Federal Court  Cour fédérale

Date: 20160407

Docket: T-1392-14

Citation: 2016 FC 382

Toronto, Ontario, April 7, 2016

PRESENT: The Honourable Mr. Justice Locke

BETWEEN:

SHIRE CANADA INC.

Applicant

and

APOTEX INC. AND THE MINISTER OF HEALTH

Respondents

and

SHIRE LLC

Respondent/Patentee

JUDGMENT AND REASONS

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I. Overview

[1] This is an application by Shire Canada Inc. (Shire) under the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 [the Regulations], for an Order prohibiting the Minister of Health (the Minister) from issuing a notice of compliance (NOC) to Apotex Inc. (Apotex) in connection with its 5, 10, 15, 20, 25 and 30 mg extended release capsules of mixed amphetamine salts (MAS) until after the expiry of Canadian Patent No. 2,348,090 (the 090 Patent).

[2] The patented composition is for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

[3] Apotex filed an Abbreviated New Drug Submission (ANDS) with the Minister seeking an NOC for approval to sell its capsules, which would be marketed under the name APO-AMPHETAMINE MIXED SALTS XR (Apotex's product). Because the 090 Patent is listed against Shire's ADDERALL XR product on the patent register maintained by the Minister under sections 3 and 4 of the Regulations, Apotex had to address the 090 Patent under section 5 of the Regulations before it could obtain its NOC.

[4] By letter to Shire dated April 24, 2014, Apotex served a notice of allegation (NOA) alleging that the 090 Patent is invalid, that it will not be infringed by Apotex's product, and that certain claims of the 090 Patent are not relevant under the Regulations and hence need not be addressed by Apotex.

[5] In response to Apotex's NOA, Shire commenced the present application on June 9, 2014, by filing a notice of application asserting that Apotex's allegations are not justified.

[6] The scope of issues in dispute in relation to the 090 Patent has since been narrowed. The claims in issue have been limited to five, being claims 22, 31, 32, 43 and 46. Apotex maintains its allegations that (i) none of these claims will be infringed by its product, (ii) in the event that the claims in issue are construed as Shire argues, they are invalid for overbreadth, ambiguity, insufficiency and lack of utility, and (iii) none of the claims in issue is relevant under the Regulations because Shire's ADDERALL XR product does not fall within the scope of said claims.

[7] For the reasons that follow, I have concluded that Apotex's allegations of non-infringement of the claims in issue are justified. Accordingly, the present application will be dismissed and the requested prohibition order will not be granted. Because Apotex's invalidity allegations apply only if the claims in issue are construed so as to encompass Apotex's product, it is not necessary to address these allegations. It is also not necessary to address Apotex's allegation that the claims in issue are not relevant under the Regulations.

II. The 090 Patent

[8] The 090 Patent has a filing date of October 20, 1999, and is based on a priority application that was filed in Germany on October 21, 1998. It was published on April 27, 2000, and is to expire on October 20, 2019. It names eight inventors: Beth A. Burnside, Xiaodi Guo, Kimberly Fiske, Richard A. Couch, Donald J. Treacy, Rong-Kun Chang, Charlotte M.

McGuinness and Edward M. Rudnic. The registered owner of the 090 Patent is Shire LLC. The applicant in the present proceeding, Shire, is a licensee of the 090 Patent.

[9] The 090 Patent is entitled “Oral Pulsed Dose Drug Delivery System”. It describes and claims a system for treating ADHD. ADHD is a psychiatric disorder characterized as a persistent pattern of inattention and/or hyperactive/impulsive symptoms that are out of the typical range for a person’s developmental level. It is common in children and adolescents (affecting 3-5% of school-age children), but is also known in some adults.

[10] Prior to the 090 Patent, favoured treatments for ADHD required at least two separate doses during the day, generally one at home in the morning and one around lunch time, usually at school. There were several disadvantages to the need for a second dose. Firstly, it would often require involving school staff to keep and then administer the second dose. This was administratively heavy, because the drugs in question are stimulants that are subject to heightened regulatory control. It also risked missed doses, as well as a loss of confidentiality and resulting stigma. Moreover, there were concerns about increased risk of diversion or misuse of these controlled drugs.

[11] Because of the problems associated with the second daily dose, there were efforts to develop a formulation that would be effective for the treatment of ADHD by means of a single daily dose. A common approach to permit reduced frequency of dosing is to develop a formulation that releases medication gradually so as to maintain a steady level in the blood

plasma over an extended period. However, it was already known, though it was not clear why, that this approach did not work for medications known in the treatment of ADHD.

[12] It had been observed that one ADHD medication, methylphenidate, had the best effect in the period between the beginning of drug absorption and the time of maximum blood plasma concentration (T_{max}). It was not clear why this was the case, but it was later theorized that, once the methylphenidate reached its maximum blood plasma concentration (C_{max}), the patient acquired an acute tolerance, being a rapidly-developing decline in pharmacological effect called tachyphylaxis.

[13] Another ADHD medication known prior to the 090 Patent was MAS (mixed amphetamine salts) taken twice a day. It was known as ADDERALL. Amphetamine is a racemate, which means that it is composed of equal amounts of two stereoisomers (also known as enantiomers). These enantiomers have the same chemical composition but in a different arrangement; they differ from one another only in that the orientation of the atoms is in mirror image. The enantiomers of amphetamine are called dextroamphetamine (d-amphetamine) and levoamphetamine (l-amphetamine).

[14] The 090 Patent describes an approach whereby multiple pulsed doses of MAS are delivered by means of a single administration comprising a first (immediate) pulse, which is released to the blood without delay at the time the medication is taken, and a second (delayed) pulse, which is released after a predetermined time. This is intended to mimic the effect in the

body of the twice daily dosing that was already known to be effective. Figure 1 of the 090 Patent shows a target plasma level profile based on the twice daily dosing.

[15] The 090 Patent describes a number of examples that illustrate the claimed invention. Example 1 is an immediate release formulation of MAS which are fully dissolved in the body within 15 minutes. Examples 2, 3 and 4 are delayed release formulations of the same MAS with different enteric coatings. Enteric coatings are designed to delay dissolution and release of active pharmaceutical ingredients until they reach the intestines. The best results are obtained in a formulation that combines Examples 1 and 2 in a hard gelatin capsule. This provides an immediate release dose and a delayed release dose in a single administration. Figure 7 of the 090 Patent shows a plasma profile that is said to be typical of results obtained from this formulation in a human study. The profile of Figure 7 (as well as Figure 8, which concerns a formulation combining Examples 1 and 3) is described in the 090 Patent as being "similar to the desired target plasma level profile shown in Figure 1."

[16] Of the five claims that remain in issue, claims 22, 31 and 32 are independent, and claims 43 and 46 are dependent. The text of these claims is reproduced here:

> 22. An oral pharmaceutical composition for delivery of one or more amphetamine base salts comprising an immediate release dosage form containing a first dosage amount of said one or more salts effective to treat Attention Deficit Hyperactivity Disorder (ADHD) in a human patient, and a second dosage form containing a second dosage amount of said one or more salts effective to treat ADHD in a human patient which has a release onset lag time sufficient that the plasma concentration/time curve of said composition has substantially the same shape as that of Figure 7, adjusted proportionally for said first and second dosage amounts.
>
> 31. An oral pharmaceutical composition for delivery of dosage amounts of one or more amphetamine base salts sufficient to

> provide an Attention Deficit Hyperactivity Disorder (ADHD) effective plasma level in said patient for at least 8 hours without further administration of amphetamine base salts and which has a plasma concentration/time curve which is substantially the same as that of Figure 7, adjusted proportionally for said dosage amounts.
>
> 32. An oral pharmaceutical composition for delivery of one or more amphetamine base salts comprising an immediate release dosage form containing a first dosage amount of said one or more salts effective to treat Attention Deficit Hyperactivity Disorder (ADHD) in a human patient, and a second dosage form containing a second dosage amount of said one or more salts effective to treat ADHD in a human patient, wherein the plasma concentration/time profile of said composition is substantially the same as that of Figure 7, adjusted proportionally for said first and second dosage amounts.
>
> 43. The pharmaceutical composition of any one of claims 14 to 41, wherein said amphetamine base salts are a mixture of dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine aspartate monohydrate and amphetamine sulfate.
>
> 46. The pharmaceutical composition of any one of claims 22 to 45 sufficient to maintain an effective level of amphetamine base salts in the patient over the course of at least 8 hours without further administration of amphetamine base salts.

[17] Each of the independent claims in issue defines an oral pharmaceutical composition for delivery of one or more amphetamine base salts sufficient to treat ADHD, and refers to the plasma profile of Figure 7.

[18] Though the key characteristics of Figure 7 and the essential elements of the claims are discussed in detail below in the Claim Construction section, it is useful at this stage to note briefly some of these features.

[19] Claims 22 and 32 each define both “an immediate release dosage form containing a first dosage amount” and “a second dosage form containing a second dosage amount.” Claim 22 specifies that the second dosage amount “has a release onset lag time”. Claim 32 does not. Claim 31 does not specify first and second dosage forms respectively containing first and second dosage amounts, and instead defines simply “dosage amounts”.

[20] With regard to Figure 7, claim 22 specifies that the plasma concentration/time curve of the claimed composition should be “substantially the same shape as that of Figure 7”, whereas claims 31 and 32 specifies that it should be “substantially the same as that of Figure 7”, without the word “shape”.

III. Apotex’s Product

[21] In this decision, I refer often to Apotex’s product and issues of infringement in the present, despite the fact that the product is not yet on the market. This is done to simplify the grammar.

[22] The parties are in general agreement as to the qualities of Apotex’s product. They disagree however on how those qualities should be characterized for the purposes of the 090 Patent.

[23] Apotex’s product is a hard gelatin capsule filled with two, four, six, eight, ten or twelve tablets depending on the dosage amount. Each tablet is a uniform monolithic matrix in which MAS and excipients are dispersed in an enteric polymer (methacrylic acid and ethyl acrylate).

Apotex's product employs an enteric polymer of the kind described in the 090 Patent, but as a matrix rather than as a coating.

[24] Apotex's product does not achieve its extended-release characteristics by a combination of coated (delayed release) and uncoated (immediate release) tablets as in Shire's ADDERALL XR product and as described for the key embodiments in the 090 Patent. Rather, Apotex's product achieves its extended-release characteristics first by a mechanism of diffusion (while the tablets are in the stomach), and later by a mechanism of diffusion and erosion (once the tablets have entered the intestines). In the low pH environment of the stomach, the enteric matrix remains intact and some of the MAS are dissolved gradually. The higher pH environment of the intestines will begin the erosion of the enteric matrix, thus facilitating further and faster dissolution of the MAS.

