Federal Court		Cour fédérale

Date: 20100120

Docket: T-118-08

Citation: 2010 FC 46

Ottawa, Ontario, January 20, 2010

PRESENT: The Honourable Mr. Justice Kelen

BETWEEN:

BIOVAIL CORPORATION
and DEPOMED, INC.

Applicants

and

THE MINISTER OF HEALTH
and APOTEX INC.

Respondents

AMENDED PUBLIC REASONS FOR ORDER AND ORDER

[1] This is an application for an Order under the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 (the NOC Regulations), prohibiting the Minister of Health from issuing a Notice of Compliance to Apotex for a generic version of metformin ER extended release 500 mg tablets, until Biovail's Canadian Patent 2,290,624 (hereafter the '624 patent) expires on June 5, 2018. Apotex alleges that Biovail's '624 patent for extended release metformin sold by Biovail under its trade name GLUMETZA is invalid for reasons of anticipation, obviousness, and double patenting so that the generic version of the drug should immediately be allowed on the Canadian market. Moreover, Apotex alleges that its formulation for extended release metformin is made in

accordance with the prior art so that its formulation does not infringe the ‘624 patent, and the Gillette defence applies.

Preliminary matter with respect to Canadian Patent No. 2,416, 671 (the ‘671 Patent)

[2] At the hearing, the parties advised the Court that the ‘671 patent was originally part of the NOA and accordingly part of this Notice of Application. The applicants advised that the ‘671 patent is no longer the subject of the application and that this Court need not address the ‘671 patent in this Judgment. After the hearing the parties advised the Court that this application should be dismissed “insofar as it relates to Canadian Patent No. 2,412,671”.

BACKGROUND

The ‘624 Patent

[3] The ‘624 patent is for an extended release drug delivery system which releases highly soluable drugs in a controlled manner over an extended period of time in order to achieve greater efficacy and more efficient use of the drug.

[4] The Applicant Depomed, Inc. owns the ‘624 patent. In Canada the Applicant Biovail Corporation markets, under licence, the drug metformin hydrochloride in accordance with the ‘624 patent under the trade name GLUMETZA.

[5] The ‘624 patent was filed on June 5, 1998, and claimed priority from U.S. Patent application 8,870,509, which was filed on June 6, 1997. The ‘624 patent was issued on December 5, 2006 and expires on June 5, 2018.

[6] The ‘624 patent teaches a drug delivery system that is a swellable, gastric retentive dosage form that releases drugs, such as metformin, in a controlled manner in the stomach over an extended period of time. The controlled-release delivery of these drugs is achieved through their synthesis into a polymeric matrix. The applicant relies on claims 6,11,16,19 and 20 of the patent. The applicant states the inventive concept disclosed in the asserted claims is the combination resulting in a controlled-release gastric retentive oral dosage form for use with metformin where the rate of drug release is dependent on dissolution and diffusion and that that the polymer stays intact during the drug delivery period, and the primary drug release mechanism is not erosional.

[7] The ‘624 patent is entitled “Gastric-retentive oral drug dosage forms for controlled release of highly soluble drugs”. The ‘624 patent explains that in the 1970s a variety of controlled delivery systems for drug doses were introduced for “sparingly soluble drugs” (see page 1, line 20 of the patent). However, these controlled release delivery systems did not work for highly soluble drugs. The patent explains the invention is a controlled release delivery system for highly soluble drugs like metformin.

The Parties

[8] The Applicant Biovail markets “once daily” GLUMETZA (metformin hydrochloride) in Canada pursuant to a Notice of Compliance (NOC) issued by Health Canada dated May 31, 2005 for the control of hyperglycaemia in type 2 diabetes. Biovail is the exclusive licensee of the ‘624 patent and has the consent of the ‘624 patent’s owner, Depomed, Inc., to include the patent on Health Canada’s Patent List.

[9] Depomed, Inc. is the owner and developer of the ‘624 patent.

[10] The Respondent Apotex Inc. is a Canadian manufacturer of generic drugs. Apotex filed an Abbreviated New Drug Submission (ANDS) with Health Canada for APO-Metformin ER extended release 500 mg tablets for oral administration for the control of hyperglycaemia in adult patients with type 2 (non-insulin-dependent, mature onset) diabetes, as an adjunct to dietary management, exercise, and weight reduction, and when insulin therapy is not appropriate. Apotex served its Notice of Allegation (NOA) on Biovail on December 11, 2007, alleging the invalidity of the ‘624 patent for anticipation, obviousness, double patenting and non-infringement based on the Gillette defence.

[11] The Minister of Health filed a Notice of Appearance, but did not participate further in this matter.

The drug in issue: Metformin Hydrochloride

[12] Biovail's GLUMETZA, and its active ingredient metformin hydrochloride, is used to treat type 2 diabetes. Metformin hydrochloride is the salt form of metformin.

[13] Metformin is a well-known and established drug recognized as an oral anti-diabetic since 1959. Oral dosage forms for the delivery of metformin and its salts were described and patented as early as 1965. For example, United States Patent No. 3, 174, 901 entitled "Process for the Oral Treatment of Diabetes" was issued on March 23, 1965 and teaches oral dosage forms containing metformin and its salts. At the time the '624 patent was filed in 1997, metformin was a popular anti-diabetic drug that was administered two or three times daily. By this time, the patent for metformin had expired and it was being made by generic drug companies.

[14] Metformin is a highly soluble drug that dissolves quickly in the stomach. As a highly soluble drug metformin presents two difficulties for formulators of an extended releases version to overcome: drug absorption location and rate of release. First, the drug needs to be retained in the stomach to promote delivery of the drug into this area. As discussed by Dr. Fass, the oral administration of formulated drugs, e.g. via tablets, capsules etc., is the most common way that humans are treated with pharmaceutical products. Therefore, oral administration drugs must be able to work within the highly variable and often extreme conditions of the digestive tract. Given that most drugs are preferentially absorbed in the upper region of the small intestine, promoting retention of metformin in the stomach is preferred.

[15] Second, highly soluble drugs remain in the stomach for short and inconsistent periods of time, resulting in poor bioavailability, a lower fraction of the drug being absorbed, and possible immediate overdosing followed by a period of underdosing.

[16] It is also desirable to reduce the number of doses of a drug taken per day as patient compliance is difficult to achieve if frequent dosing is required. Limiting the number of doses may also reduce unwanted side effects such as stomach irritation. Therefore, formulating metformin in a suitable dosage form, such as extended release, can reduce the overall amount of metformin the patient must take and can help steady the concentration of the drug in the body over time.

[17] As set out by Ms. Louie-Helm, in the early 1970's drug delivery methods were improved through the introduction of a variety of controlled delivery systems, which included systems using particular polymers to control the delivery of low or sparingly soluble drugs. Accordingly, for drugs with low solubility, extended release formulations came on the market. For water soluble drugs early polymer matrices lacked sufficient control over release of the drug and typically resulted in the drug being released within the first two hours.

[18] Glumetza is administered once-daily by taking a tablet after a meal when the stomach is in the "fed mode"**,** i.e. when the gateway between the stomach and the small intestine is constricted and only liquid and small particles can pass through. Large particles are retropelled back into the stomach for further digestion. The swelling of the polymeric matrix on contact with the gastric fluid serves two purposes: (1) it hinders passage out of the stomach, allowing the dosage form to stay in

the stomach for a longer period of time and (2) the swelling slows the rate of diffusion of the incorporated drug out of the tablet and into the upper region of the small intestine.

