Federal Court  Cour fédérale

Date: 20090618

Docket: T-1566-07

Citation: 2009 FC 638

Ottawa, Ontario, June 18, 2009

PRESENT: The Honourable Mr. Justice Kelen

BETWEEN:

PFIZER CANADA INC.,
PFIZER INC., PFIZER IRELAND PHARMACEUTICALS, AND
PFIZER RESEARCH AND DEVELOPMENT COMPANY N.V./S.A.

Applicants

and

NOVOPHARM LIMITED AND
THE MINISTER OF HEALTH

Respondents

REASONS FOR ORDER AND ORDER

[1] This is an application for an Order under the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-1333 (the NOC Regulations), prohibiting the Minister of Health from issuing a Notice of Compliance to Novopharm for a generic version of Viagra until Pfizer's Canadian Patent 2,163,446 (hereafter the '446 Patent) expires in 2014. Novopharm alleges that Pfizer's

patent for Viagra is invalid for obviousness, lack of utility, and insufficiency of disclosure so that the generic version of Viagra should immediately be allowed on the Canadian market.

TABLE OF CONTENTS

BACKGROUND

The ‘446 Patent

[2] The ’446 Patent claims the use of sildenafil citrate in the treatment of impotence, including erectile dysfunction (ED). The applicant Pfizer Ireland Pharmaceuticals, owns the ‘446 Patent, and the applicant Pfizer Canada Inc., markets the drug sildenafil cirtrate in Canada under the trade name VIAGRA.

[3] The applicants obtained the '446 Patent on July 7, 1998, from an application filed in Canada on May 13, 1994 which claimed priority from Great Britain Patent Application No. 9311920.4 filed on June 9, 1993. The '446 Patent will expire on May 13, 2014.

[4] The ‘446 patent claims the use of many compounds in Claims 1 to 7 for the treatment of ED, including sildenafil citrate, the active compound used in the VIAGRA drug. The applicant relies on claims 7, 18, 22 and 23 of the ‘446 Patent. The applicant states that all of these claims, although worded differently, cover the use of sildenafil in the treatment of ED through oral administration. Claims 1 to 7, 18, 22 and 23 of the Patent are attached hereto as “Appendix A”.

[5] Two disclaimers have been filed and recorded with respect to the ‘466 Patent. The primary effect of the two disclaimers was to limit all claims to the treatment of ED in men. The disclaimers are not relevant to this application.

The Parties

[6] The applicant Pfizer Canada Inc. is the Canadian operation of the multinational pharmaceutical company Pfizer Inc., which manufactures VIAGRA. The applicant Pfizer Ireland Pharmaceutical owns the patent, and Pfizer Canada is a licensee under the patent.

[7] The respondent Novopharm Limited filed an Abbreviated New Drug Submission with Health Canada on December 19, 2006 in respect of Sildenafil Citrate Tablets, 25 mg, 50 mg and

100 mg, for oral administration. The ANDS compared the Novopharm tablets with the applicants' VIAGRA Sildenafil Citrate Tablets, 25 mg, 50 mg and 100 mg. The Novapharm tablets are indicated for the treatment of ED. Novopharm served its Notice of Allegation, alleging the invalidity of the '446 Patent, on Pfizer on July 6, 2007.

[8] The respondent the Minister of Health did not participate in this application, as is normally the case in such proceedings.

How Sildenafil Treats ED

[9] The erectile tissue in the penis consists of two symmetrical compartments above and on either side of the urethra called the corpus cavernosa. They are made up of small blood vessels or passages surrounded by smooth muscle which can contract or relax, as with any form of muscle. Blood is supplied to the corpora cavernosa by a network of arteries, and is drained from them through veins. The flow of blood into the penis is controlled by the smooth muscle surrounding the arteries. The penis becomes erect when the penile smooth muscle relaxes and blood flows through the arterial network and into the small blood vessels. When the smooth muscles contract, the blood vessels also contract, preventing blood from flowing in. This causes the penis to become flaccid.

[10] Sildenafil inhibits a chemical in the body known as PDE_V, which otherwise stops the blood from flowing into the penis and causing an erection.

[11] Many different cascades of first and second messages, known as “pathways,” were known in 1993 to relax or contract smooth muscle tone in the penis. These included the non-adrenergic non-cholinergic (or NANC) pathway. It is now known, although it was not known in 1993, that sildenafil treats ED by virtue of its effects on the NANC pathway in which the first messenger is nitric oxide (NO), and the second messenger is cGMP, which is regulated by PDE_V.

[12] Sildenafil was initially developed by Pfizer in the mid-1980s as one of a number of compounds for the treatment of hypertension and angina, cardiovascular conditions in which smooth muscle cells are implicated. Because sildenafil is a potent and selective cGMP PDE inhibitor, it is able to treat ED in men through the operation of the NO-cGMP pathway.

AFFIDAVIT EVIDENCE

[13] The applicants have provided affidavits from five expert witness, two employees and a law clerk employed by applicant’s counsel:

Experts

1. Dr. Peter Ellis
2. Dr. Gerald B. Brock
3. Dr. George Christ
4. Professor Jeremy Heaton
5. Dr. Sharron Francis

Pfizer Employees

6. Martyn Frank Burslem
7. Madeleine Pesant

Law Clerk

8. Christine Ingham (law clerk at Torys)

[14] The respondent has provided affidavits from three experts, a witness of fact and the author of a prior art reference, and an associate employed by respondent's counsel:

Experts

1. Iñigo Saenz de Tejada, MD
2. Dr. Donald H. Maurice
3. Dr. Jonathan S. Dordick

Witness of Fact

4. Margaret A. Bush

Associate

5. Bryan Norrie (associate at Oslers)

[15] The applicants have provided reply affidavits from three of their expert witnesses, Dr. Ellis, Dr. Brock, and Dr. Francis. The respondent has provided sur-reply affidavits from two of their expert witnesses, Dr. Maurice and Dr. Dordick, both of whom also offered evidence in chief.

[16] Pfizer has accurately described the background of the key witnesses in a document attached hereto as "Appendix B".

Evidence of Dr. Peter Ellis regarding his discovery of Sildenafil for the treatment of ED

[17] Dr. Ellis, one of the inventors named in the Canadian Patent '446, deposed at paragraph 17 of his affidavit:

> In overview, the development of sildenafil as a treatment for ED arose out of a project in which a…inhibiter was being sought to treat

> hypertension. This project later evolved into a search for a drug to treat angina. Later, I determined that sildenafil could successfully treat ED based on observations of erections during Phase 1 testing in the angina project combined with my scientific knowledge.

[18] Dr. Ellis explained the many steps, and missteps, which led to the discovery of sildenafil as a solution for ED. It is clear that the discovery was a long and winding road with many twists, turns and dead ends along the way. At first, the drug was injected into the penis [to stimulate the production of the inhibiter for the treatment of impotence]. The results were disappointing. These tests were conducted on monkeys. Dr. Ellis deposed in paragraph 33:

> …this negative result probably would have ended our interest in sildenafil for impotence.

However, in studies of sildenafil as a treatment for angina, patients in the test study taking the drug orally reported "prolonged and spontaneous erections" (at paragraph 37).

[19] Following these studies on angina patients, Dr. Ellis decided that Pfizer should design a study to administer sildenafil to ED patients. A 25mg oral dose of sildenafil was given three times a day for five days to a group of healthy male volunteers. The resulting erections from the drug were surprising because, as Dr. Ellis explained at paragraph 34:

> …This too was surprising because when a drug is administered orally, it is presented to the whole body including the vascular system. Further, we knew that a…inhibiter like sildenafil could lower blood pressure, which was a known cause of impotence. Normally, drug treatments for impotence involved injection of the drug directly into the corpus cavernosum (the sponge-like tissue in the penis) to avoid systemic effects.

[20] In June 1993, Dr. Ellis testified that Pfizer filed a provisional specification for a patent in the United Kingdom, which is the "priority application" for the '446 Patent. Following this provisional

specification, Pfizer conducted a study (Study 350) wherein a group of 16 impotent men were administered an oral dose of either 25 mg of sildenafil or a placebo three times a day for a period of six days. In the evening of the sixth day, the patients were admitted to a hospital and shown sexually explicit videos and kept in the hospital overnight. They were fitted with a RigiScan transducer, a device that measured the rigidity and duration of their erections and recorded the results on a computer. The patients also kept a diary. After a suitable drug washout period, the patients repeated the test, but with the alternate of the sildenafil or placebo that they had received in the first test. As a result of this study, Pfizer concluded that sildenafil was effective in improving erectile function in men with no known organic cause of impotence.

[21] In February 1994, another study was conducted to investigate whether sildenafil could be given as a single oral dose to induce an erection between one and two hours before the anticipated opportunity for sexual activity.

The UK litigation regarding the Viagra Patent

[22] Undoubtedly a motivation to challenge the validity of the VIAGRA patent is the jurisprudence in England, which struck out the Viagra patent for obviousness: *Lilly Icos Ltd. v. Pfizer Ltd.,* [2001] F.S.R. 16 (E.C.A.).This decision of Mr. Justice Laddie of the Chancery Division, was confirmed on appeal by the U.K. Court of Appeal (Civil Division): *Lilly Icos Ltd. v. Pfizer Ltd.*, [2002] EWCA Civ 1.

Notice of Allegation

[23] In this litigation, material parts of the notice of allegation assert that the '446 Patent is invalid for reasons of obviousness, insufficient disclosure, and lack of utility.

Previous litigation before this Court relating to Pfizer's sildenafil patents

Injunction against CIALIS

[24] In 2003, the applicants filed an urgent motion for an interim injunction restraining Lilly Icos LLC and Eli Lilly Canada Inc. from importing into Canada, distributing and selling a pharmaceutical for the treatment of ED called CIALIS, which according to Pfizer infringed the VIAGRA patent.

[25] I heard the motion on October 28, 2003, and in my order dated November 3, 2003, I denied the motion: *Pfizer Ireland Pharmaceuticals v. Lilly Icos LLC,* 2003 FC 1278, 126 A.C.W.S. (3d) 856. I found that, notwithstanding the decision Mr. Justice Laddie, upheld by the UK Court of Appeal, that the VIAGRA patent was invalid for obviousness, the decision of the European Patent office to revoke the VIAGRA patent and the U.S. Patent office decision to reexamine the VIAGRA patent, the applicants had raised a serious issue, i.e. whether CIALIS infringed the VIAGRA patent. However, I found that the applicants had failed to establish irreparable harm if CIALIS was allowed in Canada, i.e. harm that could not be appropriately compensated by monetary damages.

[26] In the later disposition of the interlocutory injunction, Mr. Justice Pierre Blais (as he then was) found that the Canadian patent was valid until proven otherwise and that the alleged infringement was a serious issue. Justice Blais held, as I had, that the plaintiffs had not shown irreparable harm. He therefore dismissed the motion for an interlocutory injunction: *Pfizer Ireland Pharmaceuticals v. Lilly Icos Inc.*, 2004 FC 223, 129 A.C.W.S. (3d) 399.

