Federal Court  Cour fédérale

Date: 20180629

Dockets: T-1056-16
T-998-16

Citation: 2018 FC 637

Ottawa, Ontario, June 29, 2018

PRESENT: The Honourable Mr. Justice Fothergill

Docket: T-1056-16

BETWEEN:

APOTEX INC.

Plaintiff
(Defendant by Counterclaim)

and

SHIRE LLC AND SHIRE PHARMA CANADA ULC

Defendants
(Plaintiffs by Counterclaim)

Docket: T-998-16

AND BETWEEN:

SHIRE PHARMA CANADA ULC

Applicant

and

APOTEX INC. AND THE MINISTER OF HEALTH

Respondents

and

SHIRE LLC

Respondent/Patentee

PUBLIC JUDGMENT AND REASONS

(Identical to the Confidential Judgment and Reasons issued on June 21, 2018)

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I. Overview

[1] Attention Deficit and Hyperactivity Disorder [ADHD] is a common neurobehavioural condition in both children and adults that is characterized by a persistent pattern of hyperactivity, impulsivity and inattention. For many years, physicians have treated the symptoms of ADHD with stimulants, such as amphetamine.

[2] Amphetamine products are available as immediate and sustained release formulations, each of which produces different durations of action. In sustained release formulations, also known as controlled release, extended release and slow release, the dosage form is designed to release the drug at a continuous and controlled rate for a longer period than would normally be achieved using its conventional, non-sustained counterpart (*i.e.*, immediate release).

[3] One significant drawback of both immediate and sustained release formulations of amphetamine is their potential for abuse. The dosage forms may be ground into a powder that is

snorted or inhaled intranasally. The powder may be dissolved in water and the recovered drug may be injected intravenously. The intact or pulverized dosage forms may be ingested to produce an oral overdose.

[4] Canadian Patent 2,527,646 [646 Patent] is titled "Abuse Resistant Amphetamine Compounds", and relates generally to the compound lisdexamfetamine [LDX], its compositions, methods of delivery and use. The application for the 646 Patent was filed on June 1, 2004, and claimed priority from United States Patents US60/567,801 dated May 5, 2004 and US60/473,929 dated May 29, 2003.

[5] According to the 646 Patent, rendering amphetamines resistant to abuse, particularly by parenteral routes such as snorting or injecting, adds considerable value to this otherwise effective and beneficial prescription medication. Although formulations exist that provide sustained release, they have several shortcomings, including uneven release and the potential for abuse. There is therefore a need for an abuse-resistant dosage form of amphetamine which is therapeutically effective. There is also a need for an amphetamine dosage form which provides sustained release and sustained therapeutic effect.

[6] The 646 Patent claims to address both of these needs with the invention LDX. This is a compound that comprises amphetamine covalently bound to a chemical moiety in a manner that diminishes or eliminates the pharmacological activity of amphetamine until it is released. LDX is a prodrug, *i.e.*, a molecule which is converted into its active form in the body by normal metabolic processes.

[7] Release of amphetamine following the oral administration of LDX occurs gradually over an extended period of time, thereby eliminating the spiking of drug levels. When taken at doses above the intended prescription, the bioavailability of amphetamine, including peak levels and the total amount of drug absorbed, is substantially decreased, thereby decreasing the potential for oral overdose. LDX is also resistant to tampering, and to abuse by parenteral routes of administration. LDX therefore provides a stimulant-based treatment for ADHD with substantially decreased abuse liability compared to other stimulant treatments.

[8] The issues raised in these proceedings are whether the specified claims of the 646 Patent are valid; if so, whether they are infringed by the Plaintiff's/Respondent's generic product; and whether the Minister of Health should be prohibited from issuing a Notice of Compliance [NOC] to the Plaintiff/Respondent for its generic product under the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 [*PM(NOC) Regulations*], promulgated under the *Patent Act*, RSC 1985, c P-4.

[9] For the reasons that follow, I conclude that the specified claims of the 646 Patent are not invalid on any of the asserted grounds of anticipation, obviousness, overbreadth, or insufficiency of specification. However, the 646 Patent has not been infringed by the Plaintiff's/Respondent's manufacture and retention of its generic product for experimental or regulatory use. Finally, the Minister of Health should be prohibited from issuing a NOC to the Plaintiff/Respondent for its generic product.

II. Background

A. *Parties*

[10] Apotex Inc [Apotex] is a generic pharmaceutical company incorporated under the laws of Ontario.

[11] Shire LLC is a company incorporated in the United States of America, and the owner of the 646 Patent. Shire Pharma Canada ULC is authorized to sell LDX capsules in Canada under the trade name Vyvanse.

[12] Shire Pharma Canada ULC is a company incorporated under the laws of Canada. Shire LLC and Shire Pharma Canada ULC are wholly-owned subsidiaries of Shire PLC, a company with its head office in Ireland. Only Shire LLC and Shire Pharma Canada ULC are named as parties in the present action and application. I shall refer to them collectively as Shire.

[13] The Minister of Health is named as a Respondent in Court File No. T-998-16, but has not participated in these proceedings.

B. *Pleadings and History of the Proceedings*

[14] On February 11, 2016, Apotex filed an abbreviated new drug submission with Health Canada seeking a NOC to manufacture and sell Apo-Lisdexamfetamine, a generic version of Vyvanse.

[15] On March 24, 2016, Apotex served a first Notice of Allegation [NOA] upon Shire pursuant to s 5(3) of the *PM(NOC) Regulations*. Shire responded to the NOA by filing an application in this Court pursuant to s 6(1) of the *PM(NOC) Regulations* for an order prohibiting the Minister of Health from granting a NOC to Apotex until the expiry of the 646 Patent (Court File No. T-723-16). Apotex served a second NOA on Shire on April 7, 2016. Shire again responded with a prohibition application (Court File No. T-816-16). On June 20, 2016, these proceedings were dismissed as moot following Apotex's withdrawal of both NOAs.

[16] Apotex served Shire with a third NOA on May 13, 2016. Shire responded with the prohibition application that forms a part of these proceedings [T-998-16, or the Prohibition Application].

[17] On February 27, 2018, Apotex served Shire with a fourth NOA, pertaining to 10 mg capsules of Apo-Lisdexamfetamine.

[18] Shire initially claimed that Apotex's service of multiple NOAs, causing Shire to respond with numerous prohibition applications and potentially extending the timeframe for the assessment of damages pursuant to s 8 of the *PM(NOC) Regulations*, amounted to an abuse of process. Shire subsequently resiled from this position, while reserving its right to address the procedural history in its submissions on costs.

[19] On July 4, 2016, Apotex commenced an action against Shire pursuant to s 60 of the *Patent Act* for declarations that the 646 Patent is invalid and, in any event, Apotex's proposed

generic product will not infringe any valid claim of the 646 Patent [T-1056-16, or the Impeachment Action].

[20] The Impeachment Action and the Prohibition Application were consolidated pursuant to the order of Prothonotary Mireille Tabib dated October 3, 2016. Prothonotary Tabib directed that T-998-16 and T-1056-16 be heard together, and that T-998-16 be decided on the basis of the evidence adduced in T-1056-16, subject to relevance. Apotex appealed the consolidation order, which was upheld by Justice Cecily Strickland on February 6, 2017.

[21] The present proceedings are governed by the NOA dated May 12, 2016; the Prohibition Application dated June 24, 2016; the Second Further Amended Statement of Claim dated March 22, 2018; the Further Amended Statement of Defence and Counterclaim dated April 6, 2018; the Second Further Amended Reply and Defence to Counterclaim dated April 12, 2018; and the Further Amended Reply to Defence of Counterclaim dated December 11, 2017.

C. *Foreign Proceedings*

[22] Courts and tribunals in other countries have considered counterparts of the 646 Patent, and have consistently affirmed their validity: *Shire LLC v Amneal Pharmaceuticals, LLC,* 2015 US App LEXIS 16908 (NJ Dist Ct); *Shire LLC v Amneal Pharmaceuticals, LCC* (2015), 802 F.3d 1301 (Dist Ct App); *Shire LLC v Generics [UK] Limited* (2014), App No 04 753 925.9 (EPO (Opp Div)); *Generics [UK] Limited v Shire LLC* (2016), Case No T 2277/14 - 3.3.07 (EPO (App Board)). Shire notes that the proceedings in other countries were concerned with questions of novelty and obviousness, and an Australian patent relied upon by Apotex in these

proceedings, “Amino Carboxylic Acid Amides and Process for the Manufacture Thereof,” AU Patent No 54168/65 (20 January 1965) [AU 168], figured prominently in the foreign proceedings as well.

[23] Shire acknowledges that the factual records and applicable law may have differed in the foreign proceedings, but nevertheless argues that this Court should regard them as “instructive”. Shire cites *Harvard College v Canada*, 2002 SCC 76 at paragraph 13 [*Harvard College*] for the proposition that “[t]he mobility of capital and technology makes it desirable that comparable jurisdictions with comparable intellectual property legislation arrive (to the extent permitted by the specifics of their own laws) at similar legal results”.

[24] Apotex responds that in *Harvard College*, the Supreme Court of Canada ultimately endorsed the “discordant note” sounded by the Commissioner of Patents in refusing a patent for a higher life form, specifically a genetically-altered mouse useful for cancer research. Consistent with that decision, this Court must decide the legal issues raised by these proceedings in accordance with the factual record and Canada’s own laws.

[25] I agree with Apotex. In reaching the conclusions below, I have placed no reliance on the decisions of foreign jurisdictions regarding patents that are said to be comparable to the 646 Patent.