Polymers

[19] The term polymer describes a large class of material with a wide range of characteristics and purposes. According to Dr. Paul, polymers are compounds formed by joining together smaller units, referred to as monomers. Linking repeat units together enables a formulator to create synthetic polymers with specific structures and qualities. For example, adding hydroxyalkyl to the backbone chain of cellulose will generate a polymer that is water-loving (hydrophilic). When immersed in water such polymers will tend to swell as water is imbibed.

[20] Polymers can be combined with medical ingredients such as metformin to control the release of the drug in the stomach. There are five rate controlling mechanisms known to control drug release: diffusion, dissolution, swelling, erosion, and chemical decomposition of the polymetric matrix. The control mechanisms are not mutually exclusive. For the purposes of the '624 patent, diffusion, dissolution and swelling are the most important.

[21] Diffusion is the movement of molecules from an area of high concentration to an area of low concentration based on their random thermal motion. For controlled-release dosage forms, the drug release occurs where the solid drug (in the polymeric matrix) dissolves into the polymer or the polymer that has taken in the solvent (such as stomach fluid) and then diffuses into the surrounding environment. Dissolution describes the process of dissolving a solid into a liquid to yield a solution.

[22] As discussed above, water-loving polymers swell upon taking in a fluid. In swelling controlled-release dosage forms, the rate of drug release is dependent on the rate at which the surrounding fluid is taken into the polymeric matrix. Hydroxypropylmethylcellulose (HPMC) and polyethylene oxide (PEO) polymers, both named in the '624 patent as part of the invention, are two of the most common swellable polymers used for controlling drug release in the stomach, come in a variety of molecular weights, and have been used for approximately 25 years (see Affidavit of Dr. Digenis, paragraphs 38-42, 72).

EVIDENCE

[23] On October 15, 2008, Prothonotary Kevin Aalto ordered the "reversal of evidence", which required Apotex to deliver its evidence in support of the invalidity allegation first. Biovail then responded with its evidence.

[24] Apotex filed affidavits from three expert witnesses, an Apotex employee and a law clerk employed by the respondent's counsel:

Experts

1. Dr. Robert Langer
2. Dr. Tarun Mandal
3. Dr. George Digenis

Apotex Employee

4. Mr. John Hems

Law Clerk

5. Ms. Biserka Horvat (law clerk at Goodmans LLP)

[25] Biovail provided affidavits from two expert witnesses, one of the '624's two inventors, a fact witness, a Biovail employee, and a law clerk employed by the applicant's counsel:

Experts
1. Dr. Donald Paul
2. Dr. Ronnie Fass

Co-inventor
3. Ms. Jenny Louie-Helm

Fact Witness
4. Ms. Christine Haskett (a partner at a US law firm involved in US litigation relating to counterparts of the '624 patent).

Biovail Employee
5. Dr. Alim Mamajiwalla

Law Clerk
6. Mr. Roger Shoreman (law clerk at Lanczner Slaght Royce Smith Griffin LLP)

The backgrounds of these witnesses are set out in a document attached hereto as "Appendix A".

Evidence of Ms. Jenny Louie-Helm

[26] The named inventors of the '624 patent are Dr. John W. Shell and Ms. Jenny Louie-Helm. Dr. Shell was the President and Founder of Depomed. Dr. Shell is retired and did not provide an affidavit because of his age and health. The co-inventor Ms. Louie-Helm provided an affidavit, including her detailed laboratory notes, in which she outlined her work on metformin.

[27] In the early 1990s Dr. Shell and Ms. Louie-Helm focused on the development of controlled-release dosage forms for drugs having low solubility in water. In 1992 their work focused on developing a control-release gastic-retentive dosage form for acetylsalicylic acid ("ASA" or

"aspirin"). According to Ms. Louie-Helm, it was the experimentation with ASA that led to an understanding of the relationship between polymer type and grade to form a polymeric matrix that would swell to a size sufficient for gastric retention and provide controlled release of a low solubility drug. **[CONFIDENTIAL EVIDENCE REFERRED TO HAS BEEN REDACTED FROM THE PUBLIC VERSON OF THE REASONS FOR ORDER _____ _____]**

[28] Ms. Louie-Helm states that her goal was to identify gastric-retentive controlled release polymer based dosage forms that would be suitable for use with highly water soluble drugs without the addition of waxy additives.

[29] In 1993 Depomed prepared gastric-retentive control released dosage forms formulated with highly soluble drugs. Ms. Louie-Helm stated that the development of these dosage forms focused on a variety of factors, including: selecting appropriate polymer types, amounts, molecular weights or viscosities and combinations, and formulating the selected components into a controlled-release dosage forms in order to obtain a drug release profile.

[30] **[CONFIDENTIAL EVIDENCE REFERRED TO HAS BEEN REDACTED FROM THE PUBLIC VERSION OF THE REASONS FOR ORDER _____**

_____

_____

_____

_____

_____**]**

Evidence of Dr. Donald Paul

[31] Dr. Paul, the main expert witness for Biovail, has a Ph.D in chemical engineering. Like the main expert witness for Apotex, Dr. Langer, Dr. Paul's *curriculum vitae* demonstrates outstanding qualifications to give evidence in this case. Dr. Paul explained the state of the art for controlled-release drug delivery systems and formulations before the '624 patent was laid open to the public in 1997. During the 1970s and 1980s controlled release or delayed release drug formulations were created using polymers, but they were for drugs with low solubility, meaning that the drug did not dissolve quickly in water. For drugs with high solubility, such as metformin, these controlled-release mechanisms did not work. Dr. Paul deposes that the teachings of the '624 patent are distinguished from the controlled-release dosage forms known in the prior art for two reasons. First, the '624 patent is for a controlled-release mechanism for drugs that are defined as freely soluble in water. Second, the drug is released primarily by diffusion, not dissolution, when the drug is formulated with swellable polymers of high molecular weight.

Evidence of Dr. Robert Langer

[32] Dr. Langer has a doctorate in chemical engineering and gave evidence as an expert witness for Apotex. His *curriculum vitae* is approximately 70 pages single-spaced. He has received over 160 major awards including the 2006 United States National Medal of Science, the highest scientific honour bestowed in the United States. In 2002, he received the Charles Stark Draper Prize,

considered the equivalent of the Nobel Prize for engineers and the world's most prestigious engineering prize.

[33] The Court notes, once again, that both Dr. Paul and Dr. Langer are outstanding chemical engineers and highly regarded in their field.

[34] Dr. Langer fully reviewed the '624 patent in over 10 pages in his affidavit.

[35] Dr. Langer deposes that the Apotex extended release metformin tablets are prepared in accordance with the teachings of two DOW METHOCEL PRODUCT GUIDES published and available to the public. The first DOW GUIDE was published in 1982. The second DOW GUIDE was published in 1995. Dr. Langer undertakes a detailed analysis in his affidavit in this regard.

[36] Dr. Langer also states his opinion that the '624 patent was obvious in light of the state of the art as of the claim date of the '624 patent. Again, Dr. Langer undertakes a detailed analysis in this regard. This affidavit is detailed and technical, and comprises 143 pages, not including the aforementioned curriculum vitae.