The ‘748 Patent

[27] In 2006, the generic Apotex sought a Notice of Compliance to market tablets containing sildenafil, the active ingredient in VIAGRA, and in another Pfizer medicine called Revatio, which treats pulmonary hypertension. Apotex challenged the validity of Pfizer’s ‘748 Patent on the basis of lack of utility and sound prediction, and ambiguity. The ‘748 Patent claimed the use of a broad range of compounds (cGMP PDE inhibitors), including sildenafil, for the treatment of a number of conditions including angina, hypertension, heart failure and atherosclerosis.

[28] Mr. Justice James O’Reilly held that Pfizer had failed to establish that the compounds of the ‘748 Patent, or sildenafil in particular, had been shown or soundly predicted to be potent and selective cGMP PDE inhibitors by the priority date of the patent. He held that the language of the patent was vague, and that the patent did not enable a skilled reader to appreciate the properties in the compounds. Justice O’Reilly concluded that Pfizer had not established that the allegations of invalidity were unjustified and dismissed Pfizer’s application to prohibit the issuance of an NOC. *Pfizer Canada Inc. v. Apotex Inc.*, 2007 FC 26, 306 F.T.R. 254.

The ‘446 Patent

[29] In 2007, Apotex sought to market sildenafil citrate tablets for oral administration in strengths of 25, 50 and 100 mg tablets for the treatment of ED in men – the exact compound and dosage of the VIAGRA drug. Apotex challenged the validity of Pfizer's '446 Patent, the same patent in the case at bar. While the '748 Patent considered by Justice O'Reilly claimed the use of a number of cGMP PDE inhibitors in the treatment of a number of heart conditions, the '446 Patent claims the use of cGMP PDE inhibitors, including sildenafil, in the treatment of ED. Apotex alleged that the '446 Patent was invalid for obviousness, anticipation, and failure to meet the requirements of the legislation.

[30] Mr. Justice Richard Mosley found that the '446 Patent was not invalid for obviousness. He held that although there was a significant amount of evidence indicating that cGMP PDE inhibitors should be further explored with regard to the treatment of ED in the months leading up to the Pfizer discovery, the solution was not obvious at the time and was at best speculative. The most that could be said at the priority date is that sildenafil would be "worth a try" as a treatment for impotence. *Pfizer Canada v. Apotex Inc.,* 2007 FC 971, 319 F.T.R. 48 at paragraphs 123-129. Justice Mosley also found that the patent was not invalid for anticipation, overbreadth, or invalid disclaimer. Unlike the case at bar, Apotex did not allege that the '446 Patent was invalid for insufficient disclosure or lack of utility.

ISSUES

~~[31]~~ The issue raised by this prohibition application is whether the respondent Novopharm's allegations that the '446 patent is invalid are unjustified. While Novopharm raised a number of

issues in its NOA, the parties argued three main issues in their memoranda of fact and law and in the hearing before me:

a. whether the invention of sildenafil for the treatment of ED was obvious at the time of the priority date;

~~b.~~ whether the '446 patent meets the utility requirement by demonstrating or soundly predicting the utility of sildenafil by the Canadian filing date; and

c. whether the disclosure in the '446 Patent met the statutory requirement for disclosure set out in s. 27(3) of the Patent Act as of the '446 Patent's publication date.

ANALYSIS

Burden of proof

[32] In *Abbott Laboratories v. Canada (Minister of Health)*, 2007 FCA 153, 361 N.R. 308, the Federal Court of Appeal dealt with the issue of burden of proof and the presumption of patent validity. At paragraph 9-10, Justice Sharlow stated:

> **9** It is now beyond debate that an applicant for a prohibition order under the *NOC Regulations* bears the burden of establishing its entitlement to the order...
>
> **10** …The presumption [of validity] in subsection 43(2) is weakly worded (*Apotex Inc. v. Wellcome Foundation Limited*, [2002] 4 S.C.R. 153, per Justice Binnie at paragraph 43). It cannot determine the outcome of prohibition proceedings under the *NOC Regulations* if, as in this case, the record contains any evidence that, if accepted, is capable of rebutting the presumption (see *Rubbermaid (Canada) Ltd. v. Tucker Plastic Products Ltd.* (1972), 8 C.P.R. (2d) 6 (F.C.T.D.) at page 14, and *Bayer Inc. v. Canada (Minister of National Health and Welfare)* (2000), 6 C.P.R. (4th) 285, at paragraph 9).

[33] While the ultimate legal burden remains on the applicant, the respondent has been described as having an “evidentiary burden” to rebut the presumption of validity. In *Pfizer v. Canada Inc. v. Canada (Minister of Health)*, 2007 FCA 209. 366 N.R. 347, Justice Nadon stated at paragraphs 109-110:

> Thus, a first person under the Regulations has the overall burden of establishing, on a balance of probabilities, that the allegations of invalidity contained in a second person's NOA are not justified. Although the first person has the initial burden, because of the presumption of the validity of a patent set out in section 45 of the pre-1989 Act, it can meet this burden merely by proving the existence of the patent. The second person then has the burden of adducing evidence of invalidity and of putting the allegations of invalidity contained in its NOA "in play". To do so, the second person must adduce evidence which is not clearly incapable of establishing its allegations of invalidity. Hence, not only must the second person's NOA contain a sufficient factual and legal basis for its allegations, but it must also adduce evidence of invalidity at trial.
>
> **110** Once the second person has adduced sufficient evidence, on a balance of probabilities, the first person must, also on a balance of probabilities, disprove the allegations of invalidity set out in the NOA

[34] These cases were considered by Justice Mosley in *Pfizer v. Apotex*, 2007 FC 971, *supra*. Justice Mosley stated at paragraph 48:

> **48** When read as a whole, these paragraphs should not be taken as holding that the second person bears a legal burden on the standard of proof of a balance of probability to overcome the presumption of validity. It is clear from the Court of Appeal's reasons that the legal burden remains with the first person throughout the proceedings and does not shift to the second person. To meet that burden the first person may rely upon the presumption of validity "**in the absence of any evidence to the contrary**" as set out in subsection 43(2) of the *Patent Act* R.S.C. 1985, c. P-4 as amended, S.C. 1993, c. 15

> [emphasis added]. Should the second person lead any evidence to the contrary, the presumption is spent and the burden remains with the first person to prove validity on the balance of probability standard.

[35] Likewise, in *Pfizer*, 2007 FC 26, *supra*, Justice O'Reilly stated at paragraph 12:

> **12** To summarize, Pfizer bears the legal burden of proving on a balance of probabilities that Apotex's allegations of invalidity are unjustified. Apotex merely has an evidentiary burden to put its case "into play" by presenting sufficient evidence to give its allegations of invalidity an air of reality. If it meets that burden, then it has rebutted the presumption of validity. I must then determine whether Pfizer has established that Apotex's allegations of invalidity are unjustified. If Apotex does not meet its evidential burden, then Pfizer can simply rely on the presumption of validity to obtain its prohibition order.

[36] To summarize with respect to the burden of proof:

1. Novopharm has the evidentiary burden to present sufficient evidence to give its allegations of invalidity "an air of reality" (Novopharm's legal burden in this regard has been described in the jurisprudence as "a sufficient factual and legal basis for its allegations of invalidity with "sufficient" evidence on a balance of probabilities.") Then the burden shifts because the presumption of the patent's validity has been rebutted or overcome by Novopharm), i.e. that it can rebut the presumption of validity; and

2. Pfizer has the legal burden of proving on the balance of probabilities that Novopharm's allegations of invalidity are unjustified.

<u>Patent Claim Construction</u>

[37] The first step in a patent matter is to construe the patent claim. Claim construction is antecedent to consideration of both the validity and the infringement issues: *Whirlpool Corp. v. Camco Inc.* 2000 SCC 67, 9 C.P.R. (4th) 129 at para. 43.

[38] In construing the claims for the purposes of considering the validity of the patent, the court must look primarily to the claims. According to *Hughes & Woodley*, §26 at p. 311-12, the Court may resort to the specification only in limited circumstances:

> In construing a patent, the claims are the starting point. The claims alone define the statutory monopoly and the patentee has a statutory duty to state, in the claims, what the invention is for which protection is sought. In construing the claims, recourse to the rest of the specification is: (1) permissible to assist in understanding the terms used in the claims; (2) unnecessary where the words are plain and unambiguous; and (3) improper to vary the scope or ambit of the claims. This does not mean that claims are never to be construed in light of the rest of the specification but it means that the resort is limited to assisting in comprehending the meaning in which words or expressions contained in the claims are used.

[39] The applicants are relying on Claim 7 which is the claim for the compound sildenafil, and Claims 8, 10, 18 and 22 to the extent they relate to Claim 7. This '446 Patent has already been challenged in this Court and the Federal Court of Appeal. This Court and the Federal Court of Appeal construed the relevant patent claim as Claim 7 in the '446 patent.

[40] Claim 7 was construed by Justice Mosley in *Pfizer v. Apotex, supra*, at paragraphs 21 to 35. He concluded, at paragraph 35, as follows:

> ¶35 Taking into consideration the two disclaimers and with the aid of the expert evidence, to my mind the essential elements of the Claims in Issue can be described as follows: the use of sildenafil (or a salt thereof) in the form of an oral medicine for the treatment of erectile dysfunction in man.

[41] This construction was upheld by the Federal Court of Appeal in *Pfizer v. Apotex*, 2009 FCA 8 at paragraph 11 per Noel J.A.:

> The "solution taught by the patent" that [Justice Mosley] used for this inquiry was consistent with his claim construction, namely "the appreciation that the oral administration of sildenafil, as a potent PDE5 inhibitor, would be useful in the treatment of [ED] in men" (Reasons, para. 57).

[42] The jurisprudence establishes that where a patent has many claims, the Court will construe the relevant claim with respect to the issues. Pfizer submits that in patents such as the one in the case at bar, each claim should be considered separately for the purposes of determining which claim should be construed.

[43] In *Laboratoires Servier v. Apotex*, 2008 FC 825, 67 C.P.R. (4th) 241, Justice Snider summarized several "guiding posts" for determining demonstrated utility. At paras. 270-1, she found:

> [270] …Where a claim is to a class of compounds, lack of utility of one or more of the compounds will invalidate all of the compounds of that particular claim. (*Aventis Pharma Inc. v. Apotex Inc.*, 2006 FCA 64, 46 C.P.R. (4th) 401, at para. 276, leave to appeal to S.C.C. refused, [2006] S.C.C.A. No. 136 (QL), 55 C.P.R. (4th) vi).
>
> [271] Quite simply stated, the question is whether the invention does what the patent promises that it will do.
>
> [Emphasis added]

~~[44]~~ In *C.H. Boehringer Sohn v. Bell-Craig Ltd.*, [1962] Ex.C.R. 201, 39 C.P.R. 201, Justice Thurlow of the Exchequer Court of Canada found that an individually claimed substance was a separate invention.

