Date: 20090601

Docket: A-472-08

Citation: 2009 FCA 183

CORAM: **LINDEN J.A.**
SEXTON J.A.
SHARLOW J.A.

BETWEEN:

THE MINISTER OF HEALTH and
THE ATTORNEY GENERAL OF CANADA

Appellants
(Respondents)

and

PHARMASCIENCE INC.

Respondent
(Applicant)

Heard at Toronto, Ontario, on May 19, 2009.

Judgment delivered at Ottawa, Ontario, on June 1, 2009.

REASONS FOR JUDGMENT BY: SEXTON J.A.

CONCURRED IN BY: LINDEN J.A.
SHARLOW J.A.

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REASONS FOR JUDGMENT

SEXTON J.A.

[1] This is an appeal by the Minister of Health ("the Minister") and the Attorney General of Canada from an order of Justice Simpson of the Federal Court, allowing Pharmascience's application for judicial review of the Minister's decision requiring Pharmascience to address certain patents in respect of a supplementary abbreviated new drug submission (SANDS) under subsection 5(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 ("the *NOC Regulations*").

[2] For the reasons that follow, I conclude that the appeal should be dismissed. The Minister erred in law by failing to perform the patent-specific analysis mandated by the Supreme Court's decision in *AstraZeneca v. Canada (Minister of Health)*, 2006 SCC 49, [2006] 2 S.C.R. 560. The applications judge therefore undertook this analysis herself, and in my view her conclusion was reasonable and should be upheld.

RELEVANT LEGISLATION

[3] Subsection 5(1) of the *NOC Regulations* (as it read at the material time) requires a second person filing a submission for a notice of compliance (NOC) to address all patents listed on the register in respect of a NOC issued to a first person, where the second person compares its drug with, or makes reference to, the drug for which that NOC was issued (emphasis mine):

5. (1) Where a person files or has filed a submission for a notice of compliance in respect of a drug and compares that drug with, or makes reference to, another drug for the purpose of demonstrating bioequivalence on the basis of pharmaceutical and, where applicable, bioavailability characteristics and that other drug has been marketed in Canada pursuant to a notice of compliance issued to a first person and in respect of which a patent list has been submitted, the person shall, in the submission, with respect to each patent on the register in respect of the other drug,	**5.** (1) Lorsqu'une personne dépose ou a déposé une demande d'avis de conformité pour une drogue et la compare, ou fait référence, à une autre drogue pour en démontrer la bioéquivalence d'après les caractéristiques pharmaceutiques et, le cas échéant, les caractéristiques en matière de biodisponibilité, cette autre drogue ayant été commercialisée au Canada aux termes d'un avis de conformité délivré à la première personne et à l'égard de laquelle une liste de brevets a été soumise, elle doit inclure dans la demande, à l'égard de chaque brevet inscrit au registre qui se rapporte à cette autre drogue :
(*a*) state that the second person accepts that the notice of compliance will not issue until the patent expires; or	*a*) soit une déclaration portant qu'elle accepte que l'avis de conformité ne sera pas délivré avant l'expiration du brevet;
(*b*) allege that	*b*) soit une allégation portant que, selon le cas :
(i) the statement made by the first person under paragraph 4(4)(*c*) is false,	(i) la déclaration présentée par la première

(ii) the patent has expired,	personne aux termes de l'alinéa 4(4)*c*) est fausse,
(iii) the patent is not valid, or	(ii) le brevet est expiré,
(iv) no claim for the medicine itself and no claim for the use of the medicine would be infringed by the making, constructing, using or selling by that person of the drug for which the submission for the notice of compliance is filed.	(iii) le brevet n'est pas valide,
	(iv) aucune revendication pour le médicament en soi ni aucune revendication pour l'utilisation du médicament ne seraient contrefaites advenant l'utilisation, la fabrication, la construction ou la vente par elle de la drogue faisant l'objet de la demande d'avis de conformité.

FACTS

[4] The facts of this appeal are not in dispute and were set out in detail by the applications judge in paragraphs 2 to 30 of her reasons. The respondent is attempting to bring to market a generic version of ramipril, an ACE inhibitor. Ramipril is marketed by Sanofi-Aventis Canada Inc. ("Sanofi") in Canada under the brand name ALTACE. As of July 10, 2000, Sanofi had been granted 4 NOCs for ALTACE, against which it had listed three patents. At that time, ALTACE was approved for the treatment of hypertension.