Litigation of the '624 Patent

[37] The '624 patent has not been litigated in Canada. However, two related patents, US Patent Nos. 6, 340,475 and 6,635,280 have been considered in the United States in *Depomed, Inc. v. Ivax Corporation*. On December 20, 2006, Mr. Justice Charles Breyer issued a claims construction order

for the two US patents (see *Depomed, Inc. v. Ivax Corporation*, United States District Court, Northern District of California, (9th Cir.) case number 3:06-cv-00100 CRB (unreported)). On December 12, 2007, Justice Breyer granted the patentee Depomed, Inc.'s motion for summary judgement of infringement and denied the generic's motion for summary judgment on invalidity, no wilful infringement and inequitable conduct (see *Depomed, Inc. v. Ivax Corporation and Ivax Pharma*, 532 F. Supp. 2d 1170, (9th Cir. 2007).

ISSUES

[38] In this litigation, Apotex's Notice of Allegation ("NOA") asserts that the '624 patent is invalid for reasons of anticipation, obviousness, double patenting, and that there is no infringement based on the Gillette defence.

[39] Accordingly, the issues in this prohibition application are whether the following Apotex allegations are justified:

a. whether the '624 patent was anticipated by the prior art, which Apotex restricted to the '755 application at the hearing;

b. whether the '624 patent was disclosed in a mosaic of the prior art and was accordingly obvious to a person skilled in the art;

c. whether the '624 patent is invalid upon the principle that it is a double-patent, i.e. a patent for an invention which was the subject of another patent, patent 2,416,671 (the '671 patent); and

d. whether the Apotex formulation for extended release metformin was disclosed in the prior art, namely the Dow Publications, so that the Apotex formulation cannot infringe the '624 patent and the Gillette defence applies.

ANALYSIS

Burden of Proof

[40] As stated by Mr. Justice Roger Hughes in *Eli Lilly Canada Inc. v. Apotex Inc.*, 2009 FC 320 at paragraph 38, the issue of the burden in NOC proceedings as to invalidity should be determined as such:

1. The second person, in its Notice of Allegation, may raise one or more grounds for alleging invalidity;

2. The first person may, in its Notice of Application filed with the Court, join issue on any one or more of those grounds;

3. The second person may lead evidence in the Court proceeding to support the grounds upon which issue has been joined;

4. The first person may, at its peril, rely simply upon the presumption of validity afforded by the *Patent Act* or, more prudently, adduce its own evidence as to the grounds of invalidity put in issue;

5. The Court will weigh the evidence; if the first person relies only on the presumption, the Court will weigh the evidence led by the second person. If that evidence is weak or irrelevant, the presumption will prevail. If both parties lead evidence, the Court will weigh all the evidence and determine the matter on the usual civil standard; and

6. If the evidence weighed in step 5 is evenly balanced (a rare event), the applicant (first person) will have failed to prove that the allegation of invalidity is not justified and will not be entitled to the order of prohibition.

[41] Apotex has raised arguments in respect of validity. Each of Biovail and Apotex have led evidence and made submissions.

[42] Where a generic has alleged non-infringement, the statements that it makes in that regard in its Notice of Allegation are presumed to be true. The applicant (first person) bears the burden of

proof, on a balance of probabilities, to satisfy the Court with evidence that the allegations of non-infringement are not justified. (*Novopharm Limited v. Pfizer Canada Inc*. (2005), 42 C.P.R. (4th) 97, 2005 FCA 270 at paragraphs 19, 20 and 24).

Person Skilled in the Art

[43] Patent construction is to be done on the basis that the addressee is a person skilled in the art and the knowledge that person is expected to possess is to be considered. The hypothetical person who is skilled in the art possess the ordinary skills and knowledge of the particular art to which the invention relates, a mind willing to understand a specification, and is assumed to be someone who is going to try to achieve success and not one who is looking for difficulties or seeking failure (*Free World Trust v. Electro Sante Inc*. (2000), 9 C.P.R. (4th) 168 (S.C.C.)).

[44] Based on the affidavit evidence of both Biovail and Apotex's experts, the person skilled in the art is a person (or team) that has an advanced degree in pharmaceutical chemistry or a related degree and experience with pre-formulation and formulation methods and the design and manufacture of pharmaceutical dosage forms, including controlled release dosage forms. The person skilled in the art would also have a working knowledge of polymers, gastric anatomy and physiology combined with experience in the development of controlled-released dosage forms.

Patent Claims Construction

[45] Construction of the claims is to be performed by the Court before consideration is given to issues of validity and infringement (*Whirlpool Corp. v. Camco Inc.*, [2000] 2 S.C.R. 1067 at

paragraph 43). It applies to the whole of the patent, where necessary, and not only to the claims (*Burton Parsons Chemicals, Inc. v. Hewlett-Packard (Canada) Ltd.*, [1976] 1 S.C.R. 555 at page 563).

[46] Construction is a task for the Court alone (*Whirlpool*, above; *Burton Parsons*, above) and must be approached in an informed and purposive manner, paying close attention to the purpose and intent of the authors and a judicial anxiety to support a really useful invention (*Consolboard Inc. v. MacMillan Bloedel (Saskatchewan) Ltd.*, [1981] 1 S.C.R. 504). However, the patentee is not able to re-write a claim in claims construction (*Whirlpool*, above).

[47] The '624 patent relates to drug delivery systems that are retained in the stomach for an extended period of time while releasing a highly soluble drug in a controlled manner over the extended period in order to achieve greater efficacy and more efficient use of the drug. At page 2 of the '624 patent the patentee described the invention as such:

> It is has now been discovered that drugs that are highly soluble in water can be administered orally in a manner that will prolong their delivery time to extend substantially through the duration of the fed mode but not a substantial time beyond.

[48] At paragraph 47 of their Memorandum of Fact and Law, the applicant states that the inventive concept disclosed in the asserted claims is the combination resulting in a controlled-release gastric retentive oral dosage form for use with metformin where the rate of drug release is dependent on dissolution and diffusion, that the polymer stays in tact during the drug delivery period and that the primary drug release mechanism is not erosional.

[49] The ‘624 patent contains 23 claims. Biovail asserts claims 6, 11, 16, 19 and 20, which are set out as:

> 6. A dosage form of any one of claims 1 to 4 in which said drug is metformin hydrochloride.
>
> 11. A dosage form of any one of claims 1 to 9 in which said polymeric matrix is formed of a polymer selected from the group consisting of poly(ethylene oxide), xanthan gum, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylocellulose, and carboxymethylcellulose.
>
> 16. A dosage form of any one of claims 1 to 14 in which said weight ratio of drug to polymer is from about 30:70 to about 80:20.
>
> 19. A dosage form of any one of claims 1 to 17 in which said polymeric matrix upon immersion in gastric fluid retains at least about 60% of said drug one hour after such immersion.
>
> 20. A dosage form of any one of claims 1 to 17 in which said polymeric matrix upon immersion in gastric fluid retains at least about 80% of said drug one hour after such immersion.

[50] Each of the asserted claims depends on Claims 1-4. Claims 11, 16, 19 and 20 are clear on their face and do not need to be construed by this Court. At the hearing, Biovail confirmed that it was only relying on Claim 6 as it depended on Claim 1. Also at the hearing, Apotex confirmed that it agrees with and accepts the construction of Claim 1 as set out in the Affidavit of the Biovail expert witness Dr. Paul at paragraph 80. Accordingly, the Court will construe Claim 6 as it depends on Claim 1 as such:

> A dosage form in which the drug is metformin and the dosage has the following 8 elements as set out in Claim 1:
>
> (i) The drug has a solubility of one part by weight in less than ten parts by weight of water;
> (ii) The drug is dispersed in a solid polymeric matrix at a weight ratio of drug to polymer of about 80:20 or less;

(iii) The polymeric matrix swells to at least about twice its volume upon imbibition of water;
(iv) The dispersed drug is released from the polymeric matrix into gastric fluid by dissolution and diffusion;
(v) The polymeric matrix retains at least 40% of the dispersed drug for one hour after immersion in gastric fluid;
(vi) Substantially all of the dispersed drug is released from the polymeric matrix within about eight hours of immersion in gastric fluid;
(vii) The swollen polymeric matrix remains substantially intact until all of the drug is released; and
(viii) The swollen polymeric matrix promotes retention of the dosage form in the stomach during fed mode.