[45] In *Merck & Co. v. Apotex*, 2006 FC 524, 53 C.P.R. (4th) 1, claims for individually exemplified compounds lisinopril, enalapril and enalaprilat were considered separate inventions despite the fact that all these compounds fell within the class of compounds claimed broadly in another claim of the 340 Patent. In that case, Justice Hughes followed *Boehringer* in finding that these compounds were separate inventions, stating at paragraph 116:

> Were I to approach the matter without jurisprudential constraints, I would readily find that the '340 application is directed to but one invention, a class of compounds, of which individual compounds such as lisinopril are but illustrative. However, *Boehringer* and *Hoechst, supra*, oblige me to find otherwise…there was, in the 340 application not only examples but also specific claims to the individual compounds enalapril, enalaprilat and lisinopril, each of which…is a different invention from the class.
>
> [Emphasis added]

[46] This finding was upheld by the Federal Court of Appeal at paragraph 26 of its decision (*Merck & Co. v. Apotex (FCA), supra).* As the '446 Patent specifically claims and describes sildenafil in claim 7, the Federal Court of Appeal's ruling is applicable here and sildenafil in Claim 7 should be considered separately.

Issue No. 1: Whether the invention of sildenafil for the treatment of ED was obvious at the time of the priority date

Abuse of Process

[47] The applicants submit that re-litigating the validity of the '446 Patent for obviousness is an abuse of process given the decision of this Court in *Apotex, supra*, which was affirmed by the Federal Court of Appeal in 2009 FCA 8. In that case, Mr. Justice Mosley found that Pfizer had

sufficiently demonstrated that the allegations against the validity of the ‘446 Patent for obviousness were unjustified.

~~[48]~~ The applicants submit that Novopharm has, in this case, made substantially the same allegations made by Apotex and has not provided better evidence or argument.

[49] The applicants rely on the Federal Court of Appeal’s decision in *Sanofi-Aventis Canada Inc. v. Novopharm*, wherein the Court found that the patent-holders were could not “re-litigate a claim” that they had already made. The Court stated at paragraph 50:

> … Generics likewise must put forward their full case at the first opportunity. Multiple NOAs issued by the same generic relating to a particular drug and alleging invalidity of a particular patent will generally not be permitted, even if different grounds for establishing invalidity are put forward in each. However, where one generic has made an allegation but has failed to put forward the requisite evidence and argument to illustrate the allegation is justified, it would be unjust to preclude a subsequent generic, who is apprised of better evidence or a more appropriate legal argument, from introducing it…

[50] I will follow the decisions of Justice Mosley and the FCA where those findings are applicable on the facts before me. Novopharm has raised specific arguments in relation to obviousness attempting to distinguish the case at bar from that before Justice Mosley. I do not find this to be an abuse of process, and I will decide these arguments on their merits with reference to Justice Mosley’s decision where appropriate. The allegations of lack of utility and sufficiency raised in this application were not before Justice Mosley and there is no issue of possible abuse of process in relation to these allegations.

The law on obviousness

[51] Until recently, Canadian courts followed the test set out by the Federal Court of Appeal in *Beloit Canada Ltd. v. Valmut Oy*, (1986) 64 N.R. 287, 8 C.P.R. (3d) 289, to determine whether a patent was obvious. That test focused on whether the protected invention was "obvious to try." Justice Hugessen set out the *Beloit* test as follows:

> The test for obviousness is not to ask what competent inventors did or would have done to solve the problem. Inventors are by definition inventive. The classical touchstone for obviousness is the technician skilled in the art but having no scintilla of inventiveness or imagination; a paragon of deduction and dexterity, wholly devoid of intuition; a triumph of the left hemisphere over the right. The question to be asked is whether this mythical creature (the man in the Clapham omnibus of patent law) would, in the light of the state of the art and of common general knowledge as at the claimed date of invention, have come directly and without difficulty to the solution taught by the patent. It is a very difficult test to satisfy.

[52] The Supreme Court recently examined in detail the legal test for obviousness in *Apotex Inc. v. Sanofi-Synthelabo*, 2008 SCC 61, 381 N.R. 125. Justice Rothstein reformulated the test for obviousness at paragraph 66:

> **¶66** For a finding that an invention was "obvious to try," there must be evidence to convince a judge on a balance of probabilities that it was more or less self-evident to try to obtain the invention. Mere possibility that something might turn up is not enough.

In so formulating the test, the Supreme Court changed semantically the threshold for obviousness. Rather than showing that a person skilled in the art could "come directly and without difficulty to the solution taught by the patent to establish obviousness," now a person

challenging the patent need show that “it was more or less self-evident to try” with more than a mere possibility of success.

[53] In affirming Justice Mosley’s decision in *Pfizer v. Apotex*, the Federal Court of Appeal found that although Justice Mosley did not have the benefit of the *Sanofi-Synthlabo* decision, his reasoning accorded with the test set out by the Supreme Court in that case. The FCA stated at paragraphs 36-37:

> **36** It is apparent from the above review that the Federal Court Judge throughout his analysis looked for more than possibilities understanding that mere possibilities were not enough, and that the prior art had to show more than that. His appreciation of the matter is summed up and further demonstrated by his concluding remarks (Reasons, para. 125):
>
> Although there was a significant amount of evidence indicating that cGMP PDE inhibitors should be further explored with regards to the treatment of ED in the months leading up to the Pfizer discovery, the evidence does not in my view establish that the solution taught by the patent was obvious at the time. At best there was speculation, which in hindsight proved to be correct, that PDE5 inhibitors might treat impotence. Experiments with zaprinast, a cGMP PDE inhibitor, had been performed but in an effort to understand how the erectile process works, not how to treat ED.
>
> **37** In so holding, the Federal Court Judge drew the line precisely where the Supreme Court drew it in *Sanofi-Synthelabo* when it held that (para. 66) "the mere possibility that something might turn up is not enough".

[54] The respondent submits that it has presented better and different evidence on the issue of obviousness than was before Justice Mosley in the *Apotex* case. Specifically, the respondent submits that its evidence on the “obvious to try” issue is substantially different from the evidence before Justice Mosley. The respondent states that Apotex’s evidence did not go beyond showing

that there was a “mere possibility that the recommendation of the prior art to use cGMP PDE inhibitors to treat ED might work,” and that had the evidence shown that a skilled person would have a “fair expectation of success,” the result would have been different. According to the respondent, its expert evidence in this case demonstrates such a “fair expectation of success.”

[55] The respondent relies on the Federal Court of Appeal’s decision in *Pfizer Inc. v. Apotex Inc.* in stating that by showing that a skilled person would have had a “fair expectation of success,” it has established obviousness. The Federal Court of Appeal, commenting on the opposite outcome in proceedings in the Chancery Division involving the corresponding UK patent, stated at paragraph 41-45:

> **41** The assessment made by the Federal Court Judge is different than that made by Mr. Justice Laddie of the Chancery Division and confirmed by the English Court of Appeal in the U.K. case. The Federal Court Judge was aware of these decisions (Reasons, para. 119). However, he was entitled, indeed obliged to draw his own conclusions.
>
> **42** Furthermore, a review of Mr. Justice Laddie's decision suggests that the issue of obviousness was determined on the basis of a broader test than that adopted by the Supreme Court in *Sanofi-Synthelabo*…
>
> **43** The reasoning advanced by Mr. Justice Laddie and approved by the English Court of Appeal is that where the motivation to achieve a result is very high, the degree of expected success becomes a minor matter. In such circumstances, the skilled person may feel compelled to pursue experimentation even though the chances of success are not particularly high.
>
> **44** This is no doubt the case. However, the degree of motivation cannot transform a possible solution into an obvious one. Motivation is relevant in determining whether the skilled person has good reason to pursue "predictable" solutions or solutions that provide "a fair expectation of success" (see respectively the passages in *KSR*

> *International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007) at page 1742 and *Angiotech Pharmaceuticals Inc. v. Conor Medsystems Inc.*, [2008] UKHL 49, at paragraph 42, both of which are referred to with approval in *Sanofi-Synthelabo, supra*, at paragraphs 57 and 59).
>
> **45** In contrast, the test applied by Mr. Justice Laddie appears to be met if the prior art indicates that something may work, and the motivation is such as to make this avenue "worthwhile" to pursue (*Pfizer Ltd., supra*, para. 107, as quoted at para. 42 above). As such, a solution may be "worthwhile" to pursue even though it is not "obvious to try" or in the words of Rothstein J. even though it is not "more or less self-evident" (*Sanofi-Synthelabo, supra*, para. 66). In my view, this approach which is based on the possibility that something might work, was expressly rejected by the Supreme Court in *Sanofi-Synthelabo*, at paragraph 66.
>
> [My emphasis]

[56] Accordingly, the Federal Court of Appeal held on January 16, 2009 that the test for obviousness in England, which Mr. Justice Laddie applied to the Pfizer patent for Viagra, is a different test than the Canadian test for obviousness set out by the Supreme Court of Canada in *Sanofi-Synthelabo*. In England, the test is if the prior art indicates that something may work and the motivation is such as to make this avenue “worthwhile to pursue”, then such a solution is obvious to the skilled workman in the field. In Canada the possibility that something might work, and the motivation is such that this avenue is “worthwhile to pursue, was rejected as “obvious”. In Canada it is only obvious if the skilled person has good reason to pursue “predictable” solutions that provide a “fair expectation of success”.

Applying the Obviousness Test to the ‘446 Patent

[57] In Appendix A to the respondent’s memorandum of fact and law, the respondent has set out the findings of fact of Justice Mosley and the relevant “substantially different” evidence before this Court relevant to these findings.

[58] The respondent submits that its evidence – mainly through cross-examination of Pfizer’s experts and the evidence of Novopharm’s experts – establishes the following facts, which are contrary to Justice Mosley’s findings in *Apotex*:

a. The NANC pathway was generally recognized as the most important pathway to target in treating ED;
b. Very few researchers were working on ED and therefore, it was not true that hundreds of researchers studying ED had failed to realize the importance the NANC pathway;
c. The Murray paper pointed to the potential utility of the cGMP PDE inhibitor zaprinast, not sildenafil however, zaprinast was known to have insufficient selectivity and the fact that zaprinast was not tried does not point to the unobviousness of sildenafil;
d. The focus was not on injections and other therapies prior to sildenafil. Orally administered treatments for ED were known and were considered to be safe and effective; and
e. It was not counterintuitive to use a drug that lowered blood pressure to treat ED. Antihypertensive agents were known to be useful in treating ED
f. Dr. Heaton’s testimony that his reaction to Pfizer’s invention was surprise and skepticism is contradicted by his testimony under cross-examination.

