Federal Court Cour fédérale

Date: 20120618

Docket: T-1560-10

Citation: 2012 FC 767

Toronto, Ontario, June 18, 2012

PRESENT: The Honourable Mr. Justice Hughes

BETWEEN:

ALLERGAN INC., ALLERGAN SALES INC. and ALLERGAN, INC.

Applicants

and

THE MINISTER OF HEALTH and APOTEX INC.

Respondents

REASONS FOR JUDGMENT AND JUDGMENT

[1] This is an application made under the provisions of the *Patented Medicines (Notice of Compliance) Regulations* SOR/93-133, as amended (*NOC Regulations*) to prohibit the Minister of Health from issuing a Notice of Compliance to Apotex Inc. for a topical ophthalmic product to be known as APO-BRIMONIDINE-TIMOP, which Apotex has compared to Allergan Inc.'s product known as COMBIGAN, until the expiry of Canadian Letters Patent No. 2,440,764 (the '764 patent) on April 9, 2023. For reasons of comity, the Application is allowed.

[2] For convenience, the topics discussed can be found at the following paragraphs:

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THE PARTIES

[3] The Applicant Allergan, Inc (note the comma). is the owner of the '764 patent. The Applicant Allergan Inc. (no comma) is a Canadian pharmaceutical manufacturer which sells the COMBIGAN product in Canada. Allergan Sales Inc. played no active part in these proceedings. I will refer to the Applicants collectively as Allergan.

[4] The Respondent Minister of Health is, among other matters, responsible for granting Notices of Compliance to those wishing to distribute medicines such as those at issue here, in Canada. The Minister has notice of these proceedings but has taken no active part in them.

[5] The Respondent Apotex Inc. is a Canadian corporation which manufactures and distributes generic medicines in Canada. In the present case, it wishes to make and sell an ophthalmic drug called APO-BRIMONIDINE-TIMOP, which is a generic version of Allergan's COMBIGAN.

[6] In the parlance of the *NOC Regulations*, Allergan is a "first person", and Apotex is a "second person".

THE MEDICINE

[7] The COMBIGAN medicine is a topical ophthalmic solution to treat intraocular pressure (IOP) in persons suffering from chronic glaucoma. In short, it is an eye drop medicine used to treat glaucoma.

[8] In particular, the COMBIGAN medicine is in the form of a liquid solution having two active ingredients; 0.2% by weight/volume of brimonidine, and 0.5% by weight/volume of timolol, together with other pharmaceutically acceptable ingredients (excipients) including a stabilizer known as BAK.

THE '764 PATENT

[9] Canadian Letters Patent No. 2,440,764 (the '764 patent), entitled "*Combination of Brimonidine and Timolol for Topical Ophthalmic Use*", were issued and granted to the Applicant Allergan, Inc. on October 25, 2005.

[10] The application for the patent was filed under the provisions of the Patent Co-Operation Treaty (PCT); with an effective filing date in Canada of April 9, 2003. The application and patent are governed by the provisions of the *Patent Act*, RSC 1985, c. P-4, applicable after October 1, 1989, sometimes called the "new" *Patent Act*. The term of the '764 patent will expire twenty (20) years from its effective filing date in Canada; that is, on April 9, 2023.

[11] The '764 patent claims a priority date of April 19, 2002, which is the date when a similar application was filed in the United States Patent Office. This is the date upon which the issues of obviousness and anticipation are to be considered.

[12] The application for the '764 patent was laid open for public inspection, through the Patent Co-Operation Treaty, on October 19, 2003. This is the date to be used for construing the patent.

[13] Before reviewing the patent in detail, there a few terms used in the patent and in evidence that require explanation and upon which the parties are agreed. It is agreed that the prior art included the administration of drops to the eye in order to reduce the intraocular pressure (IOP) in the eyeball as a means to treat or control glaucoma. The known active ingredients included either timolol or brimonidine. The drops were often self-administered by the patient. Administration twice a day is

referred to as BID. Administration three times a day is referred to as TID. The precise derivation of these terms is not clear in the record but apparently the B stands for bis and the T for ter. On occasion drops of one drug would be administered closely followed (usually in five minutes or so) by drops of the other. This type of administration is sometimes called serial administration or adjuvant administration. On occasion a witness may also refer to this as a combination administration. This is not to be confused with administration of a medicine that includes both drugs in one bottle. This is sometimes referred to by a witness as administration of a combination drug.

[14] The '764 patent begins at page 1 with a statement as to the background of the invention and what the invention does. It acknowledges that two active ingredients, brimonidine and timolol, are known and have been used to treat glaucoma, including the fact that they have been used in serial application (i.e. one after the other). It is important to note what the patent says the need is; and, having regard to the conclusions on page 16 which will be discussed later, what the patent says the invention delivers; this is (a) a composition including both brimonidine and timolol that is (b) effective, (c) safe, (d) has increased stability, and (e) requires a lower effective concentration of preservative as compared to each medicine if taken as a separate dose of each of brimonidine and timolol. It says:

> *BACKGROUND OF THE INVENTION*
>
> *This invention relates to the topical ophthalmic use of brimonidine in combination with timolol when indicated for treatment of glaucoma or ocular hypertension. Such combinations or formulations are available for separate use in the ophthalmic art and have been combined in serial application during the course of treatment of glaucoma. However, there are concerns and expressed reservations in the ophthalmic community about patient compliance when the patient is required to administer separate medications to*

> *treat a single disease or condition such as glaucoma. There is, moreover, a long felt need for an effective and safe topical ophthalmic pharmaceutical composition including brimonidine and timolol which has increased stability and requires a lower effective concentration of preservative as compared to the individual agents taken alone. Finally, there is a need to increase the efficacy of many topical ophthalmic agents, without increasing the systemic concentration of such topical agents, since it is well known that many of such topically-applied ophthalmic agents cause systemic side effects, e.g. drowsiness, heart effects, etc. Unexpectedly it has been discovered that brimonidine in combination with timolol meets these criteria.*
>
> *Brimonidine is disclosed in U.S. Patent 3,890,319. The use of brimonidine for providing neuroprotection to the eye is disclosed in U.S. Patents 5,856,329; 6,194,415 and 6,248,741.*
>
> *Timolol, as an ophthalmic drug, is disclosed in U.S. Patents 4,195,085 and 4,861,760.*

[15] At pages 2 and 3 chemical depictions of brimonidine and timolol are provided, which I will not repeat, and indications as to where they may be purchased. Two paragraphs at page 3 provide for more specific dosages but it is to be noted that while one drop two times a day is recommended, the precise regimen is left to the discretion of the clinician:

> *The compositions of the present invention are administered topically. The dosage is 0.001 to 1.0, e.g. mg/per eye BID; wherein the cited mass figures represent the sum of the two components, brimonidine and timolol. The compositions of the present invention can be administered as solutions in a suitable ophthalmic vehicle.*
>
> *In forming compositions for topical administration, the mixtures are preferably formulated as 0.01 to 0.5 percent by weight brimonidine and 0.1 to 1.0 percent by weight timolol solution in water at a pH of 4.5 to 8.0, e.g. about 6.9. While the precise regimen is left to the discretion of the clinician, it is recommended that the solution be topically applied by placing one drop in each eye two times a day. Other ingredients which may be desirable to use in the ophthalmic preparations of the present invention include preservatives, co-solvents and viscosity building agents.*

[16] At the bottom of page 3 and over to page 4, the description addresses preservatives used to prevent microbial contamination. It acknowledges that benzalkonium chloride (referred to as BAK in these proceedings) is one of the known preservatives and describes, in particular, certain levels of concentration of BAK (from 0.001% to less than 0.01% e.g. from 0.001% to 0.008% preferably about 0.005% by weight) and dosages (twice a day) of the combination medicine that are advantageous, and that adequate lowering intraocular pressure can be achieved with twice-daily administration of the combination drug as compared to serial administration of Alphagan (brimonidine) and Timoptic (timolol) three times a day:

> *Antimicrobial Preservatives*
>
> *Ophthalmic products are typically packaged in multidose form. Preservatives are thus required to prevent microbial contamination during use. Suitable preservatives include: benzalkonium chloride, thimersol, chlorobutanol, methyl paraben, propyl paraben, phenylethyl alcohol, edetate disodium, sorbic acid, Onamer M, or other agents known to those skilled in the art. In the prior art ophthalmic products, typically such preservatives are employed at a level from 0.004% to 0.02%. In the compositions of the present application the preservative, preferably benzalkonium chloride, may be employed at a level of from 0.001% to less than 0.01%, e.g. from 0.001% to 0.008%, preferably about 0.005% by weight. It has been found that a concentration of benzalkonium chloride of 0.005% is sufficient to preserve the compositions of the present invention from microbial attack. This concentration may be advantageously compared to the requirement of 0.01% benzalkonium chloride to preserve timolol in the individual, commercially-available ophthalmic products. Moreover, it has been found that adequate lowering of intraocular pressure has been obtained when administering the compositions of this invention twice a day as compared to the FDA-approved regimen wherein brimonidine ophthalmic solution, i.e. Alphagan® ophthalmic solution is administered three times a day and timolol ophthalmic solution, i.e. Timoptic® ophthalmic solution is administered twice a day. This results in the exposure of the patient to 67% and 50% of benzalkonium chloride, with the compositions of this invention, as compared to the administration of Alphagan® and Timoptic®,*

> *respectively. In FDA-approved adjunctive therapy, wherein Alphagan® and Timoptic® are serially administered, the patient is exposed to almost three times the concentration of benzalkonium chloride as compared to the administration of the compositions of this invention twice a day. (It is noted that it is known that benzalkonium chloride at high concentrations is cytotoxic. Therefore, minimizing the patient's exposure to benzalkonium chloride, while providing the preservative effects afforded by benzalkonium chloride, is clearly desirable.)*

[17] At pages 4 and 5, co-solvents and viscosity agents are discussed. This discussion is not relevant to the issues in these proceedings.

[18] Example I at pages 5 and 6 provides for a preparation including 0.20% by weight/volume of brimonidine, 0.68% by weight/volume of timolol maleate, which is equivalent to 0.50% by weight/volume of timolol, and 0.005% by weight/volume of BKC, together with other excipients.

[19] Example II, beginning at page 6 and continuing to the end of the descriptive portion of the patent at page 16, provides extensive information as to the clinical testing of the combination of Example I in twice-a-day dosing in comparison with administration of solutions containing just brimonidine three times a day or just timolol twice a day.

[20] The objectives of the experiment described as Example II are stated at page 6:

> *To compare the safety and efficacy of twice-daily dosed brimonidine tartrate 0.2% timolol 0.5% ophthalmic solution combination (henceforth referred to as Combination) with that of twice-daily dosed timolol ophthalmic solution 0.5% (henceforth referred to as Timolol) and three-times-daily dosed ALPHAGAN® (brimonidine tartrate ophthalmic solution) 0.2% (henceforth referred to as*

Brimonidine) administered for three months (plus 9-month masked extension) in patients with glaucoma or ocular hypertension.

[21] The intraocular pressure (IOP) of the participating patients taking each of these doses was periodically measured. At pages 9 to 11, the patent reports the measured values and their statistical significance in respect of efficacy:

***Efficacy**:*

At baseline, mean values of diurnal IOP ranged from 22.2 mm Hg to 24.9 mm Hg in the Combination group, 22.5mm Hg to 25.0 mmHg in the Brimonodine group, and 22.3 mm Hg to 24.8 mm Hg in the Timolol group. There were no statistically significant differences between treatment groups.

Mean changes from baseline diurnal IOP at week 2, week 6 and month 3 ranged from:

-5.2 to -7.9 mm Hg in the Combination group
-3.5 to -5.7 mm Hg in the Brimonidine group
-4.5 to -6.4 mm Hg in the Timolol group

The mean decreases from baseline diurnal IOP were statistically significant within each treatment group at each follow-up timepoint ($p<0.001$).

The mean decrease from baseline diurnal IOP was statistically significantly greater with Combination that with Brimonidine at hours 0, 2 and 7 at all follow-up visits ($p<0.001$). In addition, clinically significant differences of more than 1.5 mm Hg in mean change from baseline IOP favoring Combination over Brimonidine were seen at hours 0, 2, and 7 at all follow-up visits. At hour 9, the decreases from baseline diurnal IOP were greater for the Combination group than the Brimonidine group at all follow-up visits, although the differences were not statistically significant ($p \geq 0.104$).

The mean decrease from baseline diurnal IOP was statistically significantly greater with Combination than with Timolol at hours 0, 2, 7 and 9 at all follow-up visits ($p \leq 0.041$). In addition, clinically

significant differences of more than 1.5 mm Hg in mean change from baseline IOP favoring Combinatin over Timolol were seen at week 2 (hours 0, 2, and 7), week 6 (hours 2 and 7), and month 3 (hours 0 and 2).

Mean values of diurnal IOP at week 2, week 6 and month 3 ranged from:

15.9 to 18.1 mm Hg in the Combinatin group
17.4 to 21.5 mm Hg in the Brimonidine group
17.5 to 18.9 mm Hg in the Timolol group

Mean values of diurnal IOP were statistically significantly less with Combination than with Brimonidine at hours 0, 2, and 7 at all follow-up visits ($p<0.001$) and at hour 9 at week 6 and month 3 ($p\leq 0.011$). The mean values of IOP at hour 9 at week 2 were lower for the Combination group than the Brimonidine group, although the difference was not statistically significant ($p=0.205$). In addition, clinically significant differences of more than 1.5 mm Hg in mean IOP favoring Combination over Brimonidine were seen at hours 0, 2, and 7 at all follow-up visits and at hour 9 at month 3.

Mean values of diurnal IOP were statistically significantly less with Combination than with Timolol at hour 0 at week 2 and month 3; and at hours 2, 7 and 9 at all follow-up visits ($p\leq 0.050$). The mean values of IOP at hour 0, week 6, were lower for the Combination group than the Timolol group, although the difference was not statistically significant ($p=0.102$). In addition, clinically significant differences of more than 1.5 mm Hg in mean IOP favoring Combination over Timolol were seen at week 2 (hours 0, 2, and 7), week 6 (hours 2, 7, and 9), and month 3 (hours 2 and 9).

Mean values of diurnal IOP were statistically significantly less with Combination than with Brimonidine at hours 0, 2, and 7 at all follow-up visits ($p<0.001$) and at hour 9 at week 6 and month 3 ($p\leq 0.011$). The mean values of IOP at hour 9 at week 2 were lower for the Combination group than the Brimonidine group, although the difference was not statistically significant ($p=0.205$). In addition, clinically significant differences of more than 1.5 mm Hg in mean IOP favoring Combination over Brimonidine were seen at hours 0, 2, and 7 at all follow-up visits and at hour 9 at month 3.

Mean values of diurnal IOP were statistically significantly less with Combination than with Timolol at hour 0 at week 2 and month 3; and at hours 2, 7 and 9 at all follow-up visits ($p\leq 0.050$). The mean values of IOP at hour 0, week 6, were lower for the Combination

> *group than the Timolol group, although the difference was not statistically significant (p=0.102). In addition, clinically significant differences of more than 1.5 mm Hg in mean IOP favoring Combination over Timolol were seen at week 2 (hours 0, 2, and 7), week 6 (hours 2, 7, and 9), and month 3 (hours 2 and 9).*

[22] At pages 12 to 14 the patent provides an analysis of the experiment from the point of view of safety. I repeat what is stated at page 12:

> *Safety:*
>
> *Through month 3 of the study, 53.4% (103/193) of patients in the Combination group, 61.7% (121/196) of the Brimonidine group, and 50.8% (100/197) of the Timolol group experienced one or more adverse events, regardless of causality. The incidences of oral dryness, eye pruritus, foreign body sensation and conjunctival folliculosis were statistically significantly lower with the Combination than with Brimonidine ($p \leq 0.034$), while burning and stinging were statistically significantly higher with the Combination than with Brimonidine ($p \leq 0.028$). There were no statistically significant differences in adverse events between the Combination and Timolol, except for a statistically significantly higher incidence of eye discharge with the Combination (2.6%, 5/193) compared to Timolol (0%, 0/197; $p = 0.029$).*

[23] Commencing at page 14, over to page 16, the patent reports the analysis of the pharmacokinetics of the experiment. I will not set out this portion out as no party referred to this portion of the patent in argument.

[24] The conclusions are stated at page 16. They conclude that the combination of brimonidine and timolol administered twice a day (BID) was superior to just timolol administered twice a day (BID) or just brimonidine administered three times a day (TID) in lowering interocular pressure (IOP) and delivered a safety profile comparable to timolol BID and superior to brimonidine TID :

> *Conclusions*
>
> *The Combination treatment (brimonidine tartrate 0.2%/ timolol 0.5%) administered BID for 3 months was superior to Timolol (timolol 0.5%) BID and Brimonidine (brimonidine tartrate 0.2%) TID in lowering the elevated IOP of patients with glaucoma or ocular hypertension. The Combination administered BID demonstrated a favourable safety profile that was comparable to Timolol BID and better than Brimonidine TID with regard to the incidence of adverse events and discontinuations due to adverse events.*
>
> *The invention has been described herein by reference to certain preferred embodiments. However, as obvious variations thereon will become apparent to those skilled in the art, the invention is not to be considered as limited thereto.*

[25] There are 25 claims altogether, set out in three different ways commencing at page 17. Claims 1 to 6, inclusive, are directed to a composition containing brimonidine and timolol. Claims 7 to 13 are directed to the packaging of a pharmaceutical agent for reducing intraocular pressure, including brimonidine and timolol (a form of claiming sometimes used in countries that do not permit claims to a medicine *per se*). Claims 14 to 25 are directed to use of a composition including brimonidine and timolol. The claims are drafted in "dependent" form. That is, later claims incorporate by reference the terms of earlier claims, often in cumulative fashion.

[26] Allergan is asserting claims 2 to 6 inclusive, and 14 to 25 inclusive, of the '764 patent. They are dependent in one way or another on claim 1; therefore, I recite claim 1, as well:

> *1. An ophthalmic topical pharmaceutical composition for the treatment of glaucoma or ocular hypertension comprising an effective amount of brimonidine and an effective amount of timolol in a pharmaceutically acceptable carrier therefore.*

2. A compostion according to Claim 1, wherein the amount of brimonidine is 0.01 to 0.5 percent by weight and the amount of timolol is 0.1 to 1.0 percent by weight.

3. A composition according to Claim 1, wherein the amount of brimonidine is 0.2 percent by weight and the amount of the timolol is 0.5 percent by weight.

4. A composition according to claim 1 further comprising from 0.001% by weight less than 0.01% by weight of benzalkonium chloride.

5. A composition according to claim 2 further comprising from 0.001% by weight to less than 0.01% by weight of benzalkonium chloride.

6. A composition according to claim 3 further comprising from 0.001% by weight to less than 0.01% by weight of benazalkonium chloride.

. . .

14. Topical use of a therapeutically effective amount of a composition according to claim 1 in an affected eye for treating glaucoma.

15. Topical use of a therapeutically effective amount of a composition according to claim 2 in an affected eye for treating glaucoma.

16. Topical use of a therapeutically effective amount of a composition according to claim 3 in an affected eye for treating glaucoma.

17. Topical use of a therapeutically effective amount of a composition according to claim 1 in an affected eye for lowering intraocular pressure.

18. Topical use of a therapeutically effective amount of a composition according to claim 2 in an affected eye for lowering intraocular pressure.

19. Topical use of a therapeutically effective amount of a composition according to claim 3 in an affected eye for lowering intraocular pressure.

> *20. Topical use of a therapeutically effective amount of a composition according to claim 4 in an affected eye for treating glaucoma.*
>
> *21. Topical use of a therapeutically effective amount of a composition according to claim 5 in an affected eye for treating glaucoma.*
>
> *22. Topical use of a therapeutically effective amount of a composition according to claim 6 in an affected eye for treating glaucoma.*
>
> *23. Topical use of a therapeutically effective amount of a composition according to claim 4 in an affected eye for lowering intraocular pressure.*
>
> *24. Topical use of a therapeutically effective amount of a composition according to claim 5 in an affected eye for lowering intraocular pressure.*
>
> *25. Topical use of a therapeutically effective amount of a composition according to claim 6 in an affected eye for lowering intraocular pressure.*

[27] Allergan, in its written argument at paragraph 19, puts forward claim 22 as important and representative. It depends upon claim 6, which depends upon claim 3, which depends upon claim 1. I recite these claims in descending order.