[5] On July 10, 2000, the respondent purchased ALTACE capsules in four strengths (1.25 mg, 2.5 mg, 5 mg, and 10 mg) for use as Canadian reference products. On September 4, 2001, the Minister received the respondent's abbreviated new drug submission (ANDS). This ANDS was based on the asserted bioequivalence of each strength of the respondent's ramipril capsules with the equivalent strength of ALTACE. The respondent submitted bioavailability data demonstrating the bioequivalence of its 10 mg ramipril capsule with the 10 mg ALTACE capsule. It then sought a

waiver of the requirement to submit bioavailability data in respect of the other strengths under the Minister's Proportional Formulations Policy ("the proportionality policy"). The respondent only sought approval for the use of its ramipril capsules for the treatment of hypertension.

[6] The ANDS attached the July 10, 2000 invoice for the purchase of the drug samples, and a clinical report on the bioequivalence of the 10 mg capsules stating that the ALTACE samples were received by the lab for testing on December 15, 2000.

[7] On February 24, 2003, the respondent withdrew its ANDS in respect of the 1.25 mg capsules due to a lack of stability data. On August 27, 2003, the Minister found that the respondent was entitled to a NOC for the other strengths (2.5 mg, 5 mg, and 10 mg) subject only to compliance with the *NOC Regulations*.

[8] On December 30, 2005, the respondent filed a SANDS in respect of its 1.25 mg ramipril capsules. It again sought a waiver of the requirement to submit bioavailability data under the proportionality policy, proposing to demonstrate the proportionality of its 1.25 mg capsule with its 10 mg capsule.

[9] In the period between the respondent's ANDS and its SANDS, on November 6, 2003, Sanofi was granted a further NOC ("the sixth NOC"), against which it listed Canadian Patents Nos. 2,382,387 and 2,382,549 (the 387 and 549 patents, respectively). These patents teach a new use of

ramipril, namely, for treatment following a heart attack. The respondent is not seeking approval of its ramipril capsules for this new indication.

[10] Nonetheless, on April 12, 2007, the Minister issued a decision requiring the respondent to address the 387 and 549 patents under subsection 5(1) of the *NOC Regulations* in connection with its SANDS. On May 17, 2007, the Minister, applying the proportionality policy, found that the respondent's 1.25 mg ramipril capsule is bioequivalent to the 1.25 mg ALTACE capsule. Thus, the respondent is entitled to a NOC for the last strength, subject only to compliance with the Regulations.

[11] The Minister denied the respondent's request for reconsideration of its April 12 decision on June 8, 2007, and the respondent commenced an application for judicial review.

DECISION BELOW

[12] The applications judge allowed the respondent's application on the basis of the principles set out by the Supreme Court in *AstraZeneca*. She found that *AstraZeneca* stands for the proposition that "a generic company need only address patents listed against NOC's [sic] filed at the time it purchases the comparator drug it selects for the purposes of its ANDS" (2008 FC 922 at para. 32).

[13] Since the respondent is not seeking approval of its ramipril capsules for treatment post-heart attack, the applications judge also concluded that it "has not, in fact, made use of the patented

inventions taught by the 387 and 549 patents" (at para. 31). Accordingly, she held that the respondent should not be required to address these patents under the *NOC Regulations*.

ISSUE AND STANDARD OF REVIEW

[14] The only issue on this appeal is whether the applications judge erred in holding that the respondent should not be required to address the 387 and 549 patents. In my view, *AstraZeneca* satisfactorily determined that the standard of review for an interpretation of the *NOC Regulations* is correctness (at para. 25). The factual findings made by the applications judge in applying the correct legal test are entitled to deference and must stand if they were reasonably open to her on the record.

ANALYSIS

[15] Both parties discussed the Supreme Court's decision in *AstraZeneca* at length in their submissions. In that case, the issue before the court was whether Apotex should be required to address two patents listed against NOCs granted to AstraZeneca for omeprazole after Apotex had filed its ANDS. The circumstances were somewhat unique in that AstraZeneca had never marketed any drug in Canada incorporating the inventions taught by the two after-listed patents. Writing for the unanimous court, Justice Binnie emphasized that the *NOC Regulations* were enacted to prevent abuse of the "early working exception" provided by subsection 55.2(1) of the *Patent Act*, R.S.C. 1985, c. P-4, and should be interpreted with that purpose in mind (at paras. 15-16).