III. The 646 Patent

[26] The 646 Patent describes the field of invention as follows:

> [002] The invention relates to amphetamine compounds, compositions and methods of delivery and use comprising amphetamine covalently bound to a chemical moiety.
>
> [003] The invention relates to compounds comprised of amphetamine covalently bound to a chemical moiety in a manner that diminishes or eliminates pharmacological activity of amphetamine until released. The conjugates are stable in tests that simulate procedures likely to be used by illicit chemists in attempts to release amphetamine. The invention further provides for methods of therapeutic delivery of amphetamine compositions by oral administration. Additionally, release of amphetamine following oral administration occurs gradually over an extended period of time thereby eliminating spiking of drug levels. When taken at doses above the intended prescription, the bioavailability of amphetamine, including peak levels and total amount of drug absorbed, is substantially decreased. This decreases the potential for amphetamine abuse which often entails the use of extreme doses (1 g or more a day). The compositions are also resistant to abuse by parenteral routes of administration, such as intravenous · "shooting", intranasal "snorting", or inhalation "smoking", that are often employed in illicit use. The invention thus provides a stimulant based treatment for certain disorders, such as attention deficit hyperactivity disorder (ADHD), which is commonly treated with amphetamine. Treatment of ADHD with compositions of the invention results in substantially decreased abuse liability as compared to existing stimulant treatments.

[27] According to the Background of the Invention, the invention is directed to an anti-abuse/sustained release formulation of amphetamine which maintains its therapeutic effectiveness when administered orally. The invention further relates to formulations which diminish or reduce the euphoric effect of amphetamine while maintaining therapeutically effective blood concentrations following oral administration.

[28] The Background of the Invention notes that potent central nervous system [CNS] stimulants have been used for decades to treat children with ADHD. However, the potential for abuse is a major drawback. This has earned amphetamines Schedule II status under the United States *Controlled Substances Act*, a classification that is reserved for drugs that have an accepted medical use but the highest potential for abuse. Adderall XR, another amphetamine-based ADHD medication manufactured and sold by Shire, is a product with increased abuse liability relative to single dose tablets. This is due to the higher concentration of amphetamine in the extended release formulation, and the potential for release of the full amount of the active pharmaceutical ingredient upon crushing. It may be possible for substance abusers to obtain a high dose of the pharmaceutical with rapid onset by snorting the powder or dissolving it in water and injecting it.

[29] The Background of the Invention asserts that rendering amphetamines resistant to abuse, particularly by parenteral routes such as snorting or injecting, would provide considerable value to this otherwise effective and beneficial prescription medication. Although formulations have been successfully used to manufacture dosage forms which demonstrate sustained release properties, these formulations are subject to several shortcomings, including uneven release, and are subject to abuse. The need therefore exists for an abuse-resistant dosage form of amphetamine which is therapeutically effective. Further, the need exists for an amphetamine dosage form which provides sustained release and sustained therapeutic effect.

[30] The Summary of the Invention states that the invention provides covalent attachment of amphetamine and derivatives or analogs thereof to a variety of chemical moieties. The chemical

moieties may include any substance which results in a prodrug form. The chemical moieties may be amino acids, peptides, glycopeptides, carbohydrates, nucleosides, or vitamins. The chemical moiety is covalently attached either directly or indirectly through a linker to the amphetamine. The site of attachment is typically determined by the functional group(s) available on the amphetamine.

[31] Covalent attachment of a chemical moiety to amphetamine can decrease its pharmacological activity when administered through injection or intranasally. Compositions of the invention provide amphetamine covalently attached to a chemical moiety which remains orally bioavailable. The bioavailability is a result of the hydrolysis of the covalent linkage following oral administration. Hydrolysis is time-dependent, thereby allowing amphetamine to become available in its active form over an extended period of time. In one embodiment, the composition provides oral bioavailability which resembles the pharmacokinetics observed for extended release formulations. In another embodiment, release of amphetamine is diminished or eliminated when delivered by parenteral routes. Other embodiments are also described.

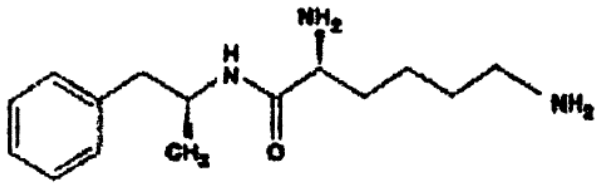
[32] The 646 Patent then provides a Detailed Description of the Invention and accompanying drawings. The claims of the 646 Patent, which number 51 in total, follow.

IV. Claims in Issue

[33] Shire alleges infringement of claims 1 to 5, 8, 10 to 12, 22, 24 to 30, 33 to 36, and 43 of the 646 Patent. Apotex challenges the validity of only these claims.

[34] Claims 1 to 5 describe compounds:

> 1. A compound selected from the group consisting of L-lysine-d-amphetamine and a pharmaceutically acceptable salt thereof.
>
> 2. The compound of claim 1, wherein the compound is L-lysine-d-amphetamine.
>
> 3. The compound of claim 1, wherein the compound is L-lysine-d-amphetamine mesylate.
>
> 4. The compound of claim 1, wherein the compound is L-lysine-d-amphetamine hydrochloride.
>
> 5. The compound of any one of claims 1 to 4 wherein the L-lysine-d-amphetamine is defined by:



[35] Claim 8 describes a composition:

> 8. A pharmaceutical composition comprising L-lysine-d-amphetamine mesylate and one or more pharmaceutically acceptable additives.

[36] Claims 10 to 12 describe compositions:

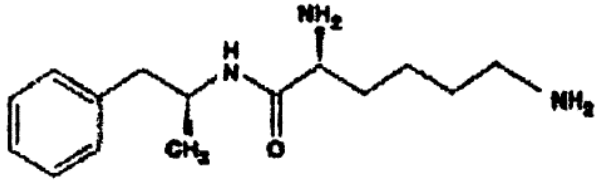
> 10. The pharmaceutical composition according to any one of claims 6-9, wherein the composition provides release of amphetamine as an active from the compound following oral administration.
>
> 11. The pharmaceutical composition according to any one of claims 6-9, wherein the L-lysine-d-amphetamine or a

pharmaceutically acceptable salt thereof provides a therapeutically effective amount of amphetamine.

12. The pharmaceutical composition of claim 11, wherein the L-lysine-d-amphetamine or a pharmaceutically acceptable salt thereof provides a reduced C_{max} of amphetamine as compared to amphetamine alone.

[37] Claim 22 describes a composition:

22. The pharmaceutical composition of any one of claims 7 to 21 wherein the L-lysine-d-amphetamine is defined by:



[38] Claims 24 to 30 describe compositions:

24. The pharmaceutical composition of any one of claims 6-15, wherein said compound is present in an amount of from 10 to 250 mg.

25. The pharmaceutical composition of any one of claims 6-15, wherein said compound is present in an amount of 20 mg.

26. The pharmaceutical composition of any one of claims 6-21, wherein said compound is present in an amount of 30 mg.

27. The pharmaceutical composition of any one of claims 6-21, wherein said compound is present in an amount of 40 mg.

28. The pharmaceutical composition of any one of claims 6-21, wherein said compound is present in an amount of 50 mg.

29. The pharmaceutical composition of any one of claims 6-21, wherein said compound is present in an amount of 60 mg.

> 30. The pharmaceutical composition of any one of claims 6-21, wherein said compound is present in an amount of 70 mg.

[39] Claims 33 to 36 describe uses:

> 33. Use of the compound of any one of claims 1-5 for the preparation of a medicament for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in a subject.
>
> 34. Use of the compound of any one of claims 1-5 for the treatment of ADHD in a subject.
>
> 35. The use according to claim 33 or 34, wherein the subject is an adult.
>
> 36. The use according to claims 33 or 34, wherein the subject is a human.

[40] Claim 43 describes a use:

> 43. The use according to any one of claims 33-42, wherein the compound is for administration once daily.

V. Issues

[41] The issues raised in these proceedings are whether the specified claims of the 646 Patent are valid; if so, whether they are infringed by Apotex's generic product; and whether the Minister of Health should be prohibited from issuing a NOC to Apotex for its generic product.

A. *Validity*

[42] Apotex alleges that the specified claims of the 646 Patent are invalid based on four grounds: obviousness, anticipation, overbreadth, and insufficiency of specification.

B. *Infringement*

[43] Shire alleges that Apotex has infringed the specified claims of the 646 Patent by manufacturing and/or retaining between 918,707 and 3,409,337 capsules of its generic product. In response, Apotex relies on the experimental and regulatory use exception recognized in ss 55.2(1) and (6) of the *Patent Act* and at common law.

C. *Prohibition Application*

[44] Shire seeks an order prohibiting the Minister of Health from issuing a NOC to Apotex, pursuant to s 6(1) of the *PM(NOC) Regulations*, on the ground that Apo-Lisdexamfetamine infringes the specified claims of the 646 Patent.

VI. Evidence

A. *Fact and Expert Witnesses*

(1) Apotex's Witnesses

[45] Apotex called the following witnesses to testify in these proceedings.

[46] **Dr. Robert Langer**. Dr. Langer is a David H. Koch Institute Professor at the Massachusetts Institute of Technology [MIT]. He holds appointments at the Department of Chemical Engineering at MIT, Whitaker College of Health Sciences Technology and Management, and the MIT Cancer Institute. He is also affiliated with the Children's Hospital Medical Center at Harvard Medical School. Dr. Langer was qualified as an expert in chemical

and biomedical engineering, pharmaceutical chemistry, drug design and formulation and drug delivery systems, including targeted drug delivery and controlled release applications.

[47] **Dr. Brian Marron**. Dr. Marron is the President and Owner of Brian Marron Drug Discovery Consulting LLC. He was qualified as an expert in synthetic organic chemistry, medicinal chemistry and the discovery, design and development of drugs.

[48] **Mr. Gordon Fahner**. Mr. Fahner is the Senior Vice President, Global Finance at Apotex. He was called as a fact witness.

(2) Shire's Witnesses

[49] Shire called the following witnesses to testify in these proceedings.

[50] **Dr. Travis Mickle**. Dr. Mickle is listed as a named inventor on the 646 Patent. He is currently the President, Chief Executive Officer and Chairman of the Board of KemPharm, a publicly-traded pharmaceutical company with its headquarters in Coralville, Iowa. He was called as a fact witness.

[51] **Dr. Scott Moncrief**. Dr. Moncrief is listed as a named inventor on the 646 Patent. He is a biologist who was formerly the head of animal testing at New River Pharmaceuticals [New River]. He was called as a fact witness.