[25] The MAS in Apotex's product are the same as those defined in claim 43, except that Apotex uses anhydrous amphetamine aspartate instead of amphetamine aspartate monohydrate. This distinction is addressed later in the Claim Construction section.

IV. Summary of the Issues in Dispute and Burden of Proof

A. *Issues in Dispute*

[26] In respect of claim 22, Apotex alleges non-infringement on the basis that its product does not comprise a first, immediate release dosage form and a second dosage form which has a

release onset lag time, and further that its product does not contain an immediate release dosage form at all.

[27] It is notable that, for reasons that were not explained, Apotex has not alleged non-infringement of claim 22 on the basis that its product does not result in a plasma concentration/time curve that is substantially the same shape as that of Figure 7. Accordingly, this feature need not be discussed in relation to claim 22.

[28] In respect of claim 31, Apotex alleges non-infringement on the basis that its product does not have a plasma concentration/time curve that is substantially the same as that of Figure 7. Apotex also asserts that its product does not have more than one dosage amount.

[29] In respect of claim 32, Apotex alleges non-infringement on the basis that its product is not comprised of first and second dosage forms, is not comprised of an immediate release dosage form, and does not have a plasma concentration/time profile that is substantially the same as that of Figure 7.

[30] In respect of claim 43, Apotex cites the dependency of this claim on claims that are not infringed, and further alleges non-infringement on the basis that its product will not contain amphetamine aspartate monohydrate.

[31] In respect of claim 46, Apotex cites the dependency of this claim on claims that are not infringed.

[32] Apotex also maintains, in the alternative, that if the claims in issue are construed broadly enough to encompass Apotex's product, then those claims are invalid for overbreadth, ambiguity and insufficiency. Further, Apotex maintains (again in the alternative) that claim 31 is invalid for lack of utility.

[33] The essence of Apotex's alternative invalidity allegations is as follows. If the claims in issue encompass a uniform monolithic formulation like Apotex's, then they are invalid for:

a) overbreadth, because they encompass any composition that achieves the desired result of providing a plasma profile effective to treat ADHD for at least eight hours (even a sustained release formulation of the type that the 090 Patent indicates it is avoiding), and hence they encompass more than was invented or disclosed in the 090 Patent;
b) ambiguity, because they do not permit a person to determine whether a formulation falls within or outside the scope of the claims without reliance on bioequivalence data, which varies from person to person;
c) insufficiency, because the 090 Patent does not describe how to make the invention using a uniform monolithic matrix so as to permit a person skilled in the art to use the invention referring only to the patent; and
d) in respect of claim 31 only, lack of utility, because the claim encompasses a uniform monolithic matrix embodiment that was neither demonstrated to have utility before the filing date of the 090 Patent, nor met the requirements of the doctrine of sound prediction.

[34] Apotex also maintains that the claims in issue are not relevant under the Regulations because Shire's ADDERALL XR product does not fall within the scope of said claims.

[35] As indicated above, because of my conclusions concerning Apotex's non-infringement allegations, it is not necessary for me to address either the alternative invalidity allegations or the assertion that the claims in issue are not relevant under the Regulations.

B. *Burden of Proof*

[36] The burden of proof in the context of an application under the Regulations is somewhat complicated and counterintuitive. It warrants some discussion.

[37] I addressed this issue in my decision in *Leo Pharma Inc v Teva Canada Limited*, 2015 FC 1237 at paras 62-64, and neither party in the present application argued that my analysis there was flawed. I reproduce it here and rely upon it:

> [62] The general principle in an application is that the applicant bears the onus of proof. This applies in the present application, even on issues of patent validity.
>
> [63] Because subsection 43(2) of the *Patent Act*, RSC 1985, c P-4 [the Patent Act], creates a presumption that a patent is valid, the jurisprudence has held that, once the existence of the patent has been established, the onus shifts to the respondent [Apotex, here] who then has the burden of putting its allegations of invalidity "into play": *Pharmascience Inc v Canada (Health)*, 2014 FCA 133 at para 32 [*Pharmascience*]. This can be done by adducing evidence which is "not clearly incapable of establishing its allegations of invalidity": *Pfizer Canada Inc v Canada (Health)*, 2007 FCA 209 at para 109. The respondent's burden in this respect has also been characterized as the requirement to "lead sufficient evidence to give its allegations 'an air of reality'." The standard of proof here is lower than a balance of probabilities: Pharmascience at para 33; *Pfizer Canada Inc v Apotex Inc*, 2007 FC 971 at para

> 51, aff'd 2009 FCA 8 [*Pfizer*]. However, the respondent's onus cannot be satisfied by the mere fact of detailing its allegations in its NOA: *Pharmascience* at para 36.
>
> [64] Once the respondent has properly put its invalidity allegations into play, the onus shifts back to the applicant [Shire, here] to establish, on a balance of probabilities, that those allegations are not justified.

[38] The burden of proof is simpler with regard to infringement issues. The applicant bears the burden of proving on a balance of probabilities that the respondent's non-infringement allegations are unjustified. There is no evidentiary burden on the respondent. Its allegation of non-infringement is "in play" by virtue of the NOA: *Bristol-Myers Squibb v Teva Canada Limited*, 2015 FCA 3 at para 11. Statements in an NOA with regard to allegations of non-infringement are presumed to be true: *Eli Lilly Canada Inc v Mylan Pharmaceuticals ULC*, 2015 FC 178 at para 81.

[39] That said, the applicant has no burden to meet any non-infringement arguments that have not been asserted in the NOA: *Apotex Inc v Pfizer Canada Inc*, 2014 FCA 250 at para 92.

V. The Witnesses

[40] The record in this application includes the evidence of eight witnesses. Shire had five witnesses (three experts and two fact witnesses) and Apotex had three witnesses (two experts and one fact witness). The witnesses and their respective testimony are each described briefly below.

[41] As often happens in patent cases, the parties' experts disagree on key questions of claim construction. I discuss in these reasons some of these opinions that I found the most compelling.

Where I have remained silent on an expert's opinion on an issue, it should be understood that I have read and considered that opinion but have not felt it necessary to discuss it in these reasons.

A. *Blinding of Expert Witnesses*

[42] Apotex argues with considerable energy that the evidence of its expert witnesses should be favoured over the evidence of Shire's experts because Apotex blinded its experts to certain unnecessary facts when seeking their opinions, whereas Shire did not. Apotex's experts never saw the NOA and were never told Apotex's legal position. Apotex's experts were essentially asked to provide a series of mini-opinions. They were asked to construe the claims of the 090 Patent without information about Apotex's product. They were given information about Apotex's product only once they were asked to give their opinion on issues of patent infringement. They were subsequently asked to opine on issues of patent validity and then to comment on the opinions expressed by Shire's experts.

[43] Apotex argues that, since claim construction should precede analysis of issues like patent infringement and validity, exposing experts to information about the allegedly infringing product or the relevant prior art could improperly taint their analysis on claim construction. One way to avoid this problem is by seeking the expert's opinion without first alerting the expert to the conclusion the party wants by sharing such unnecessary information. Apotex expresses the concern that the unblinded expert's analysis risks becoming results-oriented. Apotex argues that Shire's experts' opinions should be discounted for precisely this reason. In support of its position, Apotex cites *Teva Canada Innovation v Apotex Inc*, 2014 FC 1070 at paras 94-96; *AstraZeneca Canada Inc v Apotex Inc*, 2014 FC 638 at para 321 [*AstraZeneca*]; *Takeda Canada*

Inc v Canada (Health), 2015 FC 570 at para 29; and *Allergan Inc v Apotex Inc*, 2016 FC 344 at para 13.

[44] For its part, Shire argues that blinding of experts is not a requirement and there is no principle of law whereby testimony of blinded experts must be favoured over that of unblinded experts. Shire argues that I should consider the opinions of the experts (and whether they seem to be well-supported or are tortured) rather than focusing on the information to which they had been exposed before forming those opinions: *Eli Lilly Canada Inc v Apotex Inc*, 2015 FC 875 at para 166 [*Eli Lilly*].

[45] I agree to some extent with both parties. In some situations, the fact that an expert witness was unaware of the features of an allegedly-infringing product when they formed their opinion on claim construction may be helpful in deciding the weight to be placed on that expert's opinion. However, I agree with Shire that favouring the evidence of experts who have been blinded has not been raised to the level of a legal principle that must be applied in all cases, and is merely persuasive (*AstraZeneca* at para 322; *Eli Lilly* at para 166). I am mainly interested in the substance of an expert's opinion and the reasoning that led to that opinion. If it is well-reasoned, there may be no reason for concern about whether the witness was blinded to certain facts when giving the opinion. A concern may arise where the expert's opinion seems tortured or less well-reasoned.

[46] I am also conscious that the blinding of witnesses is no guarantee that the expert evidence before the Court is reliable. It would not be difficult (though it would be expensive) for an

unscrupulous party to seek opinions from a number of experts, keeping them all blind to unnecessary information. If one of those many experts provided the opinion that the party sought and all of the others concluded otherwise, the party would be able to retain the outlier and present him or her as a blinded (and therefore reliable) witness.

[47] In the present case, I did not find the blinding of expert witnesses to be determinative. I agree with Apotex's experts on some issues and with Shire's experts on others. I have indicated below some of my reasons for preferring the experts of one side over the other.

[48] As a complement to its arguments that the testimony of Shire's experts was less reliable, Apotex also noted that Dr. Bodmeier appears frequently as an expert witness, and cited criticism of his testimony in *Janssen Inc v Teva Canada Limited*, 2015 FC 184 [*Janssen*] and in *Eli Lilly Canada Inc v Apotex Inc*, 2015 FC 1016. However, Shire pointed to positive consideration of Dr. Bodmeier's expert testimony just a month after *Janssen* in *AstraZeneca Canada Inc v Apotex Inc*, 2015 FC 322, which was decided by the same judge as presided in *Janssen*. Shire also cited other decisions commenting positively on Dr. Bodmeier's expert testimony. In the end, I remain of the view that I am mainly interested in the substance of each expert's opinion and the reasoning that led to that opinion.

B. *Shire's Expert Witnesses*

(1) Roland Bodmeier

[49] Dr. Bodmeier obtained his PhD in Pharmaceutics in 1986 from the University of Texas at Austin. He is currently a Full Professor of Pharmaceutical Technology at the College of Pharmacy at the Free University of Berlin, Germany. In addition to being a professor, he provides consulting services to the pharmaceutical industry regarding the formulation and characterization of drug dosage forms. He has also founded two pharmaceutical firms.