[59] The applicants state that this new evidence is “not new evidence at all” but simply commentary by Novopharm’s experts on Justice Mosley’s findings on obviousness.

My Findings on Obviousness

Prior art did not suggest sildenafil as the invention

[60] In the application at bar I find that the prior art (the Rajfer Paper, the Murray Paper and the Bush Thesis) did not teach sildenafil as a solution for the treatment of ED. Dr. Rajfer did not suggest PDE_V inhibitors to treat ED. He suggested direct-acting vascodilators which were NO doners. Dr. Murray suggested PDE_V inhibitors could be developed to treat ED, but did not point to sildenafil or call for clinical trials of sildenafil. The Bush Ph.D Thesis did not mention sildenafil or any particular PDE_V inhibitor from the ‘‘446 patent. The Court has learned from the evidence that there are billions of PDE_V inhibitors, and that the only reason Dr. Ellis, at Pfizer, discovered sildenafil, was by accident in the course of testing sildenafil to treat angina patients in a clinical study. These angina patients unexpectedly experienced erections while being treated with sildenafil to lower their blood pressure.

[61] While Dr. Bush filed an affidavit in the application at bar, which she did not in *Pfizer v. Apotex* before Justice Mosley, the Court is of the view that her thesis was not widely available at the priority date of this patent and could not be considered part of the prior art at the time the patent application was filed. This Ph.D. thesis was not published; it was only filed in two copies at the universities where Dr. Bush was associated. Nevertheless, the Court has considered the content of the Bush thesis and does not find that its conclusions made it more or less self-evident to try sildenafil.

Other evidence

[62] The Court is also impressed with the evidence produced by Pfizer at this hearing. The experts in the relevant field of science studying pharmaceutical solutions for erectile dysfunction did not have any idea in late 1992, when they attended an international convention on the subject, that PDE_V inhibitors, let alone specifically sildenafil, would be effective in treating ED.

[63] The Court is persuaded on the balance of probabilities that persons skilled in the art in 1994, when this patent application was filed, were surprised that Pfizer was claiming an effective oral treatment for ED, and that none of the experts in the field were considering sildenafil as a compound for treating ED (see cross-examination of Dr. de Tejada, Dr. Maurice). Experts in the field were writing after this patent was filed that the treatment of impotence with oral medication was a desired objective for the future. It was the "holy grail" of impotence therapy. When it was finally learned that Pfizer had developed sildenafil for the treatment of impotence, experts wrote that this was a "revolutionary concept".

Detailed evidence on obviousness

[64] The Court has carefully reviewed the parties' evidence on obviousness, and prefers the evidence set out by Pfizer in a 13-page outline entitled "Obviousness," which cross-referenced the exact detailed evidence on the subject.

[65] Points raised by Novopharm in its Appendix A are either alleged erroneous findings of fact by Justice Mosley based on the evidence before me, or material reasons for me to come to a

conclusion that this patent for sildenafil in claim 7 was obvious to try with a fair expectation of success based on the prior art at the time this patent was filed in 1994.

[66] The Court, in reviewing this evidence, and in reviewing the Reasons for Judgment of Justice Mosley, concludes that Justice Mosley's analysis with respect to obviousness from paragraphs 55 to 128, represents a comprehensive and competent analysis of the evidence. I agree with and adopt Justice Mosley's conclusions on obviousness; including:

1. none of the prior art suggested the oral administration of sildenafil as a PDEv inhibitor in the treatment of ED;
2. the discovery of sildenafil's effects was a profound change in treatment method;
3. the commercial success of Viagra and the surprise that accompanied its first publication show that this solution was not obvious, or else it would not have been greeted with such surprise. The commercial success of the first effective oral treatment for ED demonstrates that there was a strong commercial motivation for other drug companies to develop sildenafil before or at the same time as Pfizer, and they would have done so if this solution was obvious;
4. the Canadian patent for Viagra was laid open in 1994. Logically, if the invention of Viagra was obvious, Novopharm or some other drug manufacturer would have challenged the validity of the Viagra patent on this basis years ago. If the Viagra patent was obvious to drug experts, why did the drug experts wait? The long delay shows that the Viagra patent was not obvious.

[67] Accordingly, the Court finds on the totality of the evidence, that the applicants have proven on the balance of probabilities that the Novopharm allegation of invalidity on the basis of obviousness is unjustified.

Issue No. 2: Whether the '446 Patent meets the utility requirement by demonstrating or soundly predicting the utility of sildenafil by the Canadian filing date

[68] Novopharm alleges that Pfizer had not demonstrated the utility of the '446 Patent by the Canadian filing date. Accordingly, Novopharm alleges that the patent is based on prediction and that the invention could not be soundly predicted at the filing date. Therefore, Novopharm alleges that the '446 Patent is invalid for lack of utility, having neither demonstrated utility nor utility based on sound prediction.

[69] There is no dispute as to the actual utility of sildenafil. Novopharm accepts that sildenafil is useful in the treatment of ED, as its goal in this action is to market a generic version of this compound as a solution for ED.

[70] In addition to showing actual utility, Pfizer must show that the inventors had demonstrated that the invention would work by the Canadian filing date, May 13, 1994. Pfizer submits that Study 350 demonstrates the utility of sildenafil and that as a result, there is no need to show that sildenafil met the test for sound prediction at the time of the Canadian filing date.

[71] Novopharm alleges the ‘446 Patent does not demonstrate utility due to Pfizer’s failure to disclose sildenafil in the patent. Novopharm submits utility must be demonstrated in the patent itself and therefore, a patent must explain what the invention is in order to have utility.

[72] Novopharm argues that because the ‘446 Patent does not demonstrate utility, it is a patent based on sound prediction. Novopharm submits that the ‘446 Patent does not meet the sound prediction test because sildenafil is not named as the active pharmaceutical ingredient (“API”) and because the results of Study 350 are not disclosed in the patent. Additionally, Novopharm alleges that Study 350 itself does not demonstrate the utility of sildenafil, nor does it soundly predict the utility of sildenafil, in the treatment of ED, because it is a flawed study.

[73] Finally, Novopharm submits that the ‘446 Patent lacks utility because it includes inoperative species, i.e. thousands of compounds which are inoperative in treating ED.

Utility - Principles of Law

[74] The utility requirement arises out of section 2 of the *Patent Act*, which provides that an invention must be “useful”:

"invention” «*invention* »	«invention » "*invention*"
"invention" means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter;	«invention » Toute réalisation, tout procédé, toute machine, fabrication ou composition de matières, ainsi que tout perfectionnement de l’un d’eux, présentant le caractère de la nouveauté et de l’utilité.

[75] *Hughes & Woodley on Patents* (2nd ed. 2005), summarizes the Canadian patent law with respect to “utility” at § 11 p. 139, Volume 1:

> An essential condition to the validity of a patent is that the invention as claimed should possess utility…Utility means primarily that the invention, as described in the patent, will work in the manner as promised by the patent.

[76] The utility of the patent must have been demonstrated in fact through tests by the Canadian filing date, or “soundly predicted”. Where sound prediction is relied upon in advance of actual testing, the doctrine of sound prediction requires the following three components to be satisfied:

a. there must be a factual basis for the prediction;

b. the inventor must have at the date of the patent application an articulable and sound line of reasoning from which the desired result can be inferred from the factual basis;

> c. there must be proper disclosure, although it is not necessary to provide a theory of why the invention works. The soundness of the prediction is a question of fact.
>
> All three criteria must be met.

(Hughes & Woodley, § 11 p. 139).

[77] In *Consolboard Inc. v. MacMillan Bloedel (Saskatchewan) Ltd*, [1981] 1 S.C.R. 504, Justice Dickson, as he then was, stated at p. 525 that usefulness, while essential for patentability, need only satisfy a low threshold:

> There is a helpful discussion in *Halsbury's Laws of England*, (3rd ed.), vol. 29, at p. 59, on the meaning of "not useful" in patent law. It means "that the invention will not work, either in the sense that it will not operate at all or, more broadly, that it will not do what the specification promises that it will do…The discussion in *Halsbury's Laws of England, ibid.*, continues:
>
> > …the practical usefulness of the invention does not matter, nor does its commercial utility, unless the specification promises commercial utility, nor does it matter whether the invention is of any real benefit to the public, or particularly suitable for the purposes suggested.

[78] Similarly, in *Aventis Pharma Inc. v. Apotex Inc*., 2005 FC 1283, 43 C.P.R. (4th) 161, Justice Mactavish stated at paragraph 271:

> **271** In order to be patentable, an invention must be novel, inventive and useful. Where the specification does not promise a specific result, no particular level of utility is required - a "mere scintilla" of utility will suffice: Fox, Canadian Law and Practice Relating to Letters Patent for Invention, 4th Ed., at p. 153.

Demonstrated Utility

[79] Pfizer submits that the Justice Dickson's explanation of utility in *Consolboard*, *supra*, sets a low threshold for demonstrating utility. According to Pfizer, as long as it can demonstrate that the invention works as promised, per *Consolboard*, it has met the utility requirement.

[80] According to Novopharm, however, this threshold must be met in the patent specification and, as a result of the failure to name sildenafil as the API, the specification does not demonstrate what the invention is or that it works as promised.

[81] The '446 Patent states, at page 10 of the disclosure:

> In man, certain especially preferred compounds have been tested orally in both single does and multiple dose volunteer studies. Moreover, patient studies conducted thus far have confirmed that one of the especially preferred compounds induces penile erection in impotent males.

This statement in the disclosure relates to Study 350, which Pfizer relies on as having demonstrated the utility of sildenafil before the filing date.

[~~82~~] The Court finds that there is no requirement in patent law that evidence of the demonstrated utility of the patent must be included in the patent. It is sufficient that the patent states that the invention has been demonstrated to be useful, as the '446 Patent does by making reference to the clinical testing of the compound (Study 350), and that the patent-holder is able to show evidence of demonstrated utility if the validity of the patent is challenged.

Demonstrated Utility in Study 350

[83] The next question is whether Study 350 adequately demonstrated the utility of sildenafil. Pfizer relies on Study 350, which it submits demonstrated the utility of sildenafil prior to the Canadian filing date. Study 350 is described at paragraph 23 of this judgment under the heading "Evidence of Dr. Peter Ellis."

[84] Novopharm submits that Study 350 was flawed and therefore cannot be the basis for either demonstrating the utility of sildenafil or soundly predicting its utility. In particular, Novopharm states that Study 350 is inadequate to demonstrate or predict the utility of sildenafil because:

a. Study 350's measure of endpoint, i.e. erections, was not clinically appropriate, and that in order to properly show utility in treating ED, successful sexual intercourse should have been the endpoint.

b. The diary data was not statistically significant (p-value greater than 0.05).

c. RigiScan results do not correlate to an ability to engage in sexual intercourse.

