
A-237-20
A-238-20

Citation: 2023 FCA 125

CORAM: **DE MONTIGNY J.A.**
GLEASON J.A.
RIVOALEN J.A.

Docket: A-234-20

BETWEEN:

ELI LILLY CANADA INC., ELI LILLY AND COMPANY, LILLY DEL CARIBE, INC., LILLY, S.A. and ICOS CORPORATION

Appellants

and

APOTEX INC.

Respondent

Docket: A-236-20

BETWEEN:

ELI LILLY CANADA INC., ELI LILLY AND COMPANY, LILLY DEL CARIBE, INC., LILLY, S.A. and ICOS CORPORATION

Appellants

and

**PHARMASCIENCE INC. and
LABORATOIRE RIVA INC.**

Respondents

Docket: A-237-20

BETWEEN:

ELI LILLY CANADA INC., ELI LILLY AND COMPANY, LILLY DEL CARIBE, INC., LILLY, S.A. and ICOS CORPORATION

Appellants

and

MYLAN PHARMACEUTICALS ULC

Respondent

Docket: A-238-20

BETWEEN:

ELI LILLY CANADA INC., ELI LILLY AND COMPANY, LILLY DEL CARIBE, INC., LILLY, S.A. and ICOS CORPORATION

Appellants

and

TEVA CANADA LIMITED

Respondent

Heard at Ottawa, Ontario, on March 1, 2023.

Judgment delivered at Ottawa, Ontario, on June 2, 2023.

REASONS FOR JUDGMENT BY: RIVOALEN J.A.

CONCURRED IN BY: DE MONTIGNY J.A.
GLEASON J.A.

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REASONS FOR JUDGMENT

RIVOALEN J.A.

I. Introduction

[1] This decision concerns four appeals of four judgments stemming from a single set of reasons by Justice St-Louis of the Federal Court (the Judge) rendered on September 10, 2020 (2020 FC 816) (the Federal Court Decision) in the context of an action by the appellants, Eli Lilly Canada Inc., Eli Lilly and Company, Lilly Del Caribe, Inc., Lilly, S.A. and ICOS Corporation (the appellants or Lilly) for infringement of Canadian Patent No. 2,371,684 (the 684 Patent). Each of the respondents, Pharmascience Inc., Laboratoire Riva Inc., Mylan Pharmaceuticals ULC, Teva Canada Limited and Apotex Inc. (the respondents) denied infringement and counterclaimed for a declaration of invalidity of the 684 Patent.

[2] The Federal Court Decision cited throughout these reasons is the public version published on the Federal Court's website and CanLII. There is a second public version, which I understand was provided to the parties with a minor correction to the numbering of paragraphs; but, for the purposes of these reasons, I will refer to the published version.

[3] In the Federal Court Decision, the Judge addressed the merits of the action and counterclaims and concluded that the asserted claims of the 684 Patent were invalid on the grounds of anticipation and obviousness. The Judge stated that, if she was wrong in her assessment of the validity of the patent and if the asserted claims were valid, Lilly had met their

burden to establish infringement and were entitled to elect between damages and accounting of profits.

[4] The Judge dismissed Lilly's action relating to the 684 Patent and granted the respondents' counterclaims with costs payable to the respondents.

[5] The appellants argue before this Court that the Judge erred in finding the asserted claims of the 684 Patent invalid for anticipation and obviousness. They ask this Court to allow the appeals, declare that the 684 Patent is valid, grant an order that the respondents have infringed the asserted claims of the 684 Patent, declare that the appellants may elect between damages and an accounting of profits, award pre-judgment and post-judgment interest, and award costs.

[6] For the reasons set out below, I would dismiss the appeals with costs.

II. The 684 Patent and its context

[7] I will first provide a brief overview of the 684 Patent.

[8] The 684 Patent is owned by Lilly ICOS LLC, US. The application for the 684 Patent was filed on April 26, 2000, claiming priority from US Patent 60/132,036 filed on April 30, 1999. It was published in Canada on November 9, 2000, it issued on October 23, 2007, and it expired on April 26, 2020.

[9] The 684 Patent relates to the use of oral pharmaceutical unit dosage forms containing tadalafil for the treatment of erectile dysfunction (ED). Tadalafil is a potent inhibitor of cyclic guanosine 3', 5'-monophosphate specific phosphodiesterase type 5 (PDE5). The appellants market 2.5 mg, 5 mg, 10 mg and 20 mg tablets of tadalafil in Canada under the brand name CIALIS for the treatment of ED.

