Date: 20080729

Docket: T-837-07

Citation: 2008 FC 922

Ottawa, Ontario, July 29, 2008

PRESENT: The Honourable Madam Justice Simpson

BETWEEN:

PHARMASCIENCE INC.

Applicant

and

THE MINISTER OF HEALTH and THE ATTORNEY GENERAL OF CANADA

Respondents

REASONS FOR ORDER AND ORDER

[1] Pharmascience Inc. (the Applicant) seeks Judicial Review pursuant to section 18.1 of the *Federal Courts Act*, R.S.C. 1985, c. F-7 of a decision of the Minister of Health (the Minister) made on April 12, 2007 (the Decision) in which he concluded that the Applicant was required to address the Canadian Patents Nos. 2,382,387 and 2,382,549 (the 387 and 549 Patents) in respect of its Supplementary Abbreviated New Drug Submission (the SANDS) for its generic 1.25 mg ramipril capsules under subsection 5(1) of the *Patented Medicines (Notice of Compliance) Regulations*, S.O.R./93-133 (the NOC Regulations).

BACKGROUND

(This section draws heavily on the Agreed Facts provided by the parties.)

[2] Prior to July 10, 2000, Sanofi-Aventis Canada Inc. (the Innovator) was granted four Notices of Compliance (the Prior NOCs) for ramipril capsules, which it marketed under the brand name ALTACE. It was first approved to treat hypertension.

[3] On July 10, 2000, the Applicant purchased ALTACE in 1.25 mg, 2.5 mg, 5 mg and 10 mg capsules for use as Canadian reference products.

[4] On February 13, 2001, the Innovator was granted a further Notice of Compliance (NOC) in association with submission number 066094 (the Fifth NOC).

[5] Pharmascience's Abbreviated New Drug Submission #073405 (the ANDS) was received by the Minister on September 4, 2001. A copy of a letter dated September 13, 2001 from the Submission and Information Policy Division, on behalf of the Minister acknowledging receipt of the ANDS on September 4, 2001 is at Tab 3 of the Agreed Documents. As acknowledged in that letter, as filed, Pharmascience's ANDS #073405 was in respect of ramipril 1.25 mg, 2.5 mg, 5 mg and 10 mg capsules.

[6] The Applicant's ANDS was based the asserted bioequivalence of its 1.25 mg, 2.5 mg, 5 mg and 10 mg ramipril capsules with the Innovator's 1.25 mg, 2.5 mg, 5 mg and 10 mg ALTACE

ramipril capsules which had been purchased by the Applicant as Canadian reference products. There is no issue that in connection with this ANDS, the Applicant was obliged to address all the patents listed on the Prior NOCs.

[7] In the ANDS, the Applicant submitted bioavailability data showing the bioequivalence of its 10 mg tablet with the Innovator's 10 mg ALTACE tablet. Pursuant to the Proportional Formulations Policy, the Applicant requested a waiver of the requirement to submit bioavailability studies showing bioequivalence of its 1.25 mg, 2.5 mg and 5 mg tablets with the corresponding ALTACE ramipril capsules strengths. Instead, the Applicant submitted data demonstrating the proportionality of its 1.25 mg, 2.5 mg and 5 mg tables with its 10 mg ramipril tablet.

[8] The ANDS included a copy of an invoice dated July 10, 2000, for the purchase from the Innovator of samples of all four strengths of ALTACE capsules (the Invoice).

[9] The ANDS also included a clinical report of Algorithme Pharma (March 23, 2001 as amended April 6, 2001) regarding bioequivalence between the Applicant's Ramipril 10 mg capsules and the ALTACE 10 mg ramipril capsules. The report states that the samples of ALTACE were received by Algorithme Pharma on December 15, 2000.

[10] On February 24, 2003, the Applicant withdrew its ANDS for the generic 1.25 mg ramipril capsules at the request of Health Canada due to a lack of stability data for those capsules. The review of the ANDS proceeded only in respect of the generic 2.5 mg, 5 mg and 10 mg capsule strengths.

[11] By letter dated August 27, 2003, the Minister agreed that the 2.5 mg, 5 mg and 10 mg ramipril capsules were bioequivalent to the respective ALTACE capsules based on the bioequivalence studies in respect of the 10 mg capsules and the demonstration of proportionality in respect of the 2.5 mg and 5 mg capsules under the Proportional Formulation Policy. Accordingly, the Applicant was entitled to a NOC for these capsules, subject only to compliance with the NOC Regulations.