<u>Issue No. 1</u>: Whether the '624 patent was anticipated by the prior art, which Apotex at the hearing restricted to the '755 application

[51] Apotex submits that the '624 patent is invalid for anticipation.

[52] The relevant date for anticipation is June 6, 1997, (see s. 28.2 of the *Patent Act*).

[53] The law of anticipation is set out by the Supreme Court of Canada in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, [2008] 3 S.C.R. 265 at paragraphs 23-37 (*Sanofi*). In *Sanofi* the Supreme Court adopted a two step approach to determine if a patent was anticipated: there must be disclosure and enablement. The steps are to be considered separately and proven. For prior disclosure, the prior art must disclose that the subject matter, if performed, would inevitably or necessarily result in infringement of that patent without trial or error. For enablement, the person skilled in the art must have been able to perform the invention without undue burden or the requirement of an inventive step.

[54] As the Supreme Court of Canada stated in *Sanofi*, anticipation and obviousness are related concepts. However, although both require an examination of the prior art, that prior art must be treated differently. In examining an allegation of anticipation (or lack of novelty), the Court must determine whether the claimed invention has already been disclosed to the public in a single disclosure in such a way as to enable it to be put into practice (see also *Synthon BV v. Smithkline Beecham plc* [2005] UKHL 59, at paragraph 25, and *Eli Lilly Canada Inc. v. Novopharm Limited*, 2009 FC 301, at paragraph 58.)

[55] Prior to the hearing there was a dispute between the parties with regard to the prior art that could be relied upon by Apotex in relation to the issues of disclosure and enablement.

[56] Biovail argued that the only allegations of anticipation were with respect to claims 6, 11 and 16 and that a careful reading of the NOA revealed that only three references were alleged to anticipate these claims. These references were: PCT Publication WO 93/ 18755 (the ‘755 application) against claims 11 and 16; United States Patent 5,273,758 (the ‘758 patent) against claims 6 and 16, and PCT Publication WO 96/32097 (the ‘097 application) against claim 11.

[57] In their Memorandum of Fact and Law Apotex asserted the ‘755 application, the ‘097 application, US Patent Number 5,582,837 (the ‘837 patent), the ‘758 patent, and an article by A. Apicella et al., “Poly(ethylene oxide) (PEO) and Different Molecular Weight PEO Blends of Monolithic Devices for Drug Release” (1993) 14(2) Biomaterials 83.

[58] At the hearing, Apotex advised the Court that it would only rely on the ‘755 application to support its anticipation allegation. Therefore, only the ‘755 application has been considered by the Court.

[59] The ‘755 application was published on September 30, 1993 and is entitled “Alkyl-Substituted Cellulose-Based Sustained Release Oral Drug Dosage Forms”. The application disclosed controlled release oral dosage forms incorporating polymeric matrices that swell and become slippery upon taking on water. The ‘755 application teaches that this will promote gastric retention of the dosage form in the stomach during the fed state.

[60] As set out by Drs. Langer and Mandal, there are many “characteristics” disclosed in the ‘755 application that are also claimed in the ‘624 patent. These include the use of controlled-release oral dosage forms for releasing a drug into the stomach and the use of alkyl-substituted cellulose-based polymers. I agree with Drs. Langer and Mandal that the polymer used to form the matrix and the ratio of drug-to-polymers in claims 6 and 11 are also set out in the ‘755 application.

[61] However, the ‘755 application does not disclose or enable the person skilled in the art to come directly to the ‘624 patent. This is due to the fact that the ‘755 application is directed to improvements to the delivery of limited solubility drugs. There maybe some overlap between the ‘755 application and the class of drugs described in the ‘624 patent and other drugs of higher solubility, but this would not result in the person skilled in the art being directly enabled by the ‘755 application.

[62] At page 3 of the ‘755 application under the heading “DESCRIPTION OF THE PREFERRED EMBODIMENT”, the ‘755 application states:

> The dosage forms of the present invention are effective for administering drugs of limited solubility in gastric fluid … Normally, the solubility of the drug (measured in water at 37°C) will be in the range of 0.001% to about 35% by weight, more normally 0.001% to 5% by weight.
>
> The invention is particularly useful for delivering drugs that are irritating to the gastrointestinal track … For instance, aspirin …

[63] Accordingly, the Court must conclude on the face of the ‘755 application itself, that this prior art is not directed to administering controlled released drug dosages of high solubility.

[64] The Court notes that the solubility of metformin is 35%, and that this falls at the very upper limit of the range discussed in the ‘755 application. But it is also clear to the Court that the ‘755 application is primarily effective and directed toward low solubility drugs.

[65] Dr. Paul, the expert witness for Biovail, was cross-examined by Apotex on this point. Dr. Paul agreed that the 35% solubility comes within the ‘755 application range, but he noted that the ‘755 application employs additional measures for higher solubility drugs. Dr. Paul also testified under cross-examination that the ‘755 application contemplates drugs more normally in the 0.001% to 5% range. See cross-examination of Dr. Paul, page 119, question 650.

[66] In Dr. Paul’s Affidavit, he deposes at paragraph 97 that a person of skill in the art would understand the ‘755 application to be applicable to drugs of “limited solubility”. He states:

> … however, the ‘755 Application employs additional measures for the higher solubility drugs. They are formulated with additional

> compounds not required in the ‘624 patent (such as long chain fatty acid esters of glycerine) in order to retard the release rate of the drug.

[67] Another important difference between the ‘624 patent and the ‘755 application is that the ‘755 application teaches the dominant release mechanism is dissolution. Dr. Paul states at paragraph 98 in his affidavit:

> This is not surprising given that the ‘755 application is directed to limited solubility drugs … where it would be expected that the dominant release mechanism would be dissolution.

[68] According to Dr. Paul on cross-examination, this is a major difference with the ‘624 patent where the drug is released over the controlled-release time period by diffusion, not by dissolution. See the cross-examination of Dr. Langer, pages 102 and 103, questions 563 to 567. On re-examination, Dr. Paul returns to the subject at questions 853 to 855 and says that a difference with the ‘755 is that the mechanism for drug release is dissolution and erosion, while the mechanism for drug release in the ‘624 patent is diffusion.

[69] Finally, another difference Dr. Paul speaks to is the rate of release of the drug disclosed in the ‘624 patent is that substantially all of the drug is released over 8 hours. In contrast, the ‘755 application demonstrates a different release profile. Dr. Paul says that his assessment of the data is that with the ‘755 application after about 8 hours approximately 70% of the drug has been released, not all of it. See the Affidavit of Dr. Paul, paragraphs 98 and 99.

[70] I have reviewed Dr. Langer’s evidence with respect to solubility. He states that a 35% solubility by weight would be considered “very soluble” and he agreed that the ‘755 application gives a range up to 35%. See the cross-examination of Dr. Langer, questions 659 to 660. However,

the Court does not find that Dr. Langer sufficiently addressed the fact that the ‘755 application is primarily effective with low solubility drugs, up to 5% solubility.