[10] The first approved PDE5 inhibitor was sildenafil. Sildenafil was commercialised by Pfizer for the treatment of ED under the brand name of VIAGRA and approved in Canada on March 9, 1999. Tadalafil is the second in a class of drug products inhibiting PDE5.

[11] Lilly's first Canadian patent for tadalafil was the Canadian Patent No. 2,181,377 (the 377 Patent). The 377 Patent identified potency data for tadalafil and claimed the tadalafil compound along with the use of that compound to treat numerous disorders and diseases, including vascular disorders. It expired on January 19, 2015.

[12] Lilly's second Canadian patent for tadalafil was the Canadian Patent No. 2,226,784 (the 784 Patent). The 784 Patent claimed, among other things, use of tadalafil for the treatment of ED. The 784 Patent described how to make tablets containing tadalafil and disclosed a dose range of 0.2–400 mg for each unit dose (tablet or capsule) of tadalafil. The application for the 784 Patent (the 784 Application) was first published in 1997. The 784 Patent expired on July 11, 2016.

[13] Lilly's third Canadian patent for tadalafil is the 684 Patent, the subject of these appeals.

[14] The respondents are generic drug manufacturers. They market a generic version of tadalafil with CIALIS tadalafil as the Canadian reference product. In 2016, after the 784 Patent expired, the respondents entered the market by selling or offering for sale their generic version of tadalafil in 2.5 mg, 5 mg, 10 mg and 20 mg tablets, except for the respondent Laboratoire Riva Inc. which offered for sale and sold 5 mg and 20 mg tablets.

[15] The 684 Patent includes 18 claims, of which the following are in issue in these appeals: Claim 10 (as it depends on Claim 9, as it in turn depends on Claims 1, 3–6) and Claims 13–16 (as they depend on Claim 12) (the asserted claims). The appellants did not argue in their memorandum of fact and law or during their oral submissions that the Judge made reviewable errors in her claim construction or in her delineation of the essential elements of the asserted claims.

[16] The Judge construed the essential elements of Claim 10 as:

> - A pharmaceutical unit dosage form (for example, a pill or tablet);
> - Suitable for oral administration;
> - Containing tadalafil;
> - At certain doses, hence Claim 3: 5–50mg, Claim 4: 2.5mg, Claim 5: 5mg, and Claim 6: 10mg;
> - For use in treating male erectile dysfunction, where inhibition of PDE5 provides a benefit[.]
>
> (Federal Court Decision at para. 211)

[17] The Judge did not read in a maximum daily dose or one dose per day limitation into Claim 10 (Federal Court Decision at para. 212).

[18] The Judge construed the essential elements of Claims 13–16 as:

- Use of a unit dose;
- Containing tadalafil (Claim 13: 2–20mg; Claim 14: about 5mg; Claim 15: about 10mg; and Claim 16: about 20mg);
- For treating sexual dysfunction (including both MED [male erectile dysfunction] and FSD [female sexual dysfunction]) in a patient.

(Federal Court Decision at para. 218)

[19] The Judge did not read in a maximum daily dose or one dose per day limitation into Claims 13–16 (Federal Court Decision at para. 219).

[20] Accordingly, the asserted claims are to be read as construed by the Judge for the purposes of assessing validity and infringement. The appellants however dispute the Judge's construction of the inventive concept, which depends on, but is not identical to, the claims construction (*Apotex Inc. v. Shire LLC*, 2021 FCA 52, 187 C.P.R. (4th) 1 at para. 68, leave to appeal to SCC refused, 39662 (7 October 2021) [*Shire*]).

[21] Prior to embarking on the issues and my analysis of the questions before me, it is useful to explain how the arguments pertaining to the essence of the invention contained in the asserted claims of the 684 Patent evolved throughout the litigation. While the construction of the

inventive concept is a question of law, the Judge was presented with different options to consider when trying to construe the correct inventive concept.