> ***Claim 22*** *– Topical use of a therapeutically effective amount of a composition according to claim 6 in an affected eye for treating glaucoma.*
>
> ***Claim 6*** *– A composition according to claim 3 further comprising from 0.001% by weight to less than 0.01% by weight of benzalkonium chloride.*
>
> ***Claim 3*** *– A composition according to Claim 1, wherein the amount of brimonidine is 0.2 percent by weight and the amount of the timolol is 0.5 percent by weight.*

> ***Claim 1*** *– An ophthalmic topical pharmaceutical composition for the treatment of glaucoma or ocular hypertension comprising an effective amount of brimonidine and an effective amount of timolol in a pharmaceutically acceptable carrier therefore.*

[28] Taking into account all of the "dependencies" relating to claim 22, that claim can be rewritten as follows:

> *22. Topical use of a therapeutically effective amount of an ophthalmic pharmaceutical composition for the treatment of glaucoma or ocular hypertension wherein the amount of brimonidine is 0.2 percent by weight and the amount of timolol is, 0.5 percent by weight, and from 0.001% by weight to less than 0.01% by weight of benzalkonium chloride.*

THE EVIDENCE

[29] As is usual in these types of applications, the evidence took the form of affidavits and transcripts of cross-examinations. No witness was examined before the Court. Thus, the Court is unable to make a truly proper assessment as to credibility of any witness, nor to weigh properly the competing opinions of the experts. However, having reviewed the transcripts of the cross-examination of Allegan's expert witness Dr. Fechtner, I find him to be evasive and less than forthright on many occasions. I will treat his evidence with great caution.

[30] The issues in this proceeding have been much reduced to those respecting invalidity of certain claims of the '764 patent. At a pre-trial conference, I invited the parties to advise the Court as to what evidence on the record no longer needs to be considered and possibly be removed from the record. The parties advised jointly by a letter from Allergan's Counsel dated May 9, 2012:

We write further to the case conference held on May 8, 2012 in respect of T-1560-10. We write with the consent of Apotex Inc. ("Apotex").

The parties are in agreement that the following evidence need not be reviewed by the Court in advance of the hearing:

Applicants' Record

- *The affidavits of Dr. Kevin Parkinson dated March 28 and May 31, 2011*
- *Paras. 5-8 and Exhibits "C" to "F" of the affidavit of Sonia Atwell dated May 31, 2011*

Respondent Apotex' Record

- *The affidavit of Biserka Horvat dated March 31, 2011*
- *The cross-examination transcript of Dr. Kevin Parkinson dated September 19, 2011*
- *Paras. 81, 83-88, 91-292 and Exhibits 3-30 to the affidavit of Dr. Harry Quigley dated March 31, 2011*

The parties are not asking the Court to strike any portions of the record.

[31] At the hearing, Counsel for each of the parties agreed that the above-referenced material could be removed from the record as it was not referred to in argument. These portions were to be removed following the hearing. None of it was referred to in argument.

[32] The Applicants Allergan filed the following evidence which remains for consideration:

1. Affidavit of Gary J. Beck, one of the named inventors in the '764 patent. His evidence is *factual*. He is the Senior Director, Global Project Management, Analysis,

at Allergan, Inc. in California. His evidence reviews the developments that led to the '764 patent, provides revenues generated by the sale of the COMBIGAN product and provides cost figures relating to the development of that product.

He was cross-examined and a transcript of that cross-examination has been filed in evidence.

2. Affidavit of Sonia Atwell, a law clerk in the offices of the Applicants' solicitors. Her evidence is *factual*; it serves to place several documents in the record.

   She was not cross-examined.

3. Affidavit of Dr. Robert Fechtner, a Professor of Ophthalmology and Director of the Glaucoma Division, Glaucoma Diagnostic Laboratory and Clinical Research Development at the Institute of Ophthalmology and Visual Science at New Jersey Medical School of the University of New Jersey. His evidence is filed as *expert* evidence. His expertise lies in the fields of study, research and teaching respecting the treatment of glaucoma and other ocular conditions. He is not a formulator of drugs used for that purpose although he has worked with such formulators. During his cross-examination he expressly stated that he was not an expert in formulation (e.g. Q's 24-26). He testified in respect of the issues of anticipation and obviousness of the '764 patent. He rebuts some of the evidence given by Apotex's experts.

He was cross-examined and a transcript of that cross-examination has been filed in evidence. I have already stated my reservations as to his evidence.

4. Affidavit of Jim Tierney, the Business Unit Director, Eye Care for Allergan Inc. His evidence is *factual*. He testified as to prescription data for bimatoprost and travoprost in Canada.

   He was not cross-examined.

[33] The Respondent Apotex filed the following evidence which remains for consideration:

1. Affidavit of Salman Hoda, a Marketing Forecast Analyst at Apotex. He is a *factual* witness. He provided marketing data, derived from a marketing survey data source, as to sales of brimatoprost, timolol, dorzolamine, dorzolamine-timolol and brimonidine-timolol products in Canada.

   He was cross-examined and a transcript of that cross-examination was filed in evidence.

2. Affidavit of Harry A. Quigley, A. Edward Maumenee Professor of Ophthalmology at the Wilmer Eye Institute at Johns Hopkins University, Baltimore, Maryland. His evidence was filed as *expert* evidence. His expertise lies in the field of study,

research and teaching in respect of glaucoma and other ocular conditions. He testified as to the issues of obviousness and anticipation of the '764 patent.

He was cross-examined, and a transcript of his cross-examination was filed in evidence.

3. Affidavit of Uday B. Kompella, a Professor in the Department of Pharmaceutical Sciences at the University of Colorado Denver. His evidence was filed as *expert* evidence. His expertise lies in the field of formulation and delivery of ocular drugs. He testified as to obviousness of the '764 patent. He also responded to the Beck affidavit.

   He was cross-examined and a transcript of his cross-examination was filed in evidence.

4. Affidavit of Aidan Hollis, a Professor of Economics at the University of Calgary. His evidence was filed as *expert* evidence. He testified in respect of COMBIGAN sales and sales of other ophthalmic products in Canada.

   He was cross-examined and a transcript of that cross-examination was filed in evidence.

PREVIOUS FEDERAL COURT DECISION RESPECTING THE '764 PATENT

[34] There has been previous litigation in the Federal Court respecting the '764 patent in the context of the *NOC Regulations*. In a decision released November 17, 2011, cited as *Allergan Inc, et al v Canada (Minister of Health) and Sandoz Canada Inc*, 2011 FC 1316, Justice Crampton (as he then was – I will refer to him as Crampton J in these Reasons.) determined that allegations made by a generic, Sandoz Canada Inc, *inter alia*, that the '764 patent was invalid for obviousness, were not justified. He wrote at paragraph 127 of that decision:

> *127 Allergan has met its burden of establishing, on a balance of probabilities, that Sandoz's allegation that the '764 Patent is invalid on the ground of obviousness is not justified. For the reasons summarized in paragraph 117 above, this would remain true even if the inventive concept of the claims of the '764 Patent did not include the uncontested surprising improvement in safety, the elimination of the afternoon reduction of effectiveness and the reduction in daily load of BAK, relative to concomitant treatment of brimonidine and timolol. These additional aspects of the inventive concept simply serve to further strengthen that the invention claimed by the '764 Patent was not obvious.*

[35] He was not asked to deal with the issue of anticipation of the ‘764 patent.

[36] I am advised that this decision is a final decision. I will refer to this decision as *Sandoz*.

PREVIOUS UNITED STATES DECISION

[37] The United States District Court, Eastern District of Texas, Marshall Division, released a decision dated August 22, 2011 in a case between *Allergan, Inc v Sandoz Inc*, cited as 2011 WL

3809882 (E.D.Tex.). I am advised that this decision is under appeal with an oral hearing expected in the fall of this year, 2012.

[38] This decision dealt with four United States patents which emerged from the same priority application as that claimed in the '764 patent; namely, a filing in the United States Patent Office on April 19, 2002 as number 10/126,790. The District Court determined that these patents were not invalid.

[39] This litigation was brought under the provisions of the United States *Hatch-Waxman Act*, [Public Law 98-417] *(formally known as the Drug Price Competition and Patent Term Restoration Act)*, of which our *NOC Regulations* are an imperfect copy.

ISSUES

[40] The basic issue before me is whether Allergan has discharged its burden of demonstrating that Apotex's allegation of invalidity of the '764 patent are not justified; thus the Court must determine whether an order for prohibition should issue.

[41] In determining this matter, there are several discrete issues:

1. Who bears the burden?
2. Effect of the previous Federal Court decision.
3. Effect of the United States Federal Court decision
4. Who is the person skilled in the art?

5. .Construction of the claims
6. Are the asserted claims of the '764 patent anticipated?
7. Are the asserted claims of the '764 patent obvious?

ISSUE #1: ***Who bears the burden?***

[42] As to the allegations of invalidity, the *Patent Act*, RSC 1985, P-4, section 43(2) affords a presumption of validity; however, once a second person, here Apotex, puts in some evidence as to invalidity, the Court must determine the matter on the usual civil burden; namely, balance of probabilities. I repeat what I wrote in *GlaxoSmithKline Inc v Pharmascience Inc*, 2011 FC 239 at paras 43 and 44:

> *43 O'Reilly J of this Court has summarized the question of burden of proof where the issue is invalidity in Pfizer Canada Inc. v. Apotex Inc., 2007 FC 26, 59 CPR (4th) 183 (aff'd 2007 FCA 195, leave to appeal refused [2007] SCCA No. 371) at paragraphs 9 and 12:*
>
> > *9 In my view, the burden on a respondent under the Regulations is an "evidential burden" -- a burden merely to adduce evidence of invalidity. Once it has discharged this burden, the presumption of validity dissolves and the Court must then determine whether the applicant has discharged its legal burden of proof. I believe this is what is meant in those cases where the Court has stated that the respondent must put its allegations "into play". It must present sufficient evidence to give its allegations of invalidity an air of reality.*
> >
> > ...
> >
> > *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.*

44 In Pfizer Canada Inc. v. Canada (Minister of Health), 2008 FC 11, 69 C.P.R. (4th) 191, I said in respect of the same thing at paragraph 32:

> *32 I do not view the reasoning of the two panels of the Federal Court of Appeal to be in substantial disagreement. Justice Mosley of this Court reconciled these decisions in his Reasons in Pfizer Canada Inc. v. Apotex Inc., [2007] F.C.J. No. 1271, 2007 FC 971 at paragraphs 44 to 51. What is required, when issues of validity of a patent are raised:*
>
> > *1. The second person, in its Notice of Allegation may raise one or more grounds for alleging invalidity;*
> >
> > *2. The first person may in its Notice of Application filed with the Court join issue on any one or more of those grounds;*
> >
> > *3. The second person may lead evidence in the Court proceeding to support the grounds upon which issue has been joined;*
> >
> > *4. The first person may, at its peril, rely simply upon or, more prudently, adduce its own evidence as to the grounds of invalidity put in issue.*
> >
> > *5. The Court will weigh the evidence; if the first person relies only on the presumption, the Court will the presumption of validity afforded by the Patent Act nonetheless weigh the strength of the evidence led by the second person. If that evidence is weak or irrelevant the presumption will prevail. If both parties lead evidence, the Court will weigh all the evidence and determine the matter on the usual civil balance.*
> >
> > *6. If the evidence weighed in step 5 is evenly balanced (a rare event), the Applicant (first person) will have failed to prove that the allegation of invalidity is not justified and will not be entitled to the Order of prohibition that it seeks.*

ISSUE #2: ***The effect of the earlier Federal Court decision***

a) The decision

[43] The Federal Court in *Allergan Inc et al v Canada (Minister of Health) and Sandoz Canada Inc*, 2011 FC 1316, (*Sandoz*) dealt with proceedings under the *NOC Regulations* involving two patents; one of them was the same '764 patent, which is the one at issue here; the other was Canadian Patent No. 2,225,626 (the '626 patent), which is not at issue in the present proceedings. The generic in that case was Sandoz Canada Inc., a different generic from Apotex Inc., the generic in these proceedings. Counsel representing the generics is also different in each proceeding.

[44] In the *Sandoz* proceeding, Allergan led evidence, including that of Mr Gary J. Beck, one of the named inventors, and that of Dr. Robert Fechtner as an expert. Both are witnesses in the present proceeding and I am advised that the affidavits of these two witnesses are in many respects essentially the same as their affidavits in the present proceedings. These persons were cross-examined in each proceeding by different Counsel. I have not been provided with the transcripts of the cross-examinations in the earlier proceeding, but I fully expect that they are different from those in the present proceedings.

[45] Sandoz provided expert evidence from different persons than those offered by Apotex in the present proceedings. Sandoz's experts were Dr. Henry Jampel and Dr. Ashim Mitra, as set out in Crampton J's reasons at paragraphs 30 and 31. I do not have copies of their affidavits or transcripts of their cross-examinations. Crampton J., at paragraph 32, expressed serious reservations as to Mitra's credibility.

[46] Crampton J, in *Sandoz*, set out the issues at paragraph 33 of his Reasons. The only issue respecting the '764 patent was that of obviousness. At paragraph 35, he sets out the same claims as Allergan relies upon in the present proceedings; and, in particular, Allergan asserted claim 22 as being representative as it does in the present proceeding. Crampton J stated at paragraph 36 that there was "*no dispute between the parties"* as to the construction of the language of these claims:

> *36 There is no dispute between the parties regarding the construction of the language in claims 1, 3, 6 and 22 of the '764 Patent (the "Representative '764 Claims"). The parties are in general agreement that those claims describe a fixed combination of brimonidine (0.2%) and timolol (0.5%) in a pharmaceutically acceptable carrier containing BAK (0.001% to 0.01%) (the "Composition") and the use of the Composition for the topical treatment of glaucoma and ocular hypertension.*

[47] At paragraph 37, Crampton J set out the test for obviousness in four steps as derived from the decision of the Supreme Court of Canada in *Apotex Inc v Sanofi-Synthelabo Canada Inc* [2008] 3 SCR 265:

> *37 The test for assessing obviousness comprises the following four steps:*
>
> > *1. Identify the person skilled in the art and the relevant common general knowledge;*
> >
> > *2. Identify the inventive concept of the claim in question or, if that cannot readily be done, construe it;*
> > *3. Identify what, if any, differences exist between the matter cited as forming part of the "state-of-the-art" and the inventive concept; and*
> >
> > *4. Without any knowledge of the alleged invention as claimed, assess whether those differences (i) constitute steps that would have been obvious to the skilled person, or (ii) required a degree of invention (Apotex Inc v Sanofi-Synthelabo Canada Inc, 2008 SCC 61, [2008] 3 SCR 265, at para 67 [Sanofi]).*

(1) Step One - The skilled person and the relevant common general knowledge

[48] As to *step one*, Crampton J defined the person skilled in the art (POSITA) at paragraphs 38 to 40, as follows:

> *38 Dr. Fechtner opined that the POSITA to whom the '764 Patent is addressed "is a person engaged in developing pharmaceutical formulations and treatment for methods for the eye, or is a specialist in treating diseases of the eye such as an optometrist or an ophthalmologist who also has experience in either developing ophthalmic pharmaceutical formulations or in designing and running clinical trials on such formulations" (emphasis added).*
>
> *39 Drs. Mitra and Jampel took a similar position, when they stated that the '764 Patent is addressed to pharmaceutical formulators and to ophthalmologists. However, Sandoz subsequently took the position that the POSITA is a composite of a practicing ophthalmologist and a pharmaceutical formulator. During the oral hearing of this application, Sandoz characterized this difference between the views expressed by Dr. Fechtner and its own experts as being a "minor" and as having no "real effect."*
>
> *40 That said, in my view, the POSITA to whom the '764 Patent is addressed is someone who is either a pharmaceutical formulator or a specialist in treating diseases of the eye, as described by Dr. Fechtner. This would include persons such as Drs. Jampel (who conceded in cross-examination that he has no experience with formulations), Fechtner, and Mitra, as well as Mr. Beck. This is consistent with the position taken by Sandoz in its NOA.*

[49] The knowledge that a person skilled in the art would possess as of the relevant date was set out at paragraphs 41 to 45 of his reasons:

41 Dr. Jampel stated in his affidavit that the common general knowledge of the POSITA as at the Priority Date included the following:

> *i. a detailed knowledge of ocular hypertension and glaucoma;*
>
> *ii. a detailed knowledge of the IOP lowering medications in use at that time, including those described at paragraphs 14 to 18, above;*
>
> *iii. the knowledge that IOP lowering medications were commonly used in combination, either in concomitant use or combined together, in order to obtain adequate IOP lowering, and that the use of two IOP lowering medications resulted in greater IOP reduction in either individual medication alone;*
> *iv. the knowledge that both brimonidine and timolol were well-established IOP lowering medications;*
>
> *v. the knowledge that brimonidine and timolol had been used in concomitant therapy and that such therapy resulted in a larger IOP reduction than with brimonidine or timolol alone;*
>
> *vi. the knowledge that commercially available combination products typically included timolol as one of the active ingredients - such products included COSOPT (combination of dorzolamide and timolol that had been available in the U.S. since 1998 and in Canada since 1999), as well as combinations of pilocarpine and timolol and of latanoprost and timolol (Xalacom) that were commercially available outside the United States prior to 2002; and*
>
> *vii. the knowledge that BAK was a commonly used preservative in ophthalmic solutions.*

42 At the oral hearing of this application, Allergan stated that while there might be some "subtle differences" between its experts and Dr. Jampel, its arguments would be based upon Dr. Jampel's above-described position regarding the common general knowledge of the POSITA as at the Priority Date. Accordingly, I am prepared to accept the foregoing summary provided by Dr. Jampel for the purposes of the present analysis, subject to the following observations.