[71] Dr. Langer also states that the drug is released from the polymer in the ‘755 application by dissolution. He does not speak to this difference with the ‘624 patent where the drug is released from the polymer primarily by diffusion. Dr. Langer does not address this difference between the ‘755 application and the ‘624 patent.

[72] The Court must conclude, after reviewing the competing evidence, that the major expert witnesses for the parties are both extremely qualified and highly regarded in their fields of chemical engineering. While Apotex has established many of the elements of the ‘624 patent are contained in the ‘755 application, the experts agree there are differences in some of the elements. Based on the competing evidence, the Court might find the competing evidence to be evenly balanced. However, there is one major difference expressly stated in the ‘755 application itself which tips the balance. The ‘755 application expressly states that the controlled release invention is for drugs of “limited solubility”, normally in the range from very low to 5% by weight (see page 3). Of course, the ‘624 patent is expressly directed to drugs of high solubility and expressly mentions metformin which is a drug with a 35% solubility rate. For these reasons, the Court must conclude that Biovail has met its burden on the balance of probabilities to demonstrate that the ‘755 application did not anticipate the ‘624 patent. The Court is mindful that the title of the ‘624 patent states that it is “FOR CONTROLLED RELEASE OF HIGHLY SOLUBLE DRUGS”. The inventors of both the ‘624

patent and the ‘755 application would not have used such express and opposite language if this difference in the inventions were not true.

[73] The U.S. patent litigation referred to above considered similar patents and prior art as before the Court in this case. It is interesting to find that Justice Breyer held at page 17 of his summary judgment decision on invalidity when speaking of the ‘837 patent, which is very similar to the ‘755 application:

> … The patented invention involves dissolution-controlled release systems (citations removed). Thus, the patented formulations are primarily used for low solubility drugs because drugs of high solubility would rapidly leach from the dosage forms and thus not sustained controlled-release.

[74] Mr. Justice Breyer continues along the same line that this Court has outlined above, which was independently concluded by this Court without prior reference to the U.S. Judgment.

[75] For these reasons the Court concludes that the ‘755 application does not anticipate the ‘624 patent.

Issue No. 2: Whether the ‘624 patent was disclosed in a mosaic of the prior art and was accordingly obvious to a person skilled in the art

[76] In accordance with section 28.3 of the Patent Act, the date to be used in assessing whether the invention claimed in the ‘624 patent was obvious is June 6, 1997.

[77] The Supreme Court adopted the following four-step approach to an obviousness inquiry in *Sanofi, supra.* at paragraph 67:

(1) (a) Identify the notional "person skilled in the art";

(b) Identify the relevant common general knowledge of that person;

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

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

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

[78] The Supreme Court noted that it may be appropriate to consider an "obvious to try" analysis, especially if there may be numerous interrelated variables with which to experiment (see paragraph 68 of *Sanofi*). The word "obvious" has been defined as "very plain" and the invention must be more or less self-evident (*Sanofi*, paragraph 66; *Pfizer Canada Inc. v. Apotex Inc.*, 2009 FCA 8 at paragraph 29).

[79] If an "obvious to try" test is warranted, Justice Rothstein set out a non-exhaustive list of factors to take into account (see paragraph 69 of *Sanofi*):

(1) Is it more or less self-evident that what is being tried ought to work?

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

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

[80] The respondent has provided a plethora of prior art from the relevant period, which is before 1997. In his affidavit, Dr. Paul specifically addressed 19 pieces of prior art put forward by Apotex and their experts to support their obvious argument. It is Apotex's position that the drug metformin was old, the use of swellable polymers for control-released tablets was known, and that the specific polymers referenced in the patent were known.

[81] Biovail does not dispute that many of the elements in Claim 1, as incorporated into the dependent claims of the '624 patent, were individually described in the art at the relevant time. It is their position that the inventiveness of the '624 patent is the combination of these features.

[82] The applicant also argues that the respondent's recitation of what was known at the relevant time is simplistic. Biovail states that the position taken by Apotex does not appreciate that there are a number of characteristics and behaviours of a formulation, vast differences between different types of polymers and that these factors ultimately contribute the dominant rate controlling mechanism of the drug from the dosage form. These variables were set out by Drs. Digenis and Mandal on their cross-examination, and will be discussed later in these reasons. Biovail submits

that the methods understood by the person skilled in the art to achieve gastric retention in 1997 were very different from the ‘624 patent, and that the art taught away from size-dependent gastric retention. Biovail also submits that highly soluble drugs present special problems for formulators, in that the polymeric matrices did not provide control over the release profile and the drug release was rapid, resulting in most of the drug being released within the first two hours. In simple terms, highly soluble drugs in a polymeric matrix, dissolve quickly upon contact with gastric fluid.

[83] Apotex submits that when considering obviousness, the court is permitted to consider a mosaic of prior art.

[84] A mosaic of prior art may be assembled in order to render a claim obvious. However, in doing so, the party claiming obviousness must be able to demonstrate not only that the prior art exists, but how the person of ordinary skill in the art would have been led to combine the relevant components from the mosaic of prior art (see *Laboratories Servier v. Apotex Inc.* (2008), 67 C.P.R. (4th) 241 at paragraph 254).

[85] It is settled law that there is no invention in discovering properties of know substances *(Pfizer Canada Inc. v. Ratiopharm Inc*. (2006), 52 C.P.R. (4th) 241 at paragraph 24 (F.C.A.)).

[86] The inventive concept in the ‘624 patent was set out by Biovail at paragraph 47 of their Memorandum of Fact and Law as such:

> The inventive concept disclosed in the Asserted Claims is the combination resulting in a controlled-released gastric retentive oral

> dosage form for use with metformin where the rate of drug release is dependent on dissolution and diffusion. The polymer stays intact during the drug delivery period: the primary drug release mechanism is not erosional. Further characteristics of the invention delineate a specific drug release profile (less than 40% of the drug released within 1 hour, substantially all of the drug released within 8 hours) and a range of drug loadings from 30:70 to 80:20. These characteristics are particularized by the dependencies of the Asserted Claims.

[87] Therefore, it is important to understand the "state of the art" with respect to: issues of special problems for highly soluble drugs; the use of polymers for controlled-release gastric retentive oral dosage forms; the methods of drug release from the polymer and drug release profiles; and drug loading.

What was known in 1997

[88] From the Memorandums of Fact and Law, submissions by counsel for the parties during the hearing, and the expert evidence, in particular that of Drs. Langer and Paul, the following can be accepted by the Court as prior knowledge:

(a) Issues of special problems for highly soluble drugs:

[89] Metformin was known to be a highly soluble drug that was absorbed in the duodenum and had a short half-life. It was known that metformin should be administered in a controlled release format, and in the "fed state". It was also known that highly soluble drugs were best formulated in high molecular weight polymers to control the drug release. The prior art taught the beneficial use of high molecular polymers, including the HMPC and PEO polymers, in the preparation of gastric retentive controlled release dosage forms for highly soluble drugs, that at least 40% of the drug is

retained after one hour, and that the dosage form is substantially intact until all the drug is released (for example, see L.S. Hermann, "Metformin: A Review of its Pharmacological Properties and Therapeutic Use" (1979) Diabetes & Metabolism 5 233; the '755 application).

(b) Use of polymers for controlled-release gastric retentive oral dosage forms:

[90] The '624 patent acknowledges, and Biovail does not dispute, that controlled-released dosage forms and their preparations and uses, including controlled release dosage forms made with swellable polymeric materials, had long been known and their benefits recognized. At page 1, line 12, the '624 patent states that "For many drugs, this pattern results in a transient overdose, followed by a long period of underdosing. This is of little clinical usefulness. The delivery pattern was improved in the 1970's with the introduction of a variety of controlled delivery systems". The person skilled in the art knew that gastric retentive dosage forms were to be administered in the fed state. The dosage forms claimed in the '624 patent were known and used in the industry for gastric retentive controlled release dosage forms.