[50] In his affidavit, Dr. Bodmeier describes the 090 Patent and the inventive concept. He then construes the claims in issue, and proceeds to address Apotex's allegations of non-infringement, disagreeing with all of them. In relation to Apotex's allegations of invalidity, Dr. Bodmeier opines that the claims of the 090 Patent are not broader than the invention disclosed, that the language of the claims can be clearly understood and the claims are therefore not ambiguous, that the patent sufficiently describes how to make the invention, and that the promised utility of the patent was demonstrated by Figure 7.

(2) James McGough

[51] Dr. McGough is a psychiatrist with specific expertise in child and adolescent psychiatry. He received his MD from the Duke University School of Medicine in 1986. He is currently a Professor of Clinical Psychiatry, Step V in the Division of Child and Adolescent Psychiatry at the University of California, Los Angeles. The treatment of ADHD is one of his principle

research interests, which is reflected in his many publications and presentations on this topic. From 1999-2002, he used grants from Shire to perform studies of Adderall XR in both children and adults with ADHD.

[52] In his affidavit, Dr. McGough presents his interpretation of the 090 Patent, defining terms such as "immediate release dosage form", and noting what he considers to be the important characteristics of the Figure 7 blood plasma concentration/time curve. He then discusses the nature of ADHD and its treatment. Finally, Dr. McGough addresses Apotex's allegations of invalidity, concluding that the 090 Patent has sufficient disclosure, that the inventors both demonstrated and soundly predicted utility, and that the claims are neither overbroad, nor ambiguous.

(3) James Polli

[53] Dr. Polli's expertise lies in pharmacokinetics and pharmacodynamics. He is a professor at the University of Maryland School of Pharmacy, where he holds the Ralph F. Shangraw/Noxell Endowed Chair in Industrial Pharmacy and Pharmaceutics. He completed his Doctorate of Pharmacy in Pharmaceutics in 1993 at the University of Michigan College of Pharmacy. He has published widely in his field, edited a number of peer-reviewed pharmaceutical journals, and been part of various boards and committees in the area of pharmaceutics.

[54] In his affidavit, Dr. Polli provides a primer on some of the science behind the 090 Patent, such as the pharmacokinetic characteristics of plasma concentration/time profiles. He provides his interpretation of the disputed claims of the 090 Patent, discussing in particular his

understanding as a pharmacokineticist of Figure 7. Dr. Polli subsequently addresses Apotex's allegations of non-infringement, asserting that the plasma concentration/time curve of Apotex's product is substantially the same as that illustrated by Figure 7, and therefore it infringes the disputed claims. Dr. Polli also addresses whether the disputed claims of the '090 Patent are relevant under the Regulations, opining that Shire's ADDERALL XR product produces a plasma concentration/time curve that is substantially the same that of Figure 7. Finally, Dr. Polli addresses Apotex's allegations of insufficiency, overbreadth, ambiguity, and inutility, concluding that they are groundless.

C. *Shire's Fact Witnesses*

(1) Beth Burnside

[55] Dr. Burnside is the lead inventor on the 090 Patent. She earned her Ph.D. in Physical Organic Chemistry from Drexel University in 1987. She has worked at a number of pharmaceutical corporations; most recently, at QRxPharma, Inc., where she is the Senior Vice President of Quality Assurance. She was employed by Shire between 1997 and 2002, her final position there being Vice President of Advanced Drug Delivery.

[56] In her affidavit, Dr. Burnside provides background on the treatment of ADHD, and on the development of Shire's ADDERALL XR product.

(2) Erin McIntomny

[57] Ms. McIntomny is a law clerk at Gowlings, solicitors for the Applicant. She provides documents related to the litigation, namely portions of Apotex's Abbreviated New Drug Submissions.

D. *Apotex's Expert Witnesses*

(1) Mario González

[58] Dr. González is President and CEO of P'Kinetics International, Inc., a pharmacokinetics and biopharmaceutics consulting company. He is also an Adjunct Professor with the College of Pharmacy at the University of Florida. He received his Ph.D. in Pharmacokinetics from the University of California, San Francisco, in 1975. Dr. González' expertise in pharmacokinetics is demonstrated by his many publications and speaking engagements in this area.

[59] In his affidavit, Dr. González describes his understanding of the 090 Patent and construes the claims in issue. He then opines on whether the essential elements of those claims are embodied in Apotex's product, concluding that the plasma concentration profiles provided by Apotex's product do not meet the essential characteristics of Figure 7. Dr. González then addresses the issue of whether the claims in issue are relevant under the Regulations, and comments on the affidavits of Drs. Burnside, Polli and Bodmeier.

(2) Ping Lee

[60] Dr. Lee is familiar with all aspects of the drug development process. He received his Ph.D. in Physical Chemistry from Michigan State University in 1975, and subsequently worked in pharmaceutical research and development and in drug delivery for several major pharmaceutical companies, most recently as the Senior Director of Pharmaceutical R&D at Schering-Plough Research Institute. Currently, he is a Professor in Pharmaceutics and Drug Delivery at the Leslie Dan Faculty of Pharmacy, University of Toronto. He has published many peer-reviewed articles, presented at many conferences, and is a named inventor of 40 patents.

[61] In his affidavit, Dr. Lee provides background information concerning the 090 Patent and explains how a skilled person would understand terms used in the disputed claims thereof. He then opines on whether all of the essential elements of any claims of the ‘090 Patent are found in Apotex’s product, concluding that since Apotex’s product uses a formulation design and drug release method different from what is contemplated in the claims, it does not infringe the 090 Patent. Dr. Lee also comments on whether the ‘090 Patent contains sufficient disclosure, whether the inventors demonstrated the promised utility of certain claims or had a basis for a sound prediction of such utility. Finally, Dr. Lee comments on the affidavits of Drs. Bodmeier, Polli, and McGough.

E. *Apotex's Fact Witness*

(1) Duane Terrill

[62] Mr. Terrill is Associate Director, Regulatory Affairs, for Apotex. He indicates in his affidavit that in this capacity, he oversaw the preparation and filing of Apotex's ANDS in respect of its product. Mr. Terrill reviews the portions of Apotex's ANDS that were provided to the applicant, and confirms their source.

VI. Claim Construction

[63] Claim construction refers to the exercise of interpreting the words of the claims in a patent. It is the claims which define the patentee's exclusive rights. In this case, as in many, the dispute turns largely on claim construction.

[64] As stated above, the parties do not disagree greatly on the nature of Apotex's product. Moreover, the words of the claims are in writing and therefore (in theory, at least) easily ascertainable. The focus of the parties' dispute is with regard to (i) the proper understanding of those claims (claim construction), and (ii) whether Apotex's product falls within the scope of the claims in issue, properly construed. The exercise of claim construction in this case is particularly challenging because the claims in issue refer to Figure 7 which is not words but a diagram of a curve.

A. *Applicable Law*

[65] Claim construction is antecedent to consideration of both validity and infringement issues: *Whirlpool Corp v Camco Inc*, 2000 SCC 67 at para 43 [*Whirlpool*]. That said, the Court is not to construe a claim without knowing where the disputes between the parties lie (where the metaphorical shoe pinches): *Shire Biochem Inc v Canada (Health)*, 2008 FC 538 at para 22; *Sanofi-Aventis Canada v Apotex Inc*, 2009 FC 676 at para 82.

[66] The same claim construction applies for all issues, including infringement and validity issues: *Whirlpool* at para 49(b).

[67] A patent is not addressed to an ordinary member of the public, but to a worker skilled in the art described as:

> [A] hypothetical person possessing the ordinary skill and knowledge of the particular art to which the invention relates, and a mind willing to understand a specification that is addressed to him. This hypothetical person has sometimes been equated with the "reasonable man" used as a standard in negligence cases. He is assumed to be a man who is going to try to achieve success and not one who is looking for difficulties or seeking failure.
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> [*Free World Trust v Électro Santé Inc*, 2000 SCC 66 at para 44 [*Free World Trust*], quoting Fox, Harold G. *The Canadian Law and Practice Relating to Letters Patent for Inventions*, 4th ed., Toronto: Carswell, 1969 at 184]

[68] The person skilled in the art may also be a team of people: *Pfizer Canada Inc v Pharmascience Inc*, 2013 FC 120 at para 28; *General Tire & Rubber Company v Firestone Tyre and Rubber Company Limited*, [1972] RPC 457 (Eng CA) at 482.

[69] As stated in the UK House of Lords decision in *Catnic Components Ltd v Hill & Smith Ltd*, [1982] RPC 183 at 242-243 [*Catnic*], and quoted in *Whirlpool* at para 44:

> A patent specification should be given a purposive construction rather than a purely literal one derived from applying to it the kind of meticulous verbal analysis in which lawyers are too often tempted by their training to indulge. The question in each case is: whether persons with practical knowledge and experience of the kind of work in which the invention was intended to be used, would understand that strict compliance with a particular descriptive word or phrase appearing in a claim was intended by the patentee to be an essential requirement of the invention so that *any* variant would fall outside the monopoly claimed, even though it could have no material effect upon the way the invention worked.
>
> [Emphasis in original]

[70] The key to purposive construction is therefore the identification by the Court, with the assistance of the skilled reader, of the particular words or phrases in the claims that describe what the inventor considered to be the "essential" elements of his invention: *Whirlpool* at para 45. For an element to be considered non-essential and thus substitutable, it must be shown either (i) that on a purposive construction of the words of the claim it was clearly <u>not</u> intended to be essential, or (ii) that at the date of publication of the patent, the skilled addressees would have appreciated that a particular element could be substituted without affecting the working of the invention, *i.e.*, had the skilled worker at that time been told of both the element specified in the claim and the variant and "asked whether the variant would obviously work in the same way", the answer would be yes: *Free World Trust* at para 55.

[71] The Supreme Court of Canada (SCC) in *Free World Trust* tied its method of determining the essentiality of a claim element to the questions posed in the UK decision in *Improver v Remington*, [1990] FSR 181 [*Improver*], which distilled the test provided in *Catnic*:

> (i) Does the variant have a material effect upon the way the invention works? If yes, the variant is outside the claim. If no: --
>
> (ii) Would this (i.e.: that the variant had no material effect) have been obvious at the date of publication of the patent to a reader skilled in the art? If no, the variant is outside the claim. If yes: --
>
> (iii) Would the reader skilled in the art nevertheless have understood from the language of the claim that the patentee intended that strict compliance with the primary meaning was an essential requirement of the invention? If yes, the variant is outside the claim.

[72] It should also be noted that identification of elements of claims as essential or non-essential is to be made based on the patent specification and without resort to extrinsic evidence: *Free World Trust* at paras 61 and following.