[22] At the start of the trial, Lilly took the position that the 684 Patent (with an asserted dose range of 2 to 20 mg) is a selection of the 784 Patent (with an identified dose range of 0.2 to 400 mg). They argued that "(…) the essence of this invention is the disclosure talks about you have efficacy with minimal side effects. You have reduced side effects. You have better side effects than sildenafil (…) but the ones that are most important are facial flushing, the vision side effects, and side effects associated with the combined effects of the, of a PDE5 inhibitor and an organic nitrate" (Federal Court Decision at para. 116, citing transcript of 5 December 2019 at p. 56, lines 2–10). Lilly submitted that "the advantage was the surprising efficacy at low dose with the improved side effects profile that gets worse above 20mg" (Federal Court Decision at para. 116, citing transcript of 5 December 2019 at p. 86, lines 12–14, 20–28).

[23] In their written closing memorandum, Lilly asserted that "[t]adalafil is a subset of the compounds disclosed in the 784 Patent and the doses and dose ranges claimed in the asserted claims of the 684 Patent are subsets of the dosage ranges set out in the 784 Patent." Lilly presented the special advantages of the 684 Patent as "the surprising efficacy at low doses with an improved side effects profile, including clear data showing flushing to be reduced in the claimed dosages ranges, as described in the 684 Patent" (Federal Court Decision at para. 117, citing Lilly Closing Memorandum at paras. 120, 122).

[24] Further, the Judge noted that, in their written closing memorandum, Lilly argued that the inventive concept of the 684 Patent includes “the surprising minimization of side effects or only of flushing as compared to Viagra sildenafil, when the maximum daily dose is set at 20mg” (Federal Court Decision at para. 263). Even if it were not construed as a selection, Lilly contended that the inventive concept should nonetheless include the “minimization of side effects as compared to VIAGRA sildenafil” (Federal Court Decision at para. 117, citing Lilly Closing Memorandum at para. 165). Lilly proposed the inventive concept to be understood as “the discovery that surprising low doses of tadalafil as claimed in each of the asserted Claims with a maximum daily dose of 20mg is effective in treating ED with a minimization of side effects as compared to Viagra sildenafil” (Federal Court Decision at para. 263, citing Lilly Closing Memorandum at para. 168).

[25] During oral closing arguments before the Judge, Lilly set out their final position. They argued that the unexpected advantage of the subset over the genus is “what the patent said, essentially eliminating the flushing”. They also said “[i]n our case, it is the surprising efficacy that it worked so well at the low doses was surprising, in combination with essentially eliminating flushing” (Federal Court Decision at para. 118, citing transcript of 4 February 2020 at p. 61, lines 27–28; p. 62, lines 15–17). The Judge described Lilly’s argument as follows: “[i]n essence, in their oral closing argument, Lilly thus eliminated the side effects comparison with sildenafil, and limited the better side effects profile to that of flushing.” (Federal Court Decision at para. 118).

[26] The Judge found that there remained uncertainty as to Lilly's position. When discussing inventive concept, "Lilly cited their experts for the proposition that the inventive concept of the 684 Patent dosage subset was that, surprisingly, low doses of tadalafil as claimed are effective in treating ED with a minimizing of side effects *as compared to Viagra sildenafil*, and narrowed the side effects to one, the flushing" (Federal Court Decision at para. 119, citing transcript of February 4, 2020 at p. 115, lines 17–27) [emphasis in original]. In light of the uncertainty as to Lilly's position on the inventive concept of the asserted claims, the Judge examined each of the two arguments presented by Lilly regarding the advantages of the 684 Patent: 1) the better flushing profile as compared to the wider range of the 784 Patent; and 2) the better flushing profile as compared to sildenafil (Federal Court Decision at para. 120).

[27] Before us, Lilly appears to have shifted their position once again. The appellants no longer claim that the 684 Patent's invention incorporates the flushing advantage compared to the wider range of the 784 Patent or to sildenafil; rather, they only claim the 684 Patent's invention incorporates the flushing advantage <u>compared to larger doses of tadalafil</u> (Appellants' Memorandum of Fact and Law at paras. 80–81, 118) [my emphasis].

[28] This synopsis of Lilly's changing position on the inventive concept demonstrates that, over a period of several years, Lilly and their experts did not agree on the solution taught by the 684 Patent.

III. Issues

[29] The appellants raised several grounds of appeal in their notices of appeal and memorandum of fact and law but, some days prior to the hearing, narrowed the issues in writing. During oral submissions, the appellants abandoned more issues and further narrowed their arguments. In the end, the appellants argue that the Judge erred in:

A. Finding Claims 10 and 13–16 were invalid for obviousness (lack of inventiveness). That is, the appellants mainly take issue with the second step of the test set out *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61, [2008] 3 S.C.R. 265 at paragraph 67 [*Sanofi*]. The appellants focused their submissions on the Judge's approach to identifying and construing the inventive concept.