[12] On November 6, 2003, the Innovator was granted a further NOC in respect of ALTACE following submission number 082094 the (Sixth NOC). It listed the 549 Patent after it was granted on March 17, 2005 and the 387 Patent after it was granted on June 21, 2005. These Patents were listed in connection with a new indication – treatment following a heart attack. The Applicant is not seeking approval for its generic ramipril capsules for the treatment of heart attacks. In other words, it does not seek to use the teaching of the 387 and 547 Patents.

[13] On December 30, 2005, after the Sixth NOC and after the 387 and 549 Patents were listed, the Applicant filed the SANDS for its generic 1.25 mg ramipril capsules.

[14] In its SANDS, the Applicant sought a waiver of the requirement to submit separate bioavailability studies showing bioequivalence of its 1.25 mg generic ramipril capsule to the 1.25 mg ALTACE capsule. Instead, it proposed to demonstrate the proportionality of its 1.25 mg generic capsule to its 10.0 mg ramipril capsule which was the subject of its original ANDS.

[15] On November 3, 2006, the Supreme Court of Canada released its decision in *AstraZeneca Canada Inc. v. Canada (Minister of Health)*, 2006 SCC 49, [2006] 2 S.C.R. 560.

[16] In *AstraZeneca*, Mr. Justice Ian Binnie, writing for a unanimous Supreme Court, described the workings and relations between the *Food and Drug Act*, R.S.C. 1985, c. F-27 and the *Food and Drug Regulations*, C.R.C., c. 870, the *Patent Act*, R.S.C. 1985, c. P-4 and the NOC Regulations. He then turned to the facts of the case and noted that *AstraZeneca* had developed Losec 20 to treat stomach hyperacidity. It was Losec 20 formulated for this purpose that Apotex sought permission to copy. However, patents were listed for a subsequent new version of Losec 20. The 037 patent described a new oral dosage form and a new manufacturing process and the 470 patent taught of a new form of omeprazole. However, this new version of Losec 20, which was designed to treat *H. Pylori*, was never marketed.

[17] The Supreme Court of Canada held in these circumstances that Apotex did not have to address 037 and 470 patents because the drug described therein had never been marketed and therefore could not have been the drug to which Apotex made reference to establish bioequivalence.

[18] The Court referred to subsection 5(1) of the NOC Regulations. It provides that:

5. (1) If a second person files a submission for a notice of compliance in respect of a drug and the submission directly or indirectly compares the drug with, or makes reference to, another drug marketed in Canada under a notice of compliance issued to a first person and in respect of which a patent list has been submitted, the second person shall, in the submission, with respect to each patent on the register in respect of the other drug,

(*a*) state that the second person accepts that the notice of compliance will not issue until the patent expires; or

(*b*) allege that

(i) the statement made by the first person under paragraph 4(4)(*d*) is false,

(ii) the patent has expired,

(iii) the patent is not valid, or

(iv) no claim for the medicinal ingredient, no claim for the formulation, no claim for the dosage form and no claim for the use of the medicinal ingredient would be infringed by the second person making, constructing, using or selling the drug for which the submission is filed.

5. 1) Dans le cas où la seconde personne dépose une présentation pour un avis de conformité à l'égard d'une drogue, laquelle présentation, directement ou indirectement, compare celle-ci à une autre drogue commercialisée sur le marché canadien aux termes d'un avis de conformité délivré à la première personne et à l'égard de laquelle une liste de brevets a été présentée — ou y fait renvoi —, cette seconde personne doit, à l'égard de chaque brevet ajouté au registre pour cette autre drogue, inclure dans sa présentation :

a) soit une déclaration portant qu'elle accepte que l'avis de conformité ne sera pas délivré avant l'expiration du brevet;

b) soit une allégation portant que, selon le cas :

(i) la déclaration présentée par la première personne aux termes de l'alinéa 4(4)*d*) est fausse,

(ii) le brevet est expiré,

(iii) le brevet n'est pas valide,

(iv) elle ne contreferait aucune revendication de l'ingrédient médicinal, revendication de la formulation, revendication de la forme posologique ni revendication de l'utilisation de l'ingrédient médicinal en fabriquant, construisant, utilisant ou vendant la drogue pour laquelle la présentation est déposée.