[85] Pfizer argues that in treating ED, an erection was the appropriate endpoint, because ED is defined in the patent as the inability to "obtain or sustain an erection adequate for intercourse". Pfizer further argues that Study 350 showed these erections to be sufficient for intercourse because 1) RigiScan readings measured whether erections were sufficient for intercourse and 2) diary data from the study reported results both in terms of erections and sexual intercourse in ED patients. Pfizer submits that for the purposes of demonstrated utility, clinical results do not have to achieve statistical significance or any other level of proof required for regulatory approval.

[86] Having reviewed the data, the Court is satisfied that the results of Study 350 indicate that the patients who received sildenafil showed a significant improvement in erectile function. The expert evidence is that RigiScan is the best available tool for measuring the rigidity and duration of an erection, which is the only objective method of determining whether an erection is adequate for intercourse (Brock Reply Affidavit, Vol. 6). The RigiScan results were statistically significant. Moreover, the diary results, although not statistically significant, nonetheless indicated a subjective measure of improved function. The small size of the study, which was objected to by Novopharm, is accounted for in the p-values measuring the statistical significance of the result.

[87] Novopharm's arguments in relation to the sample size, measurement tools and endpoints of Study 350 essentially contend that, in order to show utility, the results of the study should have been conclusive. However, this Court has held that an inventor does not need to meet a high standard of clinical testing to show utility. In *Apotex v. Wellcome,* (1998) 79 C.P.R. (3d) 193 (F.C.), Justice Wetston stated at paras. 104-5 that an inventor is not required to carry out testing meeting regulatory standards in order to show utility:

> ¶104 I must determine if an inventor can claim an invention which has utility, thus giving society proper consideration for the patent. However, A&N argues that the standard of utility to which a pharmaceutical invention must be held is safety and effectiveness….
>
> ¶105…In my opinion, these requirements are excessive in order for pharmaceuticals to be patentable and create too high a standard for a patent. Indeed, what would the effect of such a standard have on drug research?

As Justice Mactavish stated in *Aventis, supra*, a "scintilla of utility" is sufficient for the purposes of patentability.

[88] The Court finds that Study 350 established that sildenafil, when tested in humans suffering from ED, induced erections that were deemed to be sufficient for intercourse. While the study may not have met the standards for regulatory approval, the Court is satisfied that it is sufficient for the purposes of establishing the demonstrated utility of the invention. Accordingly, the patent's utility need not be established on the basis of sound prediction.

Inoperative Species

[89] Novopharm also alleges, with respect to utility, that the '446 Patent includes inoperative species, i.e. compounds that do not work to treat ED. Only one of the compounds claimed in the '446 Patent, sildenafil, is effective in treating ED. Novopharm alleges that in determining utility, the patent as a whole must be considered rather than Claim 7 alone, and that where a material portion of the invention is useless, the patent is void.

[90] Pfizer responds that as the relevant claims are only claims 7 and the related claims, the inutility of the other compounds claimed in the patent is irrelevant. Pfizer relies on s. 58 of the *Patent Act*, which provides:

Invalid claims not to affect valid claims **58.** When, in any action or proceeding respecting a patent that contains two or more	Revendications invalides **58.** Lorsque, dans une action ou procédure relative à un brevet qui renferme deux ou plusieurs revendications,

claims, one or more of those claims is or are held to be valid but another or others is or are held to be invalid or void, effect shall be given to the patent as if it contained only the valid claim or claims.	une ou plusieurs de ces revendications sont tenues pour valides, mais qu'une autre ou d'autres sont tenues pour invalides ou nulles, il est donné effet au brevet tout comme s'il ne renfermait que la ou les revendications valides.

[91] The issue of inoperative species affects the claims to those inoperative compounds, but as s. 58 of the *Patent Act* provides, the invalidity of the claims to the inoperative compounds does not affect the validity of a claim to a compound which works as promised.

Sufficiency of NOA with respect to the lack of demonstrated utility, in particular that the NOA did not allege that Study 350 was insufficient

[92] Pfizer submits that the Novopharm Notice of Allegation does not allege that Study 350 was insufficient and Novopharm cannot now raise that argument in this application.

[93] Patent '446 does not make any reference to Pfizer's 350 study. The 350 study was first raised by the inventor, Dr. Peter Ellis, in response to the allegation in Novopharm's NOA that there was no demonstrated utility or basis for sound prediction of utility.

[94] The Court finds that Pfizer knew the issue of lack of utility was raised and that Pfizer's evidence addressed this issue. In addressing the issue, Pifzer introduced Study 350 as evidence of demonstrated utility.

[95] The Court finds that a review of the NOA and the Pfizer application makes clear that the issue of utility was squarely raised. When Pfizer's expert, Dr. Ellis, responded to show that Pfizer had evidence that the compound did actually work, Pfizer produced the 350 study. At that point, Novopharm was entitled in law to respond to the 350 study presented as evidence of utility by arguing that the 350 study was flawed and not a sound basis for either demonstrated utility or sound prediction.

[96] Pfizer cannot produce the 350 study in defence of the allegation of lack of utility, and then submit that Novopharm is not able to meet this case by questioning the validity of the 350 study.

[97] Accordingly, the Court finds that the applicants have proven on the balance of probabilities that the Novopharm allegation of lack of utility is unjustified.

Issue No. 3: Whether the disclosure in the '446 Patent met the statutory requirement for disclosure set out in s. 27(3) of the Patent Act as of the '446 Patent's publication date.

1. Novopharm contention

The Act

[98] Novopharm alleges that the patent 446 is invalid because it does not provide sufficient information about the invention as required under subsection 27(3) of the *Patent Act*.

2. The law requiring full disclosure of the invention in the patent

[99] Subsection 27(3) of the *Patent Act* requires that the specification of an invention must:

1. fully describe the invention, its operation and use;

2. set out clearly the various steps in the process or method of construction of the invention to enable any person skilled in the science to which it pertains to make the invention and use it.

[100] Section 27(3) of the *Patent Act* provides:

Specification

(3) The specification of an invention must

(*a*) correctly and fully describe the invention and its operation or use as contemplated by the inventor;

(*b*) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it pertains, or with which it is most closely connected, to make, construct, compound or use it;

(*c*) in the case of a machine, explain the principle of the machine and the best mode in which the inventor has

Mémoire descriptif

(3) Le mémoire descriptif doit:

a) décrire d'une façon exacte et complète l'invention et son application ou exploitation, telles que les a conçues son inventeur;

b) exposer clairement les diverses phases d'un procédé, ou le mode de construction, de confection, de composition ou d'utilisation d'une machine, d'un objet manufacturé ou d'un composé de matières, dans des termes complets, clairs, concis et exacts qui permettent à toute personne versée dans l'art ou la science dont relève l'invention, ou dans l'art ou la science qui s'en rapproche le plus, de confectionner, construire, composer ou utiliser

contemplated the application of that principle; and	l'invention;
(*d*) in the case of a process, explain the necessary sequence, if any, of the various steps, so as to distinguish the invention from other inventions.	*c*) s'il s'agit d'une machine, en expliquer clairement le principe et la meilleure manière dont son inventeur en a conçu l'application; *d*) s'il s'agit d'un procédé, expliquer la suite nécessaire, le cas échéant, des diverses phases du procédé, de façon à distinguer l'invention en cause d'autres inventions.

The leading text

[101] In *Hughes and Woodley on Patents*, 2nd ed., Volume 1, states at paragraph 25, page 303:

> The description of the invention … is the *quid pro quo* for which the inventor is given a monopoly for a limited term of years on the invention; it is to give the public adequate details as will enable a workman skilled in the art to which the invention relates to construct or use that invention when the period of monopoly has expired ….

[102] Under paragraph 27(3)(4), the specification must end with a claim defining distinctly and in explicit terms the subject matter of the invention.

The Federal Court of Appeal

[103] The Federal Court of Appeal in *Pfizer Canada v. Ranbaxy Laboratories Ltd.* (2008), 64 C.P.R. 4th 23 per Nadon J.A. reviewed the jurisprudence about the "sufficiency" requirement under

subsection 27(3) of the *Patent Act*. The Court held that the patent must answer only two questions to meet the sufficiency requirement for the purpose of subsection 27(3):

1. What is the invention?; and

2. How does it work?

The Court held at paragraph 59:

> … if the patent specification (disclosure and claims) answers these questions, the inventor has held his part of the bargain. …

[104] At paragraph 24 Justice Nadon held that the purpose of subsection 27(3) is as follows: (I paraphrase in part)

> 1. "The disclosure requirement under the Act lies at the heart of the whole patent system ….";
>
> 2. The granting of a patent is akin to a contract between the Crown and the inventor in which the latter receives an exclusive right to exploit his invention for a certain period in exchange for complete disclosure to the public of the invention and the way in which it operates …;
>
> 3. The description of the invention is therefore the quid pro quo for which the inventor is given a monopoly for a limited term of years on the invention (20 years) …
>
> 4. The inventor must give to the public an adequate description of the invention with sufficiently complete and accurate details as will enable a workman, skilled in the art to which the invention relates, to construct or use the invention when the period of the monopoly has expired; and
>
> 5. The function of the description is also to enable others to ascertain the exact boundaries of the exclusive privilege upon which they may not trespass during the exercise of the monopoly.

[105] With respect to the scope of the disclosure requirement, Justice Nadon held at paragraph 35, and I paraphrase:

> The applicant must disclose everything that is essential for the invention to function properly. To be complete, it must meet two conditions: it must describe the invention and define the way it is produced or built.

[106] At paragraph 36, Justice Nadon refers to the leading Canadian text *Hughes and Woodley on Patents*, 2nd ed., Volume 1, at 333 and quotes from the text as follows:

> Insufficiency is directed to whether the specification is sufficient to enable a person skilled in the art to understand how the subject mater of the patent is to be made […] An allegation of insufficiency is a technical attack that should not operate to defeat a patent for a meritorious invention; such attack will succeed where a person skilled in the art could not put the invention into practice.
>
> [Emphasis added]

Accordingly, while an allegation of insufficiency normally does not operate to defeat a patent for a meritorious invention, an insufficiency attack will succeed where a person skilled in the art could not put the invention into practice.