> *43 First, I am satisfied that the evidentiary record demonstrates that a POSITA at the time of the Priority Date would also have been familiar with the fact that Allergan's second generation brimonidine product, ALPHAGAN P, contained (i) 0.15% brimonidine, rather than the 0.2% concentration that is used in the Composition, and (ii) Purite, rather than BAK as a preservative. That person also would have been aware that, when administering brimonidine and timolol concomitantly, the state-of-the-art was to administer those drugs separately, 5 minutes apart, to avoid the "wash-out" effect.*
>
> *44 Second, the record also demonstrates that the POSITA would have been aware of U.S. Patent No. 5,502,052, issued March 26, 1996 (the "DeSantis Patent"), which suggested that anti-glaucoma compositions that comprise a combination of one or more beta-blockers (such as timolol) with one or more alpha-2 agonists (brimonidine was not specifically mentioned) achieve a greater reduction in IOP than that which is achievable with the same concentration of either type of active ingredient used alone.*
>
> *45 Third, I am satisfied that the POSITA also would have been aware that the benefits associated with a fixed composition of two active ingredients for use in the topical treatment of glaucoma, relative to concomitant therapy involving those same active ingredients, likely would include: (i) less preservative being administered to patents, and (ii) greater patient compliance with the combined administration.*

[50] Crampton J then moved to *step two*, which he defined as the *"inventive concept*". He attempted to make a distinction between what is in the claims, properly construed, and the *"inventive concept…for the purposes of performing the third step of the obviousness test"*. At paragraphs 46 to 51 of his reasons, he wrote:

> *46 Sandoz submits that "it is the claims that define the invention" in any patent and that the inventive concept of the '764 Patent must be discerned solely from the language in the claims of the patent.*
>
> *47 It is settled law that the "fences" and "boundaries" of the "field" of monopoly conferred by a patent are established by the claims of the patent (Free World Trust, above, at paras 14, 33, 51, 66). That said, to achieve a "purposive construction," is permissible to have regard to other parts of the patent "through the eyes of a skilled addressee," to resolve ambiguity and to achieve flexibility and*

> *fairness in differentiating between the essential and the unessential features of the invention (Whirlpool Corp v Camco Inc, 2000 SCC 67, [2000] 2 SCR 1067, at para 48 [Whirlpool]). Given that there is no dispute in the case at bar with respect to the construction of the claims, there is no need to look beyond the claims of the '764 Patent to ascertain the field of monopoly claimed therein.*
>
> *48 The same cannot be said with respect to the inventive concept of the claims.*
>
> *49 Generally speaking, the Representative '764 Claims simply claim the Composition for topical use in an affected eye for treating glaucoma. Sandoz submits that the inventive concept of those claims must be discerned from this description alone. Dr. Jampel took the same position.*
>
> *50 I disagree. If that were the case, it would not be possible in this and similar cases to fully ascertain the differences between the state-of-the-art and the inventive concept of the claim, for the purposes of performing the third step of the obviousness test.*
>
> *51 In cases such as this, where "the inventive concept of the claims is not readily discernible from the claims themselves," it is both necessary and permissible to look to the balance of the patent "to determine its inventiveness" (Sanofi, above, at para 77). In other words, "to ascertain the nature of the invention" that is articulated in the claims, and to understand the extent to which the claimed invention differs from the prior art, the Court may "look to the whole of the disclosure" in the patent (Whirlpool, above, at para 49(g), quoting Consolboard Inc v MacMillan Bloedel (Saskatchewan) Ltd, [1981] 1 SCR 504, at 520-21). That said, it bears underscoring that "it is not permissible to read the specification in order to construe the claims more narrowly or widely than the text will allow" (Sanofi, above, at para 77).*

[51] He concluded at paragraph 58 that the *"inventive concept"* of the '764 patent also includes (i) improved safety profile (ii) BID dosing without afternoon reduction in efficiency (iii) reduction in daily load of preservative. He wrote:

> *58 I am satisfied that the inventive concept of the claims of the '764Patent also includes (i) the improved safety profile of the Composition, (ii) BID dosing without an afternoon reduction in efficiency, and (iii) the reduction in the daily load of preservative administered to patients taking both brimonidine and timolol. Although Allergan submitted that the inventive concept of the claims further includes "[i]ncreased IOP lowering of the combination as compared to monotherapy with individual agents," this was simply baldly asserted and was not further developed in Allergan's written or oral submissions. Accordingly, it will not be further addressed in these reasons.*

[52] Crampton J moved to *step three*, the differences between the state of the art and the innovative concept, beginning at paragraph 64, where he set out the differences that he found:

> *64 The differences between the prior art discussed at paragraphs 41 to 45 above and the innovative concept of the claims in the '764 Patent are the following: (i) the Composition combines brimonidine and timolol into a single, chemically stable, formulation - that combination had never previously been made or reported in the prior art, (ii) the Composition has a superior safety profile, relative to brimonidine TID, (iii) the Composition permits BID dosing without an afternoon reduction in efficiency, relative to brimonidine TID treatment, and (iv) patients who are treated with the Composition receive a significantly reduced daily load of BAK, relative to concomitant treatment of brimonidine and timolol.*

[53] Crampton J noted at paragraph 65 that much of the evidence as to these differences, as given by Beck, one of the named witnesses, was uncontradicted:

> *65 With respect to BID dosing without a reduction in afternoon efficiency, the '764 Patent disclosed, among other things, that in the clinical trial mentioned immediately above, the decreases from baseline diurnal IOP at hour 9 of the daily testing "were greater for the Combination group than for the Brimonidine group at all follow-up visits, although the differences were not statistically significant ($p > 0.104$)." Mr. Beck's uncontradicted evidence was that "[t]he*

> *frequency of administration for which a formulation is approved significantly affects its use and value because of the discomfort, difficulty, unpleasantness, and risk of infection associated with installation of eyedrops." For these reasons, Mr. Beck stated that a formulation approved for BID dosing "is, all else being equal, much better than a drug that must be administered three times a day." Once again, this evidence was not contradicted. With respect to the Composition in particular, it requires only two administrations per day, versus the five separate administrations that continue to be required in the United States for patients being administered brimonidine (TID) and timolol (BID) concomitantly, and the four separate administrations that are required elsewhere for that concomitant therapy. For this reason, Mr. Beck stated in cross-examination that a "combination product that had a dosing regimen of two times a day would be considered more advantageous, from a compliance standpoint, than monotherapies dosed" four or five times a day. Again, this evidence was not contradicted.*

[54] Crampton J rejected Sandoz's argument that the claims are simply directed to a formula, and the properties of that formula could not form part of the innovative concept. He wrote at paragraphs 68 and 69:

> *68 In addition, Sandoz submitted that since the alleged invention claimed in the '764 Patent existed once the combination itself was made, the benefits discovered in Allergan's subsequent clinical trials cannot be part of the innovative concept of the patent. Sandoz added that recognition of the superior safety profile of the Composition would require this Court to hold that the invention did not exist until the clinical trial was conducted and the results analyzed.*
>
> *69 I disagree. The cases relied upon by Sandoz on this point simply stand for the proposition that the utility of the pharmaceutical patent does not need to be demonstrated by prior human clinical trials (Apotex Inc v Wellcome Foundation Ltd, 2002 SCC 77, [2002] 4 SCR 153, at para 77; Pfizer (2009 FC 638), above, at paras 87-88; aff'd 2010 FCA 242). In the case at bar, the safety data in question was disclosed in the '764 Patent and is a legitimate part of the innovative concept of that patent.*

[55] Crampton J then moved to *step four*, which required a determination as to whether the differences between the inventive concept and the prior art were obvious, beginning at paragraph 70. He sets out four factors at paragraph 71:

> *70 In Sanofi, above, at paragraphs 69 and 70, Justice Rothstein identified a number of factors that should be taken into consideration in cases where it is appropriate to assess whether the invention was "obvious to try." In the case at bar, Allergan conceded that it is appropriate to engage in this assessment, because the Composition is a pharmaceutical invention that was achieved by experimentation (Sanofi, above, at para 68; Bridgeview Manufacturing Inc v 931409 Alberta Ltd, 2010 FCA 188, at para 42). I agree.*
>
> *71 Accordingly, it is appropriate to consider the following factors that were identified by Justice Rothstein:*
>
> > ** Is it more or less self-evident that what is being tried ought to work? Is there a finite number of identified predictable solutions known to skilled persons?*
> >
> > ** What is the extent, nature and amount of effort required? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?*
> >
> > ** Is there a motive provided in the prior art to find the solution?*
> >
> > ** What was the actual course of conduct that culminated in the invention?*
> >
> > *(a) Was it more or less self-evident that the Composition would work? Were there a finite number of identified predictable solutions known to skilled persons?*

[56] The *first* of these factors which he considered was the "self evident" factor. He wrote at paragraph 72:

> *72 Sandoz submitted that to the extent that there was any recognized need for a product with the alleged benefits of the Composition, it was well known that a combination product would offer such benefits. However, the fact that it may have been known that a combination product such as the Composition would provide particular benefits is not a sufficient basis upon which to conclude that it was more or less self-evident that the Composition would work or that there were any predictable solutions for achieving the Composition known to the POSITA. It is one thing to have an idea that a potential product would or might have certain beneficial properties. It is quite another thing to actually create that product. It is on the latter that this assessment must focus (Pfizer Canada Inc v Apotex Inc, 2009 FCA 8, at para 29 [Pfizer (2009 FCA 8)]).*

[57] Sandoz relied upon what is described as the DeSantis Patent (US Patent 5,502,052) as identified at paragraph 44 of Crampton J's Reasons, as well as "a series of articles" appended to Dr. Jampel's affidavit. Crampton J, at paragraphs 72 through 90 of his Reasons, reviewed the evidence of Allergan's and Sandoz's witnesses, particularly with respect to several of the properties of the particular formulations as found in claim 22 of the '764 patent. He concluded at paragraph 91:

> *91 In summary, given all of the foregoing, I find that (i) it would not have been more or less self-evident to the uninventive POSITA that formulating brimonidine and timolol into a chemically stable fixed combination drug ought to work, and (ii) there was not a finite number of identified predictable solutions known to skilled persons.*
>
> > *(b) What was the extent, nature and amount of effort required? Were routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?*

[58] The *second factor* considered by Crampton J was the extent of the effort required. Sandoz argued that Mr. Beck and his team were engaged in a routine exercise. Crampton J found differently. At paragraphs 103 and 104 he wrote:

> *103 In summary, before arriving at the final Composition, Mr. Beck and his team:*
>
> *i. considered other active ingredients;*
>
> *ii. encountered failures with their Brimo X and Synergel formulations;*
>
> *iii. encountered a failure with the preservative that they considered to be superior to BAK and had used in their ALPHAGAN P product (that was approved by the U.S. FDA shortly before the Priority Date); and*
>
> *iv. encountered novel degradations when brimonidine and timolol were combined with BAK.*
>
> *104 Based on the foregoing, I find that Mr. Beck and his team (i) engaged in a significant amount of difficult, non-routine work and overcame several unexpected obstacles to develop the Composition, and (ii) did not spend any significant amount of time and effort pursuing possible formulations that would not have been pursued by the POSITA.*

[59] The *third factor* considered by Crampton J was motivation, beginning at paragraph 114 of his Reasons. He accepted the uncontradicted evidence of Allergan's expert, Dr. Fechtner, at paragraphs 115 and 116:

> *115 Dr. Fechtner's uncontradicted evidence on this point, which I accept, is that:*
>
> *(i) the known difficulty in obtaining U.S. FDA approval for fixed combination drugs for the treatment of glaucoma was a major disincentive against the development of such drugs, and the POSITA would not have been motivated to develop a fixed combination drug containing timolol and brimonidine;*

> *(ii) the extent of time, effort and resources required to conduct the clinical trials described in Mr. Beck's affidavit would have given rise to a disincentive for the POSITA to pursue the development of the Composition; and*
>
> *(iii) the cost of the work required to develop such a drug would have been a further disincentive for the POSITA.*
>
> *116 Another statement made by Dr. Fechtner that is relevant to this consideration is that the POSITA would have been well aware that combining two drugs into a fixed combination may lead to the over-administration or under-administration of one of the active ingredients, which is apparently what happened with the combination product of pilocarpine and epinephrine.*

[60] In *summary*, Crampton J wrote at paragraph 117:

> *117 It follows from the conclusions reached under the headings (a) to (c) immediately above that combining brimonidine and timolol into a fixed combination drug is not something that would have been "obvious to try" for the POSITA. In short, (i) it was not more or less self-evident that the steps that were undertaken to achieve a chemically stable formulation of the Composition ought to work, (ii) the experimentation undertaken to achieve that formulation was not routine, (iii) Allergan did not have a strong motivation to pursue that experimentation, and (iv) the course of conduct undertaken to achieve the Composition does not suggest that the Composition was obvious.*

[61] Crampton J also considered the actual conduct of the inventors, which included at least three wild goose chases. He wrote at paragraph 122:

> *122 Based on the information discussed paragraphs 96 to 103 above, I find that this factor weighs in favour of a finding that the Composition was not obvious. In short, Mr. Beck and his team did not develop the Composition "quickly, easily, directly and relatively inexpensively, in light of the prior art and common general*

> *knowledge." On the contrary, they pursued at least three "wild goose chases" (Sanofi, above, at para 71) and encountered a number of other obstacles before they finally developed the Composition.*

[62] Lastly, Crampton J considered commercial success, which he acknowledged to be a secondary factor. He wrote at paragraph 125:

> *125 There is evidence to suggest that the commercial success of COMBIGAN is at least in part attributable to the favourable safety dimension of the inventive concept of the '764 Patent. In short, Dr. Fechtner's uncontradicted evidence is that "one of the reasons why COMBIGAN has been a successful product commercially (and one of the reasons I prescribed it) is because it has an advantageous side effect profile when compared to its components and other available treatment options." This evidence was not contested by Sandoz's experts.*

[63] *In conclusion*, Crampton J found that Sandoz's allegation that the '764 patent was invalid for obviousness was not justified. He set out in his conclusion at paragraph 127:

> *127 Allergan has met its burden of establishing, on a balance of probabilities, that Sandoz's allegation that the '764 Patent is invalid on the ground of obviousness is not justified. For the reasons summarized in paragraph 117 above, this would remain true even if the inventive concept of the claims of the '764 Patent did not include the uncontested surprising improvement in safety, the elimination of the afternoon reduction of effectiveness and the reduction in daily load of BAK, relative to concomitant treatment of brimonidine and timolol. These additional aspects of the inventive concept simply serve to further strengthen that the invention claimed by the '764 Patent was not obvious.*

[64] It is to be noted that Sandoz made *no allegation* of invalidity of the '764 patent on the basis of *anticipation*. Accordingly, Crampton J made no finding in respect of anticipation.

[65] There are two bases for considering the effect of the judgment of Crampton J. One is comity; the other is the jurisprudence specific to the *NOC Regulations*. I will consider comity first.

b) Comity

[66] Comity comes into consideration when a Court is faced with a decision of the same Court which deals with the same legal issues or factual circumstances. There is a general view that the subsequent Court should respect the decision of the earlier Court unless it is manifestly wrong or the jurisprudence has changed. The earlier decision should be followed unless there is strong reason to the contrary; and, in considering strong reason to the contrary, the Court does not mean a stronger or more persuasive argument of Counsel, but a showing that some jurisprudence has been clearly overlooked or is now changed. Richard J (as he then was) set out the matter in *Glaxo Group Ltd v Canada (Minister of National Health and Welfare)*, (1995), 64 CPR (3^{d}) 65 at pages 67 (line h) to 68 (line g):

The principle of judicial comity has been expressed as follows:

> *The generally accepted view is that this court is bound to follow a previous decision of the court unless it can be shown that the previous decision was manifestly wrong, or should no longer be followed: for example, (1) the decision failed to consider legislation or binding authorities which would have produced a different result, or (2) the decision, if followed, would result in a severe injustice. The reason generally assigned for this approach is a judicial comity. While doubtless this is a fundamental reason for the approach, I think that an equally fundamental, if not more compelling, reason is the need for certainty in the law, so far as that can be established. Lawyers would be in an intolerable position in advising clients if a division of the court was free to decide an appeal without regard to a previous decision or the principle involved in it.*

(Bell v. Cessna Aircraft Co. (1983), 149 D.L.R. (3d) 509 at p. 511, 36 C.P.R. 115, [1983] 6 W.W.R. 178 (B.C.C.A.).)

A similar position was taken by Mr. Justice Jackett, President of the Exchequer Court, in Canada Steamship Lines Ltd. v. M.N.R., [1966] Ex. C.R. 972 at p. 976, [1966] C.T.C. 255, 66 D.T.C. 5205:

> *I think I am bound to approach the matter in the same way as the similar problem was approached in each of these cases until such time, if any, as a different course is indicated by a higher Court. When I say I am bound, I do not mean that I am bound by any strict rule of stare decisis but by my own view as to the desirability of having the decisions of this Court follow a consistent course as far as possible.*

In R. v. Northern Electric Co. (1955), 24 C.P.R. 1 at p. 19, [1955] 3 D.L.R. 449, [1955] O.R. 431 (H.C.), McRuer C.J.H.C. stated:

> *Having regard to all rights of appeal that now exist in Ontario, I think Hogg J. stated the right common law principle to be applied in his judgment in R. ex rel. McWilliam v. Morris, [1942] O.W.N. 447 where he said: "The doctrine of stare decisis is one long recognized as a principle of our law. Sir Frederick Pollock says, in his First Book of Jurisprudence, 6th ed., p. 321: "The decisions of an ordinary superior court are binding on all courts of inferior rank within the same jurisdiction, and, though not absolutely binding on courts of co-ordinate authority nor on that court itself, will be followed in the absence of strong reason to the contrary'."*
>
> *I think that "strong reason to the contrary" does not mean a strong argumentative reason appealing to the particular Judge, but something that may indicate that the prior decision was given without consideration of a statute or some authority that ought to have been followed. I do not think "strong reason to the contrary" is to be construed according to the flexibility of the mind of the particular Judge.*

[67] Justice Barnes of this Court applied the principle of comity in NOC Proceedings in following an earlier decision wherein the same claims of the patent at issue had been construed. He

applied the same construction in *Pfizer Canada Inc v Canada (Minister of Health),* 2007 FC 446, (2007), 59 CPR (4th) 166 (FC) where he wrote at paragraph 31:

> *31 In a case like this one, the principle of comity does apply because Justice Hughes' decisions in Pharmascience, above, and Cobalt, above, turn solely on his construction of claim 22 of the 493 Patent without any reliance upon or reference to the expert opinions offered by the parties. Justice Hughes was able to construe the patent by examining only its language and, in so doing, he has made a determination on an issue of law which is deserving of deference. In such a context it does not matter if the evidentiary record before me is different from that which was placed before Justice Hughes. If he was able to construe the patent without resorting to extrinsic evidence then comity dictates that I do the same, absent a finding that Justice Hughes was "manifestly wrong".*

[68] Under the principle of comity, therefore, I must respect the decision of Crampton J in respect of the various findings that he makes unless I am persuaded that he was "manifestly wrong" in that he overlooked some relevant statute or authority, or that he misapplied the relevant statute or authority, or that there have been subsequent statutory changes or new authorities that are relevant. Where he makes factual findings on the evidence before him, I am free to make different findings if the evidence before me is different. It is in this latter respect that the jurisprudence that has developed under the *NOC Regulations* must be examined. I will do that next.

c) The jurisprudence

[69] There is no doubt that the *NOC Regulations* set out an imperfect procedure for the efficient resolution of innovator/generic pharmaceutical disputes. The United States *Hatch-Waxman Act,* including its various amendments, in general does a much better job of dealing with several of the procedural matters that vex our Court. Re-litigation is one of them.

[70] Given that this Court is overwhelmed at times with *NOC Regulation* proceedings, several attempts have been made in an endeavour to reduce or eliminate seemingly redundant litigation. The *Regulations*, section 6(5)(b), provide an opportunity for a generic (second person) to move to strike an application as an abuse of process. The Federal Courts Rules make provision for striking any proceeding on a number of grounds, including abuse. These Rules have rarely been effective in dealing with applications as opposed to actions. The Supreme Court of Canada in *Toronto (City) v CUPE Local 79*, [2003] 3 SCR 77, per Arbour J, at paragraph 35 has stated that judges have an inherent and residual discretion to prevent an abuse of the court's process. The application of such discretion appears to be tentative at best.