[52] **Dr. Michael Eldon**. Dr. Eldon is a consultant specializing in pre-clinical and clinical pharmacology, pharmacokinetics and pharmacodynamics. He is also the Principal Scientific Fellow at Nektar Therapeutics, a publicly-traded pharmaceutical company with its headquarters in San Francisco, California. Dr. Eldon was qualified as an expert in pre-clinical and clinical pharmacology, pharmacokinetics and pharmacodynamics, drug discovery, drug development, translational sciences, and the design and evaluation of drugs with reduced-abuse potential.

[53] **Dr. Bernd Clement**. Dr. Clement is Professor of Pharmaceutical and Medicinal Chemistry, and one of the Directors of the Pharmaceutical Institute at the University of Kiel, Germany. He was qualified as an expert in pharmaceutical and medicinal chemistry, including organic chemistry, synthetic chemistry, pharmacokinetics and pharmaceutics, and also drug discovery and development, and prodrugs.

B. *Observations Regarding the Evidence*

[54] To their credit, the parties largely agreed upon the qualifications of the witnesses who were called to give expert opinion evidence. However, Apotex questioned the depth of Dr. Eldon's expertise in the design and development of abuse-resistant drugs, and the depth of Dr. Clement's expertise in organic and synthetic chemistry, pharmacokinetics, pharmaceutics and drug development. I ultimately agreed to qualify Drs. Eldon and Clement in the manner proposed by Shire, with only minor adjustment to the description of qualifications tendered for Dr. Clement. In accepting the expertise of Drs. Eldon and Clement, I applied the test for expert opinion evidence articulated by the Supreme Court of Canada in *White Burgess Langille Inman v Abbott and Haliburton Co*, 2015 SCC 23 at paragraph 19: (1) relevance; (2) necessity in assisting

the trier of fact; (3) absence of an exclusionary rule; and (4) a properly qualified expert. With respect to the last of these points, I observed that the threshold for establishing expertise is relatively low: the capacity to provide information "which is likely to be outside the experience and knowledge of a judge or jury" (*R v Mohan*, [1994] 2 SCR 9 at 23). Once qualified, the depth of a particular witness' expertise, particularly in comparison to that of a competing expert witness, is a matter of weight.

[55] I found all of the witnesses called in these proceedings to be generally credible. The experts presented impressive qualifications, and all witnesses provided useful information. Unfortunately, the experts called by both parties sometimes exhibited a tendency to provide short, direct answers in examination in chief, and considerably longer, less direct answers in cross-examination. While this did not detract from their credibility, it did sometimes raise questions regarding their impartiality.

[56] Despite these reservations, I am not prepared to wholly reject or discount the evidence of any witness who was called to testify in these proceedings. My reasons for preferring some witnesses' evidence over that of others are explained in the analysis that follows.

VII. Claims Construction

A. *Legal Principles and Relevant Dates*

[57] The first step in a patent suit is to construe the claims in order to give them meaning and determine their scope (*Whirlpool Corp v Camco Inc*, 2000 SCC 67 at para 43 [*Whirlpool*]). The relevant date for construing the claims is the date of publication of the patent application:

January 6, 2005 (*Whirlpool* at paras 54-55). The Court must examine the description contained in the patent to identify its "essential elements", and may be aided by expert evidence regarding the meaning of specific terms (*Whirlpool* at paras 43, 45, 57).

[58] The canons of claims construction may be found in the Supreme Court of Canada's decisions in *Whirlpool* at paragraphs 49 to 55 and *Free World Trust v Électro Santé Inc*, 2000 SCC 66 [*Free World Trust*] at paragraphs 44 to 54. They are the following:

(a) claims are to be read in an informed and purposive way with a mind willing to understand, viewed through the eyes of the person skilled in the art as of the date of publication having regard to the common general knowledge;

(b) adherence to the language of the claims allows them to be read in the manner the inventor is presumed to have intended, and in a way that is sympathetic to accomplishing the inventor's purpose, which promotes both fairness and predictability; and

(c) the whole of the specification should be considered to ascertain the nature of the invention, and the construction of claims must be neither benevolent nor harsh, but should instead be reasonable and fair to both the patentee and the public.

B. *Person of Ordinary Skill in the Art*

[59] In order to construe the claims in issue, the Court must define the Person of Ordinary Skill in the Art [PSIA]. This is "the person to whom the patent is said to be addressed, through whose eyes the Court is to read the patent, and who stands as the criterion for determination of obviousness" (*Amgen Canada Inc v Apotex Inc*, 2015 FC 1261 at para 42).

[60] The expert witnesses called by both parties were in substantial agreement that the PSIA is a drug development team with expertise in medicinal chemistry, pharmacology, pharmaceutical formulation and medicine. Shire described the members of the team as having "knowledge of (a) medicinal chemistry; (b) pharmaceutical formulation; (c) pharmacology; and (d) the treatment of ADHD." Each of the team members would have an advanced degree such as a PhD or MD, and would have approximately three to five years of work experience.

C. *Common General Knowledge of the PSIA*

[61] The patent must be construed taking into account the "common general knowledge" shared by persons skilled in the art (*Free World Trust* at para 44; *Whirlpool* at para 53). This is the knowledge possessed by the PSIA at the relevant time, and includes what the PSIA would reasonably be expected to know (*Sanofi-Synthelabo Canada Inc v Apotex Inc*, 2008 SCC 61 at para 70 [*Sanofi-Synthelabo*]; *Whirlpool* at para 74). The common general knowledge of the PSIA must be established on a balance of probabilities, and cannot be assumed (*Uponor AB v Heatlink Group Inc*, 2016 FC 320 at para 47 [*Uponor AB*]).

[62] The assessment of common general knowledge is governed by the principles found in *Eli Lilly & Co v Apotex Inc*, 2009 FC 991 at paragraph 97 and *General Tire & Rubber Co v Firestone Tyre & Rubber Co*, [1972] RPC 457 (UKHL) at pages 482 to 483:

(a) the common general knowledge imputed to the PSIA must be carefully distinguished from what in patent law is regarded as public knowledge;

(b) common general knowledge is a different concept derived from a common sense approach to the practical question of what would in fact be known to an appropriately skilled addressee – the sort of person, good at his or her job, who could be found in real life;

(c) individual patent specifications and their contents do not normally form part of the relevant common general knowledge, although there may be specifications which are so well known that they do form part of the common general knowledge, particularly in certain industries; and

(d) regarding scientific papers generally:

i. it is not sufficient to prove common general knowledge that a particular disclosure is made in an article, or series of articles, or in a scientific journal, no matter how wide the circulation of that journal may be, in the absence of

any evidence that the disclosure is accepted generally by those who are engaged in the art to which the disclosure relates;

ii. a piece of particular knowledge as disclosed in a scientific paper does not become common general knowledge merely because it is widely read, and still less because it is widely circulated;

iii. such a piece of knowledge only becomes general knowledge when it is generally known and accepted without question by the bulk of those who are engaged in the particular art; in other words, when it becomes part of their common stock of knowledge relating to the art; and

iv. it is difficult to appreciate how the use of something which has in fact never been used in a particular art can ever be held to be common general knowledge in the art.

[63] Shire argues that prior art in an unrelated field does not form part of the common general knowledge unless it is proven to be something the PSIA would consider. Hindsight is prohibited. Shire relies on Justice Michael Manson's recent decision in *Frac Shack Inc v AFD Petroleum Ltd*, 2017 FC 104 at paragraph 146:

> […] Public knowledge is theoretical and includes each and every patent specification published, however unlikely to be looked at and in whatever language it is written. Common general knowledge, in contrast, is derived from a common sense approach to the question of what would be known, in fact, to an

> appropriately skilled person that could be found in real life, who is good at his or her job.

[64] Apotex accepts that the patent specifications it relies upon as prior art in support of its arguments regarding anticipation and obviousness do not form a part of the PSIA's common general knowledge. It does, however, rely on the discussions of prodrugs contained in scientific papers published prior to May 2003.

[65] Both parties assessed the common general knowledge as of May 2003, the relevant date for the assessment of obviousness. In its closing submissions, Shire commented in a footnote that "[t]he same teachings would have been applicable as of June 1, 2004 (the filing date) and January 6, 2005 (the publication date, the relevant date for claims construction)".

[66] The expert witnesses who testified in these proceedings were in substantial agreement that the common general knowledge of the PSIA would include the following:

(a) ADHD is a common neurobehavioural disorder in both children and adults that is characterized by a persistent pattern of hyperactivity, impulsivity and inattention.

(b) Physicians could treat the symptoms of ADHD with stimulants, including amphetamine.

(c) Amphetamine products were available as immediate and sustained release formulations, each of which produced different durations of action.

(d) In sustained release formulations, the dosage form was designed to release the drug at a continuous and controlled rate for a longer period than would normally be achieved using an immediate release formulation.

(e) One significant drawback of both immediate and sustained release formulations of amphetamine was their potential for abuse. Those who abused amphetamine wished to attain the euphoria that results from exposure to a rapid and elevated dose. In pharmacokinetic terms, abusers were seeking a short time to maximum plasma concentration [T_{max}] and a high peak plasma concentration [C_{max}] of amphetamine.

(f) As of May 2003, the PSIA would have recognized the need for an amphetamine product that could not be abused by crushing and snorting, dissolving and injecting, or taking an oral overdose.

(g) The PSIA would have understood that one of the known strategies to reduce the abuse of amphetamine was to reduce its C_{max} and extend its T_{max}.

(h) As of May 2003, no known formulation could address all principal routes of abuse of amphetamine (*i.e.*, crushing and snorting, dissolving and injection, oral overdose). Adderall XR was an extended release formulation which reduced C_{max} and extended T_{max}, but did not provide a means to prevent abusers from circumventing the extended release mechanism, either by crushing or dissolution.

(i) Concerta was a known methylphenidate composition that was designed to form a paste when crushed so it could not be snorted. However, Concerta would dissolve in water and release its active ingredient for injection or swallowing, and thus its abuse protection was limited. Further, the extended release mechanism in Concerta could be undone by crushing or chewing the tablet.