B. Finding Claims 10 and 13–16 were invalid for anticipation by the 784 Application (lack of novelty). In particular, the appellants take issue with the Judge's approach to anticipation as it relates to the disclosure requirement. They do not appeal the Judge's approach to enablement.

C. To the extent it is relevant, the appellants submit that the Judge erred in her approach when finding that the 684 Patent was not a selection patent.

[30] The appellants submit that all of the issues raised in these appeals are questions of law. They do not appeal any of the Judge's factual findings.

IV. Standard of review

[31] There is no dispute regarding the principles applicable to the standard of review. As indicated in *Housen v. Nikolaisen*, 2002 SCC 33, [2002] 2 S.C.R. 235 [*Housen*], the standard of review of correctness applies to questions of law and questions of mixed fact and law, where there is an extricable legal principle at issue. Findings of fact or mixed fact and law, absent an extricable question of law, are reviewable only where the Judge has made a palpable and overriding error (*Housen* at paras. 8, 10, 36).

[32] Questions regarding the construction of claims and the construction of the inventive concept are questions of law (*Apotex Inc. v. Allergan Inc*., 2012 FCA 308, 105 C.P.R. (4th) 371 at paras. 50, 53, leave to appeal to the SCC refused, 35184 (9 May 2013)); *Bristol-Myers Squibb Canada Co. v. Teva Canada Limited,* 2017 FCA 76, 76 C.P.R. (4th) 216 at para. 74).

[33] Questions regarding whether the asserted claims are obvious raise findings of mixed fact and law, which, absent an extricable question of law, must be assessed using the standard of review of palpable and overriding error (*Teva Canada Limited v. Pfizer Canada Inc.*, 2019 FCA 15, 163 C.P.R. (4th) 265 at para. 23 [*Teva*], *Packers Plus Energy Services Inc. v. Essential Energy Services Inc.*, 2019 FCA 96, 164 C.P.R. (4th) 191 at paras. 29, 33, leave to appeal to SCC refused, 38694 (19 December 2019) [*Packers Plus*]).

[34] The failure to characterize a patent as a selection patent is not in itself an error of law but "may reflect a lack of understanding of the patent and its factual context" (*Shire* at para. 32).

V. Obviousness

A. *The Judge's findings*

[35] The Judge applied the four-step test for obviousness laid out by the Supreme Court of Canada in *Sanofi*. The test is reproduced at paragraph 53 below.

[36] The Judge made findings regarding the person skilled in the art and the common general knowledge, which will be summarized at paragraphs 57 and 58 below.

[37] Turning to the inventive concept, the Judge examined section 28.3 of the *Patent Act*, R.S.C. 1985, c. P-4, which uses the terms "subject-matter defined by a claim" to describe the subject-matter that must not have been obvious to a person skilled in the art on the claim date. Section 28.3 of the *Patent Act* had not been considered in *Sanofi*. The Judge thoroughly examined this Court's jurisprudence since *Sanofi* and concluded that the terms "solution taught by the patent", "inventive concept" and "subject-matter defined by a claim" all "mean the same thing and […] relate to the essential elements of the claims, identified by claim construction" (Federal Court Decision at para. 300). The Judge did not have the benefit of this Court's decision in *Shire* when she undertook her review of the jurisprudence.

[38] As previously mentioned, the Judge found that the subject-matter defined by a claim "lies here in that the claimed dosages of tadalafil, orally administered, provide efficacy to treat male ED". She found that "the advantages raised by Lilly are not included [in the subject-matter defined by a claim] because they are not essential elements of the claims, the 648 Patent is not a

selection, and a viable subject-matter is discernable from the claims" (Federal Court Decision at para. 310).

[39] The Judge found that she did not need to look beyond the essential elements of the claims themselves to understand the nature of the invention of the 684 Patent. She noted that recourse to elements of the disclosure may be permitted when there is ambiguity in the claims or when the inventive concept is not discernable from the claims (Federal Court Decision at para. 301).

[40] The Judge found "the sole difference between the prior art (the 377 Patent, the 784 Application, and sildenafil) and the subject-matter defined by a claim of the 684 Patent to be the lower and narrower subset of dose range in the 684 Patent" (Federal Court Decision at para. 313).