[73] As stated in *Consolboard Inc v MacMillan Bloedel (Saskatchewan) Ltd*, [1981] 1 SCR 504 at 520:

> We must look to the whole of the disclosure and the claims to ascertain the nature of the invention and methods of its performance, (*Noranda Mines Limited v. Minerals Separation North American Corporation* [[1950] S.C.R. 36]), being neither benevolent nor harsh, but rather seeking a construction which is reasonable and fair to both patentee and public. There is no occasion for being too astute or technical in the matter of objections to either title or specification for, as Duff C.J.C. said, giving the judgment of the Court in *Western Electric Company, Incorporated, and Northern Electric Company v. Baldwin International Radio of Canada* [[1934] S.C.R. 570], at p. 574, "where the language of the specification, upon a reasonable view of it, can be so read as to afford the inventor protection for that which he has actually in good faith invented, the court, as a rule,

> will endeavour to give effect to that construction". Sir George Jessel spoke to like effect at a much earlier date in *Hinks & Son v. Safety Lighting Company* [(1876), 4 Ch. D. 607]. He said the patent should be approached "with a judicial anxiety to support a really useful invention".

[74] In construing the claims of a patent, recourse to the disclosure portion of the specification is (1) permissible to assist in understanding the terms used in the claims, (2) unnecessary where the words are plain and unambiguous, and (3) improper to vary the scope or ambit of the claims: *Monsanto Canada Inc v Schmeiser*, 2002 FCA 309 at para 37, var'd on other points 2004 SCC 34. Terms used in the claims must be read in context, and it is therefore unsafe in many instances to conclude that a term is plain and unambiguous without a careful review of the specification: *Whirlpool* at para 52, quoting from W.L. Hayhurst, "The Art of Claiming and Reading a Claim", in G.F. Henderson, ed, *Patent Law of Canada* (Toronto: Carswell, 1994) at 190.

[75] In the end, however, it is the words used in the claims which must be the focus of the exercise of claim construction: *Free World Trust* at para 40. The words chosen by the inventor will be read in the sense the inventor is presumed to have intended, and in a way that is sympathetic to accomplishment of the inventor's purpose expressed or implicit in the text of the claims. However, if the inventor has misspoken or otherwise created an unnecessary or troublesome limitation in the claims, it is a self-inflicted wound. The public is entitled to rely on the words used provided the words used are interpreted fairly and knowledgeably: *Free World Trust* at para 51.

[76] As noted by Shire, the SCC held in *Whirlpool*, at para 49(e), that an issued patent is an enactment as defined in the *Interpretation Act*, RSC 1985, c I-21, and therefore subject to

interpretation under the principles set out in the *Interpretation Act*. For the purposes of the present case, Shire cites in particular the principle set out at subsection 33(2) thereof which provides that "[w]ords in the singular include the plural, and words in the plural include the singular." Apotex notes that the SCC applied the *Interpretation Act* only for the principle that a patent must be given such interpretation according to section 12 "as best ensures the attainment of its objects." Apotex suggests that other interpretive principles are not equally applicable. In my view, nothing in the SCC's discussion of the *Interpretation Act* in *Whirlpool* suggests that its other principles should not apply. Nevertheless, I take this opportunity to note subsection 3(1) of the *Interpretation Act* which provides that its provisions apply "unless a contrary intention appears."

B. *Person Skilled in the Art*

[77] The parties appear to be in agreement as to the characteristics of the person skilled in the art. They agree that this person is a team comprising a pharmaceutical formulator, a pharmacokineticist, and a psychiatrist or clinician.

[78] Neither party has alleged that the other party's experts were not qualified in their respective fields. However, Shire notes that Apotex did not put forward an expert psychiatrist or clinician.

C. *Analysis*

[79] The key issues in dispute concerning claim construction are addressed in the following paragraphs.

(1) Claim 22

[80] The text of claim 22 is repeated here for convenience:

> 22. An oral pharmaceutical composition for delivery of one or more amphetamine base salts comprising an immediate release dosage form containing a first dosage amount of said one or more salts effective to treat Attention Deficit Hyperactivity Disorder (ADHD) in a human patient, and a second dosage form containing a second dosage amount of said one or more salts effective to treat ADHD in a human patient which has a release onset lag time sufficient that the plasma concentration/time curve of said composition has substantially the same shape as that of Figure 7, adjusted proportionally for said first and second dosage amounts.

[81] This claim clearly identifies two distinct dosage forms, each containing a distinct dosage amount. The first dosage form is defined as immediate, whereas the second has a release onset lag time.

(a) *Immediate release dosage form containing a first dosage amount*

[82] An important dispute between the parties concerns the implications of the word "immediate". The parties agree that it suggests that release of the drug begins without delay upon ingestion. However, Apotex also argues that "immediate" in the context of the 090 Patent means

that the drug is delivered as a pulse such that release of the first dosage amount must be complete within about one hour. Shire disputes this construction.

[83] Apotex points to repeated references in the 090 Patent to pulsed dosing. Apotex also relies on the evidence of its expert witnesses. Perhaps Apotex's strongest argument to construe "immediate release" as requiring rapid and complete release within a limited period of time is that, otherwise, a sustained release system (of the kind that the 090 Patent strives to avoid) would qualify as an immediate release dosage form. Apotex also notes that Shire's expert James McGough accepted in cross-examination at Q222 that it was reasonable to understand immediate release to include complete release within about one hour.

[84] Apotex argues also that "immediate release" implies that there is no intention to delay the complete dissolution and absorption of the drug: see Lee Affidavit, paras 55, 332. See also Bodmeier cross-examination at Q528-9.

[85] For its part, Shire focuses on the fact that other claims of the 090 Patent which are not in issue (*e.g.*, claims 1 to 4, as well as claims depending therefrom) define pulsed dosing and specify a period of about 60 minutes for complete dissolution. Claim 22 and the other claims in issue do not include such a limitation. Shire argues that, though the pulsed nature of the dosing and the time for complete dissolution may be essential elements of claims 1 to 4 (and claims depending therefrom), they are not essential elements of claim 22 and the other claims in issue.

[86] It should be noted first that the pulsed dosing defined in claims 1 to 4 concerns the second (delayed) dose, not the first (immediate release) dose. Therefore, Shire's argument does not apply as directly to the meaning of "immediate release" as it might seem at first blush. Nevertheless, Shire's point remains that, when the inventors intended to limit the time required for complete dissolution of a dose, they stated so explicitly.

[87] I agree with Apotex that the term "immediate release" in the claims in issue implies that there is no means for delaying release. Otherwise, I agree with Shire that "immediate release" means that release of the dose begins immediately and that there is no deadline for complete release of the dose.

(b) *A second dosage form containing a second dosage amount … which has a release onset lag time*

[88] Construction of the second dosage form is informed somewhat by the construction of the immediate release dosage form. The second dosage form is distinguished from the immediate release dosage form in two related respects: (i) it is not defined as immediate; and (ii) it has a release onset time lag.

[89] An important quality of claim 22 to draw from the distinct references to an immediate release dosage form containing a first dosage amount and a second dosage form containing a second dosage amount is that there are two distinct dosage forms containing two distinct dosage amounts.

[90] As with the immediate release dosage form, there is a dispute as to whether the second dosage form must be delivered as a pulse, such that release of the second dosage amount must be complete within a specific time.

[91] Apotex argues that the second dosage amount must be delivered as a pulse. As with the first dosage amount, Apotex relies on the testimony of its experts as well as references to pulsed dosing in the 090 Patent. However, Shire's counter-argument based on the specific time for complete dissolution of the second dosage amount in claims 1 to 4 (and not in claim 22 and the other claims in issue) is directly applicable here. The fact that the inventors did not specify a time for complete dissolution of the second dosage amount in claim 22 and the other claims in issue suggests that no deadline for such dissolution was contemplated.

[92] I conclude that the second dosage form of claim 22 is distinct from the immediate release dosage form. The onset of the release of the second dosage amount is delayed for an indeterminate amount of time, and there is no deadline for its complete release.

(c) *Substantially the same shape as that of Figure 7*

[93] Significant efforts were devoted by both parties to establishing the meaning of the phrase "substantially the same shape as that of Figure 7" in claim 22, and comparing and contrasting that phrase with "substantially the same as that of Figure 7" (without the word "shape") as appears in claims 31 and 32. Because Apotex's NOA did not address this phrase in claim 22, it is not necessary for me to construe it.

(2) Claim 31

[94] Claim 31 reads as follows:

> 31. An oral pharmaceutical composition for delivery of dosage amounts of one or more amphetamine base salts sufficient to provide an Attention Deficit Hyperactivity Disorder (ADHD) effective plasma level in said patient for at least 8 hours without further administration of amphetamine base salts and which has a plasma concentration/time curve which is substantially the same as that of Figure 7, adjusted proportionally for said dosage amounts.

[95] Claim 31 does not specify "an immediate release dosage form containing a first dosage amount" and "a second dosage form containing a second dosage amount" (as in claim 22). Rather, claim 31 defines simply "dosage amounts" and specifies that such amounts are sufficient to (i) treat ADHD for at least eight hours, and (ii) yield a plasma concentration/time curve which is substantially the same as that of Figure 7.

(a) *Dosage amounts*

[96] Shire does not identify "dosage amounts" among the essential features of claim 31 as listed in its memorandum of fact and law.

[97] Apotex construes this feature as indicating that the composition claimed in claim 31 contains more than one dosage form. Apotex argues that the use of the plural "amounts" indicates more than one dosage amount, and further that more than one dosage amount indicates more than one dosage form. Apotex also argues that the dosage forms contemplated in claim 31

should be construed as an immediate release dosage form and a delayed release dosage form, since this is what is described in the 090 Patent.

[98] Shire argues that dosage amounts are different from dosage forms, and it is an error to conflate the two. I agree that these terms are used separately in the 090 Patent and are not synonyms. Nevertheless, I agree with Apotex that the use of the plural "amounts" indicates that more than one dosage amount is contemplated.

[99] Shire counters that nothing specific should be understood by the use of the plural "amounts" in claim 31 since, as discussed above, the *Interpretation Act* (which the SCC has stated governs claim construction) provides at subsection 33(2) that "[w]ords in the singular include the plural, and words in the plural include the singular." However, Shire's proposed construction is awkward because it would read "amounts" as if it encompassed "amount". Though the guidance of the SCC arguably seems to lead to this awkward conclusion, I am comforted by subsection 3(1) of the *Interpretation Act* which provides that the provisions of the Act apply "unless a contrary intention appears." In my view, a reading of the 090 Patent as a whole and in accordance with the principles of claim construction discussed earlier in these reasons leads to the conclusion that the use of the plural "amounts" in claim 31 was deliberate and was intended to refer to at least two distinct dosage amounts. I see nothing in the 090 Patent that suggests using a single dosage amount. In fact, the clear thrust of the invention as described is to provide two pulsed doses of medication, one immediate and one delayed.