(j) An irritant could be added to a formulation that was intended to sting if snorted or injected. However, the irritant would do nothing to alter the pharmacokinetics of amphetamine, or stop someone from dissolving the drug and ingesting it orally. No formulation containing an irritant to discourage abuse had ever reached the market.

[67] The principal area of dispute is whether the PSIA's common general knowledge would encompass prodrugs and, if so, to what extent.

[68] According to Apotex, as of May 2003, prodrugs were an established concept extensively discussed in the literature as a way of developing a product with better properties to overcome barriers to a drug's usefulness, including its pharmacokinetic limitations. The field matured in the 1970s, when a number of comprehensive reviews appeared and presented the rational basis for prodrug design as applied to many drugs. Specific applications for prodrugs included controlling the release rate by reducing the C_{max}, optimizing the pharmacokinetics, and extending the duration of action of a wide range of different drug types.

[69] Shire says that, based on the scientific literature of the time, the use of prodrugs to achieve sustained release or deter abuse would not form a part of the common general knowledge of those who were engaged in the art to which the disclosure of the 646 Patent relates; namely, a compound that provides sustained release of a therapeutic quantity of amphetamine and is also resistant to abuse. A more detailed discussion of the relevant scientific literature may be found under the heading Differences between the Prior Art and the Invention, below. While prodrugs were a known concept in May 2003, using prodrugs to control release was understood to be difficult and unpredictable, and was generally avoided. There was no known use of a prodrug to render a drug less susceptible to abuse.

[70] I generally prefer the articulation of the common general knowledge proposed by Shire, which in my view is better supported by the scientific literature cited by the parties. I therefore conclude that the common general knowledge of the PSIA is as described in paragraph 66, above. However, I also accept Apotex's assertion that the PSIA's common general knowledge would include an awareness of the development of prodrugs to overcome barriers to a drug's usefulness, including its pharmacokinetic limitations. This is consistent with Shire's acknowledgment that prodrugs were an established concept as of May 2003.

D. *Claim Term Needing Construction*

[71] Patent construction is a matter of law for the judge. Expert evidence is necessary only where the meaning of a term is not apparent based on a reading of the patent specification (*Johnson & Johnson Inc v Boston Scientific Ltd*, 2008 FC 552 at para 92).

[72] The parties both maintain that the claims in issue are clear and unambiguous. However, they disagree about the meaning of the term "L-lysine-d-amphetamine". Paragraph 95 of the 646 Patent defines "amphetamine" as "any of the sympathomimetic phenethylamine derivatives which has central nervous system stimulant activity". Apotex argues that, with the exception of claims 5 and 22 (which show LDX in picture form), the claims of the 646 Patent that refer to "L-lysine-d-amphetamine" include a group of conjugates of L-lysine bound to any sympathomimetic phenethylamine derivative, as defined in paragraph 95.

[73] Apotex says its proposed construction of "L-lysine-d-amphetamine" avoids the redundancy of claims 5 and 22. This construction is also consistent with paragraph 105 of the 646 Patent, which states: "[f]or each of the recited embodiments, the amphetamine may be any of the above discussed stimulants. In one embodiment, the amphetamine is dextroamphetamine or methylphenidate".

[74] Shire responds that "amphetamine" when used alone is given the expanded definition in paragraph 95 of the 646 Patent. However, "L-lysine-d-amphetamine" is defined in paragraph 100 to exclude the various sympathomimetic phenethylamine derivatives described in paragraph 95. Moreover, Dr. Langer acknowledged that all other references to "L-lysine-d-amphetamine" in the 646 Patent specify the compound LDX. Importantly, Dr. Langer admitted that it does not make sense from a chemical perspective to have "L-lysine-d-" followed by any and all of the amphetamine variations found in paragraph 95. Apotex's proposed construction includes some compounds that cannot exist. Furthermore, Example 2 of the 646 Patent discusses the synthesis of "L-lysine-d-amphetamine" and refers the reader to Figure 2, which clearly shows LDX as

having the structure of L-lysine bound to d-amphetamine, rather than any other sympathomimetic phenethylamine derivative.

[75] I prefer the construction advocated by Shire. As a general rule, claims should be construed to avoid redundancy. However, claims may be repeated, and courts may even read claims as redundant when it is reasonable to do so (*Ratiopharm Inc v Canada (Health)*, 2007 FCA 83 at para 33; *Pfizer Canada Inc v Apotex Inc*, 2017 FC 774 at para 174). Here, the better view is that "L-lysine-d-amphetamine", as this term is used in the claims, means only LDX. Some of the claims are verbally descriptive, while some are visually illustrative (*e.g.*, Claims 5 and 22). Put simply, the claims of the 646 Patent describe LDX and its salts in two different ways. This construction avoids redundancy, as well as the absurdity of including within the claims compounds that cannot exist.

VIII. Validity

[76] Subsection 43(2) of the *Patent Act* states that a patent is presumed to be valid in the absence of evidence to the contrary. A party alleging invalidity bears the burden of establishing this on a balance of probabilities. The burden therefore falls upon Apotex.

A. *Developments Leading to the Patent*

[77] The invention claimed by the 646 Patent was developed by New River, formerly Lotus Pharmaceuticals, a small pharmaceutical company founded in Radford, Virginia in the mid-1990s. New River focused its research on developing prodrugs, and was acquired by Shire in April 2007.

[78] According to Shire, the antecedents of the 646 Patent lie in New River's attempts to create a thyroid hormone prodrug by linking the active ingredient to a long chain polypeptide of glutamic acid. However, after making and testing numerous polypeptide prodrugs, the New River researchers concluded that their approach did not work. They then redirected their efforts towards smaller, discrete prodrugs using single, di- and tri- amino acids, as well as non-peptide promoieties such as sugars, fats and vitamins.

[79] In the summer of 2002, a former employee of Shire named Suma Krishnan came to work at New River. She recommended that New River explore conjugates of d-amphetamine, in the hope that this might ultimately be of interest to Shire. Early testing with glutamic acid demonstrated that the parent compound could be released *in vivo*. However, it was not considered to be a viable candidate for a finished product, because its pharmacokinetics were not significantly different from the parent compound.

[80] Not everyone was in favour of continuing research in this area, but the team nevertheless synthesized numerous amphetamine conjugates to examine their properties. It is unclear precisely when New River settled on the goals of sustained release and abuse resistance. However, once these goals were identified, a tri-glycine promoiety covalently bound to d-amphetamine emerged as a leading contender.

[81] LDX was one of the last single amino acid conjugates tested by New River. The pharmacokinetics of LDX were measured following oral, intranasal and intravenous administration in rats and dogs. Oral administration demonstrated potential therapeutic

usefulness, while intranasal and intravenous administration demonstrated potential for abuse reduction. Shire says the discovery of these properties was both significant and unexpected.

[82] New River sought to confirm the advantageous properties of LDX through further testing. Much of this work is described in the Investigational New Drug Application [IND] submitted to the United States Food and Drug Administration [FDA] on March 22, 2004. The IND was approved by the FDA, permitting human clinical trials to compare the pharmacokinetics of LDX with Adderall XR and Dexedrine Spansules. These trials established that LDX offered a pharmacokinetic profile similar to Adderall XR.

[83] Shire's application for the 646 Patent was filed on June 1, 2004. LDX, under the trade name Vyvanse, was approved by Health Canada on February 19, 2009 for the treatment of ADHD.

B. *Selection Patents*

(1) Legal Principles

[84] In *Sanofi-Synthelabo* at paragraph 9, Justice Marshall Rothstein provided the following introduction to selection patents:

> [9] The *locus classicus* describing selection patents is the decision of Maugham J. in *In re I.G. Farbenindustrie A.G.'s Patents* (1930), 47 R.P.C. 289 (Ch. D.). At p. 321, he explained that in the field of chemical patents (which would of course include pharmaceutical compounds), there are often two "sharply divided classes". The first class of patents, which he called originating patents, are based on an originating invention, namely, the discovery of a new

> reaction or a new compound. The second class comprises patents based on a selection of compounds from those described in general terms and claimed in the originating patent. Maugham J. cautioned that the selected compounds cannot have been made before, or the selection patent "would fail for want of novelty". But if the selected compound is "novel" and "possess[es] a special property of an unexpected character", the required "inventive" step would be satisfied (p. 321). At p. 322, Maugham J. stated that a selection patent "does not in its nature differ from any other patent".

[85] Justice Rothstein identified three conditions that must be satisfied for a selection patent to be valid (*Sanofi-Synthelabo* at para 10):

> 1. There must be a substantial advantage to be secured or disadvantage to be avoided by the use of the selected members.
>
> 2. The whole of the selected members (subject to "a few exceptions here and there") possess the advantage in question.
>
> 3. The selection must be in respect of a quality of a special character peculiar to the selected group. If further research revealed a small number of unselected compounds possessing the same advantage, that would not invalidate the selection patent. However, if research showed that a larger number of unselected compounds possessed the same advantage, the quality of the compound claimed in the selection patent would not be of a special character.

[86] The specification of a selection patent must define in clear terms the nature of the characteristic which the patentee alleges to be possessed by the selection for which he claims a monopoly (*Sanofi-Synthelabo* at para 114).

[87] An assertion that the conditions for a selection patent have not been met is not an independent basis upon which to attack the validity of a patent. Rather, the conditions for a valid selection patent serve to characterize the patent and accordingly inform the analysis for the

grounds of validity set out in the *Patent Act*. A selection patent is vulnerable to attack on any of the grounds set out in the *Patent Act* (*Eli Lilly Canada Inc v Novopharm Ltd*, 2010 FCA 197 at para 27).

(2) Analysis

[88] Shire says the 646 Patent is a selection patent. Apotex disagrees.