[41] The Judge found that the difference between the prior art and the subject-matter as defined by the asserted claims would have been obvious to the person skilled in the art (Federal Court Decision at para. 324).

B. *The appellants' position*

[42] The appellants' arguments regarding obviousness focus primarily on what they say is the Judge's error in construing the inventive concept in the second step of the obviousness analysis as set out in *Sanofi*. Because of this error, they submit that the Judge also erred in her application of the third and fourth steps of the obviousness analysis.

[43] The appellants submit that the Judge erred in her approach to construing the inventive concept for two reasons:

- First, she incorrectly held that, if a patent is not a selection patent, the inventive concept means—as a matter of law—the same thing as the essential elements of the claim, identified by claim construction.

- Second, she incorrectly held that, if a patent is not a selection patent, any advantages described in the patent cannot—as a matter of law—be included in the inventive concept.

[44] As a result of these conclusions, according to the appellants, the Judge limited the inventive concept to the essential elements of the claims without ever considering "the solution taught by the patent". The appellants contend that the inventive concept of the 684 Patent is clearly more than just the essential elements of the claims.

[45] During oral submissions before this Court, for the first time, the appellants argue that Claims 1, 3–6 are to a bare chemical formula (tadalafil) and are incorporated by reference into Claim 10. As a result, they contend that it was necessary for the Judge to review the entire specification of the 684 Patent, including disclosure and the claims, in order to understand the inventive concept.

[46] The appellants maintain that, when the law is applied correctly, the inventive concept of the 684 Patent is not readily discernable from the claims as construed by the Judge. The

appellants say that it was an error of law for the Judge not to review the disclosure in order to understand the solution taught by the patent and the motivation to pursue it. The appellants rely on the Supreme Court of Canada's decision in *Teva Canada Ltd. v. Pfizer Canada Inc.*, 2012 SCC 60, 35 D.L.R. (4th) 503 at paragraph 50 for this proposition. Had the Judge reviewed the patent disclosure, the appellants say she would have included the improved side effects profile of less flushing as part of the inventive concept.

[47] The appellants say that it is critical for the court to correctly determine the inventive concept because that is the "end point" against which obviousness is measured. The appellants argue the Judge did not perform the obviousness analysis in light of the correct inventive concept. The appellants now argue the 684 Patent's inventive concept incorporates the flushing advantage compared to larger doses of tadalafil.

C. *Analysis*

(1) The law on obviousness and the proposed inventive concept

[48] It is settled that the Judge's construction of the inventive concept is one of law and I owe no deference to her finding. However, I do owe deference to the Judge on questions of fact and of mixed fact and law. The appellants have not identified any palpable and overriding errors in the Judge's factual findings, and therefore I will rely on the Judge's factual findings throughout my analysis on the issue of obviousness.

[49] As is apparent from the discussion that follows, even if I were to accept the appellants' proposed inventive concept, which now is "a minimization or elimination of flushing as compared to larger doses of tadalafil", this appeal must nonetheless be dismissed.

[50] I note that the 684 Patent was found not to be a selection patent. Whether a patent is formally classified as a selection patent or not, the approach to assessing obviousness does not change; however, the classification assists the court in understanding the "nature of the beast" and comparing the facts to previous fact scenarios. For example, selection patents "commonly attest that their inventiveness lies in 'the making of the selected compound, coupled with its advantage or advantages'" (*Shire* at paras. 32–35). Because, as noted above, I will be assessing the obviousness of the asserted claims based on the appellants' proposed inventive concept, it is not necessary for me to examine the question of whether the 684 Patent is a selection patent.

[51] The statutory basis for the obviousness analysis is found in section 28.3 of the *Patent Act*, which provides:

Invention must not be obvious	**Objet non évident**
28.3 The subject-matter defined by a claim in an application for a patent in Canada must be subject-matter that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains, having regard to	**28.3** L'objet que définit la revendication d'une demande de brevet ne doit pas, à la date de la revendication, être évident pour une personne versée dans l'art ou la science dont relève l'objet, eu égard à toute communication :
(*a*) information disclosed before the one-year period immediately preceding the filing date or, if the claim date is before that period, before the claim date by the	***a*)** qui a été faite, soit plus d'un an avant la date de dépôt de la demande, soit, si la date de la revendication est antérieure au début de cet an, avant la date de la

applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere; and	revendication, par le demandeur ou un tiers ayant obtenu de lui l'information à cet égard de façon directe ou autrement, de manière telle qu'elle est devenue accessible au public au Canada ou ailleurs;
(*b*) information disclosed before the claim date by a person not mentioned in paragraph (a) in such a manner that the information became available to the public in Canada or elsewhere.	***b*)** qui a été faite par toute autre personne avant la date de la revendication de manière telle qu'elle est devenue accessible au public au Canada ou ailleurs.