[100] That said, I am not prepared to accept Apotex's argument that the at least two dosage amounts contemplated in claim 31 should be construed as being contained within an immediate release dosage form and a delayed release dosage form. The fact that two such specific dosage forms are defined in other claims of the 090 Patent but not in claim 31 indicates that the inventors did not intend to limit claim 31 to these specific dosage forms.

(b) *Substantially the same as that of Figure 7*

[101] As indicated above, construction of the phrase "substantially the same as that of Figure 7" is particularly challenging because Figure 7 is in the form of a curve rather than words. There are many aspects to the parties' dispute over the construction of this phrase. I summarize them here and deal with each in detail below:

a) Whether the blood plasma concentration on the Y-axis of Figure 7 refers to total amphetamine (meaning d-amphetamine and l-amphetamine) or just d-amphetamine.
b) Whether the data for Figure 7 was obtained from an individual who was fed or one who was fasted.
c) The significance of the fact that Figure 7 concerns the plasma concentration/time curve for a single individual, and the statement in the disclosure portion of the 090 Patent that this curve (or profile) is typical.
d) How a reader should assess whether a composition "has a plasma concentration/time curve which is substantially the same as that of Figure 7."

(i) Total amphetamine or d-amphetamine

[102] The first of the disputed issues listed above concerns whether plasma concentration data for Figure 7 refers to total amphetamine or only d-amphetamine. The 090 Patent does not state explicitly which it is. This issue is potentially important because Shire has provided evidence on the basis of total amphetamine only. If Figure 7 concerns d-amphetamine then Shire has not provided adequate evidence on the issue of infringement.

[103] Shire argues that where one does not specify that only one of the enantiomers of amphetamine is measured (as in Figure 7) the measurement concerns total amphetamine. To support this argument, Shire refers to the fact that the patent does indicate a specific enantiomer when that is what it is referring to. An example is claim 43 (discussed in greater detail below) which specifies four amphetamine base salts, two of which are identified as dextroamphetamine salts and two of which are identified as amphetamine salts.

[104] I had some difficulty with the reference in claim 43 both to dextroamphetamine sulfate and amphetamine sulfate. I asked Shire's counsel why, if the word "amphetamine" indicates both dextroamphetamine sulfate and levoamphetamine sulfate, does claim 43 also separately identify dextroamphetamine sulfate. Shire's counsel responded that this indicates that the claimed composition includes both dextroamphetamine sulfate and levoamphetamine sulfate, but that there are not equal amounts of both; the claimed composition is fortified with additional dextroamphetamine sulfate. This seems to be a reasonable explanation, and Apotex's counsel did not take issue with it.

[105] Shire also notes that Apotex's expert Dr. González appears to agree that "amphetamine" refers to both d-amphetamine and l-amphetamine: see Q674-5 of his cross-examination.

[106] Apotex acknowledges that the 090 Patent does not indicate whether Figure 7 measures total amphetamine or only d-amphetamine, but argues against drawing the inference that "amphetamine" means total amphetamine. Apotex argues that the reader of the 090 Patent cannot determine for certain whether Figure 7 measures total amphetamine or d-amphetamine, but that it likely refers to d-amphetamine. Apotex supports this argument by reference to a passage in the 090 Patent that describes one of the aspects of the invention. At page 4f of the patent, there is reference to administration of amphetamine base salts "such that the maximum plasma concentration of dextro-salts in said mixture is about 40 ng/ml for about a 10 mg dose in each of said dosage forms." The same passage is also used in claim 51. With the support of its expert Dr. González, Apotex notes that the reference to a maximum plasma concentration of about 40 ng/ml for two doses of 10 mg each of amphetamine base salts appears to be directed to Figure 7. Otherwise, it would be an unexpected coincidence. This suggests that Figure 7 measures d-amphetamine.

[107] Apotex also notes that Shire's bioequivalence analysis for its ADDERALL XR product divided data between d-amphetamine and l-amphetamine. From Apotex's point of view, this highlights the fact that Shire recognizes the importance of the respective enantiomers of amphetamine, and is not inclined to lump them together. But this argument can cut both ways. The fact that Shire referred separately to d-amphetamine and l-amphetamine for its equivalence

analysis, but did not do so in respect of Figure 7 could suggest that Figure 7 measures total amphetamine.

[108] Moreover, Shire notes in reply that the data for Figure 1 of the 090 Patent (the desired target plasma level profile) was generated based on total amphetamine. Shire argues that, since Figure 7 was selected for its similarity to Figure 1, it stands to reason that Figure 7 also measures total amphetamine. Even though the 090 Patent itself does not state that Figure 1 measures total amphetamine, and therefore Shire's argument in reply relies on impermissible extrinsic evidence, this evidence is nevertheless consistent with the construction that I find more appropriate for the following reasons.

[109] Though the passages at page 4f of the 090 Patent and in claim 51 introduce some doubt on the question, this doubt is insufficient to displace my view that the stronger argument is that the skilled reader would understand that the word "amphetamine" (without reference to d-amphetamine or l-amphetamine) indicates total amphetamine, and that Figure 7 measures total amphetamine.

[110] I am likewise not swayed by Apotex's reference to a passage from the cross-examination of Shire's expert Dr. Bodmeier in which part of a cross-examination in a previous case in which he had acted as an expert witness on the 090 Patent was read to him. Apotex notes that in the previous case Dr. Bodmeier had acknowledged that it was possible that the reference in claim 51 to a maximum plasma concentration of about 40 ng/ml could be a reference to Figure 7. I accept Dr. Bodmeier's statement in his cross-examination in the present case that, in the earlier case, he

had not fully considered the issue of whether Figure 7 measures total amphetamine or only d-amphetamine.

(ii) Fed or fasted

[111] The next disputed aspect regarding the construction of the phrase "substantially the same as that of Figure 7" is whether the data for Figure 7 was obtained from an individual who was fed or one who was fasted. This matters because, on the issue of infringement, Shire presented only evidence based on a fed condition.

[112] Shire argues that the reference in claim 31 to the plasma level being in a "patient" indicates that the claim refers to someone who is fed, since a patient is not typically fasted.

[113] In response, Apotex notes that the 090 Patent indicates that Figure 7 was created from the results of a human study, which would typically be conducted on healthy, adult volunteers in both fed and fasted conditions. The 090 Patent does not indicate whether the subject who yielded Figure 7 was fed or fasted, and Shire provided no evidence on the point to meet its burden of proof. Apotex also argues that, if one were to focus on the word "patient" to conclude that Figure 7 referred to someone who is fed, one would have to accept also that the patient is typically a child. One would expect that the blood plasma profile for a child would be substantially different from that for an adult, and therefore Figure 7 could not be representative of a typical fed child.

[114] Shire counters this argument by arguing that it is not relevant whether the subject who yielded Figure 7 was fed or fasted. When construing this claim, what matters is the wording of

the claim. Though claim 31 refers to "a plasma concentration/time curve which is substantially the same as that of Figure 7", it does not specify that the plasma concentration/time curve should be measured under the conditions of a formal study. In fact, the claim itself does not tie Figure 7 to the study in any way. The skilled reader is therefore left to conclude from the word "patient" that no specific fasting conditions are implied by the claim.

[115] I side with Shire on this issue. I am not persuaded that Figure 7 is intended to relate to someone who is fasting. Accordingly, it is my view that a proper comparison with Figure 7 is yielded by a fed study.

[116] As regards the argument that any focus on the word "patient" should also lead to the conclusion that a proper comparison with Figure 7 would involve a blood plasma profile of a child, it is my view that there is insufficient basis for such a conclusion. It is highly likely that Figure 7 came from a subject in a study of adult volunteers. Given the difference in size between adults and children, I would have expected the patent to have addressed the point if Figure 7 was intended to relate to children.

[117] Accordingly, I am satisfied that Shire's evidence based on fed subjects is relevant.

(iii) Typical individual

[118] I now turn to a consideration of the significance of the data for Figure 7 being (i) related to an individual, and (ii) described in the 090 Patent as typical.

[119] Dr. Burnside, who was one of the inventors of the 090 Patent, explained that it was necessary to use a plasma concentration curve for an individual instead of using an average because "when the curves were plotted using the average plasma concentrations of all 20 subjects [from the crossover human study combining Examples 1 and 2], the curves of the individual subjects lost their characteristic 'peaks', 'humps', and 'troughs'." Though no such average plasma concentration curve (that was missing said peaks, humps and troughs) was put in evidence, I understand that this could be a result of the fact that those peaks, humps and troughs (which may be present in every case) might occur at different times for different individuals. Because of these different times, plotting an average would spread out and smooth out those peaks, humps and troughs, and thereby hide their importance in each individual case. I accept that it was in order to address this issue that the inventors decided to use a typical plasma concentration curve for Figure 7, rather than an average.

[120] Apotex's experts express doubt as to whether Figure 7 was indeed typical. Dr. González stated that, if Figures 7 and 8 were indeed typical, they would have been more similar to one another at least in the period before the release of the delayed release dose. However, I am not prepared to conclude from the difference in plasma concentration in this period that the statement in the 090 Patent that Figure 7 and 8 are typical should be disbelieved. It appears to be common ground that plasma concentrations following a given dose of a drug vary between individuals, and even vary between administrations of a given dose to a single individual.

[121] Apotex's other expert, Dr. Lee, was concerned that there is nothing in the 090 Patent or otherwise put into evidence to permit one to verify whether Figure 7 was indeed typical. Again, I

am not persuaded that this is a sufficient basis to disbelieve the statement in the patent. I accept Shire's argument that information provided in a patent specification should be presumed correct (*Eli Lilly Canada Inc v Novopharm Limited*, 2009 FC 301 at para 94), and Apotex has not established otherwise.

[122] Apotex also argues that Shire's reliance on evidence of one of the inventors on an issue of claim construction is inappropriate, and that such evidence should be ignored. While I accept the principle that reliance on extrinsic evidence (like an inventor's testimony) for claim construction is constrained in Canada, I do not view Shire's evidence in this regard as falling within that principle. The argument that Figure 7 represents typical results is based on a statement in the 090 Patent itself. Dr. Burnside's evidence is useful simply to explain why a typical result was used rather than a mean.