[19] In this regard, the Court said:

> 36 Viewed in this light, it seems to me inescapable that the expression "another drug" in s. 5(1) refers to the actual comparator drug — not a drug that never became available for comparison — and that the words "with respect to each patent on the register in respect of the other drug" carries the same meaning.
>
> 37 The whole obligation incurred by the generic manufacturer under the *NOC Regulations* is based on its "early working" of patents embodied in "another drug for the purpose of demonstrating bioequivalence". The only drug that fits the description is the version of *Losec 20* approved in the June 19, 1989 NOC.
>
> H. The Broader Statutory Purpose
>
> 38 I repeat that Parliament's stated purpose in authorizing the *NOC Regulations* was to permit the "early working" of the *patented invention* (s. 55.2(4)). As Apotex did not make use of the patented inventions taught by the 037 and 470 patents, Apotex is not on this occasion within the mischief aimed at by the *NOC Regulations*.
>
> 39 By imposing the 24-month delay called for by the *NOC Regulations*, the decision of the Federal Court of Appeal undermines achievement of the balance struck by Parliament between the objectives of the *FDA* and regulations thereunder (making safe and effective drugs available to the public) and the *Patent Act* and its regulations (preventing abuse of the "early working" exception to patent infringement). Given the evident (and entirely understandable) commercial strategy of the innovative drug companies to evergreen their products by adding bells and whistles to a pioneering product even after the original patent for that pioneering product has expired, the decision of the Federal Court of Appeal would reward evergreening even if the generic manufacturer (and thus the public) does not thereby derive any benefit from the subsequently listed patents. In my view, s. 5(1) of the *NOC Regulations* requires a patent-specific analysis,

> i.e. the generic manufacturer is only required to address the cluster of patents listed against submissions relevant to the NOC that gave rise to the comparator drug, in this case the 1989 version of *Losec 20*.
>
> 40 If AstraZeneca had brought to market a *Losec 20* product pursuant to the later NOCs and if Apotex had made reference to that modified product for the purpose of demonstrating bioequivalence, Apotex would have been required to file a notice of allegation with respect to the 037 and 470 patents.
>
> 41 However, it is clear that AstraZeneca did not market any product pursuant to the subsequent NOCs and that the preconditions to any obligations of Apotex under s. 5(1) were therefore not triggered.

[20] In response to *AstraZeneca*, the Minister acknowledges that he developed an informal policy (the First Policy) to the effect that generic companies were not required to address patents listed against submissions filed after the generic purchased an Innovator's Canadian comparison drugs. This meant that, in this case, the date of the Invoice would serve as the cut off date.

[21] This policy was described in the following manner by Mr. Justice Roger Hughes in *Ferring Inc. v. Canada (Minister of Health)*, 2007 FC 300, 55 C.P.R. (4th) 271 at paragraphs 63 and 64:

> 63 As soon as the *AstraZeneca* decision was released in early November, 2006, the Minister, with some prompting from some generics, set about to devise a process for dealing with the question of setting a procedure for dealing with whether a generic is required to address any particular listed patent. This process is set out in affidavits of Anne Elizabeth Bowes, Associate Director of the Therapeutic Products Directorate (TPD) which is the branch of the Minister's department dealing with the *NOC Regulations*. This process involves only ANDS applications submitted by generics

> prior to the change in the *NOC Regulations* of October 5, 2006. Ms. Bowes explains that it involves two steps:
>
> 1. First, the date on which the generic has purchased the comparator drug is used to determine which notices of compliance have been issued in respect of that comparator drug. The position of the Minister is that all patents listed in respect of the relevant NOC as of that date must be addressed by the generic.
>
> 2. Second, where further NOC's have been issued to the innovator after the date of the purchase of the comparator drug, the Minister makes a determination as to whether the generic has made use of changes made to the comparator drug since the original date of purchase. If the generic has made use of such changes, then all patents added to the patent list subsequent to the date of purchase as are pertinent to the changes of which the generic has taken advantage must be addressed.
>
> 64 The evidence shows that the Minister has regard to submissions made by the generic or its lawyers as to the date of purchase of the comparator drug and whether the generic has taken advantage of any subsequent NOC's issued to the innovator. As well, the Minister has regard to matters that are self evident on the record of the ANDS application by the generic, such as the date upon which data respecting the comparator drug was filed so as to establish a latest date upon which such drug could have been purchased. The "default date" for establishing the purchase of the comparator drug, in the absence of other information, is taken to be the filing date of the ANDS.

[22] Mr. Justice Hughes held that the Minister's First Policy was consistent with the reasons of the Supreme Court in *AstraZeneca* (*Ferring* para. 65) and his decision was upheld by the Federal Court of Appeal (2007 FCA 276).