[71] There is a concept of comity in the context of NOC proceedings was considered in the decision of Barnes J of this Court in *Pfizer Canada Inc v Canada (Minister of Health),* [2008] 1 FCR 672, at paragraph 30:

> *30 I agree with counsel for Pfizer that the principle of judicial comity may not be readily applicable to prohibition proceedings brought under section 6(1) [as am. by SOR/98-166, s. 5] of the NOC Regulations. That can be so because even in cases which involve a common generic product and challenges to an identical patent, the allegations set out in the respective NOAs of the generic challengers, or the evidence the parties present, may be sufficiently different that disparate judicial outcomes are possible. This point is recognized in the recent decision in Sanofi-Aventis Canada Inc. v. Novopharm*

> *Ltd., [2008] 1 F.C.R. 174 (F.C.A.), where, in a discussion concerning abuse of process, Justice Edgar Sexton observed at paragraph 50:*
>
> *[page 687]*
>
> > *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. Although this situation may give rise to the possibility of an inconsistent result, this concern is overridden by the potential for unfairness to the generic that is barred from bringing forward its case simply because another generic's approach was inadequate.*
>
> *The concern expressed above does not, however, apply where the issue for determination is one of patent construction. Inasmuch as this is an issue of law for the Court to decide, there should, in theory at least, be only one correct answer regardless of the expert evidence brought to bear upon it. This is particularly evident when one considers that the experts are speaking objectively for the notional person skilled in the art.*

[72] In dealing specifically with the *NOC Regulations*, the attempts by the Court to deal with re-litigation begins with the decision of the Federal Court of Appeal in *Sanofi-Aventis Canada Inc v Novopharm Inc*, 2007 FCA 163. That Court dealt with an appeal - first from a Prothonotary, then the Federal Court - from a decision arising from a motion to strike under section 6(5)(b) of the *NOC Regulations* brought by the second person (generic). The first person (innovator) had brought an application for prohibition against the generic in respect of the same patent which, in earlier NOC Proceedings against another generic, had been held to be invalid. The Prothonotary struck out the application; the trial judge reversed that decision. The Court of Appeal, in a two-to-one decision,

reversed the Trial Judge and upheld the Prothonotary in striking out the application. Sexton JA (with whom Sharlow JA concurred) wrote at paragraph 50:

> *50 Finally, Sanofi-Aventis and Schering argue that a finding of abuse of process in this case will lead to unfairness. They say that while first persons will not be permitted to defend against allegations by subsequent generics after the same allegation made by an earlier generic has been found to be justified, subsequent generics will be permitted to repeat allegations already made earlier by other generics even if the earlier allegations were found to be unjustified. However, there is no unfairness in this scenario. All parties are held to the same standard: they must each put forward their entire case, complete with all relevant evidence, at first instance. The innovator is prevented from relitigating an issue already decided in a proceeding to which it was a party with the aid of additional evidence it chose not to adduce in the earlier proceedings. 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. Although this situation may give rise to the possibility of an inconsistent result, this concern is overridden by the potential for unfairness to the generic that is barred from bringing forward its case simply because another generic's approach was inadequate. In each situation, it is necessary to balance the effect of a proceeding on the administration of justice against the unfairness to a party from precluding it from bringing forward its case.*

[73] Nadon JA dissented. He wrote at paragraph 119:

> *119 To sum up, I conclude that this is not a case where the doctrine of abuse of process should be applied. First, the parties to the proceedings herein are not the same as those that were before Mactavish J. in Sanofi Aventis, supra. Second, the issue herein and*

> *that before Mactavish J. is primarily one of fact and, as a result, it would be open to the trier of fact in this proceeding to come to a different conclusion. Third, the appellant, in seeking to prohibit the Minister from issuing a NOC to Novopharm, is simply exercising its rights under the NOC Regulations which, as I have explained, do not expressly or implicitly prevent a patentee from relitigating an issue previously litigated against another generic drug manufacturer. Fourth, there is no "additional element" in the present matter which would make of the appellant's application an abuse of process. Contrary to the situation in Hoffmann-La Roche, supra, it cannot be said that in litigating a second time the issue which it litigated against Apotex in Aventis Pharma, supra, the appellant's conduct calls for the application of the doctrine of abuse of process. Fifth, it cannot be concluded that the proceedings commenced by the appellant, following service of Novopharm's NOA, are either oppressive or vexatious.*

[74] Nadon JA revisited this decision in a later appeal, *Janssen-Ortho Inc v Apotex Inc*, 2009 FCA 212. Section 6(5)(b) was *not* at issue there. What was at issue was whether the Notice of Allegation (NOA) sent by a second person (generic) to a first person (innovator) before any application to the Court had been filed, could be considered to be an abuse of process. It was alleged that certain of the allegations had already been determined by the Courts. Nadon JA held that the remarks of Sexton JA were *in obiter;* and, in any event, a generic could not be precluded from making allegations in its NOA. He wrote at paragraphs 42 to 45:

> *42 In Sanofi-Aventis, supra, the question of abuse of process arose by reason of paragraph 6(5)(b) of the Regulations, which provides that on a motion by a second person, the Federal Court may dismiss an application for prohibition on the ground that it is redundant, scandalous, frivolous or vexatious, or that it is otherwise an abuse of process.*
>
> *43 In this appeal, however, the question is not whether the first person's application constitutes an abuse of process, but rather whether the second person's allegations found in its NOA amount to an abuse of process. Paragraph 6(5)(b) of the Regulations clearly does not apply in the present matter and this Court is not asked to*

> *dismiss an application for prohibition on a motion brought by a second person. There can be no doubt that Sexton J.A.'s comments in Sanofi-Aventis, supra, were made in obiter and, thus, are not binding and, in any event, they do not support the position adopted by the Judge.*
>
> *44 In my view, a fair reading of paragraph 50 of Sexton J.A.'s Reasons in Sanofi-Aventis, supra, does not lead to the conclusion that a second person can only put forward a NOA on grounds similar to those put forward by a different generic in other proceedings when it has better evidence to offer or better legal arguments to make. I believe that at paragraph 50 of his Reasons, Sexton J.A. was simply attempting to explain his view that notwithstanding the possibility that different judgments might be rendered with respect to identical or similar NOAs, fairness required that a generic, such as Apotex in the present case, which had not yet litigated the issues which it raised in its NOA, be allowed to have its day in court. In my view, it cannot be seriously argued that Sexton J.A. was advocating that an assessment of the second generic's evidence and legal arguments had to be made before it could send its NOA and respond to the application for prohibition.*
>
> *45 I am therefore satisfied that nothing said in our decision in Sanofi-Aventis, supra, supports the Judge's conclusion that a second person, unless it is in a position to show that it has "better evidence or a more appropriate legal argument", cannot send a NOA to a patentee and, hence, respond to the patentee's application for prohibition on grounds similar to those put forward by a different generic in other proceedings with the same patentee. I therefore conclude that the Judge erred in concluding as he did on the issue of abuse of process.*

[75] I considered these two decisions in *Pfizer Canada Inc v Canada (Minister of Health),* 2009 FC 1165 and concluded that narrow distinctions could be made. I wrote at paragraphs 45 and 46:

> *45 A narrow distinction between the Apotex and Sanofi decisions can be made on the basis that in Apotex the Court of Appeal is saying that a generic cannot be precluded from alleging something that was dealt with in a prior proceeding whereas Sanofi is saying that a Court in considering the matter at the hearing should be cautious about making a determination different from an earlier determination unless there is better evidence or more appropriate*

> *argument. If this is not the difference, then it is difficult to discern any difference other than that the decisions are contradictory.*
>
> *46 The point that I draw from these two decisions and the general jurisprudence is that the Courts have adopted a strict and narrow interpretation of the NOC Regulations and proceedings under those Regulations. The position taken by Pfizer's Counsel here is more consistent with that view and the recently expressed view of the Federal Court of Appeal in Apotex, supra, that each proceeding is to be considered on its own "stand alone" merits, without consideration as to what may have happened in, for instance, a fully litigated action respecting the same patent. Nadon J.A. wrote in Apotex, supra, at paragraphs 38, 47, 48 and 70:*
>
> . . .
>
> *Thus I find that I am to consider the NOC application proceedings in isolation from the impeachment action. In other words the findings and Judgment in the impeachment action, are not to affect the finding and Judgment in the NOC proceedings. This is particularly so since in the NOC proceedings no section 53 or fraud allegations were raised.*

[76] On the question of "*better evidence or more appropriate legal argument*" I wrote in *Pfizer Canada Inc v Canada (Minister of Health)*, 2008 FC 500, at paragraphs 23 to 26 how difficult it was, in the absence of a complete record of the earlier proceedings, to discern if something is better. Even if a difference is discerned, does that lead to a conclusion that the evidence or argument is better? How much "better" must it be? I wrote:

> *23 The Court system has been overwhelmed by NOC proceedings, many involving different generics addressing the same patent in one proceeding after another, or by the same innovator asserting the same patent time after time, even when the patent was declared in a NOC proceeding to be invalid. The United States legislation makes provision for joinder of several proceedings and interested parties. In Sanofi-Aventis Canada Inc. v. Novopharm Limited, 2007 FCA 163 (application for leave to Supreme Court dismissed [2007] S.C.C.A. No. 311) the Federal Court of Appeal stated at paragraph 50 that*

> *relitigation in an NOC context of the same patent, even if different generics are involved, is not to be permitted unless a subsequent party is apprised of "better evidence or a more appropriate legal argument".*
>
> *24 Thus parties involved in NOC proceedings engage in a "screening out" procedure:*
>
> > *1. Is the matter sufficiently raised in the Notice of Allegation;*
> >
> > *2. Has the matter been previously determined even if the generic is different, if so, does the present generic have "better evidence or a more appropriate legal argument".*
>
> *25 The question of "better evidence or a more appropriate legal argument" is often confounded because it is not readily apparent what the evidence or argument was in the earlier case. The record there is not of record here. The evidence and argument there is sometimes cloaked in secrecy by a confidentiality order. Usually all that one has is the Reasons of the earlier Court(s) and possibly memoranda of argument filed there.*
>
> *26 Not unexpectedly, Pfizer puts the three validity matters raised by Pharmascience through the "screening out" process and argues that all that is left is some portion of the utility argument. Pharmascience disagrees. Therefore I will approach each argument by looking at the "screen" and, regardless of my determination, provide my views as to the substantive arguments.*

[77] Again, I wrote on this point in *Pfizer Canada Inc v Canada (Minister of Health)*, 2008 FC 11, at paragraph 15:

> *15 I faced the question of a previous determination by the Court in respect of a patent in NOC proceedings in Eli Lilly Canada Inc. v. Novopharm Ltd., [2007] F.C.J. No. 800, 2007 FC 596. One of the difficulties canvassed there, and it is a difficulty here as well, is that the record of the earlier proceedings is not of record in these proceedings. Thus, the Court is left to determine if there is "better evidence or a more appropriate legal argument" in the present proceeding as against the earlier proceedings only from what is revealed in the Reasons of the Courts in the earlier proceedings. I said in that case at paragraphs 62 and 99:*

> *[62] The jurisprudence therefore provides that this Court, in its own discretion, can review the Reasons given in Apotex by Justice Gauthier and determine whether there is "better evidence" or "more appropriate legal argument" made by the generic in the present proceeding as to validity of the '113 patent than was presented in Apotex. If so, the better evidence and more appropriate arguments must be considered. If no better evidence or more appropriate argument is found, it would be an abuse to permit the matter to be considered again. The word "abuse" is not used in any sense so as to imply that the second generic has acted improperly, it has not; it could not have been known until a few days before the hearing of this case that the decision in Apotex would be released. The word "abuse" is used in the sense that it would be a waste of the Court's resources and possibly lead to unwanted inconsistent results, were the matter to be considered as a matter of first instance on this the subsequent occasion. The consideration in the second instance should only be one as to "better evidence" or "more appropriate" argument which, if determined to exist, must be considered as a matter of first instance. Of course if a different attack on validity is raised, one that was not raised in Apotex, it will be considered as a matter of first instance.*
>
> ...
>
> *[99] In the present proceedings therefore, I am required to determine as to each of the arguments as to invalidity raised by Novopharm:*
>
> > *1. Is the argument new and different, in which case it will be determined as a matter of first instance.*
> >
> > *2. If the matter has been dealt with by Justice Gauthier is there, having regard to her Reasons, "better evidence" or "more appropriate legal argument" in this proceeding such that Justice Gauthier's finding should not be followed.*

[78] The conclusion that I reached in *Eli Lilly Canada Inc v Novopharm Ltd*, 2007 FC 596, at paragraphs 57 to 64, in circumstances very like the present case where a different generic in earlier proceedings did not succeed on a validity issue and another generic was endeavouring to

raise the same issues before me, was that the matter could be considered on the basis of "abuse" or "comity"; but first, the Court must do its best to determine if there is "better" evidence or argument. I wrote:

> *57 Very recently, the Federal Court of Appeal in Sanofi-Aventis Canada Inc. v. Novopharm Limited [2007] F.C.J. No. 548, 2007 FCA 163, considered whether a first person could assert a patent in a proceeding under the NOC Regulations against a different second person where in a previous final decision, the Court had determined, that the patent was invalid. The decision of the Court was split, Sexton JA spoke for the majority. The matter arose on a motion brought by the generic under section 6(5)(b) of the NOC Regulations, where a second person (generic) brought a motion on the ground that it would an abuse of process for the first person to assert a patent which was previously held to be invalid against a different second person. Sexton J.A. for the majority said at paragraphs 37 and 38 of his Reasons:*
>
> > *[37] In the context of the NOC Regulations, encouraging the efficient use of scarce judicial resources is also of particular concern. Judicial resources are already taxed considerably by the voluminous proceedings brought under the regulations. An attempt to further strain the resources of parties and of the courts through repetitious litigation without any compelling justification strongly favours a finding of abuse in the process.*
> >
> > *[38] Therefore, despite the fact that Mactavish J.'s decision would not dictate the outcome of the present application and consequently, that it is not possible to say that Sanofi-Aventis has no chance of success, I nevertheless am compelled to hold that the application in respect of the Novopharm NOA is an abuse of process and therefore should be dismissed.*
>
> *58 The proceedings now before this Court arise from a different perspective. We are dealing with a different generic (second person) who is attacking the validity of a patent recently held to be valid in other NOC Regulations proceedings involving a different generic.*
>
> *59 Sexton JA, addressed the situation where a patent was held to be valid having regard to allegations raised by a first generic. He said that the first generic would be precluded from raising subsequent allegations as to invalidity of the same patent. However, he held that a different generic would not be precluded from alleging*

invalidity of the patent on better evidence or more appropriate legal argument. At paragraph 50 of his Reasons, he said:

> *...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 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. Although the situation may give rise to the possibility of an inconsistent result, this concern is overridden by the potential for unfairness to the generic that is barred from bringing forward its case simply because another generic's approach was inadequate. In each situation, it is necessary to balance the effect of a proceeding on the administration of justice against the unfairness to a party from precluding it from bringing forward its case.*

60 The question becomes how can the Court know if the evidence is "better" or the legal argument "more appropriate". As previously discussed, the NOC Regulations do not permit a first party to bring an application for abuse under section 6(5)(b). The Rules of this Court for summary judgment or to strike are inappropriate. Thus this Court can only know these matters by examination of the Reasons given in the earlier decision.

61 Notwithstanding that no motion has been brought by any party, and probably could not have been brought, there is an inherent and residual discretion in the Court itself to prevent an abuse of process. In Sanofi-Aventis Canada v. Novopharm Limited et al. 2007 FCA 163, Sexton JA at paragraph 35 of his Reasons, relies on the Supreme Court of Canada decision in Toronto (City) v. C.U.P.E. Local 79, [2003] 3 S.C.R. 77 per Arbour J. at paragraph 35 where she states:

> *"Judges have an inherent and residual discretion to prevent an abuse of the court's process"*

62 The jurisprudence therefore provides that this Court, in its own discretion, can review the Reasons given in Apotex by Justice Gauthier and determine whether there is "better evidence" or "more appropriate legal argument" made by the generic in the present proceeding as to validity of the '113 patent than was presented in

> *Apotex. If so, the better evidence and more appropriate arguments must be considered. If no better evidence or more appropriate argument is found, it would be an abuse to permit the matter to be considered again. The word "abuse" is not used in any sense so as to imply that the second generic has acted improperly, it has not; it could not have been known until a few days before the hearing of this case that the decision in Apotex would be released. The word "abuse" is used in the sense that it would be a waste of the Court's resources and possibly lead to unwanted inconsistent results, were the matter to be considered as a matter of first instance on this the subsequent occasion. The consideration in the second instance should only be one as to "better evidence" or "more appropriate" argument which, if determined to exist, must be considered as a matter of first instance. Of course if a different attack on validity is raised, one that was not raised in Apotex, it will be considered as a matter of first instance.*
>
> *63 There is another matter to consider. It is that of judicial comity. Comity was recently considered by Justice Barnes of this Court in Pfizer Canada Inc. v. Canada (Minister of Health), [2007] F.C.J. No. 596, 2007 FC 446. Justice Barnes considered the reasons of Sexton JA in Sanofi-Aventis particularly at paragraph 50 referred to previously. The principle of comity, Justice Barnes found, particularly at paragraphs 30 to 33 of his Reasons, may not be readily applicable in NOC proceedings, however, where matters such as patent construction were considered having regard to the patent itself and not the evidence, or where the evidence is not different, the need for predictability and consistency remains.*
>
> *64 Thus, the Court may approach the matter from the point of view of "abuse" or "comity" or both.*

[79] Justice Sexton may have had the last word in *Apotex Inc v Pfizer Ireland Pharmaceuticals*, 2011 FCA 77, (2011), 93 CPR (4^{th}) 42 (FCA), where he was dealing with an issue as to whether to strike out a plea by a patent owner in an action to invalidate that patent. The patent owner pleaded that, in previous NOC proceedings, the patent had been held valid as between the same parties. Thus, the patent owner pleaded that "by reason of *res judicata*, issue estoppel, comity and abuse of process" another person could not challenge the validity of a patent in a subsequent action.

[80] Sexton JA for the Court held that NOC proceedings were different from actions respecting validity. However, at paragraph 24, he wrote that "…*there is scope*…" to consider issue estoppel and abuse of process when dealing with a subsequent NOC proceeding rather than an action:

> *24 This court has repeatedly said that NOC proceedings are quite different from subsequent infringement or impeachment actions. In my view, there is scope for applying the bars of issue estoppel and abuse of process in the later proceedings to prevent the relitigation of subsidiary factual and legal issues in order to preserve judicial resources, promote the integrity of the justice system, prevent inconsistent findings, and prevent abuse. The difference between the NOC proceeding and later proceedings is an important consideration for the judge in the later proceedings, along with all of the other discretionary considerations discussed in Danyluk and C.U.P.E. Simply put, Danyluk and C.U.P.E. can apply in proceedings such as these.*

d) Conclusion as to effect of the previous Federal Court decision

[81] The resulting situation is not a good one. A court cannot be "bound" in NOC proceedings by an earlier decision respecting failed invalidity allegations made by a different generic. Some United States practitioners have raised a very real concern as to sham litigation; that is, litigation that is not strongly contested, designed to create a precedent binding all who follow, that could result if that were the case. In proceedings in the United States brought under the *Hatch-Waxman Act*, endeavours are made to join as many generics as possible in one proceeding so that all may be bound by the result. Canada has no similar provisions.

[82] Thus, what a Court in Canada must do when faced with an earlier decision in NOC proceedings involving failed invalidity allegations raised by a different generic is:

- do the best it can from the reasons of the Court in the earlier proceeding to discern what the evidence and argument was;

- compare that evidence and argument with that in the proceedings at hand;

- determine if there are meaningful differences between the evidence and argument in the earlier case and present case;

- give respect to the earlier decision but, if there are determinative differences in the evidence, the Court must make its own decision; and

- if the previous decision contains a critical error of law or if the law has changed the Court must make its own decision as to the law.

ISSUE #3: ***Effect of the United States Decision (Judge Ward)***

[83] The decision of The United States District Court, Eastern District of Texas, Marshall Division, between *Allergan, Inc v Sandoz Inc*, cited as 2011 WL 3809882 (E.D. Tex.), previously referred to, resulted from proceedings taken by Allergan, Inc. under the provisions of the *Hatch-Waxman Act*, which *Act* is in some respects a rough equivalent of our proceedings under the *NOC Regulations*.

[84] Those proceedings were in fact four consolidated proceedings, all brought by Allergan, Inc. respecting the same group of four patents, but against different defendants, all of which can be

described as generic drug companies. Those defendants were (1) Sandoz Inc., (2) Alcon Laboratories Inc., Alcon Research, Ltd., Alcon Inc. and Falcon Pharmaceuticals, Ltd., (3) Apotex Inc. and Apotex Corp., (4) Watson Laboratories, Inc.

[85] The four patents in suit all arose from the same priority document from which the Canadian '764 patent claims priority. All had essentially the same disclosure with one having an extra example. All named the same persons that the '764 patent did as inventors. Judge Ward in his reasons described the patents this way at paragraphs 33 and 34:

> *33. The four patents-in-suit generally relate to a fixed combination composition of 0.2% brimonidine and 0.5% timolol, a method of treating glaucoma or ocular hypertension by administering the aforementioned composition twice daily, or an article of manufacture comprising packaging material indicating that twice daily administration of the composition is useful for treating glaucoma or ocular hypertension. (See JTX 1-4.) Like the brimonidine tartrate and timolol maleate single agent products (Alphagan® and Timoptic®), the combination product of the patents-in-suit is applied topically to the eye. (See e.g., JTX 1 at Abstract.)*
>
> *34. The patents-in-suit also describe suitable preservatives for the combination product. (See id. At col. 2, 11. 29 et seq.) The patents-in-suit list BAK as the first such preservative. The patents-in-suit acknowledged that "typically such preservatives are employed at a level of from 0.004% to 0.02%". (Id.) The patents-in-suit further state that the preservative, preferably BAK, "may be employed at a level from 0.001% to less than 0.01%, e.g. from 0.001% to 0.008%, preferably about 0.005% by weight." (Id.)*

[86] Prior to the hearing which led to the decision of Judge Ward, that Judge held what is known as a "Markman" hearing, which is a common practice in United States patent trials. The purpose of such a hearing is for the Court to provide a construction of the claims or disputed terms of the

claims of the patents at issue prior to a hearing as to validity and infringement. Judge Ward gave his decision as to disputed terms of the claims at issue on April 27, 2011, cited as 2011 U.S. Dist LEXIS 45577. That is a lengthy and detailed decision which I will not repeat here. He rejected an argument that the claims were to be read with a limitation that the composition must meet FDA requirements for approval. He also considered the phrase "reducing the number of daily topical ophthalmic doses" as being plain on its surface and need not be interpreted as reducing the dosages from three to two per day.

