Date: 20080414

Docket: T-737-06

Citation: 2008 FC 475

Ottawa, Ontario, April 14, 2008

PRESENT: The Honourable Barry Strayer, Deputy Judge

BETWEEN:

APOTEX INC.

Applicant

and

THE MINISTER OF HEALTH
and SERVIER CANADA INC. and ADIR

Respondents

REASONS FOR JUDGMENT AND JUDGMENT

Introduction

[1] This is an application for judicial review of the decision of the Minister of Health (Minister) subjecting the Applicant's submission for a Notice of Compliance (NOC) for Apo-Perindopril 2 mg and 4 mg tablets to section 5 of the *Patented Medicines (Notice of Compliance) Regulations* (PM (NOC) Regulations). I must also dispose of a motion brought by Servier Canada Inc. and ADIR (Servier) requesting that this application be dismissed on the basis that it has become moot or that the Applicant is estopped now from asserting that it is not required to comply with section 5 of the PM (NOC) Regulations.

Legislative Provisions

[2] For ease of explanation in what follows, the most relevant legislative provisions are set out here. The sections are quoted as they were at the relevant times.

Patented Medicines (Notice of Compliance) Regulations

2. In these Regulations,	2. Les définitions qui suivent s'appliquent au présent règlement,
…	…
"notice of compliance" means a notice issued under section C.08.004 of the *Food and Drug Regulations*; (avis de conformité)	« avis de conformité » Avis délivré au titre de l'article C.08.004 du *Règlement sur les aliments et droques*. (notice of compliance)
…	…
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	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 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

the submission, with respect to each patent on the register in respect of the other drug …	cette autre drogue :

[Subsection 5(1) goes on to require such person either to state that he accepts that the NOC will not issue until the patent expires or else challenge the relevance or validity of the patent.]

Food and Drug Regulations

C.08.001.1. For the purposes of this Division,	C.08.001.1. Les définitions qui suivent s'appliquent au présent titre.
"Canadian reference product" means	« équivalent pharmaceutique » S'entend d'une drogue nouvelle qui, par comparaison à une autre drogue, contient les mêmes quantités d'ingrédients médicinaux identiques, sous des formes posologiques comparables, mais pas nécessairement les mêmes ingrédients non médicinaux.
	« produit de référence canadien » Selon le cas :
(a) a drug in respect of which a notice of compliance is issued pursuant to section C.08.004 and which is marketed in Canada by the innovator of the drug.	a) une drogue pour laquelle un avis de conformité a été délivré aux termes de l'article C.08.004 et qui est commercialisée au Canada par son innovateur;
…	…
(c) a drug, acceptable to the Minister, that can be used for the purpose of demonstrating	c) une drogue jugée acceptable par le ministre qui peut être utilisée pour la détermination de

bioequivalence on the basis of pharmaceutical and, where applicable, bioavailability characteristics, in comparison to a drug referred to in paragraph (a); (produit de référence canadien)

“pharmaceutical equivalent” means a new drug that, in comparison with another drug, contains identical amounts of the identical medicinal ingredients, in comparable dosage forms, but that does not necessarily contain the same non-medicinal ingredients; (équivalent pharmaceutique)

la bioéquivalence d’après les caractéristiques pharmaceutiques et, le cas échéant, les caractéristiques en matière de biodisponibilité, par comparaison à une drogue visée à l’alinéa a). (Canadian reference product)

…

…

C.08.002. (1) No person shall sell or advertise a new drug unless

C.08.002. (1) Il est interdit de vendre ou d’annoncer une drogue nouvelle, à moins que les conditions suivantes ne soient réunies :

(a) the manufacturer of the new drug has filed with the Minister a new drug submission or an abbreviated new drug submission relating to the new drug that is satisfactory to the Minister;

a) le fabricant de la drogue nouvelle a, relativement à celle-ci, déposé auprès du ministre une présentation de drogue nouvelle ou une présentation abrégée de drogue nouvelle que celui-ci juge acceptable;

…

…

C.08.002.1. (1) A manufacturer of a new drug may file an abbreviated new drug submission for the new drug where, in comparison with a Canadian reference product,

C.08.002.1. (1) Le fabricant d'une drogue nouvelle peut déposer à l'égard de celle-ci une présentation abrégée de drogue nouvelle si, par comparaison à un produit de référence canadien :

(*a*) the new drug is the pharmaceutical equivalent of the Canadian reference product;

(*b*) the new drug is bioequivalent with the Canadian reference product, based on the pharmaceutical and, where the Minister considers it necessary, bioavailability characteristics;

(*c*) the route of administration of the new drug is the same as that of the Canadian reference product; and

(*d*) the conditions of use for the new drug fall within the conditions of use for the Canadian reference product.