[89] Shire maintains that LDX is selected from the class of compounds encompassed by AU 168, with the clearly described advantages of sustained release coupled with abuse resistance. According to Shire, the unselected compounds encompassed by AU 168 do not possess these advantageous properties. Moreover, Table 46 of the 646 Patent demonstrates that LDX has special advantages over other single amino acid conjugates, some (but not all) of which are encompassed by AU 168. The only compound in Table 46 that approaches the advantageous properties of LDX is GGG-d-amphetamine, which is not encompassed by AU 168.

[90] According to Apotex, the 646 Patent describes its invention as providing improvements over the parent compound (amphetamine) and related stimulants, not over other conjugates of amphetamine. Apotex says the 646 Patent provides insufficient description of its advantages over the purported genus patent to be classified as a selection from AU 168, citing *Hoffman-La Roche Ltd v Apotex Inc*, 2013 FC 718 [*Hoffman-La Roche*].

[91] *Hoffman-La Roche* concerned a NOC application rather than an impeachment action, and any appeal of the judgment by the unsuccessful patentee would likely have been moot (see

Amgen Canada Inc v Apotex Inc, 2016 FCA 196 at para 12). The patent in issue claimed the compound valganciclovir in various forms. Valganciclovir is a prodrug of ganciclovir, which was disclosed in the prior art as an antiviral medication used to treat cytomegalovirus infections such as herpes. Valganciclovir was said to offer better bioavailability than its parent compound when administered orally. The main issues were whether the patent was invalid for anticipation and obviousness.

[92] A preliminary question arose in *Hoffman-La Roche* whether the patent in issue was a selection patent. Curiously, the patentee's position appears to have evolved as the case progressed. In the words of Justice Catherine Kane, "[t]he applicant also asserts that the '721 Patent is probably, likely, or is definitely a selection patent from the genus of EP 329" (at para 33). She later observed that "[t]he assertions of the applicant and respondent and the words of the claims themselves are not determinative of whether this is a selection patent" (at para 135), and noted that "[i]n the claims of the patent there is no reference to special advantages (as there need not be) and there is no reference to it as a selection patent" (at para 161).

[93] Like the patent at issue in *Hoffman-La Roche*, the 646 Patent makes no mention of AU 168 or any other genus or originating patent. The advantageous qualities of LDX are assessed in relation to the conjugates of d-amphetamine described in Table 46, only some of which are encompassed by AU 168. The claimed advantages of LDX are principally in comparison to the parent compound amphetamine, not to other conjugates of d-amphetamine.

[94] In *Hoffman-La Roche*, the patentee argued that there was no anticipation because the previous patent did not disclose examples of its drug, did not disclose the results of any biological testing of its drug, and encompassed more than 500,000 compounds that were distinct from its drug. Justice Kane nevertheless concluded, in light of the PSIA's common general knowledge, that the identification of the drug as among the preferred class of compounds was sufficient to constitute an anticipatory disclosure, notwithstanding that it was not exemplified (at paras 230-236).

[95] *Hoffman-La Roche* has been criticized by Professor Norman Siebrasse in his online blog, Sufficient Description (Norman Siebrasse, "Time to Abandon the Doctrine of Selection Patents?" (26 July 2013), *Sufficient Description* (blog), online: <http://www.sufficientdescription.com/2013/07/time-to-abandon-doctrine-of-selection.html>). There was no dispute in that case that valganciclovir was encompassed within the very many compounds described in the genus patent. However, it was not disclosed in any of the examples. The question was whether the disclosure was sufficiently specific to anticipate. Professor Siebrasse takes issue with Justice Kane's conclusion that valganciclovir was "disclosed" by the prior patent for the purposes of the two-part test for anticipation set out in *Sanofi-Synthelabo*, which requires both disclosure and enablement. He concludes that *Hoffman-La Roche* was very similar in its facts to *Sanofi-Synthelabo*, and the two decisions cannot be reconciled.

[96] Professor Siebrasse's criticisms may be reason to approach *Hoffman-La Roche* with caution. However, in my view the case is distinguishable on its facts. As explained below, the

differences between AU 168 and the 646 Patent are more profound than those between the purported genus and selection patents at issue in *Hoffman-La Roche*.

[97] Nevertheless, Professor Siebrasse's general remarks regarding this potentially confusing area of patent law are worth bearing in mind. By statute, the basis for assessing anticipation cannot depend on whether the patent is a selection patent or not. The jurisprudence does not imply that anticipation and obviousness in respect of a selection patent are to be assessed over the genus patent from which it is a selection, rather than over the prior art read as a whole. A selection patent "does not in its nature differ from any other patent" (*Sanofi-Synthelabo* at para 9), there is no reference to selection patents in the *Patent Act*, and the conditions for a valid selection patent do not constitute an independent basis upon which to attack the validity of a patent. A selection patent, like any other patent, is therefore vulnerable to any attack set out in the *Patent Act*, but no other.

[98] Taking all of this into consideration, I am left in some doubt whether the 646 Patent may be properly characterized as a selection patent. However, as will be seen in the analysis that follows, nothing ultimately turns on this point.

C. *Anticipation*

(1) Legal Principles

[99] Pursuant to s 28.2 of the *Patent Act*, a patent claim will be invalid for anticipation if the subject matter defined by the claim was disclosed in such a manner that it became available to

the public more than one year before the filing date of the application, and was enabled to a skilled person (*Eli Lilly Canada Inc v Mylan Pharmaceuticals ULC*, 2015 FC 125 at para 145). Disclosure need not reveal an exact description of the subject matter of a claim, but must be sufficient so that, when read by a person skilled in the art and willing to understand the invention, it can be understood without undue burden, taking into account the nature of the invention (*Sanofi-Synthelabo* at para 33). The requirement of prior disclosure means that the prior patent must disclose subject matter which, if performed, would necessarily result in infringement of the patent (*Sanofi-Synthelabo* at para 25).

[100] If the disclosure requirement is satisfied, the second requirement to prove anticipation is enablement, which means that the PSIA would have been able to perform the invention. While trial and error experimentation is permitted at the enablement stage, it is not at the disclosure stage. For purposes of enablement, the question is no longer what the skilled person would think the disclosure of the prior patent meant, but whether he or she would be able to work the invention (*Sanofi-Synthelabo* at paras 26-27). The parties agree that no issue of enablement arises in this case.

(2) Analysis

[101] Apotex says that AU 168 discloses claims 1 to 5, 8, 10 to 12, 22, 24 to 30, 33 to 36 and 43 of the 646 Patent. Shire disagrees.

[102] Apotex asserts that AU 168 discloses LDX, its pharmaceutical formulation, its pharmaceutically acceptable salts, including hydrochloride and mesylate salts, and its

compositions with dosages of 20 and 50 milligrams, with the instruction to adjust dosage as needed. Apotex also maintains that AU 168 contemplates unprotected LDX: it provides instruction on how to de-protect any protected compounds; the l-series of amino acids are contemplated as an advantageous choice by formula IV; and lysine is preferred since its use generally results in end products of greater therapeutic value.

[103] Shire denies that AU 168 discloses LDX, its properties, or any of its pharmaceutically acceptable salts. Shire states that AU 168 contains no pharmacokinetic data; no mention of dosing frequency; no discussion of amphetamine abuse; and no discussion of treatment for ADHD.

[104] AU 168 discloses a very large class of d-, l-, and dl-amphetamine amino acid conjugates, both protected and unprotected. LDX is included as one of the many possible configurations in the "advantageous" class described on page 4 of AU 168. However, LDX is not included within the "especially advantageous subgenera" described on pages 5 and 6 of AU 168.

[105] According to Shire, three of the 30 Examples in AU 168 contain lysine conjugates of amphetamine, but these are either in the form of d-lysine (Examples 22 and 23) and/or in protected form (Examples 22 to 24), which Dr. Marron acknowledged would not fall within the scope of claims 1 to 5 of the 646 Patent. Shire therefore asserts that the examples do not disclose LDX or any LDX salt.

[106] The expert evidence adduced in these proceedings raises many unanswered questions regarding the invention disclosed by AU 168. It appears that the claimed invention is primarily concerned with appetite suppressants that are substantially free of CNS stimulatory activity. However, AU 168 also seems to suggest that anorexic and stimulatory effects may be "tuned" (the word chosen by Dr. Langer), and it may be possible to achieve CNS stimulation without suppressing appetite. This is not possible if the compounds envisaged by AU 168 are prodrugs that release their active pharmaceutical ingredient through enzymatic cleavage. It is common ground that the administration of amphetamine results in both CNS stimulatory and anorexic effects at similar dosage levels.

[107] AU 168 never mentions prodrugs, and no pharmacokinetic data are provided. Dr. Langer was prepared to infer that the compounds are indeed prodrugs, but Dr. Clement observed that the manner in which the compounds disclosed by AU 168 are intended to function is never explained. None of the compounds described were manufactured or tested by the inventors. It is therefore unclear whether the PSIA would understand the compounds described in AU 168 to be prodrugs that achieve their therapeutic effect by enzymatic cleavage in the body.

[108] The process of making of LDX is not disclosed by AU 168. Nor are any of the compounds encompassed by AU 168 said to provide a sustained release treatment for ADHD with, or even without, a reduced potential for abuse.

[109] I therefore conclude that Apotex has not met its burden of demonstrating that the 646 Patent is anticipated by AU 168.

D. *Obviousness*

(1) Legal Principles

[110] Pursuant to s 28.3 of the *Patent Act*, a patent cannot be issued for an invention that was obvious on the priority date to a person skilled in the art or science to which the patent pertains. The parties agree that obviousness is to be assessed as of May 29, 2003.

[111] Obviousness is generally considered to be a factual determination, or a question of mixed fact and law (*Wenzel Downhole Tools Ltd v National-Oilwell Canada Ltd*, 2012 FCA 333 at para 44). It must be assessed on a claim-by-claim basis (*Zero Spill Systems (Int'l) Inc v Heide*, 2015 FCA 115 at para 85).