[107] The jurisprudence also states that the language in the patent cannot obfuscate, obscure or bewilder the skilled reader of the patent. The description in the patent must be "free from avoidable obscurity or ambiguity and be as simple and distinct as the difficulty of the description permits". The description must not be misleading or calculated to deceive or render it difficult for the skilled reader, without trial and experimentation, to comprehend what the invention is. The description must give all the information necessary for the successful use of the invention without leaving such result to the chance of successful experiment. The inventor must provide all of the information in

good faith. See *Noranda Mines v. Minerals Separation North America Corp.*, [1947] Ex.C.R. 306, 12 C.P.R. 99 at 102, rev'd on other grounds [1950] S.C.R 36, 12 C.P.R. 99 AT 182, aff'd 15 C.P.R. 133 (Privy Council), per Thorson P, followed in *Pioneer Hi Bred. Ltd. v. Canada (Commissioner of Patents)*, [1989] 1 S.C.R. 1623, per Lamer J., as he then was, at para. 27; *Corning Glass Works v. Canada Wire and Cable Ltd.*, (1984) 81 C.P.R. (2d) 39, 26 A.C.W.S. (2d) 54, (F.C.T.D.) per Strayer J. at p. 71; *TRW Inc. v Walbar of Canada Inc. et al*, (1991) 132 N.R. 161, 39 C.P.R. (3d) 176 (F.C.A.), per Stone J.A. at p. 194; *Eli Lilly Canada Inc. v. Novopharm Ltd.*, 2009 FC 235, per Justice Hughes at para. 99.

Relevant Date

[108] The relevant date for construing the '446 patent with respect to the sufficiency of the disclosure is the date that the patent was placed open for public inspection, December 22, 1994. *Eli Lilly Canada Inc. v. Novopharm Ltd.* (2007), 58 C.P.R. (4th) 214 per Hughes J. at paragraph 141; *Whirlpool Corp. v. Camco Inc.*, [2000] 2 SCR 1067 at paragraphs 42 to 62. Whirlpool established that the language of the patent should be construed as of the date the patent is published.

3. What Patent '446 does disclose

[109] The patent specification consists of the disclosure and 27 claims.

(a) The disclsoure

The '446 patent disclosure is 12 pages. At page 1 the disclosure states:

> This invention relates to the use of a series of pyrazolo [4, 3-d] pyrimidin-7-ones (PDEv inhibitors) for the treatment of impotence.

The disclosure defines impotence and states that clinical trials in men to date have shown that only certain drugs are effective in treating impotence but these drugs have to be injected into the penis.

[110] At page 2 the disclosure discusses a variety of other interventions to treat impotence which have been problematic. The disclosure then states that the "compounds of the invention" (patent '446) are "potent inhibitors" which:

> Unexpectedly, it has been found that these disclosed compounds are useful in the treatment of erectile dysfunction. Furthermore, the compounds may be administered orally, thereby obviating the disadvantages associated with (injection).

At page 2, the disclosure states:

> Thus the present invention concerns the use of a compound of formula I:

The disclosure then provides the complex chemical formulae for a range of compounds (which total 260 quintillion, in more understandable language, hundreds of billions of compounds), or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of erectile dysfunction.

[111] Then, from pages 5 to 7, the disclosure breaks down this range of compounds into different categories (which are each separate claims in the patent) respectively called "a preferred group of compounds"; "a more preferred group of compounds", "a particularly preferred group of compounds" and "especially preferred individual compounds". This last category is stated to "include" nine compounds listed.

[112] The Court notes that these ranges of compounds (from 260 quintillion to 9 compounds in the "especially preferred individual compounds list") include sildenafil. However, at no point in the patent is sildenafil identified as the compound which is the actual embodiment of the invention on which Pfizer relies exclusively for this invention.

[113] At page 9 the disclosure states that the compounds of the invention have been tested in-vitro and found to be "potent and selective inhibitors of the cGMP – specific PDEv". At page 10 the disclosure states that none of the compounds of the invention tested in rat and dog has shown any sign of toxicity.

[114] Also at page 10 the disclosure states that "especially preferred compounds" have been tested orally in both single dose and multiple doses. And then, most importantly, at page 10 the disclosure states:

> "Moreover, patient studies conducted thus far have confirmed that one of the especially preferred compounds induces penile erection in impotent males".
>
> (Underlining added)

The disclosure does not state that this compound is sildenafil.

(b) The Claims

[115] The patent includes 27 claims. (There have been two disclaimers which are not pertinent to this NOC application.) The first seven claims relate to a number of compounds for use as a medication for the treatment of impotence.

[116] Claim 1 is the use of a compound of formula I, which is a formula for a range of compounds which number 260 quintillion.

[117] Claim 2 is for a compound in a smaller range of the same compounds. Each successive claim cascades downward in the number of compounds included to Claim 5 which is the use of a compound from one of nine compounds contained in formula I. Claim 6 and Claim 7 both refer to only one compound each. Claim 7 is for a formula which is sildenafil.

4. What Patent '446 does not disclose

[118] Patent '446 does not disclose that Claim 7 and sildenafil is the only claimed compound that Pfizer found in its patient studies to induce penile erection in impotent males and is the only active compound in the invention sold commercially under the trade name Viagra. Patent '446 does not disclose that the many of other claims and compounds in the patent are "red herrings", i.e. they are for claimed compounds which have been found not to work for treating erectile dysfunction.

5. The expert evidence: What does the '446 Patent teach the person skilled in the art?

(a) Claim 7 clearly describes Sildenafil

[119] Dr. Jonathan S. Dordick, an expert witness for Novopharm, deposed that Claim 7 of the '446 Patent claims the use of sildenafil (Affidavit of Dr. Dordick, para. 55). This evidence is uncontradicted and there is no argument between the parties that Claim 7 clearly describes the use of sildenafil to treat ED.

[120] Dr. Peter Ellis, the inventor named in the ‘446 Patent and a witness for Pfizer, testified that sildenafil was the only compound in the patent found to induce erections.

[121] Pfizer submits that as Claim 7 is a separate invention, a skilled person seeking to make the invention would be, by definition, a person seeking to use the particular invention claimed in Claim 7, i.e. the use of sildenafil for the treatment of ED. Thus, the skilled person would not have to select sildenafil, as it is the only invention disclosed in Claim 7.

(b) Evidence that a skilled person would not be able to select Sildenafil from the patent as a whole

[122] Novopharm submitted that a skilled person reading the disclosure and claims as a whole would not know to select sildenafil as the patent does not disclose which of the compounds claimed in the patent was the compound tested in ED patients.

[123] In support of this contention, Novopharm produced evidence from its own experts as well as testimony from Pfizer’s experts. During cross-examination, Dr. Gerald B. Brock, an expert witness for Pfizer, confirmed that a person reading page 10 of the disclosure (wherein the patent states that one of the especially preferred compounds was tested in patients with ED and found to induce erections) would not know that the tested compound was sildenafil (Cross-examination of Dr. Brock, p. 1964, Q. 242). Dr. George Christ, also an expert witness for Pfizer, deposed under cross-examination that he did not know the basis on which the especially preferred compounds listed on page 6 of the disclosure were selected (Cross-examination of Dr. Christ, p. 2414, Q. 434).

[124] Dr. Inigo Saenz de Tejada, an expert for Novopharm, testified that the 446 Patent did not identify the compound used in the disclosed testing (Affidavit of Dr. Saenz de Tejada, para. 92):

> Dealing now with the second sentence: "Moreover, patient studies conducted thus far have confirmed that one of the especially preferred compounds induces penile erection in impotent males," this appears to refer to the 350 Study. As with the description of the healthy volunteer studies, virtually no information is given regarding these studies. The disclosure of the study fails to identify the compound that was tested…

[125] Dr. Donald H. Maurice, an expert for Novopharm, deposed in his evidence in chief that a person skilled in the art wishing to make the invention would choose between the extremely large number of compounds claimed in Claim 1 (Affidavit of Dr. Maurice, para 109):

> Faced with a dearth of information about the invention, the person skilled in the art who wishes to practice the invention would have to start by selecting a compound from the enormous number of compounds in formula (I).

[126] Dr. Dordick stated in his affidavit that the "concealment of the identity of the compound tested is nothing short of astounding", and that such an action prevents effective peer review and is poorly viewed in the scientific community (Affidavit of Dr. Dordick, para. 30).

(c) Evidence that an expert would know to choose sildenafil from the patent as a whole

[127] Pfizer states that in making the above statements, the experts were asked to make reference only to the disclosure, and not to the claims. Pfizer's experts deposed that a skilled person making reference to the relevant claim would know to select sildenafil. First, Pfizer submits that the

subsequent claims in the ‘446 Patent significantly narrow the number of compounds that could potentially be the tested compound.

[128] Professor Jeremy Heaton, an expert witness for Pfizer, stated that a person skilled in the art would need look only to the “especially preferred compounds” referred to in the disclosure, as the disclosure stated that the compound tested was one of these nine compounds (Affidavit of Prof. Heaton, para 69). Dr. Brock deposed in his affidavit that in reading the claims, a skilled person would be aware that only two compounds of the preferred group are individually claimed and would be able to narrow their focus to these compounds (Affidavit of Dr. Brock, para. 220):

> …Furthermore, in the claims only two compounds of the preferred group are selected for individual claiming. Sildenafil is one, and is claimed in Claim 7. A skilled person would understand that sildenafil is one of two compounds that the inventors thought to be most important for the treatment of erectile dysfunction.

6. Construction of the patent specification

[129] To determine whether patent ‘446 sufficiently describes the invention, the specification is to be construed as addressed to a person skilled in the art. The specification includes the disclosure and all the claims. The Court must construct the patent to determine whether the specification is sufficient to enable a person skilled in the art to understand and make the invention as of the date the patent was laid open to the public. See *Burton Parsons Chemicals, Inc. v. Hewlett Packard (Canada) Ltd.*, [1976] 1 SCR 555 per Pigeon J. at pages 4, 5 and 7 and *Hughes & Woodley on Patents*, above, paragraph 25(3) at page 304-5.

[130] Novopharm alleges that the patent does not sufficiently describe the invention because the skilled reader could not determine from the 7 claims for compounds, which of the compounds embodied the invention. Pfizer submits that the only relevant claim is Claim 7, which is a claim for a single compound, sildenafil. Accordingly, the skilled reader would know from looking at Claim 7 that sildenafil is the invention.

[131] Each of the claims, according to the law, represents a separate monopoly and each claim must be viewed separately in relation to the disclosure. In the alternative, as discussed, the evidence of Dr. Brock, an expert witness for Pfizer, is that a skilled reader of the patent would understand see that Claim 7 and sildenafil is the relevant invention. Dr. Brock stated:

> … in the claims only two compounds of the preferred group are selected for individual claiming. Sildenafil is one, and is claimed in Claim 7. A skilled person would understand that sildenafil is one of two compounds that the inventors thought to be most important for the treatment of erectile dysfunction. A skilled person would and could choose these compounds.

The importance and value of Patent '446

[132] I cannot disregard the jurisprudence which has condoned the claiming of classes of compounds and single compounds within that class as separate monopolies, and construes only the claim for the single compound which contains the relevant commercial product. I have not been referred to any case, and I cannot find any case, which considers the issue of sufficiency with respect to a patent which contains many claims, but does not disclose the claim embodied in the invention found to be the commercial product. While the Federal Court of Appeal in *Ranbaxy*,

supra., comprehensively reviewed the law with respect to sufficiency of disclosure, it did not deal with this aspect of the issue.