…

C.08.004. (4) A notice of compliance issued in respect of a new drug on the basis of information and material contained in a submission filed pursuant to section C.08.002.1 shall state the name of the Canadian reference product referred to in the submission and shall constitute a declaration of equivalence for that new drug.

SOR/84-267, ss. 1 to 3; SOR/85-143, s. 3; SOR/86-1009, s. 1; SOR/86-1101, s. 1; SOR/88-42, s. 1; SOR/88-257, s. 1; SOR/95-411, s. 6.

a) la drogue nouvelle est un équivalent pharmaceutique du produit de référence canadien;

b) elle est bioéquivalente au produit de référence canadien d'après les caractéristiques pharmaceutiques et, si le ministre l'estime nécessaire, d'après les caractéristiques en matière de biodisponibilité;

c) la voie d'administration de la drogue nouvelle est identique à celle du produit de référence canadien;

d) les conditions thérapeutiques relatives à la drogue nouvelle figurent parmi celles qui s'appliquent au produit de référence canadien.

…

C.08.004. (4) L'avis de conformité délivré à l'égard d'une drogue nouvelle d'après les renseignements et le matériel contenus dans la présentation déposée conformément à l'article C.08.002.1 indique le nom du produit de référence canadien mentionné dans la présentation et constitue la déclaration d'équivalence de cette drogue.

DORS/84-267, art. 1 à 3; DORS/85-143, art. 3; DORS/86-1009, art. 1; DORS/86-1101, art. 1; DORS/88-42, art. 1; DORS/88-

257, art. 1; DORS/95-411, art. 6.

Facts

[3] On March 6, 2001 Canadian Patent 1,341,196 (‘196 Patent) issued to ADIR. Servier apparently has the rights of exercising the patent in Canada. The patent contains claims for Perindopril and its pharmaceutically acceptable salts. Servier obtained a Notice of Compliance for a medicine containing one of these salts in dosages of 2 mg, 4 mg, and 8 mg tablets on or about October 16, 2002. On or about March 15, 2001 Servier had filed patent lists under section 4 of the PM (NOC) Regulations listing the ‘196 patent in respect of COVERSYL 2 mg and 4 mg tablets. It did not file a patent list in respect of COVERSYL 8 mg tablets. This omission remains unexplained. Because of it, we have this whole proceeding before the Court.

[4] On December 1, 2005 the Applicant filed its abbreviated new drug submission (ANDS) for 2 mg, 4 mg and 8 mg Apo-Perindopril. According to the evidence of an officer of Health Canada, Therapeutic Products Directorate (TPD) (I cannot find such submissions in the material filed) this submission used as Canadian reference products COVERSYL 2 mg, 4 mg and 8 mg tablets. The Applicant was advised by TPD that the Applicant was required to address the ‘196 patent in respect of COVERSYL 2 mg and 4 mg tablets but confirmed that the PM (NOC) Regulations did not apply to 8 mg tablets because they were not listed on the patent register. Thereupon the Applicant withdrew its application and submitted a new ANDS on December 23, 2005. In this ANDS, it removed comparative data for 2 mg and 4 mg APO-Perindopril. It included bioavailability studies