[112] When considering obviousness, hindsight is prohibited. To determine whether a claim is obvious, courts generally follow the four-part test found in *Sanofi-Synthelabo* at paragraph 67:

(a) identify the notional "person skilled in the art" and the relevant common general knowledge of that person;

(b) identify the inventive concept of the claim in question or, if that cannot readily be done, construe it;

(c) identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed; and

(d) viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

[113] The fourth step of the inquiry may require consideration of whether the claimed invention was "obvious to try". This aspect of the test tends to arise in areas of endeavour where advances are often made through experimentation, and where numerous interrelated variables may affect the desired result (*Sanofi-Synthelabo* at paras 68-71). The development of pharmaceutical products is such an endeavour, and it is therefore necessary to ask whether the claimed invention in this case was "obvious to try". This involves a consideration of the following non-exhaustive factors:

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

(b) what is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?

(c) is there a motive provided in the prior art to find the solution the patent addresses?

(2) The PSIA and Common General Knowledge

[114] The PSIA and the common general knowledge are discussed under the heading Claims Construction, above.

(3) Inventive Concept of the Patent

[115] The Federal Court of Appeal has recently observed that there may be cases in which the inventive concept may be grasped without difficulty; however, because "inventive concept" is undefined, the search for it has brought considerable confusion into the law of obviousness. That uncertainty may be reduced by avoiding the inventive concept altogether, and pursuing the alternative course of construing the claim. This avoids distraction or engaging in unnecessary "satellite debate" (*Ciba Specialty Chemicals Water Treatments Limited v SNF Inc*, 2017 FCA 225 at para 77 [*Ciba*], leave to appeal to SCC refused, 37915 (June 14, 2018)).

[116] Apotex argues that, following *Ciba*, "inventive concept" should no longer be used in the obviousness analysis, pending clarification of its meaning by the Supreme Court. Rather, the question of obviousness should be determined by reference to the claims alone.

[117] In my view, this is a misreading of *Ciba*. As a matter of *stare decisis*, *Ciba* cannot be understood to have overruled *Sanofi-Synthelabo*. Furthermore, the patent in issue in *Ciba* pertained to a process, while *Sanofi-Synthelabo* concerned bare chemical compounds and therefore bears a closer resemblance to the present case. Here, there is no need to resort to the

"alternative course" endorsed by *Ciba*, because the inventive concept may be grasped without difficulty, and there is no danger of distraction or engaging in unnecessary satellite debate.

[118] According to Shire, the inventive concept of the claims in issue is the use of LDX as a once-daily administration for the treatment of ADHD, and in a manner that is less susceptible to abuse than existing amphetamine formulations. Shire argues that the inventive concept must reflect the practical problems that LDX is intended to solve: the creation of a sustained release, amphetamine-based ADHD treatment with decreased abuse potential. Shire relies on *Sanofi-Synthelabo* at paragraphs 77 and 78:

> [77] […] A bare chemical formula in a patent claim may not be sufficient to determine its inventiveness. In such cases, I think it must be acceptable to read the specification in the patent to determine the inventive concept of the claims. Of course, it is not permissible to read the specification in order to construe the claims more narrowly or widely than the text will allow.
>
> [78] In the present case, it is apparent that the inventive concept of the claims in the '777 patent is a compound useful in inhibiting platelet aggregation which has greater therapeutic effect and less toxicity than the other compounds of the '875 patent and the methods for obtaining that compound.

[119] Apotex cautions that the *Patent Act* as applied in *Sanofi-Synthelabo* did not include s 28.3, which specifically refers to "[t]he subject-matter defined by a claim". Shire responds that the same approach has been applied in many subsequent cases by both the Federal Court of Appeal and this Court (see, for example, *Apotex Inc v Allergan Inc*, 2012 FCA 308 [*Allergan*] and *Sanofi-Aventis v Apotex Inc*, 2013 FCA 186 [*Sanofi-Aventis*]). In *Allergan*, the Federal Court of Appeal held that a purposive and complete reading of the patent supported the conclusion that an improved safety profile formed part of the claimed invention (at paras 74-75).

[120] Shire suggests that another viable approach may be the "problem-solution" analysis favoured in European jurisdictions, which is consistent with the analysis prescribed by *Sanofi-Synthelabo*. This inquiry necessarily takes into account the special properties of LDX. There is no dispute among the expert witnesses called by both parties that the problem addressed by the 646 Patent is achieving a sustained release formulation of a therapeutically useful dose of amphetamine that is resistant to abuse.

[121] Apotex makes the reasonable observation that including a "once daily" administration to treat ADHD within the inventive concept is not supported by the language of the claims. Claim 44 relates to the administration of LDX more than once daily, and other claims specify that LDX may be used to treat narcolepsy and obesity, as well as ADHD.

[122] In *Sanofi-Synthelabo*, the Supreme Court identified a single inventive concept for all claims of the patent in issue. In my view, a similar approach is warranted here. I conclude that the inventive concept of the 646 Patent is a sustained release formulation of a therapeutically useful dose of amphetamine that is resistant to abuse.

(4) Differences between the Prior Art and the Invention

[123] Apotex relies on the following patent specifications and scientific papers as prior art:

(a) "Active Agent Delivery Systems and Methods for Protecting and Administering Active Agents," US Patent No 2002/0099013 A1 (22 August 2001) [US 013]; and "A Novel Pharmaceutical Compound Containing Dextroamphetamine and

Methods of Making and Using Same," Int'l Patent No WO 03/034980 A2 (14 November 2001) [WO 980]:

- US 013 and WO 980 disclose prodrugs consisting of active agents (including, among many others, amphetamine) that are covalently attached to a promoiety (including, among many others, a chain of natural amino acids that may be as short as two amino acids) to control release of the active agent. The release of the active agent is in part controlled by cleavage of the key bond.

(b) AU 168; "Method for Preparation of Aminocarboxylic Acid Amides," NL Patent No 6414901 (21 December 1964) [NL 901]; and "Procede pour la preparation d'aminocarboxamides," FR Patent No 142130 (20 January 1965) [FR 130]:

- NL 901 and FR 130 are substantially similar to AU 168. They disclose a very large class of d-, l-, and dl-amphetamine amino acid conjugates, both protected and unprotected, aimed at creating appetite suppressants that are substantially free of CNS stimulatory activity. LDX is encompassed as one of the many possible configurations. Various pharmaceutically acceptable salts, compositions and dosage strengths are also disclosed.

(c) GB Baker et al, "Carbamate Prodrugs of Phenylethylamines: A Neurochemical Investigation" (1984) 27 Proc West Pharmacol Soc 523 [Baker]; and AJ

Verbiscar et al, “Carbamate Ester Latentiation of Physiologically Active Amines” (1970) 13:6 J of Med Chem 1176 [Abood]:

- Baker and Abood teach the use of carbamate prodrugs to deliver intact prodrug to the brain, in part by increasing lipophilicity.

(d) FE King, JW Clark-Lewis & GR Smith, “Synthesis from Phthalimido-acids. Part V. Amides of Glycine, DL-Alanine, and L-Glutamic Acid with Amphetamine, Benzocaine, and Procaine” (1954) J Chem Soc 1044 [King]:

- King teaches the preparation of certain amide derivatives of amphetamine, benzocaine and procaine. With respect to amphetamine, King discusses the synthesis of glycylamphetamine hydrochloride and DL-glutamic acid amphetamine.

(e) “Abuse-Deterrent Pharmaceutical Compositions of Opioids and Other Drugs,” US Patent No 2004/0052731 A1 731 (7 July 2003) [US 731]; and “Abuse-Resistant Prodrugs of Oxycodone and Other Pharmaceuticals,” US Patent No 2004/0058946 A1 (3 July 2003) [US 946]:

- US 731 and US 946 describe the use of prodrugs to curb abuse, with US 731 including amphetamine as a preferred drug.

[124] Shire makes the following observations regarding the prior art cited by Apotex:

(a) US 013 and WO 980 teach that delivery of the active agent in certain applications is controlled in part by the unfolding of the polypeptides, not single amino acids. The patents do not include data concerning the making or testing of amphetamine conjugates, and disclose only general teachings about a very broad class of compounds. These patents teach the PSIA only that polypeptide conjugates are preferred over the excluded single amino acid conjugates to control release of the active pharmaceutical ingredient.

(b) AU 168, NL 901 and FR 130 do not explicitly use the term prodrug, and the PSIA would not understand them to describe prodrugs (see the discussion of AU 168, above). Lysine is not said to have favourable properties or advantages, and all final products are protected amino acid conjugates. The patents provide no data regarding the relative properties of the different conjugates encompassed, and teach only that unprotected compounds and lysine are less favoured than the other compounds.

(c) Baker and Abood do not explicitly seek to reduce abuse potential or obtain sustained release.

(d) There are no pharmacologic data discussed in King, nor is the word “prodrug” used.

(e) US 731 and US 946 post-date the relevant date. US 731 does not focus on prodrugs, and the reduced abuse potential is achieved very differently from the operation of LDX. US 946 relies on a two-step cleavage process, which the PSIA would understand cannot be used with amphetamine.

[125] More generally, Shire objects that the literature searches relied on by Apotex do not objectively canvass the art as a whole. The search terms used by Apotex's experts included, *inter alia*, "prodrugs" and "amino acids", betraying the hindsight inherent in the analysis conducted by Apotex's expert witnesses.

[126] Apotex says the prior art fully discloses the essential elements of the invention claimed by the 646 Patent, and there is therefore no difference between the prior art and the invention.

[127] In the alternative, Apotex argues that the differences between the starting and end points for claims 1 to 5 and 8 are: first, obtaining LDX by de-protecting N-tosyl-lisdexamfetamine to prepare LDX (as in NL 901, Example 24), or switching the D-lysine in Example 23 of NL 901 for L-lysine, or moving from a two amino acid promoiety for an amphetamine prodrug (as in US 013/WO 980) to the single amino acid promoiety, L-lysine; and second, preparing the hydrochloride and mesylate salts of LDX and including these in a composition which would be part of routine salt screening activities.

[128] With respect to claims 10 to 12, 22, and 24 to 30, in addition to the assertions respecting claims 1 to 5, Apotex argues that the differences between the prior art and the invention are the

specific dosage strengths, and the recognition that LDX is a prodrug that releases therapeutic amounts of amphetamine with a lower C_{max} than that of amphetamine alone.