(c) The use and properties of the high-molecular weight polymers in the '624 patent were known

[91] The use and properties of high-molecular weight polymers in the '624 patent were known, including their behaviours, the molecular weight grades of each, that they have hydrophilic polymeric matrices in swellable, controlled release dosage forms and are good for gastric retention. It was known that release rates were dependent on, *inter alia*, the molecular weight of the polymer and that high molecular weight HMPC polymers swelled and absorbed water more slowly than low molecular weight HMPC polymers (for example, see Waleed S.W. Shalaby, "In vitro and in vivo

studies of enzyme-digestible hydrogels for oral drug delivery" (1992) 19 J. of Controlled Releases 131; K. Park, "Enzyme-digestible swelling hydrogels as platforms for long-term oral drug delivery: synthesis and characterization" (1988) 9 Biomaterials 435; the '755 application).

(d) The methods of drug release from the polymer:

[92] In swellable controlled release dosage forms prepared with high molecular weight polymers, it was known that drug release could be controlled by the swelling of the polymer matrix, drug dissolution and diffusions, among other release mechanisms. For example, in A. Pham and P. Lee's article, listed below, the authors conducted experiments on high viscosity HPMC to "elucidate the mechanism [regulating drug release] involved". The aim of the U. Conte et al.'s works, listed below, was to determine the influence of the swelling and dissolution properties of the system on drug release, and the movement of the interfaces between solvent and system was measured during the release process.

[93] It was also known that high molecular weight polymers, such as HPMC, result in dosage forms in which swelling rather than erosion is the dominant drug release mechanism (for example, see U. Conte et al., "Swelling-activated drug delivery systems" (1988) 9(6) Biomaterials 489; A. Pham and P. Lee "Probing the mechanism of drug release from hydroxypropylmethyl cellulose (HMPC) matrices" (1993) 20 Proceedings of the International Symposium on Controlled Release of Bioactive Materials 220; Dow Publications: Formulating for Controlled Release with METHOCEL Premium cellulose ethers (Dow Chemical Company: 1995) and Formulating Sustained Release Pharmaceutical Products with METHOCEL (Dow Chemical Company: 1982)).

(e) Drug loading:

[94] It was recognized that drug to polymer ratios are an important factor in controlling drug release. In Ford et al, listed below, the authors found that the major factor controlling drug release was the drug to polymer ratio. (For example, see Ford et al, "Importance of Drug Type, Tablet Shape and Added Diluents on Drug Release Kinetics from Hydroxyproplylmethylcellulose Matrix Tablets" (1987) 40 Int. Journal of Pharmaceutics 223; the '755 application).

Metformin

[95] Biovail also submits that metformin was not directly addressed in the disclosure of the prior art. However, the problems of highly soluble drugs were known in 1997. **[CONFIDENTIAL EVIDENCE REFERRED TO HAS BEEN REDACTED FROM THE PUBLIC VERSION OF THE REASONS FOR ORDER]** Accordingly, the Court does not agree that identifying metformin for a controlled release dosage is inventive in itself.

The mechanism of action

[96] Biovail argues that the mechanism of action in the '624 patent was not known.

[97] Drug release mechanisms have elements of swelling, dissolution, diffusion and erosion, even if one element is more pronounced than another. Dr. Mandal explained that erosion is an inherent characteristic of polymers (see his cross-examination, pages 36-37, 39), and Dr. Paul

agreed that all polymers will at some point erode (see his cross-examination, Q170). Dr. Paul also agreed that it was known that the molecular weight of the polymer affects the drug release mechanisms. The ‘718 application and Pham and Lee articles taught that a higher molecular weight PEO swelled faster than it eroded and that the drug release will be via diffusion or a mixture of dissolution and diffusion.

[98] On cross-examination, Dr. Paul agreed that the ‘755 application taught how to deal with more soluble drugs and speaks to the drug being dispersed in a solid polymeric matrix, in that case hydroxyethyl cellulose, at a weight ratio of drug to polymer of about 80:20 or less. Dr. Paul also agreed that that the ‘755 application includes a discussion of the solubility of the drugs that can be used in the controlled-release oral dosage forms, with normal solubility in a range up to 35%, which is the upper end of the range listed in the ‘624 patent. However, Dr. Paul stated that what the ‘755 application does not address the question of what controls the release of the drug. At question 709 on his cross-examination, he stated “But what controls that release is what is at issue, in my mind…”.

[99] However, mechanisms of action, even if not known as of 1997, are inherent properties of high molecular weight polymers in controlled-release systems containing highly soluble drugs. In *AstraZeneca AB v. Apotex Inc*. (2007), 60 C.P.R. (4th) 199 at paragraph 103 per Barnes J., the applicant argued that the new use disclosed by the patent was the discovery of a mechanism of action. Justice Barnes held that a new use is not satisfied by identifying an inherent effect of a known therapy.

[100] As stated by Justice Hughes in *Shire Biochem Inc. v. Canada (Minister of Health)* (2008), 67 C.P.R. (4th) 94 at paragraph 79, the fact that a number of routes exist to the invention does not mean that the alleged invention is not obvious.

[101] Viewed without any knowledge of the alleged invention as claimed, any "new" learnings were with regard to the mechanism of action of the drug release. These are inherent properties and not patentable. The non-inherent elements of the '624 invention were known.

[102] Biovail argues that the work on metformin was based on a culmination of years of research and development. The difficulty in selecting a polymer, based on the variable factors that need to be considered, were acknowledged by Dr. Digneis and Dr. Mandal on cross-examination.

[103] On cross-examination Dr. Digenis noted that there are numerous factors that have an impact on the speed of delivery of a drug out of the dosage form. At questions 126 – 146 Dr. Digneis agreed that molecular weight and viscosity of the polymer, if the polymer is cross-linked or branched, solubility of the drug, the presence or absence of food, any coatings, excipients or fillers, compression during manufacturing, and the shape of the dosage form are all factors that would effect the delivery of the drug.

[104] Dr. Mandal agreed on cross-examination that the way a polmeric matrix behaves is dictated by a number of different variables (page 27, lines 8-16). Dr. Mandal also agreed that there are a

huge range of polymers and that within each of those types, there is a vast variation (page 28, lines 1-25). At page 29, starting at line 10, Dr. Mandal agreed that there are numerous types of cellulosic polymers that could be used and that these can be substituted with a number of different functional groups, such as hydroxyl groups.

[105] The evidence from Ms. Louie-Helm on this subject is contained in her affidavit, her voluminous lab note books, and her cross-examination.