[133] The importance and value of this patent should not be invalidated by such an objection 13 years after the patent was laid open for public inspection because it was allegedly not clear to the notional skilled reader that sildenafil was the active compound which made the invention work. The credibility of this allegation is undermined since it has only been raised in 2007, 13 years after the patent was laid open for public inspection.

[134] Moreover, if I dismissed this application for an order prohibiting the NOC for a generic version of Viagra, an appeal would be moot since the NOC would have issued.

8. *Obiter*

[135] I prefer to express in *obiter* my discomfort with the existing jurisprudence which condones a patent description by way of cascading claims for groups of compounds such that the skilled reader must undertake a minor research project to determine which claim is the true invention. In my mind, the disclosure plays games with the reader. Why did the disclosure not simply state that that compound in Claim 7 was sildenafil? The patent plays “hide and seek” with the reader. The reader is expected to look for the “needle in the haystack”, or “the tree in the forest”. Remember, Claim 1 is for a range of compounds which includes 260 quintillion compounds.

[136] By withholding from the public the identity of the only compound tested and found to work, sildenafil, the patent did not fully describe the invention. Obviously Pfizer made a conscious choice not to disclose the identity of the only compound found to work, and left the skilled reader guessing. This is contrary to the statutory requirement to fully disclose the invention.

[137] The applicants are putting the “cart before the horse”. The applicants submit that only Claim 7 is relevant because Novopharm seeks to introduce a generic version of sildenafil. But sildenafil is “the cart”. It is impossible to understand from the patent that sildenafil (the cart) is the invention which works without researching whether the other compounds identified in the other claims do not work.

[138] On the other hand, there is comfort in the disclosure stating that “one of the especially preferred compounds induces penile erection in impotent males”. Then in Claim 6 and Claim 7 only single compounds are described and the expert witness Dr. Brock deposed that the skilled reader would know that the compound which worked must be one of those two compounds. Then the skilled reader would conduct tests on those two compounds to determine which of those two compounds worked.

[139] Moreover, in view of the jurisprudence, the relevant claim is Claim 7 and Claim 7 does clearly describe sildenafil as the compound for the invention.

9. The Court's conclusion with respect to sufficiency of disclosure

[140] Novopharm alleges that the Pfizer patent '446 for Viagra is invalid for insufficiency of disclosure under subsection 27(3) of the *Patent Act*. An attack based on insufficiency has been held by the Federal Court of Appeal in *Ranbaxy*, *supra*, quoting with approval from *Hughes & Woodley*, as one which should not defeat a meritorious invention unless a skilled reader of the invention would not be able to know "what is the invention?" and "how does it work?".

[141] First, Patent '446 includes within its claims a meritorious invention. The proof of the pudding is in the tasting. The patent includes claims encompassing the commercially successful drug popularly known as Viagra.

[142] Second, the patent was laid open to the public in Canada on December 22, 1994, the relevant date for assessing whether a skilled reader would have sufficient information in the patent to answer the two above-mentioned questions. The Novopharm allegation of insufficiency comes in 1997, 13 years after it was laid open to the public, 11 years after Pfizer publically identified sildenfil as the active ingredient in the drug, and 9 years after Viagra was introduced (in the Unites States) and available for analysis.

[143] Third, the fact that this patent has not been challenged for insufficiency of disclosure until 2007 raises the question "why not". Surely the patent would have been attacked on this basis before 2007 if there was any possibility of success. Moreover, such an attack was not pursued before the

Federal Court of Canada, the Federal Court of Appeal or the English Courts in other legal proceedings seeking to invalid this same patent for Viagra.

[144] Fourth, the skilled reader knows, and has known for years, that sildenafil is the active ingredient in the invention and will be able to make the invention when the patent expires in 2014.

[145] Fifth, the jurisprudence with respect to sufficiency of disclosure condones the claiming of classes of compounds, and single compounds within a patent, and considers only the relevant claim with the disclosure when deciding whether the patent clearly describes the patent and how it works.

[146] Sixth, in any event, the disclosure in patent 446 does state that “One of the especially preferred compounds” has been found to work, and in that group of compounds there are only nine compounds. Then the skilled reader would see that Claim 6 and Claim 7 each describe a single compound, and the expert witness Dr. Brock deposed that the skilled reader would know that one of those two single compounds was the invention which worked. A skilled reader would then conduct tests on those two compounds and determine which of those compounds worked. In this case, Claim 7 is the compound which works and Claim 7 does sufficiently and clearly describe sildenafil.

[147] Accordingly, Pfizer has demonstrated, on the balance of probabilities, that the allegation of invalidity based on insufficiency of disclosure is unjustified.

10. Appeal if wrong

[148] While I found in *obiter* the construction and language in the patent obfuscated the reader and did not simply and distinctly describe the true invention for the skilled reader, I followed the jurisprudence that Claim 7 is a separate monopoly, and that Claim 7 alone with the disclosure can be read by the Court to determine whether the patent sufficiently described the invention and how it works. If I am wrong in reading or following this jurisprudence, I welcome judicial correction on appeal.

CONCLUSION

[149] The Court concludes that the applicants have met their legal burden to establish the validity of the ‘446 Patent and have established on the balance of probabilities that the Novopharm allegations that Pfizer’s ‘446 Patent is invalid for obviousness, lack of utility and insufficiency of disclosure are unjustified. Accordingly, the Minister of Health will be prohibited from issuing a Notice of Compliance to the respondent Novopharm until after the expiry of the patent.

ORDER

THIS COURT ORDERS that:

1. This application is allowed and the Minister of Health is prohibited from issuing a Notice of Compliance to Novopharm for a generic version of Viagra until Pfizer's Patent '446 expires in 2014; and

2. The applicants are entitled to their costs on the mid scale of the tariff.

"Michael A. Kelen"
Judge

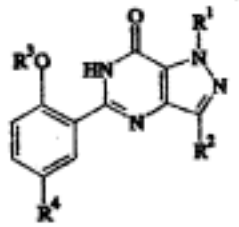
APPENDIX “A”

DISCLAIMER - RENONCIATION
See Form 2 for details - voir Formule 2 pour détails

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

Disclaimer - Renonciation

1. The use of a compound of formula (I):



(I)

wherein R^1 is H, C_1-C_3 alkyl, C_1-C_3 perfluoroalkyl, or C_3-C_5 cycloalkyl;

R^2 is H, C_1-C_6 alkyl optionally substituted with C_3-C_6 cycloalkyl, C_1-C_3 perfluoroalkyl, or C_3-C_6 cycloalkyl;

R^3 is C_1-C_6 alkyl optionally substituted with C_3-C_6 cycloalkyl; C_1-C_6 perfluoroalkyl; C_3-C_5 cycloalkyl; C_3-C_6 alkenyl, or C_3-C_6 alkynyl; R^4 is C_1-C_4 alkyl optionally substituted with OH, NR^5R^6, CN, $CONR^5R^6$ or CO_2R^7; C_2-C_4 alkenyl optionally substituted with CN, $CONR^5R^6$ or CO_2R^7; C_2-C_4 alkanoyl optionally substituted with NR^5R^6, (hydroxy)C_2-C_4 alkyl optionally substituted with NR^5R^6; (C_2-C_3 alkoxy) C_1-C_2 alkyl optionally substituted with OH or NR^5R^6, $CONR^5R^6$, CO_2R^7, halo, NR^5R^6, $NHSO_2NR^5R^6$, $NHSO_2R^8$, $SO_2NR^9R^{10}$, or phenyl, pyridyl,

pyrimidinyl, imidazolyl, oxazolyl, thiazolyl, thienyl or triazolyl any of which is optionally substituted with methyl; R^5 and R^6 are each independently H or C_1-C_4 alkyl, or together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino, 4-N(R^{11})-piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or OH;

R^7 is H or C_1-C_4 alkyl;

R^8 is C_1-C_3 alkyl optionally substituted with NR^5R^6;

R^9 and R^{10} together with the nitrogen atom to which they are attached form a pyrrolidinyl, piperidino, morpholino or 4-N(R^{12})-piperazinyl group wherein said group is optionally substituted with C_1-C_4 alkyl, C_1-C_3 alkoxy, $NR^{13}R^{14}$ or $CONR^{13}R^{14}$;

R^{11} is H; C_1-C_3 alkyl optionally substituted with phenyl; (hydroxy)C_2-C_3 alkyl; or C_1-C_4 alkanoyl;

R^{12} is H; C_1-C_6 alkyl; (C_1-C_3 alkoxy)C_2-C_6 alkyl; (hydroxy)C_2-C_6 alkyl; ($R^{13}R^{14}$N)C_2-C_6 alkyl; ($R^{13}R^{14}$NOC)C_1-C_6 alkyl; $CONR^{13}R^{14}$; $CSNR^{13}R^{14}$; or $C(NH)NR^{13}R^{14}$;

and R^{13} and R^{14} are each independently H; C_1-C_4 alkyl; (C_1-C_3 alkoxy)C_2-C_4 alkyl; or (hydroxy)C_2-C_4 alkyl;

or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic

treatment of an erectile dysfunction in a male animal or sexual dysfunction in a female animal.

2. The use according to claim 1 wherein in the compound of formula (I) R^1 is H, methyl or ethyl; R^2 is C_1-C_3 alkyl; R^3 is C_2-C_3 alkyl or allyl; R^4 is C_1-C_2 alkyl optionally substituted with OH, NR^5R^6, CN, $CONR^5R^6$ or CO_2R^7; acetyl optionally substituted with NR^5R^6; hydroxyethyl optionally substituted with NR^5R^6; ethoxymethyl optionally substituted with OH or NR^5R^6; CH=CHCN, CH=CHCONR^{5}R^6, $CH=CHCO_2R^7$, $CONR^5R^6$, CO_2H; Br; NR^5R^6; $NHSO_2NR^5R^6$; $NHSO_2R^8$; $SO_2NR^9R^{10}$, or pyridyl or imidazolyl either of which is optionally substituted with methyl; R^5 and R^6 are each independently H, methyl or ethyl, or together with the nitrogen atom to which they are attached form a piperidino, morpholino, 4-N(R^{11})-piperazinyl or imidazolyl group wherein said group is optionally substituted with methyl or OH; R^7 is H or t-butyl; R^8 is methyl or $CH_2CH_2CH_2NR^5R^6$, R^9 and R^{10} together with the nitrogen atom to which they are attached form a piperidino or 4-N(R^{12})-piperazinyl group wherein said group is optionally substituted with $NR^{13}R^{14}$ or $CONR^{13}R^{14}$; R^{11} is H, methyl, benzyl, 2-hydroxyethyl or acetyl; R^{12} is H, C_1-C_3 alkyl, (hydroxy)C_2-C_3 alkyl, $CSNR^{13}R^{14}$ or $C(NH)NR^{13}R^{14}$, and R^{13} and R^{14} are each independently H or methyl.