[87] The United States patents are similar to the '764 patent at issue here, but the claims are not identical.

[88] The Plaintiff Allergan led the evidence of one of the named inventors, Mr. Gary Beck, the same person who gave evidence in these proceedings. They also led the evidence of another named inventor, Ms. Amy Batoosingh. The Reasons mention only one expert, whose evidence was led by Allergan; Dr. Noecker, whom Judge Ward described in paragraph 158 of his Reasons as a very credible witness whose testimony was well supported by the evidence presented at trial.

[89] The Defendants collectively appear to have led the evidence of two expert witnesses; Dr. Tanna and Dr. Laskar. At paragraphs 156 and 157 of his reasons, Judge Ward appears to be sceptical about some of their evidence.

[90] The Defendants did not contest infringement. They attacked the validity of the four patents at issue on a number of grounds including, principally, anticipation having regard to DeSantis US

Patent No. 5,502,052, and obviousness having regard to the same DeSantis reference, plus common general knowledge.

[91] The Court, at paragraph 161, stated that it adopted Allergan's definition of a person skilled in the art (POSITA) which was set out at paragraph 159 of the Reasons as follows:

> *159. Dr. Noecker opined that a person of ordinary skill in the art is "a person engaged in developing pharmaceutical formulations and treatment methods for the eye, or is a specialist in treating diseases of the eye such as an optometrist or ophthalmologist who also has experience either in developing ophthalmic pharmaceutical formulations or in designing and running clinical trials on such formulations. This person may also work in collaboration with other scientists and/or clinicians who have experience developing ophthalmic pharmaceutical formulations, running clinical trials related to such formulations, and/or treating patients using such formulations." (D.I. 242, Trial Tr. Day 3 (AM) at 90:15-91:17 (Noecker).)*

[92] With respect to anticipation, the test under United States law as stated by Judge Ward is not very different from that under Canadian law. He wrote at paragraphs 163 and 165:

> *163. A patent is invalid as "anticipated" under 35 U.S.C. § 102 if a single prior art reference discloses each element of the claimed invention.*
>
> . . .
>
> *165. To anticipate, the identical subject matter must not only be disclosed by the single prior art reference, but also the disclosure must be sufficiently enabling to place the information in the possession of the public.*
>
> . . .

[93] Judge Ward then considered the US DeSantis patent at considerable length and determined that it did not anticipate any of the four patents. I repeat what he wrote at paragraphs 173, 187, 190 and 191:

> *173. At best, DeSantis discloses a very large genus of potential fixed combinations of alpha-agonists and beta-blockers, listing all known beta-blockers and alpha-agonists for theoretical use. (D.I. 242, Trial Tr. Day 3 (AM) Tr. 96:6-9, 17-19 (Noecker).) "It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus. There may be many species encompassed within a genus that are not disclosed by a mere disclosure of the genus." Atofina v. Great Lakes Chem Corp., 441 F.3d at 999.*
>
> . . .
>
> *187. One of ordinary skill in the art would thus not read DeSantis' disclosure of an enormous genus of potential fixed combinations to anticipate a brimonidine and timolol combination. (D.I. 242, Trial Day 3 (AM) at 123:4-12 (Noecker).) Indeed, as a testament to the difficulties in developing combination drugs, the only claimed combination in DeSantis, apraclonidine and betaxolol, was never marketed or approved anywhere in the world. (D.I. 242, Trial Day 3 (AM) at 119:18-25 (Noecker); D.I. 240, Trial Tr. Day 2 (AM) at 131:22-24 (Tanna).)*
>
> . . .
>
> *190. Thus, DeSantis does not disclose a fixed composition of 0.2% brimonidine and 0.5% timolol, as required by independent claim 1 of the '976 patent, independent claims 1 and 7 of the '258 patent, independent claim 4 of the '149 patent, and independent claims 1 and 4 of the '463 patent. (D.I. 242, Trial Day 3 (AM) at 120:20-121:3; 121:24-122:11 (Noecker).) DeSantis does not disclose a fixed composition of 0.2% brimonidine and 0.5% timolol with a specific BAK concentration, as required by claims 2, 3, 8, and 9 of the '258 patent and claims 2, 3, 5, and 6 of the '463 patent (D.I. 242, Trial Day 3 (AM) at 124:7-17; 125:1-10 (Noecker).) DeSantis does not disclose a method of reducing the dose of brimonidine from three times a day to two times a day without losing efficacy in the treatment of glaucoma. (D.I. 242, Trial Day 3 (AM) at 127:10-21 (Noecker).)*

> *191. For all these reasons, the Court is not persuaded that Defendants have established by clear and convincing evidence that the patents-in-suit are anticipated by DeSantis.*

[94] Next, Judge Ward turned to the issue of obviousness. Again, the United States law as he set out is not very different from Canadian law. He wrote at paragraphs 192 to 196:

> *192. A determination of obviousness is a legal determination based on four factual inquiries: (1) the scope and content of the prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations of non-obviousness. See Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966), cited in KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 127 S. Ct. 1727, 1734 (2007).*
>
> *193. When the patented invention is a combination of known elements, the Court must "determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue" by considering the teachings of multiple references, the effects of demands known to the design community or present in the marketplace, and the background knowledge possessed by a person having ordinary skill in the art. KSR, 127 S. Ct. at 1740-41.*
>
> *194. [K]nowledge of a problem and motivation to solve it are entirely different from motivation to combine particular references to reach the particular claimed [invention]." N.V. v. Abbott Labs., 512 F.3d 1363, 1373 (Fed. Cir. 2008) (concluding that the district court correctly dismissed an expert's vague and conclusory obviousness testimony, which did not offer any motivation for one skilled in the art to combine the particular references he cited in order to practice the claimed invention); see also Graham, 383 U.S. at 36 (discussing the "importance of guarding against hindsight…and resist[ing] the temptation to read into the prior art the teachings of the invention in issue" when considering the obviousness of a patent).*
>
> *195. Additionally, "[t]wo ingredients might be therapeutically effective when use separately as part of an overall treatment regimen, yet be incompatible or ineffective when combined in a single solution." In re Brimonidine, 643 F.3d 1366 (Fed. Cir. May 19, 2011) at Section B.2 (pinpoint cite unavailable); see also Pozen*

> *Inc. v. Par Pharmaceutical, Inc., et al., C.A. No. 6:08-cv-00437, Slip Opinion at 4, 40.*
>
> *196. Secondary considerations that provide evidence of non-obviousness include copying, commercial success, failure of others, long-felt need, general scepticism of those in the art, and unexpected results. See KSR, 127 S. Ct. at 1734. "As (the Federal Circuit) has repeatedly explained, this evidence is not just a cumulative or confirmatory part of the obviousness calculus but constitutes independent evidence of nonobviousness." Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc., 520 F.3d 1358, 1365 (Fed Cir. 2008) (Citing Catalina Lighting, Inc. v. Lamps Plus, Inc., 295 F.3d 1277, 1288 (Fed. Cir. 2002) ("Objective indicia may often be the most probative and cogent evidence of nonobviousness in the record.")).*

[95] The arguments of the Defendants as to invalidity for obviousness were summarized by Judge Ward at paragraph 204:

> *204. Defendants contend that the claims of the patents-in-suit are obvious based on the teachings of DeSantis alone, and combined with what was known by a person of ordinary skill in the art prior to April 2002 regarding the concentrations of brimonidine, timolol, and BAK in the commercial products Alphagan® and Timoptic®. The commercial product Alphagan®, available since 1996, was 0.2% brimonidine tartrate preserved in 0.005% BAK. The commercial product Timoptic®, available since 1978, was 0.5% timolol maleate preserved in 0.01% BAK. Thus, Defendants argue that a person of ordinary skill in the art would have considered the concentrations of brimonidine, timolol, and BAK recited in the claims of the patents-in-suit could be achieved through routine optimization by a person of ordinary skill in the art at the time. See Bayer Schering Pharma AG v. Barr Labs., Inc., 575 F.3d 1341 (Fed. Cir. 2009).*

[96] Judge Ward reviewed the evidence at considerable length in his Reasons. He summarized at paragraphs 241 and 242:

> *241. For all of the reasons set forth above, none of the references cited by Defendants discloses or suggests a combination ophthalmic product consisting of brimonidine and timolol as claimed in the patents-in-suit. The mere existence in the art of fixed combination products with other constituents, and the available information about the concomitant or adjunctive administration of brimonidine and timolol does not provide a substantial reason for one of ordinary skill in the art to create a fixed combination product of brimonidine and timolol as claimed in the patents-in-suit. In particular, one of skill in the art would not expect that, simply because two active ingredients are effective and marketed separately, they could or should be put together in a single, workable formulation that is safe and therapeutically effective for glaucoma treatment. (See D.I. 238, Trial Tr. Day 1 (AM) at 58:13-59:9 (Whitcup).) Moreover, given the significant difference in the efficacy between brimonidine BID and brimonidine TID at hours 9 and 11, one of skill in the art would not have expected that adding timolol to brimonidine would enable a reduction in dose of brimonidine from three to two times a day without loss of efficacy.*
>
> *242. This is particularly true given the nature of the field, factors that teach away from the invention, and several secondary considerations of non-obviousness.*

[97] The Judge went on to consider a number of other factors, such as long-felt need and commercial success, which he described as a secondary factor. He concluded that the Defendants had failed to make out their case on obviousness. He wrote at paragraph 295:

> *295. In sum, the Court is not persuaded that Defendants have established by clear and convincing evidence that the patents-in-suit are obvious in light of the prior art. The Court finds that there are significant differences between the prior art and the claimed inventions, such that a person of ordinary skill in the art would not have been motivated to create a fixed combination composition of 0.2% brimonidine and 0.5% timolol, In addition, there exist a number of secondary considerations that severely undermine the defendants' claims of obviousness. Accordingly, the court concludes that the patents-in-suit are not invalid as obvious under 35 U.S.C. § 103.*

[98] As previously stated, this decision is under appeal to the United States Court of Appeal for the Federal Circuit (US CAFC) with a hearing expected in a few months.

[99] This determination, therefore, is not a final determination. It involves somewhat different patents, but not very different - but with different claims; somewhat different law, but not very different; as well as different evidence. The principal piece of prior art is a DeSantis United States Patent and not the DeSantis published international patent application relied upon here; they are not very different. The witness, Mr. Beck, is the same person who gave evidence here, but it is unclear as to what the evidence was that he gave in the United States actions. The experts are different.

[100] This United States decision is not binding upon me, and I do not treat it as binding in any way. It is interesting and informative, but it goes no further than that. No Counsel argued differently before me.

ISSUE #4: ***Who is the person skilled in the art?***

[101] Among the first tasks to which a Court must attend in a patent action is to define the "person of ordinary skill in the art" (POSITA) or more briefly, "person skilled in the art". This is the notional person to whom the patent is addressed, and who takes his or her place in the spectrum of other fictional legal persons, such as the "reasonable person" in tort law.

[102] Allergan, through its expert Dr Fechtner, describes the person skilled in the art this way in paragraph 52 of his affidavit:

> *It is my opinion that the POSITA is a person engaged in developing pharmaceutical formulations and treatment methods for the eye, or is a specialist in treating diseases of the eye such as an optometrist or ophthalmologist who also has experience either in developing ophthalmic pharmaceutical formulations or in designing and running clinical trials on such formulations. This person may also work in collaboration with other scientists and/or clinicians who have experience developing ophthalmic pharmaceutical formulations, running clinical trials related to such formulations, and/or treating patients using such formulations.*

[103] Apotex asserts that the person skilled in the art is, in addition to that as described by Dr. Fechtner, a person skilled in the formulation of topical ophthalmic medicines. It supports this assertion with reference to the evidence of its expert witnesses; Dr. Quigley, at paragraphs 48 and 296 of his affidavit, and Dr. Kompella at paragraphs 17(b) and 38 to 40 of his affidavit. I repeat paragraphs 38 to 40 of Dr. Kompella's affidavit:

> *38. The '764 patent concerns the topical ophthalmic use of brimonidine in combination with timolol when indicated for the treatment of glaucoma or ocular hypertension. The '764 patent acknowledges that brimonidine and timolol are each available for separate use and have been combined in serial application (adjunctive therapy) during the course of treatment of glaucoma.*
>
> *39. The compositions of the '764 patent are described as being preferably formulated with 0.01 to 0.5 percent by weight brimonidine and 0.1 to 1.0 percent by weight timolol solution in water at a pH of 4.5 to 8.0. Additionally, the compositions may contain other ingredients, such as preservatives, co-solvents and viscosity building agents; numerous examples of each are provided.*
>
> *40. Based on the above, it is my opinion that the '764 patent addresses itself to an individual or individuals with experience in ophthalmology (the treatment aspects) and experience in the formulation of ophthalmic compositions (the formulation aspects).*

[104] I am persuaded that, in addition to the skills of a person skilled in the art as set out by Dr. Fechtner, must be added the skill of a person with experience in the formulation of topical ophthalmic compositions. The description set out in the '764 patent makes it clear that the formulation of a topical composition is what is addressed by the patent. I repeat just a few passages of the description by way of illustration (emphasis added):

> *[page 1 – lines 8-12]*
>
> *This invention relates to the topical ophthalmic use of brimonidine in combination with timolol when indicated for treatment of glaucoma or ocular hypertension. Such combinations or* ***formulations*** *are available for separate use in the ophthalmic art and have been combined in serial application during the course of treatment of glaucoma.*
>
> *[page 3 – lines 11 & 12]*
>
> *In* ***forming*** *compositions for topical administration, the mixtures are preferably* ***formulated****…*
>
> *[page 5 – lines 26 & 27]*
>
> *The Brimonidine-Timolol* ***formulation****…The* ***formulation****…*
>
> *[page 6 – lines 1 & 2]*
>
> *The* ***formulation*** *preservative is…The* ***formulation*** *passes…*

[105] Therefore, I conclude that a person skilled in the art can be described, briefly, as set out in paragraph 40 of Dr. Kompella's affidavit:

> *An individual or individuals with experience in ophthalmology and experience in the formulation of ophthalmic compositions.*

[106] I appreciate that, in first reading, my characterization of the person skilled in the art may seem different from that characterized by Crampton J in the Sandoz decision. Crampton J seems to say that the person skilled in the art has experience in ophthalmology or formulation of ophthalmic compositions. However, in paragraph 40 of his Reasons, Crampton J describes the person skilled in the art by adding the words "…as described by Dr. Fechtner". That description is set out in paragraph 38 of Crampton J's Reasons and adds the words "…who also has experience in either developing ophthalmic formulations or in designing and running clinical trials on such formulations". This qualification, which I assume Crampton J meant to include, makes his definition of a person skilled in the art very close to mine.

[107] Counsel for Allergan has sought to characterize the definition of a person skilled in the art as a *legal* finding. He had no authority for such a proposition. At best, it is a finding of mixed fact and law. Therefore, I do not feel compelled by comity to follow the finding of Crampton J in this regard.

[108] The difference between Crampton J's conclusions and mine are small. Mine requires that more regard be given to the viewpoint of a formulator. Only Apotex put forward an expert formulator, Dr. Kompella. Allergan's witness, Dr. Fechtner, indicated that he had worked with formulations; but he declined to answer certain questions, as I have previously indicated, on the basis that he was not a formulator. I have also previously stated that, given the manner in which he gave answer during his cross-examination, I would treat his evidence with some care.

ISSUE #5: ***Claim construction***

[109] I repeat what I wrote in *Merck & Co v Pharmascience Inc*, 2010 FC 510 after a lengthy review of the history of the law relating to patent claiming, at paras 68 to 70:

> *68 Having looked at the history of patent claims and claim construction in Canada as influenced by Great Britain, it can be seen that, originally, it was essential for a Court to construe the patent and its claims because the "invention" - hence, the monopoly - was to be found in the specification. As the statutes became clearer in respect of claims, the specification became divided into two parts. The description served the purpose of "purchasing" the monopoly by describing the invention in sufficient detail so that a person skilled in that art could understand what the invention was and how to put it into practice. The other part of the specification was the claims, which served to define and set limits as to the monopoly that the patent was intended to secure.*
>
> *69 Construction of the claim no longer meant that the Court had to scour the description so as to arrive at what the monopoly was; rather, the Court now begins with the claim and determines what a person skilled in the art would understand it to mean. This is done using the description as a context and, if necessary, using expert evidence to assist in putting the Court in a position of understanding at the level of a person skilled in the art. The purpose of the exercise is to understand what the patentee is claiming as its monopoly.*
>
> *70 Thus, claims construction today in the Canadian Courts is an easier task than in earlier days, because the function of the claims has been made clearer by statute. That function is to define distinctly and in explicit terms what the claimed monopoly is. To the extent that the claim is now to be "construed", that is the function of the Court alone. Experts may assist in two ways; first, they may inform the Court as to the knowledge that a person skilled in the art would have had at the relevant time, so as to bring that knowledge to bear reading both the description and the claims; second, an expert may assist in explaining any technical terms not within the experience expected of a Court. Thus, while construction is for a Court alone, the Court may have to make certain factual findings as to the knowledge of a person skilled in the art. The findings of the Court in this respect may best be considered as findings of mixed fact and law.*

[110] Claim construction can be efficiently conducted by the Court focusing on the issues of contention raised by the parties. This has been characterized as considering where “the shoe pinches” by the late Sir Nicholas Pumfrey of the UK Chancery (Patents) Court and latterly, the UK Court of Appeal. I repeat what I wrote in *Shire Biochem Inc v Canada (Minister Health)*, 2008 FC 538 at paras 21 to 23:

> *21 The Court, however is not to construe a claim without knowing where the disputes between the parties lie. To quote Justice Floyd of the England and Wales High Court (Patent Court) in Qualcomm Incorporated v Nokia Corporation [2008] EWHC 329 (Pat) at paragraphs 7 to 11, who in turn quoted the late Justice Pumfrey (as he then was) in Nokia v Interdigital Technology Corporation [2007] EWHC 3077 (Pat), "it is essential to see where the shoe pinches so that one can concentrate on the important points." Justice Floyd also quoted Jacob L-J. and further stated that, just as is the case in our Courts, construction is for the Court not expert witnesses save the well known exception as to technical terms with a special meaning. He raises at paragraph 11 some of the same concerns that our Court has encountered, particularly in NOC proceedings, where affidavit evidence is given, that experts will endeavour to put their own construction on the claims (possibly assisted by lawyers):*
>
> > *7. It is often said that a patent specification should be construed without reference to the infringement. Yet one cannot sensibly identify the point of construction without understanding what it is about the alleged infringement which is said to take it outside the claims. Pumfrey LJ (sitting at first instance) identified the necessary process in Nokia v Interdigital Technology Corporation [2007] EWHC 3077 (Pat) (unreported 21st December 2007), when he said (in another case about mobile telephone standards):*
> >
> > > *"Although one construes a claim 'as if the defendant had never been born', in any complex case it is essential to see where the shoe pinches so that one can concentrate on the important points. It is important nevertheless that the opportunity thus presented to construe the document with one eye on the infringement must be rejected, as far as possible.*

> *So when the claim calls for A, and the standard requires B, the right question is not whether A means B, or covers B, or might with hindsight be said to be another example of the genus of which B is also a member, but whether in the context of the specification the skilled man would appreciate that A in the claim encompassed B."*

8. Jacob LJ was not saying anything different in Technip France SA's Patent (2004) RPC 46,

> *"Although it has often been said that the question of construction does not depend on the alleged infringement ("as if we had to construe it before the Defendant was born" per Lord Esher MR in Nobel v Anderson (1894) 11 RPC 519 at 523), questions of construction seldom arise in the abstract. That is why in most sensible discussions of the meaning of language run on the general lines 'does it mean this, or that, or the other?' rather than the open-ended 'what does it mean'?"*

9. It is for the court and not the witnesses to come to conclusions about what the claim means. Subject to the well known exception about technical terms with a special meaning, the construction of a patent is a question of law. So an expert report which seeks to parse the language of the claim, and opine that a particular ordinary English word can only in his opinion have a particular meaning is not admissible, or helpful. Both sides in the present case are guilty of adducing evidence of this kind.