[106] Ms. Louie-Helm deposes that the effort to develop the invention spanned years of research, dating back to 1992 and Depomed's work on ASA, and that there was a need to address the multiple dosing problem by prolonging the release of freely soluble drugs over an extended period of time. However, the evidence with regard to metformin does not demonstrate the rigour that is often associated with pharmaceutical research. **[CONFIDENTIAL EVIDENCE REFERRED TO HAS BEEN REDACTED FROM THE PUBLIC VERSION OF THE REASONS FOR ORDER]**

Conclusion with respect to obviousness

[107] When the Court applies the law to the evidence in this case, the Court concludes that:

1. The difference between the state of the art and the inventive concept in the '624 patent is the "right" combination of known elements with a highly soluble drug like metformin. The known elements include a high molecular weight polymer which swells to enhance gastric retention. The result is a mechanism of action which releases the metformin predominantly by diffusion and dissolution, not erosion, over an eight hour time period;

2. The resulting “mechanism of action” is an inherent property of the particular polymer chosen and, in law, is not patentable;

3. The experimentation which defined a polymer with the right molecular weight and other characteristics to control the release of the highly soluble drug metformin is the alleged invention. The evidence is evenly divided as to whether this experimentation was such that it could be considered “obvious to try” or not;

4. The question is whether the experimentation would have been “obvious to try” by a person skilled in the art. In this regard, the Court has weighed the evidence adduced by both sides of the case and finds the evidence evenly balanced;

5. The parties agree that the elements of the invention were known in the prior art and it was their combination, including the right choice of polymer, which caused the “mechanism of action” claimed in the ‘624 patent;

6. The evidence showed that high molecular weight polymers were known to be more viscous and to retain the drug for a longer period of time, than lower molecular weight polymers;

7. It was known that the solubility of the polymer decreases as the molecular weight increases. Moreover, the higher molecular weight polymer imbibes water which slows the release of the drug;

8. The polymers identified in patent ‘624 were well-known, readily available polymers;

9. The parties recognized that a controlled release dosage form for highly soluble drugs such as metformin was required. There was a motive to find the solution;

10. The evidence as to the extent, nature and amount of experimentation required to achieve the ‘624 patent were as a result of trials on a number of polymers; and

11. The Court finds the evidence evenly balanced as to whether these trials were the type of routine experimentation which were “obvious to try” by a person skilled in the art.

Because the applicant has the onus of proof and because the Court has concluded that the evidence on this important “obvious to try” test criteria is evenly balanced, the applicant has not satisfied its onus to prove, on a balance of probabilities, that the allegation in this regard was unjustified. For this reason, the Court must dismiss this application.

[108] I recognize that in *Depomed Inc. v. Ivax Corporation*, United States District Court, Northern District of California, case number 3:06-cv-00100 CRB, per Judge Charles Breyer (December 12, 2007) Judge Breyer denied Ivax's motion for summary judgement of invalidity as he found that Ivax had failed to meet its burden of demonstrating that the asserted claims of the patents at issue in that case were obvious in light of two prior art references, US Patent No. 5,582, 837 and the Dow publications. I note that this matter was heard in a foreign jurisdiction under different law, did not involve the '624 patent, that only two pieces of prior art were considered, and that this case is based on a different record.

[109] In the event that I am wrong on this issue of obviousness, I will proceed to consider the remaining two issues.

Issue No. 3: Whether the '624 patent is invalid upon the principle that it is a double-patent, i.e. a patent for an invention which was the subject of another patent, patent 2 414 671 (the '671 patent)

[110] Apotex submits that the '624 patent is invalid on the principle of "double-patenting". Mr. Justice Hughes clearly explained the principle against double-patenting in *Bristol-Myers Squibb Canada Co. v. Apotex Inc*., [2009] F.C. 137 at paragraphs 173 and 174:

> ¶ 173. Double patenting, put simply, involves the concept that a person cannot get a second patent for the same thing for which they already have received a patent. A patent is a monopoly for a limited period of time and that period should not be extended by the expedient of getting a subsequent patent for the same thing.
>
> ¶ 174. Double patenting only applies when dealing with the same person getting two or more patents. If some other person has

> received an earlier patent, then the second patent is to be considered in the context of anticipation and obviousness or, in the case of pre-October 1989 patent applications, the first to invent.

[111] Apotex submits that the asserted claims of the ‘624 patent are invalid on the basis of the claims in Canadian ‘671 patent. The Supreme Court of Canada in *Whirlpool Corp. v. Camco Inc.*, [2000] 2 S.C.R. 1067 at paragraph 63 per Binnie J. explained that:

> Prohibition against double patenting relates back to the “evergreen” problem mentioned at the outset. The inventor is only entitled to “a” patent for each invention. If a subsequent patent issues with identical claims, there is an improper extension of the monopoly.

[112] In the case at bar the Court is satisfied that the ‘624 patent expires before the ‘671 patent. Accordingly, the ‘624 patent does not evergreen a prior patent with the same invention. The ‘624 patent expires on June 5, 2018. The ‘671 patent expires on February 26, 2021. Without the Court needing to go into further detail, it is clear that the ‘624 is not a subsequent patent to the ‘671 patent within the meaning of the principles of law against double patenting and the mischief of “evergreening”.

[113] Since it is clear to the Court that the double patenting law is not applicable to the ‘624 patent, it is not necessary for the Court to consider whether the ‘624 patent claims are “identical or conteriminous” with the ‘671 patent.

<u>Issue No. 4:</u> Whether the Apotex formulation for extended release metformin was disclosed in the prior art, namely the Dow Publications, so that the Apotex formulation cannot infringe the ‘624 patent and the Gillette defence applies.

[114] The Gillette defence is made out when it is established that the alleged infringing product is based on the teachings of a prior art and that the alleged infringer is simply doing something that is already known (*Gillette Safety Razor Co. v. Anglo-American Trading Co. Ltd*. (1913), 30 R.P.R. 465 (H.L.)).

[115] Hughes and Woodley on Patents (Hughes, Roger T., John H. Woodley, Neal Armstrong and David Smith, Hughes and Woodley on Patents , 2nd ed. (Markham, Ont.: LexisNexis Butterworths, 2005 at para 38A) described this defence as follows:

> The House of Lords in England gave rise to a defence to an allegation of infringement that has commonly been called the Gillette Defence after the case of that name(1). The Court said:
>
> > The defence that "the alleged infringement is not novel at the date of the plaintiff's Letters Patent" is a good defence in law, and it would sometimes obviate the great length and expense of Patent cases if the defendant could and would put forth his case in this form and thus spare himself the trouble of demonstrating on which horn of the well-known dilemma the plaintiff had impaled himself, invalidity or non-infringment.
> >
> > This defence as such has been raised in Canadian cases(2) and been successful in one.(3)

1.*Gillette Safety Razor Co. v. Anglo-American Trading Co. Ltd. (1913), 30 R.P.C. 465 at 480-481* (H.L.); *Eli Lilly Canada Inc. v. Apotex In.*, [2008] F.C.J. No. 171, 63 C.P.R. (4th) 406 at paras. 185 and 186.
2. Citations omitted.
3. *Eli Lilly Canada Inc. v. Apotex Inc.*, [2009] F.C.J. No. 413, March 26, 2009, 2009 FC 320 at paras. 60 to 64.

[116] Apotex alleges that it is merely practicing the teachings of the prior art in a manner that is consistent with the knowledge of a person skilled in the art. It is their position that their extended release metformin tablets are made in accordance with the teachings of the two Dow Chemical publications referred to above in the obviousness section.

[117] The parties disagree as to whether a successful Gillette defence is entirely reliant on an anticipating prior art reference and that absent this conclusion, the defence is unsustainable and unjustified. Apotex relies on the original text from the House of Lords decision in *Gillette Safety Razor Company v. Anglo-American Trading Company Ltd*. and an excerpt from Fox, Canadian Patent Law and Practice (4th ed. 1969) at 352-252 for their position that the question should be whether Apotex's tablets are made in accordance with the prior art, not whether the prior art anticipates the claims.