3. The use according to claim 2 wherein in the compound of formula (I) R^1 is methyl or ethyl; R^2 is C_1-C_3 alkyl; R^3 is ethyl, n-propyl or allyl; R^4 is $CH_2NR^5R^6$,

$COCH_2NR^5R^6$, $CH(OH)CH_2NR^5R^6$, $CH_2OCH_2CH_3$, $CH_2OCH_2CH_2OH$, $CH_2OCH_2CH_2NR^5R^6$, $CH{=}CHCON(CH_3)_2$, $CH{=}CHCO_2R^7$, $CONR^5R^6$, CO_2H, Br, $NHSO_2NR^5R^6$, $NHSO_2CH_2CH_2CH_2NR^5R^6$, $SO_2NR^9R^{10}$, 2-pyridyl, 1-imidazolyl or 1-methyl-2-imidazolyl; R^5 and R^6 together with the nitrogen atom to which they are attached form a piperidino, 4-hydroxypiperidino, morpholino, 4-N(R^{11})-piperazinyl or 2-methyl-1-imidazolyl group; R^7 is H or t-butyl; R^9 and R^{10} together with the nitrogen atom to which they are attached form a 4-carbamoylpiperidino or 4-N(R^{12})-piperazinyl group; R^{11} is H, methyl, benzyl, 2-hydroxyethyl or acetyl; and R^{12} is H, C_1-C_3 alkyl, 2-hydroxyethyl or $CSNH_2$.

4. The use according to claim 3 wherein in the compound of formula (I) R^1 is methyl or ethyl; R^2 is n-propyl; R^3 is ethyl, n-propyl or allyl; R^4 is $COCH_2NR^5R^6$, $CONR^5R^6$, $SO_2NR^9R^{10}$ or 1-methyl-2-imidazolyl; R^5 and R^6 together with the nitrogen atom to which they are attached form a morpholino or 4-N(R^{11})-piperazinyl group; R^9 and R^{10} together with the nitrogen atom to which they are attached form a 4-N(R^{12})-piperazinyl group; R^{11} is methyl or acetyl; and R^{12} is H, methyl, 2-propyl or 2-hydroxyethyl.

5. The use according to claim 4 wherein the compound of formula (I) is selected from:

5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-(5-morpholinoacetyl-2-n-propoxyphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-[2-allyloxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]-pyrimidin-7-one;

5-{2-ethoxy-5-[4-(2-propyl)-1-piperazinylsulphonyl]-phenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]-pyrimidin-7-one;

5-{2-ethoxy-5-[4-(2-hydroxyethyl)-1-piperazinyl-sulphonyl]phenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one;

5-{5-[4-(2-hydroxyethyl)-1-piperazinylsulphonyl]-2-n-propoxyphenyl}-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo-[4,3-d]pyrimidin-7-one;

5-[2-ethoxy-5-(4-methyl-1-piperazinylcarbonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; and

5-[2-ethoxy-5-(1-methyl-2-imidazolyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one, or a pharmaceutically acceptable salt thereof.

6. The use according to claim 4 wherein the compound of formula (I) is 5-(2-ethoxy-5-morpholinoacetylphenyl)-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one or a pharmaceutically acceptable salt thereof.

7. The use according to claim 4 wherein the compound of formula (I) is 5-[2-ethoxy-5-(4-methyl-1-piperazinyl-sulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one or a pharmaceutically acceptable salt thereof.

Disclaimer - Reconciliation

8. The use according to any one of claims 1 to 7 wherein the said male animal is man.

Disclaimer - Reconciliation

9. The use according to any one of claims 1 to 7 wherein the said female animal is woman.

Disclaimer - Reconciliation

10. A pharmaceutical composition for the curative or prophylactic treatment of erectile dysfunction in a male animal, including man, comprising a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable diluent or carrier.

Disclaimer - Reconciliation

11. A pharmaceutical composition for the curative or prophylactic treatment of sexual dysfunction in a female animal, including woman, comprising a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable diluent or carrier.

Disclaimer - Reconciliation

12. A process for the preparation of a pharmaceutical composition for the curative or prophylactic treatment of

18. The use of a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, for the curative or prophylactic treatment of erectile dysfunction in man.

Disclaimer - Reconciation

19. The use of a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, for the curative or prophylactic treatment of sexual dysfunction in woman.

Disclaimer - Reconciation

20. A commercial package containing, as active pharmaceutical ingredient, a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with instructions for its use for the curative or prophylactic treatment of erectile dysfunction in a male animal.

Disclaimer - Reconciation

21. A commercial package containing, as active pharmaceutical ingredient, a compound of formula (I) according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, together with instructions for its use for the curative or prophylactic treatment of sexual dysfunction in a female animal.

Disclaimer - Reconciation

22. The use according to any one of claims 1 to 9 wherein the medicament is adapted for oral treatment.

Disclaimer - Reconciation

23. A pharmaceutical composition according to claim 10

or 11 which is adapted for oral treatment.

Disclaimer - Reconciliation

24. A commercial package according to claim 20 or 21 wherein the active pharmaceutical ingredient is adapted for oral treatment.

Disclaimer - Reconciliation

25. The use of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the oral treatment of erectile dysfunction in man.

Disclaimer - Reconciliation

26. The use of a cGMP PDE inhibitor, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition containing either entity, for the manufacture of a medicament for the curative or prophylactic oral treatment of erectile dysfunction in man.

Disclaimer - Restrictive

27. The use according to claim 25 or 26 wherein the inhibitor is a cGMP PDE$_5$ inhibitor.

SMART & BIGGAR
OTTAWA, CANADA

PATENT AGENTS

59387-204

APPENDIX “B”

Witness List

Pfizer Witnesses

1. **Dr. Peter Ellis** - one of the inventors named in the 446 Patent; a pharmacologist; current position at Pfizer is Executive Director and Development Team Leader in the Genito-urinary Therapeutic Area.

2. **Dr. Gerald B. Brock** - a urologist and surgeon; professor of surgery in the Faculty of Medicine, Division of Urology at the University of Western Ontario in London; researched neuro-urology under Dr. Tom Lue, leading researcher in erectile dysfunction; focus of research was on the causes and treatments of erectile dysfunction; studied non-adrenergic non-cholinergic (NANC) pathway, and the neuro-regulation of erections in rats and dogs; involved in clinical trials of sildenafil, tadalafil and vardenafil.

3. **Dr. George J. Christ** - professor of urology, physiology and pharmacology, and regenerative medicine at the Wake Forest Institute for Regenerative Medicine in North Carolina; an Affiliate Faculty Member at the Virginia Tech-Wake Forest University School of Biomedical Engineering and Sciences; has expertise in smooth muscle physiology; researches urology and penile smooth muscle, with particular interest in erectile dysfunction.

4. **Professor Jeremy P.W. Heaton** - medical specialist in urology; was a professor of urology, pharmacology and toxicology at Queen's University in Kingston, Ontario until 2006; extensive research experience in impotence and sexual dysfunction, including the study of physiology of erections, erectile dysfunction and pharmacology of drugs for erectile dysfunction; studied the NO/cGMP pathway for penile erection in late 1980s; began focusing on neural stimulation of the NANC pathway for ED in 1990.

5. **Dr. Frank Burslem** - Senior Director, Discovery Biology of Pfizer Global Research & Development; was a research biochemist in the Cardiovascular Biology Group (a group within Discovery Biology) at Pfizer from 1987 to 1992; was responsible for the biological testing of potential candidate drugs, including sildenafil.

6. **Dr. Sharon Francis** - research professor in the Department of Molecular Physiology and Biophysics at the Vanderbilt University School of Medicine (Nashville); an expert in PDEs, with a special emphasis on PDE5; has extensive knowledge and experience in the fields of cell physiology, enzymology and cell signaling.

Novopharm Witnesses

1. **Dr. Donald Maurice** - professor of pharmacology and toxicology and pathology and molecular medicine at Queens University in Kingston, Ontario; a pharmacologist; researches PDEs; consulted for Bayer-AG on the development of a PDE5 inhibitor for the treatment of male erectile dysfunction; research at Queens focuses on the roles of PDEs in the cardiovascular system.

2. **Dr. Inigo Saenz de Tejada, M.D.** - Director of the Institute for Sexual Medicine and President of the Foundation for Research and Development in Andrology in Madrid, Spain; began studying impotence in 1982 at Boston University; a member of various specialist professional associations in the fields of impotence, andrology, sexual medicine and urology; research focuses on erectile dysfunction, penile erection, sexual dysfunction, pharmaceutical compounds that effect erectile dysfunction (including sildenafil, vardenafil and tadalafil).

3. **Jonathan Dordick** - professor in the departments of Chemical Biological Engineering and Biology at Rensselaer Polytechnic Institute in Troy, New York; has expertise in enzymology, protein-protein and protein-ligand interactions, biosynthetic chemistry, medicinal and natural products chemistry, and bio-engineering; research interests include drug discovery, biocatalysis, formulations for active and stable biologicals, protein- and DNA-based nanoscale architectures, metabolic pathway engineering, and biopolymer synthesis and characterizations.

4. **Margaret Bush** - author of the "Bush Thesis"; completed a Ph.D. in pharmacology at UCLA in 1993; in the early 1990s, researched the role of nitric oxide and cyclic GMP in relaxation of corpus cavernosum smooth muscle under the direction of Louis Ignarro.

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-1566-07
STYLE OF CAUSE:	PFIZER CANADA INC. ET AL. v. NOVOPHARM LIMITED ET AL.
PLACE OF HEARING:	Toronto, Ontario and Ottawa, Ontario
DATE OF HEARING:	April 28, 29, 30, 2009 (Toronto, Ontario) May 5, 2009 (Ottawa, Ontario)
REASONS FOR ORDER AND ORDER:	KELEN J.
DATED:	June 18, 2009

APPEARANCES:

Andrew Shaughnessy, Andrew Bernstein, Vincent de Grandpré and Sandra Perri	FOR THE APPLICANTS
David Aitken Marcus Klee	FOR THE RESPONDENT (NOVOPHARM LTD.)

SOLICITORS OF RECORD:

Andrew Shaughnessy, Andrew Bernstein and Vincent de Grandpré Torys LLP Toronto, Ontario	FOR THE APPLICANTS
David Aitken Marcus Klee	FOR THE RESPONDENT (NOVOPHARM LTD.)

Osler, Hoskin & Harcourt, LLP
Ottawa, Ontario

John H. Sims, Q.C.
Deputy Attorney of General of Canada

FOR THE RESPONDENT
(MINISTER OF HEALTH)