10. What is both admissible and helpful expert evidence is something rather different: evidence about the technical inter-relationship between rival claim meanings and the teaching of the specification. The expert is well able to assist the Court about the impact of different assumptions about the correct legal construction of the claim. It may be that it is only on one construction of the claim that general technical statements made in the body of the patent about what the invention achieves will hold good. It is perfectly legitimate for an expert to point that out, and to give a technical explanation of why, if the rival construction is adopted, the

> *claim would extend to embodiments which would not achieve the patent's technical objective.*
>
> *11. None of the above requires the expert to go through the claim and give his definition (wide or narrow) of every word or phrase in it. The written evidence in the present case suffered from this excess. Some of the cross examination did as well. It sometimes takes longer to intervene and stop it than it does to let it happen. It should not start.*

> *22 A patent is to be construed by the Court in light of the description in the specification, assisted, where necessary, by expert evidence as to the meaning of technical terms if they cannot be understood by reading the specification. This is not intended to open the door for experts to rush in through the portal of "explanation" to construe the claim themselves. The claims are to be read through the eyes of a person skilled in the art as of the relevant date which here is the date of publication, April 18, 1996. The fixing of such date is often not of any particular concern where the specification is clear and can be understood. It is only when some particular piece of "common knowledge" has or has not come into the public domain, such that it would be accepted as part of the knowledge and understanding of the notional person skilled in the art, that a meaningful difference in interpretation of the claims might occur.*
>
> *23 In this instance, for the purpose of interpreting the claims of the '967 patent, there is no significant event put in evidence that occurred after April 18, 1996, that would be relevant in considering claim interpretation.*

[111] In the present case, Allergan has put forward claim 22 as representative. As previously discussed, that claim depends on previous claims 6, 3 and 1. I have rewritten claim 22 as follows:

> *22. Topical use of a therapeutically effective amount of an ophthalmic pharmaceutical composition for the treatment of glaucoma or ocular hypertension wherein the amount of brimonidine is 0.2 percent by weight and the amount of timolol is, 0.5 percent by weight, and from 0.001% by weight to less than 0.01% by weight of benzalkonium chloride.*

[112] Construction of this claim is quite straightforward. It is couched in the form of a "use" claim; thus, it can be stated as:

- the use in topical fashion of an ophthalmic pharmaceutical composition

- for a particular purpose, the treatment of glaucoma or ocular hypertension

- of a composition of a particular formula containing two active ingredients in particular quantities, namely:
  - brimonidine at 0.2 percent by weight; and
  - timolol at 0.5 percent by weight

  together with a particular preservative, benzalkonium chloride, present in a range from 0.001% by weight to less than 0.01% by weight.

[113] The claim does not state the advantages of such a formulation. The patent, at page 1, promises that the formulation will overcome a number of difficulties experienced in the past:

> *This invention relates to the topical ophthalmic use of brimonidine in combination with timolol when indicated for treatment of glaucoma or ocular hypertension. Such combinations or formulations are available for separate use in the ophthalmic art and have been combined in serial application during the course of treatment of glaucoma. However, there are concerns and expressed reservations in the ophthalmic community about patient compliance when the patient is required to administer separate medications to treat a single disease or condition such as glaucoma. There is, moreover, a long felt need for an effective and safe topical*

> *ophthalmic pharmaceutical composition including brimonidine and timolol which has increased stability and requires a lower effective concentration of preservative as compared to the individual agents taken alone. Finally, there is a need to increase the efficacy of many topical ophthalmic agents, without increasing the systemic concentration of such topical agents, since it is well known that many of such topically-applied ophthalmic agents cause systemic side effects, e.g. drowsiness, heart effects, etc. Unexpectedly it has been discovered that brimonidine in combination with timolol meets these criteria.*

[114] I summarize what advantages the formulation is promising to deliver:

- the combination product in a single dose improves patient compliance
- it contains brimonidine and timolol
- which is effective
- is safe
- has increased stability
- requires lower effective concentration of preservative than separate doses of each; and
- has increased efficacy without increased concentration of brimonidine or timolol

[115] I repeat, these advantages are not part of the claim. I will discuss this point further in considering the "inventive concept".

ISSUE #6: ***Are the asserted claims obvious?***

ANTICIPATION AND OBVIOUSNESS

[116] Apotex has alleged invalidity of the '764 patent on two grounds; anticipation and obviousness. These concepts are related, but have important differences. Anticipation arises from the statutory definition of "invention" in section 2 of the *Patent Act* in that, in order to be patentable, the invention must be "new". Obviousness arises from the concept of invention itself.

[117] I described these two concepts with reference to the reasons of Desjardins JA in the *Imperial Tobacco* case and with reference to a lecture of Professor Carl Moy. In *Eli Lilly Canada Inc v Apotex Inc*, 2008 FC 142, at paragraphs 127 and 128, I wrote:

> *127 Anticipation and obviousness are closely related concepts having their foundation based on the requirement that there be an "invention" and that the invention be "new". Justice Desjardins of the Federal Court of Appeal explained the concepts in Imperial Tobacco Ltd. v. Rothmans Benson & Hedges Inc. (1993), 47 C.P.R. (3d) 188 at pages 197-199. She explained that anticipation and obviousness are different concepts although both are questions of fact. Prior art may be used in the application of both tests but is to be used differently. She said:*
>
> > *Prior art may be used in the application of both tests but differently. H.G. Fox, Canadian Patent Law and Practice, 4th ed. (Toronto: Carswell, 1969) at p. 137 states:*
> >
> > > *Prior specifications are generally used to show anticipation if they disclose exactly and fully what the patentee has claimed. If such disclosure is not made by the prior specification and it cannot be used as an*

> > *anticipation, it may be used as indicating the state of the art at the time that the patentee made his alleged invention and as showing that what the patentee did was so slight a contribution to existing knowledge as to lack the essential element of invention and to be merely obvious.*
>
> *Anticipation must therefore be found in a single document which already gives a skilled person what is claimed and which teaches it all. In the case of obviousness, however, "the prior art should be reviewed and its cumulative effect considered", op. cit., p. 72.*
>
> *128 A useful way to consider those concepts was given by Professor Carl Moy (author of the United States multi-volume patent treatise, Moy's Walker on Patents, Thompson West, updated annually) to students at the Osgoode Intellectual Property Masters Programme in considering the bargain theory of patents. He said, as best I can recall:*
>
> > *"You do not pay the price of a monopoly for something you already have, nor do you pay the price for something you could get anyway"*

[118] In the present case, since the '764 patent is governed by the provisions of the "new" *Patent Act*, both anticipation and obviousness are to be considered from the viewpoint of a person skilled in the art as of the priority date, April 19, 2002.

A) <u>Anticipation</u>

[119] In order for an invention as claimed in a patent to be considered to be anticipated by a prior reference, that reference, as understood by a person skilled in the art as of April 19, 2002, must both disclose what is claimed and enable that person to make what is claimed. Layden-Stevenson JA put the matter very clearly in *Eli Lilly Canada Inc v Novopharm Inc*, 2010 FCA 197, at paragraphs 43 to 45:

> *43 Section 2 of the Act stipulates that an invention must be novel. When approaching an inquiry as to novelty, the invention must not have been anticipated. The reformulated approach to anticipation is articulated in Sanofi. To succeed in invalidating a patent on grounds of anticipation, an alleged infringer (here Novopharm), must satisfy the requirements of prior disclosure and enablement, considered separately.*
>
> *44 With respect to disclosure, section 28.2 of the Act is the governing section. Among other things, it requires that the invention was not disclosed "in such a manner that it became available to the public in Canada or elsewhere" more than one year before the patent was filed. Although Sanofi addressed disclosure in the context of the predecessor Act, the principles enunciated in Sanofi remain applicable. The POSITA reads the particular piece of prior art to understand whether it discloses the second invention. The evidence to be considered is comprised solely of the prior art, as the POSITA would understand it. No trial and error or experimentation is permitted.*
>
> *45 Where disclosure is found to exist, the second requirement (enablement) requires the POSITA to be able to perform the invention. Enablement is assessed having regard to the particular piece of prior art as a whole. The prior art must provide the POSITA, using his or her common general knowledge, with enough information to allow the subsequently claimed invention to be performed without undue burden. Where the invention arises in a field of technology where trials and experiments are generally carried out, routine trials are acceptable.*

[120] I will recite again claim 22 of the '764 patent as set out in full, including all dependencies in prior claims:

> *22. Topical use of a therapeutically effective amount of an ophthalmic pharmaceutical composition for the treatment of glaucoma or ocular hypertension wherein the amount of brimonidine is 0.2 percent by weight and the amount of timolol is, 0.5 percent by weight, and from 0.001% by weight to less than 0.01% by weight of benzalkonium chloride.*

[121] Apotex's allegation as to anticipation rests on a DeSantis International (PCT) patent application (*not* the US DeSantis patent), application number WO 89/10126, laid open for public inspection on November 2, 1989. This is several years before the priority date claimed in the '764 patent. The US and PCT DeSantis references are not materially different in their disclosures; however, they do have different claims.

[122] I will briefly summarize this DeSantis (PCT) reference. It begins by stating that it relates to the field of ophthalmology, particularly the treatment of glaucoma, by providing a topical composition comprised of a combination of two active ingredients; which, for short, can be called alpha and beta:

> *1. Field of the Invention*
>
> *The present invention relates to the field of ophthalmology. More particularly, the invention relates to the treatment of glaucoma and associated elevations of intraocular pressure, and to the treatment of ocular hypertension associated with other diseases or conditions. The invention is directed to providing topical, ophthalmic, pharmaceutical compositions which include, as principal active ingredients, combinations of one or more alpha-2 agonists, such as clonidine derivatives (e.g., para-amino clonidine) and one or more beta-blockers (e.g., betaxolol).*

[123] Alpha ingredients are described to include compounds such as substituted 2-(arylimino) inadozolidines. It is to be noted that brimonidine is *not* specifically mentioned. The beta ingredients are identified as a number of choices, but timolol and another, betaxolol are specifically mentioned. The proportions of each are left to skilled clinicians:

> *The antiglaucoma compositions of the present invention comprise a combination of a therapeutically effective amount of one or more alpha-2 agonists and a therapeutically effective amount of one or more beta-blockers. The ratio of the alpha-2 agonist component to the beta-blocker component may vary considerably depending on the relative potency of the specific components utilized and other factors, such as the degree of intraocular pressure reduction desired and the nature of the condition being treated. The ratio of the components employed is therefore left to the discretion of skilled clinicians. The ratio on a percent by weight concentration basis will typically be in the range of about 0.1:10 to 10:0.1 alpha-2 agonist:beta-blocker.*

[124] There are a large number of candidates proposed for use as a preservative, including benzalkonium chloride (BAK). One example is provided, which uses BAK but not timolol or brimonidine.

[125] At the hearing, Apotex stated that, in respect of anticipation, it would not be making oral submissions, but would rely on its written submissions. The essential part of those written submissions is as follows:

> *94. …DeSantis discloses the concept of combining an alpha-2 agonist and beta blocker into a topical composition for the treatment of glaucoma. The skilled person reviewing DeSantis in 2002, and considering the common general knowledge in the art, would know that there was but one alpha-2 agonist at a single concentration that was available for chronic use and which had been used adjunctively in the treatment of glaucoma, brimonidine 0.2%. The skilled person would also know that the "gold standard beta blocker" that had been used was timolol 0.5%. The skilled person would "go straight for the money" and select BAK (which is discussed in DeSantis) at concentrations of less than 0.01% for the reasons discussed above, as well as the clinical concentrations of the drugs rather than trying an infinite number of combinations.*
>
> *95. While Allergan notes that DeSantis does not specify the vehicle, buffer, pH adjusting agent, and tonicity adjusting agent to be used in a fixed combination of brimonidine and timolol, this is not a*

> *legitimate point of distinction. The 764 patent similarly encompasses a wide range of options encompassing common excipients and amounts. All of the comments regarding the "advantages" asserted by Allergan apply to this aspect of the case as well.*
>
> *96. To be enabled, it is only required that the skilled person would be able, reading DeSantis and having regard to their common general knowledge, to prepare an ophthalmic composition comprising brimonidine and timolol, and in particular a composition with 0.2% brimonidine, 0.5% timolol and between 0.001 and less than 0.01% BAK. This would have posed no difficulty for the skilled person, and actually posed no difficulty for Allergan, all as stated above.*

[126] These submissions require a person skilled in the art to make a number of choices in selecting particular ingredients and choosing specific proportions of those ingredients from the large number of ingredients indicated or suggested by DeSantis, and from the very general ranges of proportions suggested by DeSantis. DeSantis neither discloses nor enables the specific active ingredients, nor the proportions of them, nor the specific use of BAK as the preservative in the specific proportion required by claim 22 of the '764 patent, which is the only claim with which we need to be concerned.

[127] These arguments are really directed to the issue of obviousness rather than anticipation. Apotex's allegations as to anticipation are not justified.

B) <u>Obviousness</u>

[128] Apotex also alleges that the '764 patent is invalid for obviousness. This is a question previously considered by Crampton J, albeit with somewhat different evidence; including, for the generic in that case, different expert witnesses.

[129] Obviousness has been described by Oliver LJ in *Windsurfing International Inc v Tabur Marine (Great Britain) Ltd*, [1985] RPC 59 (Eng CA) at page 71 as *"a kind of jury question"*. No judge can be expected to have the kind of knowledge necessary to put him or her in the position of a person skilled in the art as of the relevant time without suitable instruction from credible experts. Even when the judge has been put in that position, the Courts have endeavoured to formulate some kind of structure for assessing what is obvious and what is inventive and distinguishing between them.

[130] In *Novopharm Limited v Janssen-Ortho Inc*, 2007 FCA 217, the Federal Court of Appeal reviewed and improved upon a set of criteria that I had gleaned from a variety of sources for the purpose of considering obviousness.

[131] In the European Patent Office, guidelines have been established for considering obviousness; sometimes called the problem-solution approach. Jacob LJ of the United Kingdom Court of Appeal in *Actavis v Novartis* [2010] FSR 18 at paragraph 22 described this approach as follows:

> *[22] I am conscious that some appear to think that this structured process is something peculiarly British. I do not think it is. It merely makes explicit that which is implicit in all other approaches. No one would dispute for instance, that obviousness must be considered through the eyes of the skilled man (steps 1(a) and (b)). Nor that you have to identify the target of alleged obviousness (step 2). Nor that you have to identify the differences between the target and the prior art (step 3).*

[132] The United Kingdom jurisprudence has settled upon what is described as the *Windsurfing/Pozzoli* test, which was postulated in *Windsurfing International Inc. v Tabur Marine (Great Britain) Ltd*, supra, and refined by Jacob LJ in *Poszzoli SPA v BDMO SA*, [2007] EWCA Civ 588. It is this test that the Supreme Court of Canada called *Windsurfing/Pozzoli* and adopted as the test for obviousness in *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at paragraphs 67 to 69:

> *67 It will be useful in an obviousness inquiry to follow the four-step approach first outlined by Oliver L.J. in Windsurfing International Inc. v. Tabur Marine (Great Britain) Ltd., [1985] R.P.C. 59 (C.A.). This approach should bring better structure to the obviousness inquiry and more objectivity and clarity to the analysis. The Windsurfing approach was recently updated by Jacob L.J. in Pozzoli SPA v. BDMO SA, [2007] F.S.R. 37 (p. 872), [2007] EWCA Civ 588, at para. 23:*
>
> > *In the result I would restate the Windsurfing questions thus:*
> >
> > *(1) (a) Identify the notional "person skilled in the art";*
> > *(b) Identify the relevant common general knowledge of that person;*
> >
> > *(2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;*
> >
> > *(3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;*
> >
> > *(4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention? [Emphasis added.]*
>
> *It will be at the fourth step of the Windsurfing/Pozzoli approach to obviousness that the issue of "obvious to try" will arise.*
>
> > *i. When Is the "Obvious to Try" Test Appropriate?*

> *68 In areas of endeavour where advances are often won by experimentation, an "obvious to try" test might be appropriate. In such areas, there may be numerous interrelated variables with which to experiment. For example, some inventions in the pharmaceutical industry might warrant an "obvious [page294] to try" test since there may be many chemically similar structures that can elicit different biological responses and offer the potential for significant therapeutic advances.*
>
> *ii. "Obvious to Try" Considerations*
>
> *69 If an "obvious to try" test is warranted, the following factors should be taken into consideration at the fourth step of the obviousness inquiry. As with anticipation, this list is not exhaustive. The factors will apply in accordance with the evidence in each case.*
>
> *1. Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?*
>
> *2. What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?*
>
> *3. Is there a motive provided in the prior art to find the solution the patent addresses?*

[133] The Federal Court of Appeal considered this test in *Pfizer Canada Inc v Apotex Inc*, 2009 FCA 8. That Court expressly rejected the “worth a try” test as not being the standard by which obviousness is measured. Noel JA wrote at paragraphs 28 and 29:

> *28 I take it from this that the test adopted by the Supreme Court is not the test loosely referred to as "worth a try". After having noted Apotex' argument that the "worth a try" test should be accepted (para. 55), Rothstein J. never again uses the expression "worth a try" and the error which he identifies in the matter before him is the failure to apply the "obvious to try" test (para. 82).*

> *29 The test recognized is "obvious to try" where the word "obvious" means "very plain". According to this test, an invention is not made obvious because the prior art would have alerted the person skilled in the art to the possibility that something might be worth trying. The invention must be more or less self-evident. The issue which must be decided in this appeal is whether the Federal Court Judge failed to apply this test.*

[134] That Court went on to consider that more than a possibility that something might work is required. Noel JA wrote at paragraphs 43 to 46:

> *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.*

> *46 The Federal Court Judge rendered his decision on the basis that more than possibilities were required. He concluded based on the evidence before him that Apotex had failed to establish more than that. In so doing, he applied the correct test.*

What is the "Inventive Concept"?

[135] Difficulty in applying the Supreme Court of Canada test in *Sanofi* has arisen in the context of steps (iv) and (v), identifying the "inventive concept". The question is whether the "inventive concept" is something different from the claim at issue, even when that claim has been construed by the Court. Is the Court to embark on two separate missions; one to construe the claim, the other to define the inventive concept?

[136] It is appropriate to begin by considering what Jacob LJ wrote about "inventive concept" in *Pozzoli,* supra, at paragraphs 14 to 21:

> *14. The place of "inventive concept" in relation to obviousness also calls for some discussion. It will be recalled that it forms the first step of the well-known Windsurfing test of Oliver LJ [1985] FSR 59 at 73. The test provides a structured approach to the problem and is often useful. I set it out adding my own numbering:*
>
> > *(1) The first step is to identify the inventive concept embodied in the patent in suit.*
> >
> > *(2) Thereafter, the court has to assume the mantle of the normally skilled but unimaginative addressee in the art at the priority date and to impute to him what was, at that date, common general knowledge in the art in question.*
> >
> > *(3) The third step is to identify what, if any, differences exist between the matter cited as being "known or used" and the alleged invention.*

> *(4) Finally, the court has to ask itself whether, viewed without any knowledge of the alleged invention, those differences constitute steps which would have been obvious to the skilled man or whether they require any degree of invention.*

15. I think the test requires some restatement and elaboration. First one must actually conduct the first two operations in the opposite order - mantle first, then concept. For it is only through the eyes of the skilled man that one properly understand what such a man would understand the patentee to have meant and thereby set about identifying the concept.