[129] With respect to claims 33 to 36 and 43, in addition to the assertions respecting claims 1 to 5, Apotex argues that the differences between the prior art and the invention are the use of LDX to treat ADHD and the "once daily" dosage frequency.

[130] I am unable to accept Apotex's position regarding the differences between the prior art and the invention. A review of the scientific literature and patent specifications cited by both parties demonstrates that in May 2003, formulations were the primary, perhaps the only, method used to reduce a drug's potential for abuse. At this time, no prodrug had yet been developed as a means of reducing abuse potential. The development of prodrugs was expensive and time-consuming, in part because the FDA considers prodrugs to be new chemical entities. Even minor covalent structural changes are capable of producing major changes in the activity of a drug in an unpredictable manner, and it was therefore necessary for a new prodrug to undergo extensive testing (GS Banker & CT Rhodes, eds, *Modern Pharmaceutics*, 3rd ed, rev and expanded (New York: Marcel Dekker Inc, 1996) at 596; AA Sinkula, "Sustained drug action accomplished by the prodrug approach" in H Bundgaard, ed, *Design of Prodrugs* (Amsterdam: Elsevier, 1985) 156 at 157).

[131] Without testing, it would be impossible to predict whether any particular conjugate of amphetamine would cleave upon administration, at what rate it would cleave, whether saturation at a desired concentration would occur, or whether active transportation would occur (VJ Stella,

WNA Charman & VH Naringrekar, "Prodrugs: Do They Have Advantages in Clinical Practice?" (1985) 29 Drugs 455 at 467; NL Pochopin, *Amino Acid Amides As Water-Soluble Prodrugs of Primary Aromatic Amines* (PhD Thesis, University of Kansas and Victorian College of Pharmacy, 1991) at 141-142; RE Notari, "Pharmacokinetic aspects of prodrug design and evaluation" in H Bundgaard, ed, *Design of Prodrugs* (Amsterdam: Elsevier, 1985) 135 at 148). Furthermore, it was commonly understood that amides were too stable *in vivo* to be useful prodrug forms for amines (KE Uhrich et al, "Polymeric Systems for Controlled Drug Release" (1999) 99 Chem Rev 3181 at 3195). Alternatively, there was a risk that cleavage of an amide bond between amino acids and active ingredients could occur too quickly (NL Pochopin, WN Charman & VJ Stella, "Pharmacokinetics of Dapsone and Amino Acid Prodrugs of Dapsone" (1994) 22:5 Drug Metabolism & Disposition 770; NL Pochopin, WN Charman & VJ Stella, "Amino acid derivatives of dapsone as water-soluble prodrugs" (1995) 12 Int J Pharmaceutics 157). The area was fraught with uncertainty.

[132] I therefore conclude that the key difference between the state of the art and the inventive concept is the compound LDX and its advantageous properties. Nothing in the prior art indicated or suggested that LDX would provide a sustained release treatment of amphetamine with a reduced potential for oral, intravenous and intranasal abuse.

(5) Whether the Differences were Obvious or Required Invention

[133] According to Apotex, the prior art taught that amino acid amide prodrugs of amphetamine would be resistant to chemical hydrolysis and provide controlled release. The

PSIA would prepare LDX, among a very few other compounds, and determine its relative pharmacokinetics in routine screening tests.

[134] Apotex says the PSIA would be motivated to prepare amino acid prodrugs of amphetamine, including LDX, in an effort to obtain a form of amphetamine that was resistant to abuse by intranasal, intravenous and oral routes. The PSIA would immediately focus on prodrugs, particularly if a formulation approach had failed. The PSIA would understand that amphetamine would make a good prodrug, given its single functional group and resemblance to phenylalanine. Masking an amine with a promoiety would make the intact prodrug inactive, and the added molecular weight (and charge, depending on the promoiety chosen) of the prodrug in comparison with the active moiety would be expected to slow absorption and thus reduce abuse. Enzymatic hydrolysis would become saturated and the body's elimination mechanism would clear any excess prodrug before the active moiety was released, thereby preventing oral overdose. The PSIA would choose a natural amino acid because this would form an amide bond with amphetamine resembling a natural dipeptide, which would permit a time-dependent, enzymatic hydrolysis on ingestion without additional toxicity.

[135] Apotex maintains that the PSIA would prepare prodrugs using all 20 natural amino acid prodrugs of amphetamine and measure their relative chemical and enzymatic stability in standard assays within a few days. Alternatively, the PSIA would start with cationic amino acids (L-lysine, L-arginine, L-histidine), because they would be charged in the body and switch absorption from passive diffusion to active transport, adding a further mechanism of rate control.

[136] Shire says the analysis proposed by Apotex amounts to a series of extrapolations. The uncertainty involved at each step is ignored, as is the cumulative uncertainty of the development project as a whole. I agree.

[137] Nothing in the prior art suggested the properties of LDX, and these properties could not be predicted. The prior art taught away from single amino acid conjugates to extend release, and did not suggest this ought to work. Moreover, the prior art did not suggest the use of prodrugs for the purpose of deterring abuse. The use of prodrugs to achieve sustained release was unpredictable and complex. This is confirmed by the extensive work undertaken by New River researchers that preceded the 646 Patent.

[138] None of the prior art, with the exception of AU 168, contemplated single amino acid conjugates of amphetamine. While the PSIA may have considered the use of prodrugs to achieve sustained release, there was nothing in the prior art to suggest this would also render the drug less susceptible to abuse. Indeed, this advantageous property of LDX appears to have emerged unexpectedly in the course of New River's research.

(6) Whether the Invention was Obvious to Try

[139] Apotex says that claims 1 to 5 and 8 were obvious to try, as it was more or less self-evident that the contemplated tests would overcome the differences between the starting point and end point. The prior art taught that LDX would be a prodrug of amphetamine, would resist chemical hydrolysis (*i.e.*, tampering), and would provide sustained release by shortening C_{max} and lengthening T_{max}. Moreover, the PSIA would be aware of other extended release

products, such as Adderall XR. There would be a finite number of identifiable and predictable solutions, and the specific pharmacokinetics and relative pharmacokinetics among the 20 options would be quantified in routine testing. This would not take an excessive amount of effort, as the test procedures were common in the field and would be completed quickly and in a straightforward manner.

[140] Apotex dismisses as irrelevant Dr. Clement's opinion that a formulation approach would be the obvious first choice of the PSIA, because the existence of several obvious paths does not make choosing one such path inventive. A formulation approach would not address abuse by extraction with water, or by oral overdose.

[141] With respect to claims 10 to 12, 22, and 24 to 30, Apotex argues that inventive ingenuity would not be required, as the PSIA would understand that a prodrug's gradual release of amphetamine would decrease C_{max} relative to amphetamine alone. Apotex says this is disclosed by NL 901. Furthermore, once LDX was prepared in accordance with claims 1 to 5 and 8, it would necessarily behave in the manner described in claims 10 to 12. Dosage could be calculated based on known dosages of marketed amphetamine products.

[142] With respect to claims 33 to 36 and 43, Apotex again argues that inventive ingenuity would not be required to bridge the gap, because the PSIA would know that LDX and amphetamine could be used treat ADHD with a "once daily" administration.

[143] According to Apotex, the work of the inventors confirms that the 646 Patent was obvious. They reached the subject matter of the claims of the 646 Patent in a direct and straightforward manner, with no difficult or prolonged effort, extensive research or deliberation. Rather, the inventors adopted the precise approach envisaged by Drs. Marron and Langer, and never contemplated or pursued other methods of abuse deterrence. Apotex says that obviousness is also corroborated by the general academic literature, which encouraged the use of prodrugs long before 2003 to modify a drug's pharmacokinetic properties.

[144] The difficulty with Apotex's analysis is that there was no way of knowing what the properties of LDX might be without testing. LDX could not therefore be "obvious to try", because it was not more or less self-evident that it ought to work. This is true even if the testing may itself have been routine. In *Sanofi-Aventis,* the Federal Court of Appeal held at paragraph 81 that the unknown nature of the properties was fatal to the "obvious to try" analysis, even though the means of ascertaining these properties was part of the common general knowledge:

> [81] […] Put another way, the distance between the common general knowledge and the inventive concept of the '777 Patent could not be bridged by routine experimentation since the results to be obtained were unknown. On the facts, this was confirmed by the fact that the inventors, who had more knowledge that the person of ordinary skill in the art, attempted to resolve a number of other compounds before finally trying PCR 4099 […]

[145] For similar reasons, I conclude that LDX, its compositions, methods of delivery and uses were not obvious to try. It was not more or less self-evident that the contemplated tests would overcome the differences between the starting point and end point.

E. *Overbreadth*

(1) Legal Principles

[146] In order to be valid, the claims of a patent must not exceed the invention made or the invention disclosed. A claim cannot be stretched to grant the patentee a monopoly on anything that achieves a desired result (*Free World Trust* at para 32).

(2) Analysis

[147] Apotex's allegation of overbreadth is premised on its assertion that, with the exception of claims 5 and 22 (which show LDX in picture form), the claims of the 646 Patent that refer to "L-lysine-d-amphetamine" include a group of conjugates of L-lysine bound to any sympathomimetic phenethylamine derivative, as defined in paragraph 95.

[148] In light of my conclusion that "L-lysine-d-amphetamine", as the term is used in the claims, means only LDX, Apotex's allegation of overbreadth must fail.

F. *Insufficiency of Specification*

(1) Legal Principles

[149] Pursuant to s 27(3)(a) of the *Patent Act*, the specification of a patent must correctly and fully describe the invention and its operation or use as contemplated by the inventor. Subsection 27(4) of the *Patent Act* further provides that the specification must end with claims that define

the subject matter of the invention in distinct and explicit terms. Adequate disclosure in the specification is a "precondition for the granting of a patent" (*Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60 at para 34 [*Teva*]).