[52] The question to be answered pursuant to section 28.3 of the *Patent Act* is whether the subject-matter defined by the asserted claims of the 684 Patent is obvious to a person skilled in the art with regard to the prior art as of the claim date of April 30, 1999. If the "invention" is obvious, the patent or its asserted claims are invalid.

[53] In *Sanofi*, the Supreme Court of Canada adopted the four-step approach to an obviousness inquiry first outlined in *Windsurfing International Inc. v. Tabur Marine (Great Britain) Ltd.*, [1985] R.P.C. 59 (C.A.):

> In the result I would restate the Windsurfing questions thus:
>
> (1) (a) Identify the notional "person skilled in the art";
>
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;

> (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?
>
> (*Sanofi* at para. 67, citing *Pozzoli SPA v. BDMO SA*, [2007] F.S.R. 37 (p. 872), [2007] EWCA Civ 588 at para. 23) [emphasis in original]

[54] In *Shire*, this Court reminded us that obviousness is assessed on a claim-by-claim basis; each claim is evaluated against the four-part *Sanofi* test (*Shire* at para. 55).

[55] I will rely on the Judge's findings on the prior art while embarking on the *Sanofi* analysis. The Judge found that the prior art includes sildenafil, the 377 Patent and the 784 Application. Regarding the 784 Application, the Judge found that it relates to the use of tadalafil to treat ED, discloses potency data for tadalafil, describes how to make tablets containing tadalafil, and discloses a dose range of 0.2–400 mg for each tablet of tadalafil for the treatment of ED (Federal Court Decision at paras. 174, 177, 180, 181, 262).

> (2) The first step of the *Sanofi* test for obviousness: Identify the notional person skilled in the art and the relevant common general knowledge

[56] The first step of the *Sanofi* test for obviousness and the Judge's key findings were not at issue before this Court. They are summarized below.

> (a) *Person skilled in the art*

[57] The person skilled in the art is not in dispute. It consists of a drug development team—which could include physicians, clinicians, research scientists, pharmacologists, toxicologists and statisticians—with expertise in pharmacology, pharmacokinetics, physiology, dose ranging

and safety assessment of candidate therapeutics, and with experience in the treatment of ED (Federal Court Decision at para. 171).

(b) *Common general knowledge*

[58] The Judge found the respondents' expert more reliable than Lilly's expert and defined the common general knowledge as follows:

- The person skilled in the art would seek to identify the minimum effective dose of tadalafil in the treatment of ED (Federal Court Decision at para. 196);
- In order to identify the minimum effective dose of tadalafil for the treatment of ED, the person skilled in the art would be "making a judgment call with what the team knows" based upon pharmacokinetic data, the information in the journal articles and from sildenafil, as well as the specific International Index of Erectile Function questions (Federal Court Decision at para. 196);
- A blueprint of the testing conducted with sildenafil was widely distributed by Pfizer, "revealing the whole slate of studies (preclinical and clinical studies), the doses actually tested, the potency of 3.0–3.9nM, the poor selectivity for PDE5 relative to PDE6 leading to transient vision abnormalities, the efficacy in low doses of 5 and 10 mg, and the efficacy plateau in the 50–100 mg range" (Federal Court Decision at paras. 176, 196).

(c) *Claim date*

[59] The claim date for the asserted claims is April 30, 1999 (Federal Court Decision at paras. 187, 196, 242).

(3) The second step of the *Sanofi* test for obviousness: Identify or construe the inventive concept of the claim in question

[60] As mentioned, the appellants argue that the Judge erred in law when she identified the inventive concept as claimed dosages of tadalafil, orally administered, that provide efficacy to treat male ED without including the advantages raised by Lilly.

[61] For the sake of argument only, I will accept Lilly's new construction of the inventive concept of the asserted claims in the 684 Patent as being "the claimed dosages of tadalafil, orally administered, provide efficacy to treat male ED, including the minimization or elimination of flushing as compared to larger doses of tadalafil". However, the appellants' constant shift in their identification of the inventive concept undermines the strength of their argument.