[23] However, in obiter, in *Ferring*, Mr. Justice Hughes went on to suggest a revision to the Minister's First Policy. Starting at para. 65, Justice Hughes stated:

> If I were to modify this policy, I would do so in two respects…A better date [than the date of purchase of the comparator drug] would be the filing date of the ANDS by the generic as that is a date of record and is logically, the last date upon which the comparator drug could have been obtained by the generic.

[24] Following Justice Hughes's suggestion in *Ferring*, the Minister changed his policy so that all patents had to be addressed as of the date an ANDS or a SANDS for the generic version of a drug was filed (the Second Policy)

[25] Based on *AstraZeneca* and the First Policy, the Applicant asked the Minister to confirm that it was not required to address the 387 and 549 Patents in connection with its SANDS for the 1.25 mg generic ramipril capsules. The Minister did not reply to this request although apparently Novopharm and Apotex received approvals for their generic versions of ramipril on the basis of the First Policy.

[26] On April 12, 2007, the Minister Issued the Decision requiring the Applicant to address the 387 and 549 Patents under section 5 of the NOC Regulations in connection with the 1.25 mg generic ramipril capsules which were the subject of the SANDS of December 30, 2005.

[27] By letter dated April 30, 2007, the Applicant requested reconsideration of the part of the Decision relating to the 1.25 mg capsules and by letter dated June 8, 2007, the Minister denied the Applicant's request.

[28] By letter dated May 17, 2007, the Minister granted the waiver of bioavailability data for the SANDS and accepted that the Applicant's 1.25 mg strength of ramipril is bioequivalent to 1.25 mg ALTACE capsules under the Proportional Formulations Policy. Accordingly, the Applicant is entitled to a NOC for the 1.25 mg capsules, subject to compliance with the NOC Regulations.

[29] The following table is based on one provided in the Agreed Statement of Facts. It lists the NOCs that were issued to the Innovator for ALTACE and the submissions that gave rise to those NOCs and the patents listed on the Patent Register in respect of those submissions:

NOC Date	Submission No.	Submission Date of Filing	Reason for Submission	Patent No.	Patent Date of Filing	Date Added
The Prior NOCs						
Oct 3, 1993	08257	Jul 7, 1992	New drug submission	206	Oct 20, 1981	Apr 11, 2001
				948	Nov 26, 1991	Jun 25, 2004
Sep 30, 1994	24206	Mar 10, 1994	Provides for a revised manufacturing process	206	Oct 20, 1981	Apr 11, 2001
				089	Aug 10, 1990	Nov 10, 2003
				948	Nov 26, 1991	Jun 25, 2004

Jun 5, 1996	043465	May 13, 1996	(Company merger)	206	Oct 20, 1981	Apr 11, 2001
				089	Aug 10, 1990	Nov 10, 2003
				948	Nov 26, 1991	Jun 25, 2004
Dec 31, 1996	033131	Dec 24, 1994	Additional indication: treatment following acute myorcardia infarction	206	Oct 20, 1981	Apr 11, 2001
				089	Aug 10, 1990	Nov 10, 2003
				948	Nov 26, 1991	Jun 25, 2004

July 10, 2000 - The Invoice

The Fifth NOC

Feb 13, 2001	066094	Apr 3, 2000	New indication: management of patients at increased risk of cardiovascular events	206	Oct 20, 1981	Apr 11, 2001
				089	Aug 10, 1990	Nov 10, 2003
				948	Nov 26, 1991	Jun 25, 2004

Sept. 4, 2001 – The ANDS

The Sixth NOC

Nov 6, 2003	082094	Jan 15, 2003	Update the Action and Clinical Pharmacology Section of the Product Monograph with regards to management of patients with increased risk of cardiovascular events	206	Oct 20, 1981	Nov 19, 2003
				948	Nov 26, 1991	Jun 30, 2004
				549	Aug 30, 2000	Mar 17, 2005
				387	Aug 25, 2000	Jun 28, 2005

Dec. 30, 2005 – The SANDS

May 29, 2006	105810	May 8, 2006	Manufacturer name change	206	Oct 20, 1981	Jun 2, 2006
				089	Aug 10, 1990	Jun 2, 2006
				948	Nov 26, 1991	Jun 2, 2006
				549	Aug 30, 2000	Jun 2, 2006
				387	Aug 25, 2000	Jun 2, 2006

[my emphasis]

[30] As shown in the above table, as of July 10, 2000, the date of purchase of the ALTACE samples used for the purposes of the Applicant's comparative testing, the NOCs issued to the Innovator in respect of ramipril were the Prior NOCs. As of September 4, 2001, the date of filing of the Applicant's ANDS, the Fifth NOC had also been issued to the Innovator in respect of Submission #066094 but no new patents had been listed in association with the Fifth NOC. However, by the time the SANDS was filed, the Sixth NOC had been issued and the 549 and 387 Patents had been listed.