[150] In *Pioneer Hi-Bred Ltd v Canada (Commissioner of Patents)* (1989), 25 CPR (3d) 257 at page 268, the Supreme Court of Canada described the adequacy of disclosure as follows:

> […] The applicant must disclose everything that is essential for the invention to function properly. To be complete, it must meet two conditions: it must describe the invention and define the way it is produced or built [citation omitted]. The applicant must define the nature of the invention and describe how it is put into operation. A failure to meet the first condition would invalidate the application for ambiguity, while a failure to meet the second invalidates it for insufficiency. The description must be such as to enable a person skilled in the art or the field of the invention to produce it using only instructions contained in the disclosure [citations omitted] […]

[151] The analysis of insufficiency requires answers to three questions: (i) what is the invention? (ii) how does it work? and (iii) having only the specification, can a PSIA successfully produce the invention using only the instructions contained in the disclosure? (*Uponor AB* at para 172, citing *Teva* at paras 50-51). The Court must look at the specification as a whole to determine whether the patent meets the disclosure requirements.

(2) Analysis

[152] Apotex argues that, with the exception of claim 2, each of the asserted claims embraces not only LDX, but one or more of its pharmaceutically acceptable salts, including specifically the mesylate in claims 3 and 8, and hydrochloride salts in claim 4. According to Drs. Langer and

Marron, as of the filing date, the named inventors had determined that the hydrochloride salt could be isolated only as an oil or a foam, and the mesylate salt of L-lysine-d-amphetamine was the only salt that was likely to be useful for inclusion in solid oral dosage forms. Apotex therefore says the 646 Patent's failure to mention this renders its teachings insufficient.

[153] I disagree. There is no dispute among the experts that LDX's advantageous properties exist regardless of whether the composition is a mesylate salt, a hydrochloride salt, in free base form, or any other pharmaceutically acceptable salt. The invention of the 646 Patent does not relate to scale-up synthesis or to a particular crystal form of LDX, and the PSIA would be capable of making the compounds of claims 1 to 5 simply by following the 646 Patent.

IX. Infringement

A. *Legal Principles*

[154] Section 42 of the *Patent Act* grants the patent holder the exclusive right, privilege and liberty of making, constructing and using the invention and selling it to others to be used. A patent is infringed by any act that interferes with the patentee's full enjoyment of the monopoly granted (*Monsanto Canada Inc v Schmeiser*, 2004 SCC 34 at para 34 [*Monsanto*]).

[155] Pursuant to s 55(1) of the *Patent Act*, any person who infringes a patent is liable for all damages sustained by the patentee after the grant of the patent by reason of infringement. Infringement is determined by comparing the products that are said to infringe the patent with the patent's claims as construed by the Court.

[156] The burden of proving infringement rests with the party that alleges it (*Monsanto* at para 29). The burden therefore falls upon Shire.

B. *Experimental and Regulatory Use Exception*

[157] Pursuant to s 55.2(1) of the *Patent Act*, it is not an infringement of a patent for any person to make, construct, use or sell a patented invention for uses reasonably related to the development and submission of information required under any law of Canada, a province, or any other country that regulates the manufacture, construction, use or sale of any product. Subsection 55.2(1) is "sufficiently broad so as to exempt from infringement such samples taken pursuant to such regulations and needed for submission of information to the relevant government authorities if and when required" (*Merck & Co Inc v Apotex Inc*, 2006 FC 524 at para 158; var'd on other grounds, *Merck & Co Inc v Apotex Inc*, 2006 FCA 323).

[158] Subsection 55.2(6) of the *Patent Act* preserves the common law experimental use and fair dealing exemptions that permit manufacturers to make and use a patented invention in the course of experimental research and development work designed to establish and implement a commercial process or product made in accordance with the patent.

C. *Analysis*

[159] Shire alleges that Apotex has acquired and used, or holds in inventory, a total of approximately 212.7 kilograms of LDX dimesylate at a cost of $1,535,760 USD. From this material, Apotex has formulated 122.904 kg of LDX into finished dosage form to produce 3,409,337 LDX dimesylate capsules.

[160] Mr. Fahner testified that Apotex has retained only 918,707 capsules in inventory. His testimony was not contradicted. Shire nevertheless argues that Apotex has provided no reasonable explanation for producing and retaining so many capsules of LDX dimesylate, and must therefore be found liable for infringement.

[161] With respect to the capsules retained in inventory, Mr. Fahner testified that Apotex has an "internal policy that these materials could not be used commercially". Shire says this bare statement is insufficient to meet Apotex's burden of showing that its actions fall within the experimental or regulatory use exception.

[162] I accept Apotex's defence of experimental or regulatory use. Mr. Fahner's evidence establishes that Apotex obtained product for the purpose of (i) developing suitable formulations and processes, (ii) obtaining regulatory approval to sell commercial formulations, (iii) demonstrating that its manufacturing process could be carried out on a commercial scale, and (iv) ensuring that it tested the active pharmaceutical ingredient when it received and retained samples, in accordance with the regulatory requirements for future testing. Moreover, Mr. Fahner's uncontested evidence is that all retained capsules will be used entirely for future research or making demonstration batches. No use will result in a product that will be sold commercially.

[163] Shire's Counterclaim alleging infringement of the 646 Patent must therefore be dismissed.

X. Prohibition Application

A. *Legal Principles*

[164] The applicant bears the burden of establishing its entitlement to a prohibition order on a balance of probabilities (*Abbott Laboratories v Canada (Health)*, 2007 FCA 153 at para 9).

[165] In *Eli Lilly Canada Inc v Mylan Pharmaceuticals ULC*, 2015 FC 178 at paragraph 137, Justice Yves de Montigny held that the purpose of s 5(3)(b) of the *PM(NOC) Regulations* is to ensure that a patentee is not taken by surprise, and has all of the necessary information to confidently decide whether to resist the issuance of a NOC. A second person may not rely on any facts not cited in the NOA. If a document is the source of a new factual basis, it shall properly be excluded if it has not been disclosed in the NOA. However, there is currently no support for the view that every single document relied upon to substantiate allegations must be disclosed in the NOA.

B. *Analysis*

[166] Shire says the result of the Impeachment Action governs the Prohibition Application. The Prohibition Application need not be considered, except in the unlikely event the Court finds in favour of Apotex based on documents or allegations that are material to the ultimate decision but are not referenced in the NOA. Shire notes that many documents adduced in the Impeachment Action are not included in the NOA, notably NL 901, FR 130 and Baker.

[167] Apotex agrees that the result of the Impeachment Action governs the Prohibition Application, except in the rare and unusual circumstance where the Court finds the evidence to be evenly balanced and there is a "tie" respecting the question of validity. Shire would then prevail in the Impeachment Action, because Apotex has the burden of proof; and Apotex would prevail in the Prohibition Application, because Shire has the burden of proof. However, even in this unlikely scenario, there would be a final judgment from the Court that the 646 Patent is valid. If Apotex were to obtain a NOC based upon its success in the Prohibition Application, this would be of little moment because any manufacture or sale of its generic product would necessarily infringe a patent that had previously been declared valid.

[168] None of the exceptional circumstances identified by the parties are present here. I am therefore satisfied that the result of the Impeachment Action should govern the Prohibition Application. Shire is entitled to an order prohibiting the Minister of Health from issuing a NOC to Apotex pursuant to s 6(1) of the *PM(NOC) Regulations*, on the ground that Apo-Lisdexamfetamine infringes the specified claims of the 646 Patent.

XI. Conclusion

[169] Claims 1 to 5, 8, 10 to 12, 22, 24 to 30, 33 to 36, and 43 of the 646 Patent are not invalid on any of the asserted grounds of obviousness, anticipation, overbreadth, or insufficiency of specification. The Impeachment Action is therefore dismissed.

[170] Apotex benefits from the experimental and regulatory use exception recognized in ss 55.2(1) and (6) of the *Patent Act* and at common law, and has therefore not infringed the specified claims of the 646 Patent by manufacturing and retaining capsules of its generic product. Shire's Counterclaim is therefore dismissed.

[171] Shire's application for an order prohibiting the Minister of Health from issuing a NOC to Apotex for Apo-Lisdexamfetamine pursuant to s 6(1) of the *PM(NOC) Regulations* is granted.

[172] If the parties are unable to agree upon costs, they may make written submissions, not exceeding seven pages, within 21 days of the date of this Court's judgment. Responding submissions, not exceeding three pages, may be made within 10 days thereafter.

JUDGMENT

THIS COURT'S JUDGMENT is that:

1. Claims 1 to 5, 8, 10 to 12, 22, 24 to 30, 33 to 36, and 43 of the 646 Patent are not invalid on any of the asserted grounds of obviousness, anticipation, overbreadth, or insufficiency of specification.

2. Apotex's Impeachment Action (T-1056-16) is dismissed.

3. Shire's Counterclaim (T-1056-16) is dismissed.

4. Shire's application (T-998-16) for an order prohibiting the Minister of Health from issuing a Notice of Compliance to Apotex for Apo-Lisdexamfetamine pursuant to s 6(1) of the *PM(NOC) Regulations* is granted.

5. If the parties are unable to agree upon costs, they may make written submissions, not exceeding seven pages, within 21 days of the date of this Judgment. Responding submissions, not exceeding three pages, may be made within 10 days thereafter.

"Simon Fothergill"
Judge

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-1056-16
STYLE OF CAUSE:	APOTEX INC. v SHIRE LLC AND SHIRE PHARMA CANADA ULC
AND DOCKET:	T-998-16
STYLE OF CAUSE:	SHIRE PHARMA CANADA ULC v APOTEX INC. AND THE MINISTER OF HEALTH AND SHIRE LLC
PLACE OF HEARING:	TORONTO, ONTARIO
DATES OF HEARING:	APRIL 16, 17,19, 20, 24, 25, 26, 30 AND MAY 1, 2, 3, 7, 8, 9, 22, 23, 24, 2018
JUDGMENT AND REASONS:	FOTHERGILL J.
CONFIDENTIAL JUDGMENT AND REASONS:	JUNE 21, 2018
PUBLIC JUDGMENT AND REASONS:	JUNE 29, 2018

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