(4) The third step of the *Sanofi* test for obviousness: Identify the differences between the state of the art and the inventive concept

[62] The proposed inventive concept is "the claimed dosages of tadalafil, orally administered, provide efficacy to treat male ED, including the minimization or elimination of flushing as compared to larger doses of tadalafil".

[63] The prior art includes sildenafil, the 377 Patent and the 784 Application. Regarding the 784 Application, the Judge found that it relates to the use of tadalafil to treat ED, discloses potency data for tadalafil, describes how to make tablets containing tadalafil, and discloses a

dose range of 0.2–400 mg for each tablet of tadalafil for the treatment of ED (Federal Court Decision at paras. 174, 177, 180, 181, 262).

[64] Therefore, with the proposed inventive concept including a minimization or elimination of flushing as compared to larger doses of tadalafil, the differences between the prior art—in particular the 784 Application—and the inventive concept are the lower and narrower subset of dose ranges in the 684 Patent and the improved side effects profile of minimization or elimination of flushing.

(5) The fourth step of the *Sanofi* test for obviousness: Do the differences constitute steps that would have been obvious to the person skilled in the art?

[65] I agree with the Judge when she relied on paragraph 78 of *Sanofi* and found that it was appropriate to apply the obvious to try test in this case because the 684 Patent is in an area of endeavour where advances are often won by experimentation (Federal Court Decision at para. 323).

[66] Where the "obvious to try" test is appropriate, the Supreme Court of Canada has identified the following non-exhaustive list of factors to take into consideration at the fourth step of the obviousness test:

1. Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?
2. What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?

3. Is there a motive provided in the prior art to find the solution the patent addresses?

(*Sanofi* at para. 69)

[67] Another important factor to consider is the actual course of conduct that culminated in the making of the invention (*Sanofi* at para. 70). The relative knowledge of the inventor compared to the skilled person can be helpful when assessing the actual course of conduct (*Sanofi* at paras. 70–71).

[68] I agree with the Judge when she considered the factors set out at paragraph 69 of *Sanofi*, recognized that those factors were non-exhaustive, and was satisfied that the difference between the prior art and the subject-matter as defined by the asserted claims "would have been obvious to the [person skilled in the art] on April 30, 1999" (Federal Court Decision at paras. 323–24).

[69] As I will demonstrate, even if the inventive concept is the one now proposed by the appellants, the Judge's findings that it was obvious to try must stand. The improved side effects profile—in particular the advantages relating to the minimized or eliminated flushing—is included in the Judge's findings on safety and tolerability of the different doses of tadalafil. Indeed, the Judge found that the routine work carried on by the person skilled in the art included identifying the dose range and any side effects. The Judge repeatedly stated that, as part of identifying the dose range, the person skilled in the art identifies "side effect occurrences" or the doses that best balance efficacy, safety and tolerability. The Judge understood that the side effects occurrences being identified included flushing (Federal Court Decision at paras. 116–20, 122, 132, 135, 190, 222, 246, 255–56, 263, 308, 321, 325, 327–28).

[70] Regarding the first factor, the Judge found:

> [T]he number of predictable solutions is not infinite, but rather well defined with a final outcome with minor possible variations. The ultimate aim is to select a dose range that offers the best balance between efficacy, and safety and tolerability. There is only really one method to identify the dose range: trials have to be performed in order to graph the efficacy of the drug in relation to the dose, and to identify the side effect occurrences in relation to the dose […].
>
> (Federal Court Decision at para. 327).

[71] As noted by this Court in *Hospira Healthcare Corporation v. Kennedy Trust for Rheumatology Research*, 2020 FCA 30, 316 A.C.W.S. (3d) 537:

> It should be noted that, whereas being "more or less self-evident to try to obtain the invention" (per *Sanofi* at para. 66) is a requirement for obviousness to try, being "more or less self-evident that what is being tried ought to work" (per *Sanofi* at para. 69) is not a requirement but merely a factor to be considered.

[72] The Judge's findings regarding the first factor would still apply to the proposed inventive concept because the ultimate aim of the person skilled in the art would not change in this particular case. It continues to be the selection of a dose range that offers the best balance between efficacy, safety and tolerability. The Judge relied on the expert evidence to determine that the number of predictable solutions is not infinite.