[123] Finally, Dr. González states that the skilled person comparing two different formulations of a drug would normally look for bioequivalence to a reference product. Assessment of bioequivalence could include parameters such as the maximum plasma concentration (C_{max}), the time at which C_{max} occurs (T_{max}), and the area under the curve (AUC) which provides an indication of the total exposure of the drug in the subject's blood. Apotex argues that comparisons for bioequivalence are done using mean figures and that it is impractical to do such a comparison with data concerning an individual such as Figure 7. Apotex argues that Shire improperly treats the "typical" results of Figure 7 as being a mean of the results of the crossover human study. Citing Dr. González' affidavit, Apotex argues that the reference in the 090 Patent to Figures 7 and 8 being typical means that they are similar to the target plasma profile provided

in Figure 1. I reject this argument. In my view the portion of the disclosure that describes Figures 7 and 8 makes clear that they are typical of the results obtained in the crossover human study. It is clear from the 090 Patent that the claims in issue were to be construed on the basis of Figure 7 and that infringement of said claims would require comparison with Figure 7. I will comment below on the merit of comparing to Figure 7 using parameters such as C_{max}, T_{max}, and AUC, but to the extent that they are applicable, they must apply to Figure 7 as it is provided in the 090 Patent.

(iv) How to assess "substantially the same"

[124] Finally, I turn the disputed question of how a reader should assess whether a composition "has a plasma concentration/time curve which is substantially the same as that of Figure 7." Though the parties disagree on many points on this question, those disagreements can initially be distilled to a debate over whether the comparison of the curve of Figure 7 to a possibly infringing composition should be an objective (statistical, quantitative) one or a subjective (graphical, qualitative) one. Shire's position is that the comparison can, and should, be made using objective (statistical, quantitative) criteria. Apotex, on the other hand, argues that the comparison requires a determination of the key characteristics of the claimed curve, and is necessarily subjective (graphical, qualitative).

[125] Reliance on objective criteria in construing a patent claim is generally preferable because it can make infringement analysis more straightforward and remove or reduce the negative effect of issues like unpredictability and bias. The SCC in *Free World Trust* (at para 42) recognized that a patent of uncertain scope becomes a public nuisance.

[126] The objective criteria that Shire argues should be applied in determining whether a curve is substantially the same as Figure 7 are those frequently used by skilled persons in assessing bioequivalence. Shire focuses on C_{max} and AUC. Shire also argues that the 80/125 rule used in assessing bioequivalence should apply in determining the scope contemplated by the word "substantially". That is, a curve is substantially the same as that of Figure 7 if its C_{max} and AUC are both within 80% and 125% of Figure 7.

[127] I note that the 090 Patent does not provide any criteria as to how one should assess "substantially the same". However, there are hints from the statement that the plasma profiles of Figures 7 and 8 are similar to the desired target plasma profile of Figure 1, and from the fact that the curve of Figure 7 was claimed while that of Figure 8 was not. In my view, these hints suggest that characteristics of Figure 7 that are common to Figure 1 are important characteristics of Figure 7, as are characteristics of Figure 7 that are <u>different</u> from Figure 8.

[128] For convenience, I reproduce Figures 1, 7 and 8 here:

FIG. 1

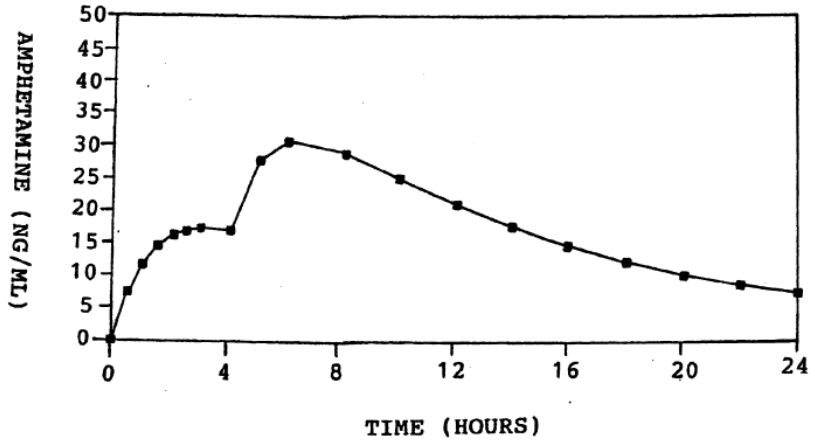


FIG. 7

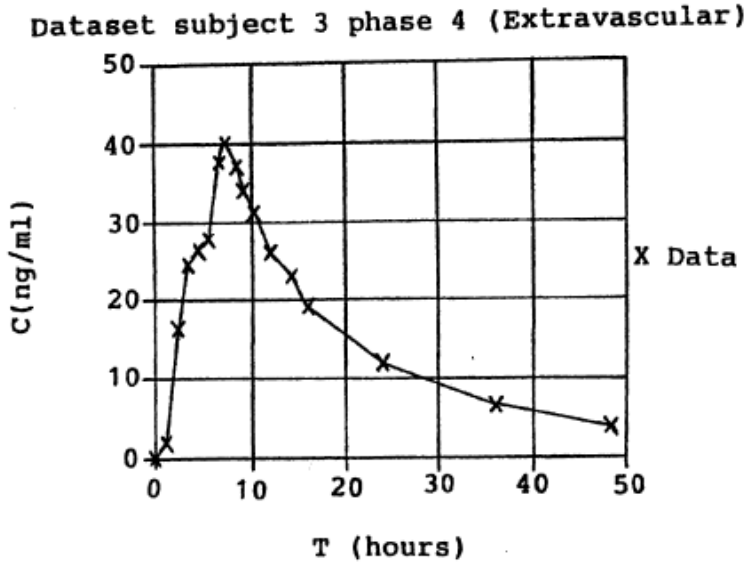
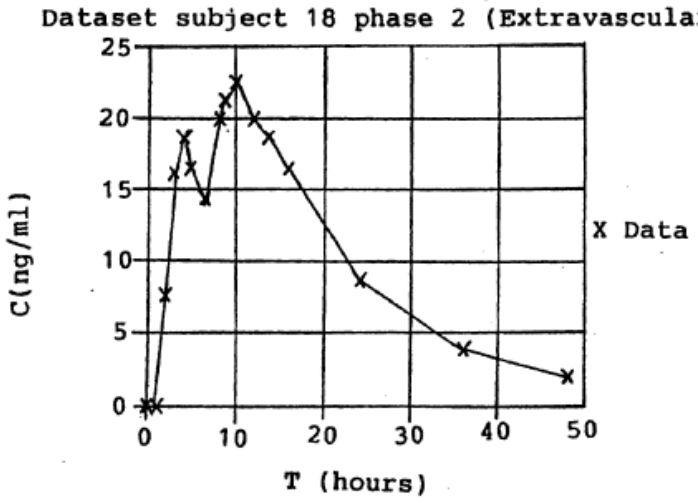


FIG. 8



[129] I agree with Apotex that construction of the term "substantially the same" requires a subjective (graphical, qualitative) consideration of the key characteristics of Figure 7 in the context of the 090 Patent as a whole. I am concerned that Shire's focus on statistical criteria like

C_{max} and AUC to determine the key characteristics of a complex curve like Figure 7 could result in a scope of the claim that encompasses curves that appear substantially different from Figure 7. It is not difficult to create a curve having the same C_{max} and AUC as Figure 7 but which would not be seen as substantially the same as Figure 7 by a casual observer. An example would be a straight line up from zero blood plasma at zero time to 40 ng/ml at 7 hours (the same C_{max} and T_{max} as in Figure 7), followed by another straight line down from that point to zero at some point between 30 and 40 hours which results in the same AUC as in Figure 7. I am not persuaded that a skilled person would be any more likely than a casual observer to see such a curve as being substantially the same as Figure 7.

[130] Based on the hints from the 090 Patent (similarities to Figure 1 and differences from Figure 8), I see five key characteristics in Figure 7:

a) A first ascent (of about 3 hours);

b) A shoulder without descent (following the first ascent);

c) A second ascent (after the shoulder);

d) A sharp peak at about 7 hours (following the second ascent); and

e) A steady descent (after the peak).

[131] I note that Apotex's expert Dr. Lee discussed essentially these characteristics at paragraph 324 of his report.

[132] Shire argues that the key features of the patented composition are those that affect treatment of ADHD in the eight hours after administration. Shire therefore focuses on the ascent

profile of the curve. Shire argues that the shoulder in Figure 7 has no therapeutic value and therefore should not be considered as an essential characteristic of Figure 7. Moreover, based on evidence that the beneficial effects of the ascent profile continue for three hours after C_{max}, the key characteristics of Figure 7 are those in the first five hours or so.

[133] I have difficulty accepting Shire's argument in this regard because it focuses on a small portion of the curve shown in Figure 7 and ignores many of its characteristics. Figure 7 provides data over a period of 48 hours. In my view, the inventors would not have included this period of time in the figure if they had intended the phrase "substantially the same" to be focused on the first five hours. Further, if one focuses on the first five hours and ignores the shoulder as Shire argues, then the only remaining characteristic of Figure 7 is the ascent. Again, in my view, the inventors would not have provided a curve such as that shown in Figure 7 if this had been their intention. Finally, I consider that a characteristic that clearly appears as part of Figure 7 but which may be unnecessary (like the shoulder) operates against Shire as a self-inflicted wound upon which the public is entitled to rely.

(v) Aside on claim construction principles

[134] Since this is a discussion on the essential elements of a claim, and because I have been asked to consider both the intended meaning of the claim and whether certain elements thereof affect the working of the invention, I take this opportunity to comment on an aspect of the test for determining whether a claim element is essential or not. Consideration of that test begins with an extract from paragraph 55 of the SCC decision in *Free World Trust* which is discussed above and which is reproduced here for convenience:

> For an element to be considered non-essential and thus substitutable, it must be shown either (i) that on a purposive construction of the words of the claim it was clearly *not* intended to be essential, or (ii) that at the date of publication of the patent, the skilled addressees would have appreciated that a particular element could be substituted without affecting the working of the invention, i.e., had the skilled worker at that time been told of both the element specified in the claim and the variant and "asked whether the variant would obviously work in the same way", the answer would be yes: *Improver Corp. v. Remington*, supra, at p. 192. In this context, I think "work in the same way" should be taken for our purposes as meaning that the variant (or component) would perform substantially the same function in substantially the same way to obtain substantially the same result. In *Improver Corp. v. Remington*, Hoffmann J. attempted to reduce the essence of the *Catnic* analysis to a series of concise questions, at p. 182:
>
> (i) Does the variant have a material effect upon the way the invention works? If yes, the variant is outside the claim. If no: –
>
> (ii) Would this (i.e.: that the variant had no material effect) have been obvious at the date of publication of the patent to a reader skilled in the art? If no, the variant is outside the claim. If yes: –
>
> (iii) Would the reader skilled in the art nevertheless have understood from the language of the claim that the patentee intended that strict compliance with the primary meaning was an essential requirement of the invention? If yes, the variant is outside the claim.
>
> [Emphasis in original]

[135] A careful reader will note that the series of three questions from *Improver* which is quoted by the SCC does not appear to be entirely consistent with the two-part analysis earlier in the paragraph for determining whether or not an element is essential. The first part of the SCC's characterization of the analysis ("on a purposive construction of the words of the claim [the element] was clearly *not* intended to be essential") corresponds roughly to the third question in *Improver*. The second part of the SCC's characterization ("at the date of publication of the patent, the skilled addressees would have appreciated that a particular element could be

substituted without affecting the working of the invention") corresponds roughly to the first and second questions in *Improver*. However, under the *Improver* test, the defendant need only be successful on one of the questions. In order for the patentee to establish that a claim element is not essential, it must succeed on all three questions. On the other hand, the SCC's characterization of the analysis appears to indicate that the defendant must be successful on both parts of the analysis, and that the patentee can establish that a claim element is not essential by succeeding on just one part.