DISCUSSION

[31] The Applicant says that *AstraZeneca* applies on the facts of this case. However, there are factual differences. In this case, unlike *AstraZeneca*, the drug to which the 387 and 549 patents apply is being marketed. However, the evidence is that, as in *AstraZeneca*, the comparator drug, which was approved for the treatment of hypertension, is not the subject of the 387 and 549 patents and the Applicant does not seek approval for the drug in connection with treatment of patients with increased risk of heart attack. This means that the Applicant, to paraphrase the words of *AstraZeneca* at paragraph 38, has not, in fact, made use of the patented inventions taught by the 387 and 549 patents.

[32] The fact that the Applicant in this case could have made use of the later patents (while in *AstraZeneca*, such use was an impossibility) doesn't alter what I view to be the gravamen of *AstraZeneca*. *AstraZeneca* stands for the proposition that a generic company need only address patents listed against NOC's filed at the time it purchases the comparator drug it selects for the purposes of its ANDS. The Minister therefore erred in law when he required the Applicant to address the 387 and 549 patents.

Standard of Review

[33] In *AstraZeneca* at para. 25, the Supreme Court said that the applicable standard of review is correctness. However, in light of its decision in *Dunsmuir v. New Brunswick*¸ 2008 SCC 9, the Court might now conclude that the standard is reasonableness. Even if that were the case, the application of the Minister's Second Policy in the Decision in this case, does not represent a reasonable interpretation of *AstraZeneca* because the Decision ignores the requirement to make a patent specific analysis, ignores the reality of the Invoice and requires the Applicant to address patents which have nothing to do with the purpose for which it is making a generic version of ramipril.

The Minister's Submissions

[34] The Minister wants to avoid the requirement to conduct the patent specific analysis mandated by the Supreme Court in *AstraZeneca*. He suggested that, if there were issues about which patents should be addressed, a prohibition proceeding should be undertaken and any such issues could then be resolved by the Court on a motion for summary judgment under subsection 6(5) of the NOC Regulations.

[35] I have rejected this approach for three reasons:

(a) First, in paragraph 22 of the *AstraZeneca*, the Supreme Court of Canada says that it is the Minister's role to identify the precise patents which are relevant to a generic manufacturer's early working of a copycat product.

(b) Second, since prohibition proceedings under the NOC Regulations have been described as "draconian" by the Supreme Court of Canada, because of the automatic stay they mandate, they should not be used as a tool to relieve the Minister of his responsibilities (see *Merck Frosst Canada Inc. v. Canada (Minister of National Health and Welfare*, [1998] 2 S.C.R. 193 at paragraph 33).

(c) Third, patent specific analysis is not difficult. In most cases invoices will show which drug was purchased by the generic company as the reference or comparator drug. In other cases, related study reports or FDA filings may show which drugs were used as comparators and it can be assumed that they were purchased prior to the study. However, if there is a dispute or lack of credible evidence, the submission date of the ANDS or SANDS can be used as a fallback position. If there is a problem with the Minister's decision, it can be judicially reviewed.

ORDER

UPON reviewing the material filed and hearing the submission of counsel for both parties in Toronto, Ontario on February 12, 2008;

NOW THIS COURT ORDERS that, for the reasons given above, that this application for judicial review is hereby allowed and the Minister is directed to reconsider the Applicant's request applying the First Policy so that the Applicant need not address the 387 and 549 Patents.

"Sandra J. Simpson"
Judge

FEDERAL COURT

NAME OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	T-837-07
STYLE OF CAUSE:	PHARMASCIENCE INC. v. MINISTER OF HEALTH ET AL
PLACE OF HEARING:	TORONTO
DATE OF HEARING:	FEB 12, 2008
REASONS FOR ORDER AND ORDER:	SIMPSON, J.
DATED:	JULY 29, 2008

APPEARANCES:

DONALD MACODRUM MARK MITCHELL	FOR APPLICANT
FREDERICK WOYIWADA	FOR RESPONDENT

SOLICITORS OF RECORD:

LANG MICHENER LLP BARRISTERS & SOLICITORS TORONTO, ON	FOR APPLICANT
JOHN H. SIMS, QC OTTAWA, ON	FOR RESPONDENT