[73] Regarding the second factor, the Judge found that the steps the person skilled in the art would take were routine (Federal Court Decision at para. 328). As part of her anticipation analysis, the Judge had previously found that "[d]ose selection is a routine pharmaceutical work performed without undue burden, and forms part of Phase II clinical studies at the end of which,

typically, a dose response curve is typically drawn for the final selection of doses for large-scale studies" (Federal Court Decision at para. 255). The Judge found that "[t]he skilled team, in attempting to dose tadalafil, would use available information from the 784 Application and the 377 Patent, including information on tadalafil bioavailability, potency and selectivity for PDE5, as well as information from sildenafil" (Federal Court Decision at para. 325).

[74] While I agree with the Judge's findings that drug dosing of tadalafil for the treatment of ED here is routine work having regard to the prior art, I would not endorse this statement at large. There may be cases where dosage selection is not routine (see *Teva Canada Limited v. Janssen Inc.*, 2023 FCA 68, [2023] F.C.J. No. 467 (QL) at para. 66).

[75] Turning to the question of side effects, the Judge's factual findings are that Phase II clinical studies include identifying the efficacy plateau using "a host of factors from previous work in preclinicals and Phase I, including, for example, […] the side effect profile […] which offer the best balance between safety-tolerability and effectiveness" (Federal Court Decision at para. 255).

[76] The Judge also found that, using all the available information in the prior art, "the skilled team can design a Phase II dose ranging study, graph the dose response curve from data gathered during the study, identify the side effects, and select the dose range that provides the best balance between efficacy, and safety and tolerability" (Federal Court Decision at para. 325).

[77] As a result, the Judge's findings regarding the second factor apply to the proposed inventive concept. In particular, the Judge found that the routine steps taken by the person skilled in the art would include identifying side effects (such as flushing) and the safety profile of the dose range.

[78] Regarding the third factor, the Judge found that, having already identified a viable compound for the PDE5 inhibition and treatment of ED, a person skilled in the art "would certainly be motivated to identify the doses that offer the best balance between efficacy, and safety and tolerability to push the compound one-step closer to the market" (Federal Court Decision at para. 328).

[79] The Judge's findings regarding the third factor would still apply to the proposed inventive concept because the person skilled in the art would continue to be motivated in this case to identify and commercialize the doses that offer the best balance between efficacy, and safety and tolerability.

[80] This review of the Judge's factual findings leads me to conclude that, even if the inventive concept includes the minimization or elimination of flushing as compared to larger doses of tadalafil, the Judge's finding on obviousness must stand. The differences between the prior art and the proposed inventive concept would have been obvious for the person skilled in the art and would not have required any degree of invention.

[81] In sum, based on the Judge's factual findings made during her obviousness analysis, in my view, notwithstanding the proposed inventive concept, the asserted claims remain obvious. Accordingly, the asserted claims are invalid.

VI. Anticipation and selection patent

[82] Having reached the conclusion that the asserted claims are obvious, it is not necessary to address the appellants' arguments on the issues of anticipation and whether the 684 Patent is a selection patent. These reasons, however, should not be viewed as endorsing the Judge's findings or reasons in respect of these issues.

VII. Conclusion

[83] For these reasons, I conclude that Claims 10 and 13–16 of the 684 Patent are invalid on the ground of obviousness.

[84] I would dismiss the appeals with costs.

"Marianne Rivoalen"
J.A.

"I agree.
Yves de Montigny J.A."

"I agree.
Mary J.L. Gleason J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKETS:	A-234-20, A-236-20, A-237-20, A-238-20
DOCKET:	A-234-20
STYLE OF CAUSE:	ELI LILLY CANADA INC., ELI LILLY AND COMPANY, LILLY DEL CARIBE, INC., LILLY, S.A. and ICOS CORPORATION v. APOTEX INC.
DOCKET:	A-236-20
STYLE OF CAUSE:	ELI LILLY CANADA INC., ELI LILLY AND COMPANY, LILLY DEL CARIBE, INC., LILLY, S.A. and ICOS CORPORATION v. PHARMASCIENCE INC. and LABORATOIRE RIVA INC.
DOCKET:	A-237-20
STYLE OF CAUSE:	ELI LILLY CANADA INC., ELI LILLY AND COMPANY, LILLY DEL CARIBE, INC., LILLY, S.A. and ICOS CORPORATION v. MYLAN PHARMACEUTICALS ULC
DOCKET:	A-238-20
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