[136] It seems unlikely that the SCC intended this apparent difference. Its decision does not acknowledge any inconsistency between the *Improver* questions and its own test for determining essentiality. Nor does the SCC suggest any disapproval of the *Improver* questions. In fact, the SCC clearly relies in *Improver*.

[137] In my view, the SCC likely intended that, in order for a patentee to establish that a claim element is non-essential, it must show both (i) that on a purposive construction of the words of the claim it was clearly not intended to be essential, and (ii) that at the date of publication of the patent, the skilled addressees would have appreciated that a particular element could be substituted without affecting the working of the invention.

[138] It seems clear enough that a claim element should be considered essential if that is what the words of the claim indicate, regardless of whether skilled addressees would have appreciated that a particular element could be substituted without affecting the working of the invention. At para 51 of *Free World Trust*, the SCC stated as follows:

> The words chosen by the inventor will be read in the sense the inventor is presumed to have intended, and in a way that is sympathetic to accomplishment of the inventor's purpose expressed or implicit in the text of the claims. However, if the inventor has misspoken or otherwise created an unnecessary or troublesome limitation in the claims, it is a self-inflicted wound. The public is entitled to rely on the words used *provided* the words used are interpreted fairly and knowledgeably.
>
> [Emphasis in original]

[139] Moreover, the SCC makes clear that the onus is on the patentee to establish known and obvious substitutability (non-essentiality) of a claim element: *Free World Trust* at para 57.

[140] This issue of apparent inconsistency between the test in *Free World Trust* and that in *Improver* was alluded to shortly after the SCC rendered its decision, in D. Clarizio, "*Whirlpool* and *Free World Trust*: Claim Construction and the Test for Patent Infringement", (2001) 18 C.I.P.Rev. 139. At p 145, Clarizio attempted to reconcile the conjunctive test in *Improver* and the disjunctive test in *Free World Trust* as follows:

> With the "primacy of the language of the claims" as the overriding principle, the test to determine if an element is essential or not requires answering two questions, although not necessarily in this order:
>
> 1. Is it the intention of the inventor as expressed or implied in the claims language that the element is essential? If yes, then the element is essential.
>
> 2. If no, then:
>
> (a) Has the patentee shown on a purposive construction of the words of the claim that the element was clearly not intended to be essential? or
>
> (b) Would the skilled worker have appreciated that the element could be substituted without affecting the working of the invention?

> If yes to either (a) or (b), then the element is not essential. If no to (a) and (b), then the element is essential.

[141] This reconciliation is somewhat unsatisfying because question 1 (which asks about the intention of the inventor that the element is essential) is basically the other side of the coin of question 2a (which asks about whether the element was clearly not intended to be essential). The main difference is the additional word "clearly". In my view, that additional word does not explain why the *Free World Trust* characterisation of the test is disjunctive while the *Improver* characterisation of the test is conjunctive.

[142] More recently, Donald M. Cameron addressed this issue in Canadian Patent Law Benchbook, 2nd ed., D.M. Cameron ed., Carswell, 2014, at p 375, making another attempt at reconciling the inconsistency which effectively reads the *Free World Trust* characterisation of the test as conjunctive. Though there is sparse mention of this issue in the jurisprudence, the Federal Court of Appeal did inherently adopt the same approach in *Halford v Seed Hawk Inc*, 2006 FCA 275 at paras 13-15 where it stated:

> [13] In the process of construing the claims of a patent, a court will identify some elements of the invention as essential. The determination of which elements are essential depends upon the language of the claims, read purposively, and informed by evidence as to how persons skilled in the art would understand the claims (*Whirlpool* at paragraph 45). An element may be found to be essential on the basis of the intent of the inventor as expressed or inferred from the claims, or on the basis of evidence as to whether it would have been obvious to a skilled worker at the time the patent was published that a variant of a particular element would make a difference to the way in which the invention works (*Free World* at paragraphs 31 and 55).
>
> [14] … In that decision, Binnie J. defined an element as being essential if it is required for the device to work as contemplated and claimed by the inventor. It is non-essential if it may be

> substituted or omitted without having a material effect on either the structure or operation of the invention described in the claims (*Free World* at paragraph 20).
>
> [15] …if it was not obvious at the date of patent publication that the substituted member had no material effect upon the way the invention works, then there is no infringement. Alternatively, if the functional equivalence was obvious, but the patentee intended strict compliance with the claim, then there is also no infringement (*Free World* at paragraph 55).

[143] Moreover, Justice Johanne Gauthier appears to have recognized the same reasoning in *Bauer Hockey Corp v Easton Sports Canada Inc*, 2010 FC 361 at para 144, aff'd 2011 FCA 83.

[144] Applying the foregoing discussion to the present case, the onus is on Shire to establish that a feature is not essential. As discussed above, my view is that the five listed features of Figure 7 are essential to claim 31. In addition, I conclude that Shire has failed to establish that, on a purposive construction of the words of claim 31, these features were clearly not intended to be essential.

(vi) Conclusion on construction of "substantially the same as that of Figure 7"

[145] To conclude on this issue, I find that the phrase "substantially the same as that of Figure 7" refers to blood plasma concentration of total amphetamine in a fed state. The essential features of Figure 7 are the first ascent, shoulder, second ascent, peak and steady descent as discussed in paragraph [130] above.

(3) Claim 32

[146] Claim 32 reads as follows:

> 32. An oral pharmaceutical composition for delivery of one or more amphetamine base salts comprising an immediate release dosage form containing a first dosage amount of said one or more salts effective to treat Attention Deficit Hyperactivity Disorder (ADHD) in a human patient, and a second dosage form containing a second dosage amount of said one or more salts effective to treat ADHD in a human patient, wherein the plasma concentration/time profile of said composition is substantially the same as that of Figure 7, adjusted proportionally for said first and second dosage amounts.

[147] Claim 32 differs from claim 22 only toward the end. Specifically, claim 32 removes reference to the release onset lag time (for the second dosage amount) that appears in claim 22. Also, claim 32 employs the phrase "the plasma concentration/time profile of said composition is substantially the same as that of Figure 7" instead of "the plasma concentration/time curve of said composition has substantially the same shape as that of Figure 7" [emphasis added] which appears in claim 22.

[148] Removal of the reference to the release onset lag time indicates that claim 32 does not require that onset of release of the second dosage amount be delayed.

[149] I have been given no reason to find any substantive difference between the word "profile" in claim 32 and "curve" in claim 22.

[150] As mentioned earlier, I have not found it necessary to reach a conclusion as to the relevance of the additional word “shape” in the phrase as used in claim 22. The phrase “substantially the same as that of Figure 7” used in claim 32 is identical to that used in claim 31. I conclude that it has the same meaning in both claims.

(4) Claim 43

[151] Claim 43 reads as follows:

> 43. The pharmaceutical composition of any one of claims 14 to 41, wherein said amphetamine base salts are a mixture of dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine aspartate monohydrate and amphetamine sulfate.

[152] Focusing on where the shoe pinches, it is necessary only to construe the term “amphetamine aspartate monohydrate”. Shire argues that the word “monohydrate” is not essential, and that the term encompasses anhydrous amphetamine aspartate. Shire points to evidence that anhydrous amphetamine aspartate is bioequivalent to amphetamine aspartate monohydrate, and that substituting one for the other has no therapeutic effect. Apotex does not appear to disagree with this. However, as discussed in some detail in my aside beginning at paragraph [134] above, it does not necessarily follow from this that the word “monohydrate” should be considered non-essential and thus substitutable. I have seen no evidence that, on a purposive construction of the term, it was clearly not intended to be essential.

[153] The term “amphetamine aspartate monohydrate” is clear and there is no suggestion that the skilled reader would understand the inventor using this term to mean that compound as well

as other similar compounds such as anhydrous amphetamine aspartate. In fact, the parties' respective arguments make it clear that they understand these two terms to be distinct.

(5) Claim 46

[154] Claim 46 reads as follows:

> 46. The pharmaceutical composition of any one of claims 22 to 45 sufficient to maintain an effective level of amphetamine base salts in the patient over the course of at least 8 hours without further administration of amphetamine base salts.

[155] There are no issues of claim construction for discussion in relation to claim 46. This claim specifies that an effective level of amphetamine base salts is maintained in the patient over the course of at least eight hours without further administration. This feature is already an element of claim 31, and nothing turns on this.

VII. Non-Infringement

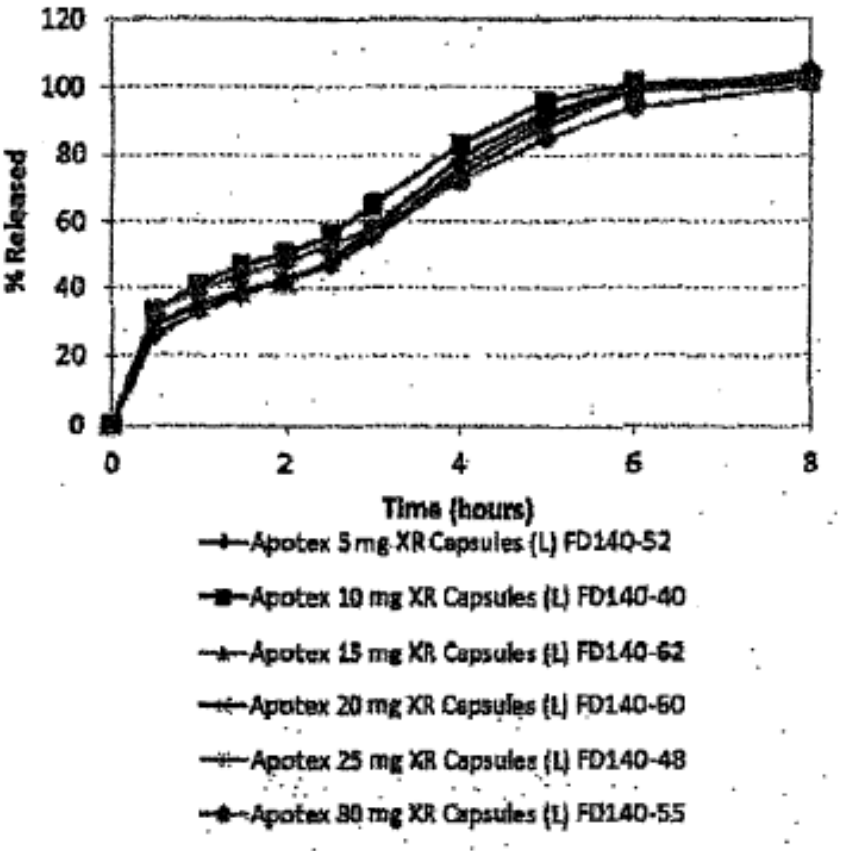
A. *Applicable Law*

[156] Infringement is not defined in the *Patent Act*. However, infringement has been defined in the jurisprudence. For the purposes of this case, it is enough to say that infringement of a patent claim requires that all essential elements of that claim (properly construed) be present: *Free World Trust* at para 68(4). There is no infringement if an essential element is different or omitted. There may still be infringement, however, if non-essential elements are substituted or omitted: *Free World Trust* at para 31(f).