16. Next, that first step actually involves two steps, identification of the attributes of the notional "person skilled in the art" (the statutory term) and second identification of the common general knowledge ("cgk") of such a person.

17. What now becomes stage (2), identifying the inventive concept, also needs some elaboration. As I pointed out in Unilever v Chefaro [1994] RPC 567 at page 580:

> *It is the inventive concept of the claim in question which must be considered, not some generalised concept to be derived from the specification as a whole. Different claims can, and generally will, have different inventive concepts. The first stage of identification of the concept is likely to be a question of construction: what does the claim mean? It might be thought there is no second stage - the concept is what the claim covers and that is that. But that is too wooden and not what courts, applying Windsurfing stage one, have done. It is too wooden because if one merely construes the claim one does not distinguish between portions which matter and portions which, although limitations on the ambit of the claim, do not. One is trying to identify the essence of the claim in this exercise.*

18. So what one is seeking to do is to strip out unnecessary verbiage, to do what Mummery LJ described as make a précis.

19. In some cases the parties cannot agree on what the concept is. If one is not careful such a disagreement can develop into an unnecessary satellite debate. In the end what matters is/are the difference(s) between what is claimed and the prior art. It is those differences which form the "step" to be considered at stage (4). So if a disagreement about the inventive concept of a claim starts getting

> *too involved, the sensible way to proceed is to forget it and simply to work on the features of the claim.*
>
> *20. In other cases, however, one need not get into finer points of construction - even without them the concept is fairly apparent - in Windsurfing, for instance, it was the "free sail" concept. In yet other cases it is not even practical to try to identify a concept - a chemical class claim would often be a good example of this.*
>
> *21. There is one other point to note. Identification of the concept is not the place where one takes into account the prior art. You are not at this point asking what was new. Of course the claim may identify that which was old (often by a pre-characterising clause) and what the patentee thinks is new (if there is characterising clause) but that does not matter at this point.*

[137] Thus, the "inventive concept" was intended by Jacob LJ to be a statement of what the claim, properly construed, says "stripped of unnecessary verbiage". It is not a reformulation of the claim. As Lord Hoffman wrote in *Conor v Angiotech*, [2008] RPC 716, at paragraph 19:

> *19. In my opinion, however, the invention is the product specified in a claim and the patentee is entitled to have the question of obviousness determined by reference to his claim and not to some vague paraphrase based upon the extent of his disclosure in the description.*

[138] The Canadian jurisprudence respecting "inventive concept" began to develop after the Supreme Court adopted the *Windsurfing/Pozzoli* test in *Sanofi*, supra. The Federal Court of Appeal in *Laboratoires Servier v Apotex Inc*, 2009 FCA 222, determined that where the inventive concept was not readily discernable from the claims, such as where a bare chemical formula is claimed, recourse to the specification may be appropriate. Layden-Stevenson JA, for the Court, wrote at paragraphs 58 and 59:

> *58 Whirlpool Corp. v. Camco Inc., 2000 SCC 67, [2000] 2 S.C.R. 1067 (Whirlpool) decides that claims construction is antecedent to issues of both infringement and validity. It also stands for the proposition that purposive construction requires a court to have regard to the whole of the patent (including the claims and the disclosure) when ascertaining the nature of the invention. Indeed, several of the authorities cited in Apotex's memorandum of fact and law illustrate the application of these principles. More recent authority indicates that the inventive concept need not be readily discernable from the claims, even in circumstances where construction of the claims is not in issue. A bare chemical formula may require recourse to the specification to determine the inventive concept of the claims: Apotex Inc. v. Sanofi-Synthelabo Canada Inc., 2008 SCC 61, [2008] 3 S.C.R. 265 (Sanofi).*
>
> *59 The trial judge proceeded precisely in accordance with the holdings of the above-noted jurisprudence. She examined the patent as a whole to ascertain its invention in circumstances where there was really no debate as to the construction of the claims. When confronted with competing positions as to the nature of the invention, she turned to relevant jurisprudence where a broad class of compounds was described in the disclosure and narrower claims to compounds were stated in the claims. To assist in her analysis, she referred to Boehringer, Hoechst and the decision of this Court in Merck & Co. Inc. v. Apotex Inc., 2006 FCA 323, [2007] 3 F.C.R. 588, leave to appeal refused, [2006] S.C.C.A. No. 507 (Merck lisinopril).*

[139] This is the approach taken by Mactavish J in *Novo Nordisk Canada Inc v Cobalt Pharmaceuticals Inc*, 2010 FC 746, where she wrote at paragraph 113:

> *113 Given that repaglinide's allegedly advantageous pharmacokinetic properties are not referred to anywhere in Claims 1 through 9 of the patent, I am of the view that these properties are not part of these claims. That said, any advantageous properties possessed by repaglinide would indeed be inherent to the compounds described in those claims, and thus should be taken into account when examining issues such as anticipation and obviousness.*

[140] A similar approach was adopted by the Federal Court of Appeal in *Eli Lilly Canada Inc v Novopharm Limited*, 2010 FCA 197, in respect of selection patents. Layden-Stevenson JA, for the Court, wrote at paragraph 57:

> *57 In the context of a selection patent, the obviousness analysis considers the special properties of the compound, along with its alleged advantages, as described in the selection patent disclosure, for it is there that the inventiveness of the selection lies.*

[141] Thus, where the claim is something that is only a chemical compound or compounds selected from a larger class, and the utility is not found in the claim, it is permissible to go to the description in order to determine that utility and combine that utility with what is said in the claim in order to determine the "inventive concept" for purposes of examining obviousness of the claim.

Inventive Concept of Claim 22

[142] Claim 22 is said by Allergan to be representative. I have previously expressed that claim, so as to include all dependencies, as follows:

> *22. Topical use of a therapeutically effective amount of an ophthalmic pharmaceutical composition for the treatment of glaucoma or ocular hypertension wherein the amount of brimonidine is 0.2 percent by weight and the amount of timolol is, 0.5 percent by weight, and from 0.001% by weight to less than 0.01% by weight of benzalkonium chloride.*

[143] Stripping from this claim any unnecessary verbiage, I have construed the claim previously as follows :

- *the use in topical fashion of an ophthalmic pharmaceutical composition*
- *for a particular purpose, the treatment of glaucoma or ocular hypertension*
- *of a composition of a particular formula containing two active ingredients in particular quantities, namely:*
    - *brimonidine at 0.2 percent by weight; and*
    - *timolol at 0.5 percent by weight*

together with a particular preservative, benzalkonium chloride (BAK), present in a range from 0.001% by weight to less than 0.01% by weight.

[144] As I have previously found, that composition promises to deliver:

- *the combination product in a single dose improves patient compliance*
- *it contains brimonidine and timolol*
- *which is effective*
- *is safe*
- *has increased stability*
- *requires lower effective concentration of preservative than separate doses of each*
- *has increased efficacy without increased concentration of brimonidine or timolol*

[145] The "inventive concept" is, therefore, that a particular composition of ingredients including brimonidine, timolol and benzalkonium chloride, in particular quantities, achieves the above results as promised.

[146] At this stage, I will consider what Counsel for Allergan has argued as being part of the "inventive concept"; something which Allergan's Counsel calls the afternoon trough. Crampton J in paragraph 58 of his Reasons has referred to this as an afternoon reduction in efficiency. Allergan places much stress on an assertion that its combination drug can be used only twice a day (BID) with as much effectiveness as the prior use of timolol or brimonidine alone, three times a day (TID). However, this property is not clearly stated in the patent. At page 3 of the patent it is stated that the precise regimen is left to the discretion of the clinician. At page 4 it is stated that adequate lowering of interocular pressure has been obtained when administering the compositions of the invention twice a day when compared to commercially approved brimonidine and timolol solutions twice or three times a day. In Example II, the combination as used twice a day (BID) is said to be superior to a certain concentration of timolol used twice a day (BID), or a certain concentration of brimonidine, used three times a day (TID). I repeat the conclusions at page 16:

> *Conclusions*
>
> *The Combination treatment (brimonidine tartrate 0.2%/ timolol 0.5%) administered BID for 3 months was superior to Timolol (timolol 0.5%) BID and Brimonidine (brimonidine tartrate 0.2%) TID in lowering the elevated IOP of patients with glaucoma or ocular hypertension. The Combination administered BID demonstrated a favourable safety profile that was comparable to Timolol BID and better than Brimonidine TID with regard to the incidence of adverse events and discontinuations due to adverse events.*

[147] The patent draws no general proposition from these conclusions or the previous comments as to comparative frequency of administration. The evidence shows that while some countries, including, apparently, Canada, approve the combination drug for twice-a-day use; the United States does not. Therefore, unlike Crampton J, I do not accept the avoidance of an afternoon trough (or ability to dose only twice a day) as part of the inventive concept of the patent. The patent at best describes the possibility of twice-daily dosing in the discretion of a clinician as a resulting property of the combination but not as an inventive feature.

[148] Allergan's Counsel argues that the interpretation of a patent is a legal matter; thus, Crampton J's finding as to what constitutes the inventive concept is an interpretation of law and must, as a matter of comity, be followed by me. I reject that argument.

[149] Allergan's argument rests on an interpretation as to what Binnie J, for the Supreme Court of Canada, wrote in *Whirlpool Inc v Camco Inc*, [2000] 2 SCR 1067, at paragraph 49 (c) where he refers to "letters patent" as being a "regulation" as defined in section 2(1) (a) of the *Interpretation Act*, RSC 1985, c. I-21. As the late W. K. Hayhurst pointed out in his article written in respect of this comment*, "The Distinction between 'Letters Patent' and 'Patent Specification', How Did We Get Where We Are?"* (2007), 57 CPR (4^{th}) 161, the regulation spoken of is the one-page document attached to the patent specification, which is the page *granting* the patent, not the patent itself. The specification is a document drafted by the patentee, not Parliament or the Governor in Council. Interpretation of the specification is like the interpretation of a contract drafted by one or more parties. The level of comity owed by one judge in the interpretation of the same contract by another judge is not as great as the level of comity owed when a statute or regulation has been interpreted.

Differences between the State of the Art and the Inventive Concept

[150] Put very generally, Apotex's submission is that each of the ingredients; brimonidine, timolol and BAK, at or about the quantities specified in claim 22, had been used separately for quite a long time. There had been patent applications and scientific articles indicating that ingredients like these could be blended into a single-dose product. To do so, Apotex alleges, was obvious.

[151] Allergan agrees that the use of these ingredients separately was known and that a combination product had been seen as desirable. However, Allergan asserts, to combine these particular products in those particular quantities to achieve desirable results was inventive.

[152] What we have in claim 22 is a "recipe" for a particular combination of ingredients which achieve a safe, stable, effective result. The ingredients were known and the drugs had been used separately for the same purpose for some time. Was this "recipe" for combining them into a single dose composition inventive?

[153] The differences between the "state of the art" and the "inventive concept" can be described as follows:

- administration of brimonidine as a single dose three times a day to glaucoma patients;

- administration of timolol as a single dose three times a day to glaucoma patients;

- the use of BAK as a preservative in formulations such as the above, for use in eye drops;

- illustrations in patent applications such as DeSantis that Alpha drugs, without specifying brimonidine; and beta drugs, of which timolol is specifically mentioned as one; could be combined in the same bottle for single-dose administration, and that compounds such as BAK could be used as a preservative;

- a competitor had been marketing a combination product, COSOPT, which was a combination of dorzolamide and timolol;

The "inventive concept" includes:

- the successful combination of the drugs brimonidine and timolol in a single bottle at levels that do not exceed the previous dose levels, together with the preservative BAK at a lower level than was used for either as a single-dose drug;

- the combination, in the proportions claimed, is effective, safe and has increased stability

[154] In dealing with the "recipe" of claim 22, one must be careful not to focus on a commercial product which may fall within the parameters of the claim. One must focus on the claim itself. In this case, claim 22 provides a permissible range of BAK; namely, 0.001% by weight to less than

0.01% by weight. While the commercial product COMBIGAN includes BAK at the 0.005% by weight level, claim 22 monopolizes recipes that include anything from 0.001% by weight to 0.01% BAK by weight level. Thus, prior art, and what it would mean to a person skilled in the art, must be considered having that range in mind, and not just a particular level of BAK provided in the commercial product.

Were these differences obvious?

[155] As Crampton J did in his Reasons at paragraph 71, this question can be approached by addressing four questions:

1) Is it more or less self-evident that what is being tried ought to work? Is there a finite number of identified predictable solutions known to skilled persons?

2) What is the extent, nature an amount of effort required? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?

3) Is there a motive provided in the prior art to find the solution?

4) What was the actual course of conduct that culminated in the invention?

1) Is it more or less self-evident that what is being tried ought to work? Is there a finite number of identified predictable solutions known to skilled persons?

[156] As expected, the experts differ in respect of this issue. Dr. Fechtner expressed the reluctance that a person skilled in the art would have even to try combining two drugs together at paragraphs 154 to 157 of his affidavit:

> *154. The POSITA would have understood that differences in pharmacokinetics, the additive of adverse effects with multiple drugs, and potential drug interactions were all difficulties be overcome in developing a fixed combination drug. Of particular importance is the cumulative nature of adverse effects with multiple drugs. As I discuss more fully above, all ophthalmic drugs have side effect profiles, and some of these are severe enough to cause patients to discontinue treatment.*
>
> *155. The POSITA would have expected the side effects observed for a fixed combination product to be at least as poor for the combination product as it was for the individual components (and possibly worse). In other words, I would expect the side effects in a fixed combination to be no better than, and possibly worse than, the sum of the side effects of the individual components.*
>
> *156. For the reasons I describe in detail above, the POSITA would understand the formulations of fixed combination drug with two components could potentially lead to a worsening of the side effect profile as compared to the components. For example, Strohmaier et al reported that the side effect profile of the fixed combination drug (dorzolamide and timolol) was worse than the side effect profile for adjunctive use of the two components with respect to eyelid pain and discomfort.*
>
> *157. The POSITA would not have expected that combining two IOP lowering drugs together in a fixed combination would result in an improved safety profile for the fixed combination in comparison to one of its components. Clineschmidt et al reported the results of a study comparing the fixed combination of timolol and dorzolamide with timolol BID and dorzolamide TID each administered monotherapy. Clineschmidt et al report that a significantly higher percentage of patients reported having a drug-related adverse experience when receiving the combination (41%) than when receiving timolol (23%) and an equivalent number of patients*

> *reported a drug-related adverse experience receiving the fixed combination of dorzolamide (41%) thus, the adverse events for the fixed combination drug were as bad as the adverse events for the worst individual component. The POSITA would not expect that a fixed combination would show an improved safety profile with respect to one of its components.*

[157] It must be remembered that Dr. Fechtner was not an expert in formulation.

[158] Dr. Quigley, who also was not an expert in formulation, expressed that, from an ophthalmologist's point of view, co-formulations of drugs previously used separately would be expected to achieve results similar to those found in the use of the drug separately. He said at paragraphs 78 to 80 and 360 and 361 of his affidavit:

> *78. Prior to reviewing any of the documents that Mr. Naiberg ultimately provided me, Mr. Naiberg asked if an ophthalmologist as of April 19, 2002, would have sought to improve the treatment of patients who were prescribed a combination of timolol maleate and brimolidine tartrate for lowering IOP and/or treating glaucoma and, if so, how the ophthalmologist would have done so.*
>
> *79. My immediate answer to this question was that the ophthalmologist would have known to combine the two medicines together at their previously used concentrations (0.2% brimonidine; 0.5% timolol) into a single bottle (with appropriate excipients) for topical use as a way of improving patient treatment.*
>
> *80. I said this because, by 2002, ophthalmologists were routinely using timolol maleate drops in combination with brimonidine tartrate drops (from separate bottles) at these respective concentrations to lower IOP and treat glaucoma. The two medicines, given together, were known to be more effective in lowering IOP than either medicine given alone and there were no observed incompatibilities between the medicines. Providing the medicines in a single bottle, as COSOPT had done with dorzolamide and timilol, would be expected to achieve similar IOP…*
>
> . . .

> *360. As noted above, the use of combinations of brimonidine and timolol to lower IOP and treat glaucoma was well established. The combinations were safe and efficacious and displayed no incompatibilities that might discourage an ophthalmologist from wanting to prescribe the combination in a co-formulation. The ophthalmologist would expect that a co-formulation of brimonidine and timolol would allow patients access to their brimonidine/timolol combination with increased convenience.*
>
> *361. Moreover, ophthalmologists knew that co-formulations could be prepared, as had occurred in the case of dorzolamide and timolol. The ophthalmologist considering the question of how to improve treatment in patients prescribed a combination of brimonidine and timolol would immediately suggest that a co-formulation of the two be prepared, expect that it would be, and that it would provide the same increase in efficacy over monotherapy as had been seen in sequential, combination treatment.*

[159] Dr. Kompella, the only formulation expert, stated in his affidavit that, given the COSOPT precedent, a formulator would find confirmation that two active ingredients at the same concentrations would form the principal approach in his or her mind. He said at paragraph 33 of his affidavit:

> *33. Even without knowing about Cosopt, the formulator would immediately perceive that combining brimonidine tartrate and timolol maleate in a single formulation would benefit the patient. Rather than administering the two drugs in adjunctive therapy, where one drug was administered to the eye followed by the second drug a short time (a few minutes) later, preparing a single formulation for the two drugs to be used together in therapy would made administration much easier for the patient since it would require administering only a single drop rather than two different drops with a gap between administrations. The Cosopt model would confirm combining the two active ingredients at concentrations the same as those in the individual formulations as a principal approach in the mind of the formulator.*

[160] In cross-examination, Dr. Kompella frankly stated that until a formulator had actually combined the two, such a person could not be certain that the combination would be stable, safe and effective. I repeat Questions and Answers 607 to 621, in which it must be noted that pH is not part of claim 22 or the inventive concept.

607. Q. Would you agree that pH and buffering of an ophthalmic solution is probably of equal importance to proper preservation, since the stability of most commonly used ophthalmic drugs is largely controlled by the pH of their environment?

A. Yes.

608. Q. In addition to stability effects, pH adjustments can influence comfort, safety and activity of the product?

A. Yes.

609. Q. Ideally, every product would be buffered at a pH of 7.4, considered the normal physiological pH of tear fluid?

A. Yes.

610. Q. If the formulator had two products, two active ingredients with two different pH's, and the two products were combined, it would have to be formulated at the same pH?

A. Yes.

611. Q. You wouldn't know in advance of testing what the pH would be?

MR. NAIBERG: For a particular compound? I am not sure of the question. Particular compound or the combination one?

<u>BY MR. MASON:</u>

612. Q. For the combination of the two products.

A. I mean, it would be one pH for the two molecules in the same bottle, yes.

613. Q. And you wouldn't know in advance of testing what the pH would be?

A. I mean, that's correct. I mean, you have to look at a number of vehicles to come to a final vehicle.

614. Q. Right. But in determining what the pH would be of the combined product, you wouldn't know that in advance of testing, correct?

A. Right, unless you have some prior products that have already developed with very close pH that guides you.

615. Q. Assuming they don't have very close pH, you wouldn't know in advance of testing what the pH of the combined product would be, correct?

A. Yes.

616. Q. The optimal pH of timolol is 7, correct?

A. Yes.

617. Q. The optimal pH of brimonidine or Alphagan is 6.3?

A. Yes.

618. Q. You would agree with me that pH is measured on the log scale?

A. Yes.

619. Q. When a pH is above 7, the solution is basic or alkaline?

A. Yes.

620. Q. When the pH is below 7, the solution is acidic?

A. Yes.

621. Q. A formulator would know that the difference in each unit on the log scale is a significant difference?

A. Yes, it's a clear difference, but there are many products for ophthalmics in a wide range of pH.

[161] The question for the Court is whether "it is *more or less* self-evident" that what is claimed *ought* to work. This is not about "worth a try"; it is about what the Court of Appeal in *Pfizer*, supra, has characterized as "very plain" or "more or less self evident". There is always, especially in chemistry, an element of doubt that can only be dispelled by actually doing a test or experiment. However, I am satisfied, on the evidence before me - particularly that of Dr. Kompella, the only expert formulator - that it is *more or less* self evident that the combination formulation *ought to work*.