[118] Two recent decisions of this Court support Biovail's position that, essentially, the Gillette defence is an attack on validity and lack of novelty: *Eli Lilly Canada Inc. v. Apotex Inc.*, 2009 FC 320 and *Sanofi-Aventis Canada Inc. et al. v. Apotex Inc. et al.*, 2009 FC 676.

[119] In *Eli Lilly Canada Inc. v. Apotex Inc.* Justice Hughes found at paragraph 64 that, on the facts of that NOC proceeding, Apotex's allegations as to the Gillette defence were justified as the Apotex product was to be produced in accordance with the process outlined in a piece of prior art that would fall within the scope of the claims of the patent at issue in that matter. However, Justice Hughes had previously found that product set out in the prior patent anticipated the product as

claimed in the patent at issue and therefore the claims were not valid and no valid claim had been infringed.

[120] In *Sanofi-Aventis Canada Inc. et al. v. Apotex Inc. et al.*, 2009 above at paragraphs 347 to 349, Justice Snider interpreted the conclusion of Justice Hughes in *Eli Lilly Canada Inc. v. Apotex Inc*, above. According to Justice Snider, Justice Hughes' conclusion on the Gillette defence was entirely reliant on his conclusion on anticipation and that absent his finding of anticipation, the Gillette defence would not have been available to Apotex. Justice Snider therefore determined that the Gillette defence could not be sustained in the matter before her as Apotex had not made a claim on invalidity due to anticipation by the prior patent.

[121] Based on these decisions, it is clear to the Court that the Gillette defence has only ever applied in Canada when the prior art anticipates the patent. In the case at bar, Apotex has not asserted that the 2 Dow Chemical publications in 1982 and 1995 anticipate the '624 patent. The Court would have expected Apotex to rely on these Dow publications in its argument on anticipation if these publications really did disclose and enable the invention claimed in the '624 patent.

[122] In this case Apotex did not assert the Dow Chemical publications in its allegations on anticipation. As discussed, I have found that Biovail has shown that Apotex's allegation of invalidity for anticipation is not justified. Therefore, absent a finding that Biovail has failed to show that the anticipation allegations are not justified, Apotex's Gillette defence argument must fail.

CONCLUSION

[123] The Court concludes that the applicants have established on the balance of probabilities that the Apotex allegations that the Biovail ‘624 patent is invalid for anticipation, double-patenting and infringement are not justified. However, the Court has also concluded that the applicants have not met their legal burden to establish on the balance of probabilities that the Apotex allegation that the Biovail ‘624 patent is invalid for obviousness are not justified. Accordingly, the application for an Order prohibiting the Minister of Health from issuing a Notice of Compliance to Apotex for a generic version of the metformin extended release tablets will be dismissed with costs.

COSTS

[124] At the hearing, the parties indicated that if they cannot agree upon the scale of costs and the number of counsel, they will make submissions to the Court. Accordingly, the Court will make a subsequent order detailing the scale of the tariff and the number of counsel if the parties do not reach an agreement.

ORDER

THIS COURT ORDERS that:

This application for an Order prohibiting the Minister of Health from issuing a Notice of Compliance to Apotex for a generic version of metformin extended release tablets is dismissed with costs.

"Michael A. Kelen"
Judge

Appendix A

Background of Witness

Unless noted, all witnesses were cross-examined.

APOTEX'S WITNESSES:

Dr. Robert Langer: Dr. Langer is a chemical engineer whose work focuses on the areas of chemical engineering, biomedical engineering, biotechnology, pharmaceutical chemistry and formulation development. He is one of 14 Institute Professors at the Massachusetts Institute of Technology, has authored or co-authored over 1,000 articles, and has approximately 600 issued or pending patents world wide. Dr. Langer has sat on numerous Boards, such as the United States Food and Drug Administration's Science Board, and received over 160 major awards.

Dr. Tarun Mandal: Dr. Mandal is a pharmaceutical formulator and is the McCaffrey/Norwood Professor of Pharmacy and Pharmaceutics at Xavier University of Louisiana. He has served as a reviewer or on the editorial board for numerous peer-reviewed journals. Dr. Mandal also has an extensive record of peer-reviewed publications including original research papers.

Dr. George Digenis: Dr. Digenis is an Emeritus Professor of Medicinal Chemistry and Pharmaceutics at the College of Pharmacy at the University of Kentucky, as well as an Emeritus Professor in the Departments of Nuclear Medicine and Toxicology at the College of Medicine at the University of Kentucky. He has more than 190 peer-reviewed scientific articles or books to his name, and holds 14 patents. Dr. Digenis' research interests include drug design and delivery and the release behaviour and bioavailability of dosage forms. In particular, he has studied metformin and its absorption in the stomach intestine.

Mr. John Hems: Mr. Hems is the Director, Regulator Affairs, Canada, at Apotex. Mr. Hem's affidavit included excerpts from Apotex's drug submission. He was not cross-examined.

Ms. Biserka Horvat: Ms. Horvat is a law clerk at Goodmans LLP whose affidavit included copies of the references listed in the NOA. She was not cross-examined.

BIOVAIL'S WITNESSES:

Dr. Donald Paul: Dr. Paul is the Director of the Texas Materials Institute, the Earnest Cockrell Sr. Chair in Chemical Engineering, and Director of the Center for Polymer Research, all at the University of Texas at Austin. He is a member of numerous professional societies such as the American Institute of Chemical Engineers, has authored over 600 peer-reviewed scientific publications, and is on the editorial board for peer-reviewed journals such as the Journal of Applied Polymer Science.

Dr. Ronnie Fass: Dr. Fass is a Professor of Medicine at the University of Arizona, Chief of Gastroenterology at Southern Arizona VA Health Care System, and Director of GI Motility Laboratory at both Southern Arizona VA Health Care System and the University of Arizona Health Sciences Centre. He holds numerous awards and honours for his work, is extensively involved in the gastroenterology community, and is a reviewer for numerous academic journals. Dr. Fass has a particular expertise in gastrointestinal motility.

Ms. Jenny Louie-Helm: Ms. Louie-Helm is a co-inventor of the 624 Patent.

Ms. Christine Haskett: Ms. Haskett is a partner at a US law firm involved in US litigation relating to the counterpart of the '624 Patent. Ms. Haskett was not cross-examined.

Dr. Alim Mamajiwalla: Dr. Mamajiwalla is the Senior Director, Intellectual Property at Biovail, who provided patent listing information. He was not cross-examined.

Mr. Roger Shoreman: Mr. Shoreman is a law clerk at Lanczner Slaght Royce Smith Griffin LLP whose affidavit included a certified copy of the '624 Patent. He was not cross-examined.

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-118-08
STYLE OF CAUSE:	BIOVAIL CORPORATION and DEPOMED, INC. v. THE MINISTER OF HEALTH and APOTEX INC.
PLACE OF HEARING:	Toronto, Ontario
DATE OF HEARING:	November 23, 24, 25 and 26, 2009
AMENDED REASONS FOR ORDER AND ORDER:	KELEN J.
DATED:	January 20, 2010

APPEARANCES:

Marguerite Ethier Elizabeth Dipchand	FOR THE APPLICANTS
Andrew Brodkin Dino Clarizio Belle Van	FOR THE RESPONDENT (APOTEX INC.)

SOLICITORS OF RECORD:

Lenczner Slaght Royce Smith Griffin LLP Toronto, ON	FOR THE APPLICANTS
Goodmans LLP Toronto, ON	FOR THE RESPONDENT (APOTEX INC.)
John H. Sims, Q.C. Deputy Attorney General of Canada	FOR THE RESPONDENT (MINISTER OF HEALTH)