[16] He described the Regulations as part of a balancing exercise, whereby generic drug companies are given the right to early work an innovator's patented inventions to satisfy the

requirements under the *Food and Drugs Act*, R.S.C. 1985, c. F-27 and Regulations (C.R.C. 1978, c. 870) for a NOC. However, if the innovator initiates an application for an order prohibiting the Minister from issuing a NOC to the generic, a 24 month stay of ministerial action arises automatically. The Supreme Court had previously described this stay as "draconian" in *Merck Frosst Canada Inc. v. Canada (Minister of National Health and Welfare)*, [1998] 2 S.C.R. 193 at para. 33.

[17] Justice Binnie concluded that in principle, a generic need only address patents relevant to the NOC that gave rise to the comparator drug (*AstraZeneca* at para. 39, emphasis mine):

> In my view, s. 5(1) 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*.

The comparator drug in that case was the drug that Apotex had actually purchased and analyzed for the purposes of demonstrating the bioequivalence of its own omeprazole tablets (at paras. 34-37).

[18] The dispute in the instant case is how "the comparator drug" should be identified. The appellants submit that legally, ALTACE is not simply a physical compound. Rather, ALTACE is defined as the sum total of all submissions approved for it as of a given date—that is, the initial new drug submission in respect of which its first NOC was issued, and all subsequent supplemental new drug submissions giving rise to later NOCs. Therefore, the appellants argue that the comparator drug in this case is the version of ALTACE available to be copied as of the date the respondent submitted its SANDS—namely, the version for which Sanofi received its sixth NOC, against which it listed the 387 and 549 patents.

[19] The respondent, on the other hand, submits that the comparator drug is the drug it actually purchased in July 2000 and analyzed for the purpose of demonstrating the bioequivalence of its ramipril capsules. Although it withdrew its initial ANDS in respect of the 1.25 mg capsules and later submitted an SNDS, it argues that it still relied only on the drug it purchased in 2000 to demonstrate bioequivalence with ALTACE.

[20] Despite the very able argument of counsel for the appellants, I am unable to agree with their interpretation of *AstraZeneca*. In that case, Justice Binnie wrote (at para. 28):

> I accept the linguistic point made by Noël J.A. in the Federal Court of Appeal that the words "in respect of which" in s. 5(1) refer to "the other drug", i.e. the Canadian reference product, and not to a particular patent list or amended patent list. However, it seems to me that the "other drug" is the drug to which the generic manufacturer makes reference "for the purpose of demonstrating bioequivalence".

AstraZeneca also emphasized that "it is the actual drug, from which samples can be taken and used for comparative purposes that is relevant to the application of subsection 5(1) of the *NOC Regulations*" (at para. 34, quoting from the judgment of Justice Noel of this court, 2005 FCA 189, [2006] 1 F.C.R. 297 at para. 46, emphasis Justice Binnie's).

[21] In *Ferring Inc. v. Canada (Minister of Health)*, 2007 FC 300, [2008] 1 F.C.R. 19, aff'd 2007 FCA 276, 370 N.R. 263, Justice Hughes acknowledged the importance of the date the generic purchased the comparator drug to the patent specific analysis required by *AstraZeneca*. However, in

obiter dicta, he expressed concern that the purchase date of the samples would only be known to the generic itself. As an evidentiary matter, he suggested that the Minister have regard to the date the generic filed its ANDS, as this would be "logically the last date upon which the comparator drug could have been obtained by the generic". He was also of the view that the Minister should require a generic to address after-listed patents only if the generic had made use of changes made to the comparator drug since the date of purchase, for the purposes of demonstrating bioequivalence (at para. 65).

[22] Thus, the jurisprudence is clear that the patent specific analysis requires a generic to address only those patents in respect of which it takes advantage of the early working exception in the *Patent Act* for the purposes of demonstrating bioequivalence and obtaining a NOC.

[23] The appellants' position is that the generic should be required to address any patent that is notionally available for early working (i.e. any patent listed prior to an ANDS or SANDS) and that the Minister should not have to determine on the evidence whether a patent was in fact early worked. Thus, they say that in cases where there is a dispute, the proper forum for that dispute is a NOC proceeding in which the innovator may participate. The appellants seek to distinguish *AstraZeneca* on the basis that in that case a drug had never become available incorporating the teachings of the after-listed patents, and that unlike in this case, early working was a factual impossibility.