[162] There was an issue raised in respect of the inclusion of BAK at the indicated levels in the "recipe". The evidence of Mr. Beck was that his research team first endeavoured to use a compound called Purite as a preservative, and that it was not satisfactory. He next turned to BAK. Purite is *not* one of the preservatives indicated to be suitable for use at page 3 of the patent.

[163] Mr. Beck, one of the named inventors, in his affidavit, testified that his team first attempted to use Purite as a preservative since it did not have a significant side effect profile. It degraded the timolol. The team then turned to BAK, found that it produced some degradants, but they were not toxic. Thus, BAK was acceptable. He wrote at paragraphs 8, 11, 12 and 14 of his affidavit:

> *8. Allergan initially attempted to use purite as the preservative for COMBIGAN® because purite did not have as significant a side effect profile as was associated with other preservatives known at the time. The development of COMBIGAN® using purite as the preservative failed. The formulation was not chemically stable. We discovered that purite degraded timolol maleate in the combined product solution.*
>
> . . .

> *11. As a result of this initial failure, Allergan investigated BAK as the preservative.*
>
> *12. Allergan discovered that novel degradants were being formed in the combination formulation that contained BAK. Those degradants were not detectable in short term studies (e.g. less than a few weeks), but rather were only detectable after the product had been stored under accelerated stability conditions for a period of many weeks or a few months. At Allergan, we determined that the novel degradants were being formed as a result of the interaction between brimonidine tartrate and timolol maleate. Allergan did not predict that there would be novel degradants formed as a result of the interaction between brimonidine tartrate and timolol maleate. Allergan had to investigate each of these novel degradants and ultimately decided to use in vivo animal toxicity models to establish the safety and efficacy of the formulation in the presence of the discovered formation of these novel degradants.*
>
> . . .
>
> *14. One of the reasons Allergan was able to create a formulation that was sufficiently stable was because the novel degradants in the combined product formulated with BAK turned out to be non-toxic at the levels predicted from our accelerated stability studies. The adequate stability of the combination product was not predicted by us, nor predictable until we completed the toxicity studies.*

[164] Again, the point is not whether, historically, the named inventive team first turned to something that, in the end result, did not work. The question is whether the notional person skilled in the art would have turned to BAK as something that it was more or less self evident ought to work. The answer from Dr. Kompella is yes. He said at paragraphs 98 and 116 of his affidavit:

> *98. Although numerous preservatives were known for use in ophthalmic formulations prior to 2002, by far the most common preservative in use was BAK. This is demonstrated, for example, in Noecker, a 2001 review, which discussed the commonly used ophthalmic preservatives and their effects on the eye. Typically, as shown in Table 1 of Noecker, BAK was known to be used in*

> *concentrations of 0.005% to 0.02% in topical, multiuse ophthalmic compositions.*
>
> . . .
>
> *116. In claims 4 to 6 and 20 to 25, there is a requirement that the compositions also include the preservative BAK in an amount of 0.001% to less than 0.01% by weight. As I have discussed above, as of April 2002, formulators were aware of the requirement for a preservative in ophthalmic multidose formulations and that BAK was the most commonly used preservative in glaucoma medications. In my opinion, there would be no inventiveness in the selection of BAK for use as the preservative in a further ophthalmic composition, particularly given it was already known to be used in the individual compositions of both brimonidine and timolol. The formulator would thus immediately and unhesitatingly choose to include BAK in the combined formulation of brimonidine and timolol.*

[165] It must be remembered that while Mr. Beck's team tried Purite first, it immediately turned to BAK next. And it worked satisfactorily. The fact that more than one preservative may have been more or less self evident as something that ought to work and that, as it turned out, one of them didn't work, does not mean that any other candidate preservative from the class of those that a formulator would have readily considered is inventive. BAK was a more or less self-evident candidate for something that ought to work.

[166] Crampton J, on the evidence before him, found differently. He concluded at paragraph 90 of his Reasons:

> *90 Sandoz further submitted that the POSITA would not have considered using Purite because that substance is patented by Allergan. However, this fails to recognize that the POSITA is a hypothetical person who is able to take into consideration all prior art, including that which may enjoy patent protection (see, for example, Eli Lilly Canada Inc v Apotex Inc, 2009 FC 320, at para 50, and Roger T. Hughes, Hughes and Woodley on Patents, 2ed., loose-leaf (Markham, Ont.: Lexis Nexis Butterworths, 2005), ch 5 at 166.4).*

[167] The basis in evidence for his findings can best be seen in paragraph 85 of his Reasons:

> *85 I also accept Dr. Fechtner's statements that the POSITA would have known that (i) potential problems might be encountered when formulating brimonidine and timolol into a fixed combination drug, and (ii) "differences in pharmacokinetics, the additive nature of adverse effects with multiple drugs, and potential drug interactions were difficulties to be overcome in developing a fixed combination drug." The various unexpected difficulties encountered by Mr. Beck and his team are discussed at paragraphs 96 to 103 below. The significant time and effort that Mr. Beck and his team spent overcoming those difficulties lend credence to Dr. Fechtner's statement that it would not have been self-evident or obvious to the POSITA that a chemically stable Composition could be achieved. Dr. Fechtner's conclusion on this point is further supported by Mr. Beck's statement, which I find credible, that each time he and his team began with a new potential formulation, they believed that it could fail at any stage of the process.*

[168] With all due respect to all of his reasoning, Crampton J seems not to have focused on the question at hand. The question is: Was it more or less self evident that the combination ought to work? Crampton J shifted to addressing what are really the second, third and fourth questions postulated by Rothstein J in *Sanofi*, supra, in introducing evidence as to various supposed difficulties apparently encountered by Mr. Beck's team in carrying out their tests. That is not what the first question is directed to.

2) What is the extent, nature an amount of effort required? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?

[169] This is the second question postulated by Rothstein J in *Sanofi*, supra. The question clearly implies that trials are considered to be routine. The Court must ask itself what is the extent, nature

and amount of effort required; is the testing prolonged or arduous? In other words, is it more than routine?

[170] Mr. Beck gave evidence as to what his team actually did. They combined brimonidine with timolol, first using Purite. It was unsatisfactory. Then, they tried BAK instead of Purite. It was satisfactory. Then, they did clinical studies for the purpose of obtaining regulatory approval. The timeline, according to paragraphs 8 and following was; January 8, 1999, the team was given the task of developing a combination product; in February 1999, it was decided that Purite was unsatisfactory; there is a delay, then in March 2001, the team turned to BAK; in May 2001, it was determined that BAK worked (Beck, Exhibit E).

[171] Mr. Beck states at paragraph 37 of his affidavit that the project cost approximately 26.4 million (US) dollars. This includes the cost of clinical studies. In cross-examination (Questions 131 to 142) Mr. Beck admits that this number is simply unconfirmed hearsay.

[172] Dr. Fechtner, at paragraphs 198, 202, 205 and 208 of his affidavit, states that considerable time, effort and resources were expended. But they were expended at the clinical trial stage. I repeat paragraph 208:

> *208. I am familiar with the conduct of Phase I, II and III clinical trials. Having reviewed the clinical trials attached to Mr. Beck's affidavit, it is clear that Allergan expended considerable time, effort and resources into designing and conducting the clinical trials required to bring its fixed combination drug to the market. The extent of time, effort and resources required for these clinical trials would have been a disincentive against the POSITA pursuing the development of the invention claimed in the '764 Patent.*

[173] A distinction must be made between considering the time and effort expended in clinical studies for purposes of obtaining regulatory approval, and time and effort expended in considering whether there has been an invention. Binnie J for the Supreme Court of Canada in *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 (AZT) put the matter quite clearly at paragraph 77:

> *77 The appellants take issue with the trial judge's conclusion. In their factum (though not in oral argument), they argue that utility must be demonstrated by prior human clinical trials establishing toxicity, metabolic features, bioavailability and other factors. These factors track the requirements of the Minister of Health when dealing with a new drug submission to assess its "safety" and "effectiveness". See now: Food and Drug Regulations, C.R.C. 1978, c. 870, s. C.08.002(2), as amended by SOR/95-411, s. 4(2), which provides in part:*
>
> *[page190]*
>
> > *A new drug submission shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug ... .*
>
> *The prerequisites of proof for a manufacturer who wishes to market a new drug are directed to a different purpose than patent law. The former deals with safety and effectiveness. The latter looks at utility, but in the context of inventiveness. The doctrine of sound prediction, in its nature, presupposes that further work remains to be done.*

[174] The evidence as to time and effort expended as far as invention is concerned was addressed by Dr. Kompella at paragraphs 17(g) and 127 of his affidavit:

> *17. (g) The information in Mr. Beck's affidavit does not reveal that, in the creation of the formulation of the '764 patent, the inventors encountered any particular difficulties in arriving at the subject matter claimed in the '764 patent.*
>
> . . .

> *127. At paragraphs 12 to 14, Mr. Beck discusses a degradant that appeared over an extended stability test of the brimonidine/timolol combination. It should be apparent that this degradant was discovered after the preparation of the combined formulation and reflects testing undertaken for the purpose of obtaining regulatory approval. The appearance of such a degradant does not indicate that that the combination of brimonidine/timolol initially proposed would not work, at least for some time. In any event, Mr. Beck's comments confirm that the existence of this degradant did not prevent the FDA approval of the combination formulation.*

[175] I find, on the evidence, that in order to arrive at the alleged inventive concept, no more than routine laboratory work was required. As Floyd J said in *Teva UK Limited v Merck & Co Inc* [2009] EWHC 2952 (Pat) at paragraph 95, it is a basic proposition of patent law that the doctrine of obviousness exists to prevent a patentee from monopolizing products or activities that a skilled person should feel free to make or perform without worrying about the existence of a patent.

[176] Crampton J, at paragraphs 92 to 113 of his Reasons, found differently. I put this down to two reasons. First is on the evidence. In *Sandoz*, Mr. Beck was intensively cross-examined, and during the course of the questioning apparently put in a great deal of evidence not set out in his affidavit as to the work involved. In the case before me, Mr. Beck was not questioned in this way and had no opportunity to provide additional evidence of this kind. Further, in *Sandoz*, the cross-examination of Dr. Fechtner failed to reveal the serious problems with his testimony that have been revealed in the evidence before me. Second, it does not appear that Crampton J's attention was drawn to the *AZT* case, supra, where a distinction between effort expended in clinical studies for regulatory approval must be made from effort expended in arriving at the alleged invention.

3) <u>Is there motive provided in the prior art to find the solution?</u>

[177] I am satisfied that the evidence is compelling that prior to April 2002 there was sufficient motivation to provide a combination drug for use in treating glaucoma. One combination product, COSOPT, was already on the market. A competitor would have been strongly motivated to come up with a comparable or better product.

[178] Dr. Quigly states at paragraphs 72 to 74 of his affidavit:

> *72. By 1995, and long before, ophthalmologists knew that prescribing multiple medications to patients, while necessary to adequately lower IOP, was undesirable from a patient compliance standpoint. The more complicated a dosage regimen, the less likely it is that the patient will follow it. Further, taking multiple drops creates the possibility of having the second drop wash out the medicine delivered by the first, before the first can penetrate the eye. Often, the patient would be required to wait some number of minutes between administering each component of the combination. This would be a source of frustration for the patient as it added further complexity (and the risk that the patient would forget which medicine he or she took first) and added to the time required to take the medication.*
>
> *73. Further, the antibacterial preservatives used in eye drops were known to be irritating to the eye. Administering multiple eye drops exposes the patient to multiple doses of antibacterial preservatives. Ophthalmologists knew that administering a combination of medicines from a single bottle would reduce the number of exposures to preservative.*
>
> *74. For all the above reasons, ophthalmologists knew that, for patients prescribed a combination of IOP-lowering medicines, it would be much more desirable to have a single co-formulation of the medicines available. The first such co-formulation, called COSOPT, was approved in the United States in 1998. COSOPT is an eye drop formulation that contains both dorzolamide and timolol, each well-known IOP lowering medicines that had been used separately and together (from separate bottles) in the past.*

[179] Dr. Kompella states at paragraphs 29 and 112 of his affidavit:

> *29. Beginning in the mid-late 1990's, the administration of multiple drugs to treat glaucoma and ocular hypertension was improved by the development and approval of Cosopt, an ophthalmic composition containing two glaucoma medications.*
>
> . . .
>
> *112. While the '764 patent also describes the reduced exposure of the patient to BAK owing to the change to a combined formulation and reduction in the dosing schedule (five drops per day to two drops per day), this would have been apparent to the formulator. Also, it was k known for COSOPT®, the dorzolamide and timolol combination, that the amount of BAK used (0.0075%) could be reduced when compared to the amount used in the available formulation of timolol (0.0075% BAK for known dorzolamide formulation and 0.01% BAK for the known timolol formulation).*

[180] Dr. Fechtner, in cross-examination, agreed that in 2001 he held the opinion that fixed combinations offer convenience to the patient and make business sense to manufacturers: In answer to questions 601 to 606, he said (with a rather grudging answer to question 606):

> *601. Q. You thought that the convenience factor of fixed combinations were quite compelling such that you expected that fixed combination products would likely gain in popularity?*
>
> *A. I thought you said something about patients the first time you asked me that. I believe the fixed combinations would gain in popularity with physicians as they grow to appreciated the benefits.*
>
> *602. Q. And you considered that this popularity would grow notwithstanding that clinicians would not be able to titrate the components in a fixed combination?*
>
> *A. Are you asking me as of 2000?*
>
> *603. Q. As of 2002.*

A. As of 2002, I believed they would grow in popularity. I have said many other things about fixed combinations as well, that they have drawbacks and that the physician needs to assess them in their patients.

604. Q. Can you give the witness Exhibit 7, please. This is your paper with Paul J. Lama, "The Future of Glaucoma Diagnosis and Therapy".

A. Let me be precise. This is a chapter written in a book directed to optometrists.

605. Q. All the better. What you were writing and communicating to ophthalmologists –

A. No, I said optometrists, which is different from ophthalmologists.

606. Q. Fair enough. You wrote in the first full paragraph in 423:

> *"The first new combination drug in many years is a fixed combination of dorzolamide/timolol. About 50% of patients treated with IOP lowering drugs received more than one medication. Additional new combinations are under development, and fixed combination products will likely gain in popularity. Although the clinician sacrifices the ability to titrate the components in a fixed combination, the convenience factor for patients is quite compelling. With several pharmaceutical manufacturers having proprietary compounds in different classes and with the generic availability of timolol, these fixed combinations offer convenience to the patient and make business sense to the manufacturers; they gain additional market share if patients remain on their products as therapy is advanced."*

I take it that statement is something that you believed when you wrote it and published it in this textbook?

A. I think we visited this paragraph earlier today and I pointed out that even though there is not a footnote to it, that

> *50 percent number I cited refers back to the ocular hypertension treatment study. The rest of it looks like opinion I held in 2001 when I wrote it.*

[181] Crampton J dealt with motivation at paragraphs 114 to 116 of his Reasons. He relies on uncontradicted evidence of Dr. Fechtner. Here, Fechtner is contradicted both by other experts and in his own cross-examination. Crampton J also refers to the clinical trials necessary for government approval. As previously discussed, this is not relevant to the question of inventiveness.

4) What was the actual course of conduct that culminated in this invention?

[182] The actual course of conduct of Mr. Beck's team has been discussed in the context of the previous questions. The team was motivated to come up with a combination drug. A competitor already had one; COSOPT. They took their own product ALPHAGAN (brimonidine), mixed it with another well-known glaucoma drug, timolol, and stabilized it with a stabilizer, Purite. That stabilizer, within a couple of months, was determined to be unsatisfactory. They reached for another well-known stabilizer, BAK. It worked. They worked with some differing concentration levels of the principal ingredients and at different pH levels: pH is not part of the claimed invention.

[183] Once it was determined that BAK was satisfactory, and appropriate pH levels (not part of the "inventive concept") were obtained, the rest of the efforts were directed at clinical trials for regulatory approval. The US gave approval only for thrice-daily use (TID). Canada and some other countries have approved twice-daily use (BID). The patent says that dosage is left to the discretion of the clinician.

[184] On the evidence before me I find that no more than routine testing was required. This does not rise to the level of inventiveness. No unusual obstacles were presented. The initial choice of Purite was no more than a matter of choosing among several candidates. When it proved unsatisfactory within a short period of time, another obvious candidate BAK was chosen and was successful. The testing as to how low the limits of BAK could be established was no more than routine and involved, if anything, the selection of an appropriate pH which is not part of the inventive concept.

[185] Crampton J addressed this question at paragraph 121 of his Reasons. He addressed, to an extent, evidence of Mr. Beck that is not before me. The so-called "wild goose chase" was simply the preference in choosing Purite first, which didn't work. An obvious alternative, BAK, was chosen next and did work.

[186] My conclusions are different from those arrived at by Judge Ward in the United States. I point out that he had live witnesses before him; the evidence and the claims of the patents appear to have been somewhat different than that before me.

5) <u>Commercial Success</u>

[187] Just as Crampton J said at paragraph 123 of his Reasons, commercial success is a secondary factor when it comes to a consideration of obviousness. Unlike Crampton J, who discussed the matter at paragraphs 123 to 126 of his Reasons, I do not have uncontradicted evidence. The evidence of Dr. Quigly and to some extent, Dr. Hollis, whose evidence is rebutted by Dr. Fechtner,

reveal that the commercial success of COMBIGAN may be due to market factors other than the "inventiveness" of the product.

[188] Suffice it to say that COMBIGAN has enjoyed some success, and is sufficient to motivate Apotex to seek to market a generic version. I am satisfied, however, that commercial success has little impact on the issue of obviousness.

CONCLUSIONS AS TO OBVIOUSNESS

[189] As is apparent, I would find on the evidence before me that Apotex's allegations as to obviousness are justified. In this regard, my findings are in line with the decision of O'Reilly J of this Court in *Merck & Co Inc v Canada (Minister of Health),* 2010 FC 1042, where he held that a similar patent directed to the earlier combination product COSOPT was obvious, and with the decision of Justice Floyd of the High Court of Justice, Chancery Division, Patents Court of England and Wales in *Teva UK Limited v Merck & Co Inc*, supra, where he held the European COSOPT patent to be obvious.

[190] That is, however, not the end of the matter.

[191] I must consider the question of comity. Is the evidence and argument before me "different" from or "better" than the evidence and argument before Crampton J in *Sandoz*? There is no real way to measure "different" or "better". The evidence and argument is of the same *kind*. In some cases Crampton J had unrebutted evidence whereas I have rebutted evidence. The difference in the

evidence and argument is more one of *quality* to the best that can be discerned from the record that I have, and this Court not having the record as to what was before Crampton J.

[192] If I were to dismiss this application on the basis that Allergan did not discharge its burden of proving that Apotex's allegations as to obviousness were not justified; then, within a matter of hours - if not days - the Minister would give Apotex a Notice of Compliance, and the issue as to whether the Court should grant a prohibition order would be moot. The Court of Appeal, in all likelihood, would not hear an appeal.

[193] I believe that there have been serious issues raised as to comity. The somewhat contradictory decisions of the Court of Appeal should be considered by that Court and clear instruction given as to how, in an NOC context, previous decisions of a Court on the same issues respecting the same patent, should be considered.

[194] The only practical way to get the matter before the Court of Appeal is for me to grant the Order for prohibition in the likely expectation that Apotex will appeal.

[195] In the circumstances, I will not award costs to any party.

JUDGMENT

FOR THE REASONS PROVIDED:

THIS COURT'S JUDGMENT is that:

1. The application is allowed;

2. The Minister is prohibited from issuing a Notice of Compliance to Apotex in respect of its ophthalmic drug APO-BRIMONIDINE-TIMOP until the expiry of Canadian Letters Patent No. 2,440,764; and

3. No costs are awarded.

"Roger T. Hughes"
Judge

FEDERAL COURT

SOLICITORS OF RECORD

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