B. *Analysis*

[157] Apotex's product is described generally earlier in these reasons. The key difference already mentioned between Apotex's product and the composition of the 090 Patent is that the former does not achieve its efficacy over an extended period by a combination of immediate release tablets and delayed release tablets, as described in the 090 Patent. Instead, Apotex's product employs tablets having a uniform monolithic matrix of an enteric polymer of methacrylic acid and ethyl acrylate in which is dispersed amphetamine salts and other excipients.

[158] Though the matrix of Apotex's product is made up of an enteric polymer, there is some dissolution of amphetamine salts before the product reaches the intestine. This dissolution occurs by a mechanism of diffusion, whereby gastric juices in the stomach gradually penetrate the tablets dissolving some of the salts that are dispersed in the enteric matrix, though the matrix remains intact. Shire's expert Dr. Bodmeier provided the following graph of the release profile of Apotex's product:



[159] This graph shows dissolution of about 40-50% of the amphetamine salts in the first two hours while the product is in the stomach. The graph also shows that the rate of dissolution increases once the product enters the intestine. This second stage of dissolution occurs by the addition of a new mechanism, erosion, as the enteric matrix breaks down, thus exposing more of the salts for dissolution.

[160] It is important in this discussion not to confuse the dissolution (or release) profile in the graph above with the plasma concentration profile shown in Figure 7 of the 090 Patent. The dissolution profile shows the dissolution of the amphetamine salts over time, whereas the plasma concentration profile shows the absorption thereof over time in the patient's blood.

[161] Data for the plasma concentration profile for Apotex's product (total amphetamine, and in a fed state) is found in Exhibit 23 of Dr. González' affidavit. This exhibit provides separate profiles for each subject who was studied. Dr. González also provides a graph of the mean plasma profile at Exhibit 21 of his affidavit. However, a mean plasma profile of Apotex's product is unhelpful in much the same way as Dr. Burnside indicated in her affidavit that a mean curve would not have been useful for Figure 7: because it would not reflect the characteristic "peaks", "humps" and "troughs" of the individuals' curves.

[162] Exhibit 23 comprises 21 individual plasma profiles. It is clear from an examination of the profiles in Exhibit 23 that there is considerable variation between subjects.

[163] Another notable difference between Apotex's product and that described in the 090 Patent is that the former contains anhydrous amphetamine aspartate instead of amphetamine aspartate monohydrate, as in the latter.

(1) Claim 22

[164] The non-infringement issues concerning claim 22 are whether Apotex's product has

a) an immediate release dosage form containing a first dosage amount; and
b) a second dosage form containing a second dosage amount which has a release onset lag time.

[165] As discussed earlier in relation to construction of claim 22, the term "immediate release" implies that there is no means for delaying release. I conclude that Apotex's product does not

include an immediate release dosage form since it comprises a single dosage form that includes an enteric matrix which operates to delay release of the active ingredient.

[166] This is sufficient to conclude that Apotex's allegation of non-infringement of claim 22 is justified. In addition, though it is not necessary for my decision, I would have difficulty finding that Apotex's product has a second dosage form containing a second dosage amount which has a release onset lag time. Firstly, though Apotex's product has means for delaying release of the active ingredient, it does not appear that there is a delay in the onset of release. Moreover, I cannot agree that Apotex's product comprises distinct first and second dosage forms. It is true that Apotex's product employs two separate drug release mechanisms, but there is only a single dosage form.

(2) Claim 31

[167] The non-infringement issues concerning claim 31 are whether Apotex's product has

a) more than one dosage amount; and
b) a plasma concentration/time curve which is substantially the same as that of Figure 7.

(a) *More than one dosage amount*

[168] As discussed in the preceding section concerning claim 22, Apotex's product comprises only one dosage form. I must ask therefore whether this single dosage form comprises more than one dosage amount.

[169] Shire argues in the affirmative, referring to the distinct mechanisms of release (diffusion and then erosion) that are employed in Apotex's product. However, it is clear that Apotex's product is uniform and monolithic. In my view, it would be straining the term "dosage amount" to conclude that Apotex's product comprises two of them.

[170] Shire also refers to page 3 of the 090 Patent which mentions bimodal drug release as one of the mechanisms that is contemplated. The passage indicates that "[b]imodal release is characterized by a rapid initial release, followed by a period of constant release, and finalized by a second rapid drug release." In my view, this passage is insufficient to establish that the reference in claim 31 to "dosage amounts" was intended to encompass a product like Apotex's. The reference to bimodal release is drawn from the Background of the Invention section. It is not clear that it is intended to define "dosage amounts" in claim 31.

[171] Therefore, I conclude that Apotex's allegation of non-infringement of claim 31 is justified.

(b) *A plasma concentration/time curve which is substantially the same as that of Figure 7*

[172] I reach the same conclusion in respect of whether Apotex's product has a plasma concentration/time curve which is substantially the same as that of Figure 7. As stated in discussion of the construction of claim 31, this element requires that the plasma profile of an infringing pharmaceutical composition have a plasma profile with the five characteristics identified in paragraph [130] above. Having reviewed all of the plasma profiles in Exhibit 23 of

Dr. González' affidavit, I find that almost all are missing both (i) a shoulder, and (ii) either a sharp peak or a steady descent or both. Arguably, the plasma profiles for subjects 2 and 10 would be substantially the same as that of Figure 7 if one ignored one or two anomalous data points. One might also have to ignore a substantially lower C_{max} for subject 10. Shire argues that this establishes at least that Apotex's product will sometimes infringe, and that therefore the product should be found to infringe the claim.

[173] However, since Figure 7 is based on a typical profile, it is my view that one should consider a typical profile when assessing whether Apotex's product infringes. Despite the fact that subject 2 (and possibly also subject 10) had plasma profiles that were arguably substantially the same as that of Figure 7, these profiles are not typical. In my view, a typical plasma profile from Exhibit 23 is not substantially the same as that of Figure 7.

(3) Claim 32

[174] The non-infringement issues concerning claim 32 are whether Apotex's products has

a) an immediate release dosage form containing a first dosage amount;
b) a second dosage form containing a second dosage amount; and
c) a plasma concentration/time profile which is substantially the same as that of Figure 7.

[175] All of these issues have been addressed in considering infringement issues in relation to claims 22 and 31.

[176] Apotex's product does not have an immediate release dosage form in that its product includes means for delaying release of the amphetamine salts. Moreover, Apotex's product does not include distinct first and second dosage forms.

[177] In addition, Apotex's product does not yield a plasma concentration/time profile which is substantially the same as that of Figure 7 since a typical subject's profile would be missing the essential characteristics of both a shoulder and either a sharp peak or a steady descent or both.

[178] For these reasons, I conclude that Apotex's allegation of non-infringement of claim 32 is justified.

(4) Claim 43

[179] The only issue in dispute in relation to claim 43 is whether Apotex's product contains amphetamine aspartate monohydrate. It is common ground that Apotex's product contains anhydrous amphetamine aspartate. Based on my construction of claim 43 above, the term "amphetamine aspartate monohydrate" does not encompass anhydrous amphetamine aspartate, and therefore Apotex's product does not infringe claim 43.

(5) Claim 46

[180] Though the additional limitation introduced by claim 46 (maintenance of an effective level of amphetamine base salts in the patient over the course of at least eight hours without further administration) is presumably present in Apotex's product, this claim is nevertheless not

infringed because it is a dependent claim and no claim from which it depends has been shown to be infringed.

C. *Conclusion on Infringement*

[181] For the foregoing reasons, I conclude that none of the claims in issue is infringed by Apotex's product, and that Shire has not established that Apotex's allegations of non-infringement are unjustified.

VIII. Invalidity Issues

[182] As indicated above, because I have concluded that Apotex's non-infringement allegations are justified, its alternative invalidity allegations are not in issue.

IX. Claims Not Relevant to the Regulations

[183] Similarly, because I have concluded that Apotex's non-infringement allegations are justified, it is not necessary for me to decide whether its allegations that the claims in issue are not relevant to the Regulations are justified.

X. Conclusion

[184] Based on the foregoing analysis, I have concluded that Apotex's allegations of non-infringement concerning the 090 Patent are justified. In view of this, Shire's application will be dismissed.

[185] Apotex should have its costs. If the parties are unable to agree on the quantum of costs, I will receive submissions from the parties as contemplated in the Judgment below.

JUDGMENT

THIS COURT'S JUDGMENT is that:

1. The present application is dismissed;

2. Costs will follow the event. If the parties are unable to agree on the quantum of costs payable by Shire Canada Inc. to Apotex Inc., the latter shall serve and file its costs submissions, of no more than 15 pages, within 30 days following the date of this decision. Shire shall have 15 days following receipt of Apotex's submissions to serve and file its responding costs submissions, which likewise shall be limited to 15 pages. Thereafter, Apotex may, within five (5) days following receipt of Shire's responding submissions, serve and file reply costs submissions of no more than five (5) pages

"George R. Locke"
Judge

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-1392-14
STYLE OF CAUSE:	SHIRE CANADA INC. v APOTEX INC. AND THE MINISTER OF HEALTH AND SHIRE LLC
PLACE OF HEARING:	OTTAWA, ONTARIO
DATE OF HEARING:	FEBRUARY 15-18, 2016
JUDGMENT AND REASONS:	LOCKE J.
DATED:	APRIL 7, 2016

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