[24] I cannot accept this argument, which would require a generic to address patents as fast as an innovator could list them, with no regard to whether the generic has taken advantage of the early working exception. As Justice Binnie wrote in *AstraZeneca* (at paras. 21 and 23, underlining mine):

> There is no linkage between the 037 and 470 patents and the submissions that lead to the *Losec 20* product copied by Apotex. Those after-acquired patents were listed in relation to a SNDS dated January 22, 1999 by AstraZeneca for a new medical use for *Losec 20* (treatment of *H. Pylori*), a use for which the Apotex product is *not* approved, and to an administrative SNDS submitted by AstraZeneca dated July 12, 2000, which submission has nothing at all to do with the technology incorporated in *Losec 20*.
> …
>
> …On this view a "first person" could carry on "evergreening" its product indefinitely by the addition of new patents of marginal significance which would trigger an indefinite series of 24-month statutory freezes <u>even though such subsequently listed patents are not the subject of "early working" by the generic manufacturer, and from which (as in the circumstances here) the generic manufacturer derives no advantage.</u>

[25] As the applications judge noted, it is the Minister's responsibility to conduct the patent specific analysis and "to identify the precise patents which are relevant to a generic manufacturer's early working of a copycat product" (at para. 35, citing *AstraZeneca* at para. 22). In my view, the date the comparator drug was purchased is the starting point. The Minister must then evaluate the evidence before him to determine whether the generic has taken advantage of the teachings of any after-listed patents. Evidence including invoices for the purchase of drug samples, clinical studies stating when drug samples were received for testing, and the generic's product monograph listing the proposed uses of the drug, is generally before the Minister when an ANDS or a SANDS is filed and can be marshalled for this purpose. In cases where the evidence is unclear or there is an absence of reliable evidence, we agree with the applications judge that the Minister may use the filing date of an ANDS (or a SANDS, where appropriate) as a fallback position.

[26] The Minister failed to conduct this analysis. Thus, it was open to the applications judge to do so. In this case, there was evidence before the Minister (in the form of the July 2000 invoice) as to when the respondent purchased the comparator drug. It submitted bioavailability data that relied exclusively on those samples. While it withdrew its ANDS in respect of the 1.25 mg capsules and later submitted a SANDS, it did so only due to an initial lack of stability data for those capsules and not for the purpose of conducting new bioequivalence studies or modifying its drug to incorporate any new technologies.

[27] As the respondent points out, a SANDS is not a stand-alone submission. The Minister must take into account the relationship between a particular SANDS and an earlier-filed ANDS when conducting the patent specific analysis.

[28] Most significantly in this case, the respondent has never sought approval for the new use of ramipril capsules for treatment post-heart attack, as taught by the after-listed patents. The appellants argue that this fact goes to the ultimate question of infringement and not to whether the respondent should have to address the new patents. However, the Supreme Court saw fit to consider this factor in *AstraZeneca*, when it noted at least twice that Apotex was not seeking to take advantage of a new indication taught by the after-listed patents in that case (at paras. 21 and 42).

[29] The applications judge found as a fact that the respondent has not made use of the patented inventions taught by the 387 and 549 patents (reasons for order at para. 31), and is not “on this

occasion within the mischief aimed at by the *NOC Regulations*" (*AstraZeneca* at para. 38). Indeed, the appellants were not able to refer this court to any evidence in the record contrary to this finding. Accordingly, this conclusion was reasonably open to the applications judge, and there is no basis for this court to interfere.

CONCLUSION

[30] I therefore conclude that the applications judge was correct to conclude that the respondent should only be required to address the patents listed against the NOC giving rise to the comparator drug it actually purchased and analyzed for the purposes of demonstrating bioequivalence, in the circumstances of this case. The Minister erred in requiring it to address the 387 and 549 patents.

[31] For these reasons, I would dismiss the appeal with costs.

"J. Edgar Sexton"
J.A.

"I agree
A.M. Linden J.A."
"I agree
K. Sharlow J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-472-08

APPEAL FROM AN ORDER OF THE HONOURABLE MADAM JUSTICE SIMPSON DATED JULY 29, 2008, DOCKET NO. T-837-07

STYLE OF CAUSE:	THE MINISTER OF HEALTH and THE ATTORNEY GENERAL OF CANADA v. PHARAMASCIENCE INC.
PLACE OF HEARING:	Toronto, Ontario
DATE OF HEARING:	May 19, 2009
REASONS FOR JUDGMENT:	Sexton J.A.
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DATED:	June 1, 2009

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