only in respect of COVERSYL 8 mg and requested a waiver for submitting additional bioavailability data for its 2 mg and 4 mg strength invoking Health Canada's Proportional Formulations Policy. According to this policy issued by TPD, it is said to be generally accepted that when a product is marketed in more than one strength, and if the formulation of each strength contains the same ingredients in the same proportion, a single comparative bioavailability study to one strength of the Canadian reference product can be extrapolated to all strengths in the series. Thus the Applicant contended that it need make bioavailability comparisons only to the COVERSYL 8 mg dosage and it could be assumed that its 2 mg and 4 mg dosages represented comparable bioavailability. It therefore contended that it was not comparing its 2 mg and 4 mg dosages to drugs on the patent list, namely COVERSYL 2 mg and 4 mg tablets. While there was considerable discussion and correspondence back and forth between the Applicant and the TPD, the latter's position complained of in these proceedings is perhaps best set out in a letter of January 12, 2006 from the TPD to Dr. B. Sherman, Chairman and CEO of the Applicant, part of which reads as follows:

> Rather, our position is that Apotex must, in accordance with the *Patented Medicines (Notice of Compliance) Regulations*, address the patents listed for the 2 mg and 4 mg Coversyl strengths because an abbreviated new drug submission, under section C.08.002.1 of the *Food and Drug Regulations*, requires inclusion of a comparison with a Canadian reference product for the purpose of demonstrating bioequivalence. This is sufficient to trigger the application of subsection 5(1) of the *Patented Medicines (Notice of Compliance) Regulations* and requires that Apotex address the patents listed against 2 mg and 4 mg Coversyl strengths.
>
> Stated another way, waiving the requirement to submit bioavailability studies for your 2 mg and 4 mg strengths in accordance with the TPD policy for "Bioequivalence of Proportional

> Formulations – Solid Oral Dosage Forms" does not preclude the fact that the 2 mg and 4 mg Coversyl strengths will, if a NOC is issued, stand as Canadian reference products for your 2 mg and 4 mg strengths, respectively. Not requiring Apotex to address the patents listed for the 2 mg and 4 mg Coversyl strengths on the ground that it has only submitted bioequivalence studies in respect of the Coversyl 8 mg strength would, in the TPD's view, amount to a circumvention of the *Patented Medicines (Notice of Compliance) Regulations*.
>
> As such, you must address the patents listed for 2 mg and 4 mg Coversyl pursuant to section 5 of the *Patented Medicines (Notice of Compliance) Regulations*.
>
> In the alternative, the TPD notes that even if it were to agree that subsection 5(1) of the *Patented Medicines (Notice of Compliance) Regulations* were not applicable, subsection 5(1.1) would apply to your situation. The Supreme Court of Canada's decision in *Bristol-Myers Squibb Co. v. Canada (Attorney General)*, 2005 1 S.C.R. 533 confirms that in such cases "[i]f the approval of the generic drug is related to the work of another drug manufacturer in respect of which a patent list has been filed […], it will be caught by s. 5(1.1)."

It is agreed by the parties here that subsection 5(1.1) of the PM (NOC) Regulations is no longer relevant in these proceedings.

[5] Notwithstanding its rather vigorous correspondence with the TPD insisting that section 5 of the PM (NOC) Regulations did not apply in respect of the Applicant's 2 mg and 4 mg formulations, on February 15, 2006 the Applicant filed Form V's certifying that it compared or made reference for the purpose of demonstrating bioequivalence of its 2 mg and 4 mg tablets to COVERSYL 2 mg and 4 mg tablets and acknowledging that the NOC would not be issued until the expiration date of patent '196. On November 27, 2007, the day that this present application was argued before me, and

unknown to the Court, the Applicant sent to Servier a Notice of Allegation under section 5 of the PM (NOC) Regulations alleging the invalidity of patent ‘196. Counsel for Servier upon learning of this brought it to the attention of the Court and I gave directions allowing Servier to bring a motion in writing for dismissal of the application on the basis of mootness or estoppel. Submissions were subsequently filed by all three parties. On January 11, 2008 Servier commenced, in response to the Applicant’s Notice of Allegation of November 27, 2007, an application in this Court in file no. T-45-08 seeking prohibition to prevent the Minister from issuing an NOC to the Applicant in respect of Apo-Perindopril 2 mg and 4 mg tablets until the expiry of the ‘196 patent.

Analysis

Motion to Dismiss the Application

[6] I believe the main issue on this motion is as to whether I should exercise my discretion to dismiss for mootness on the criteria set out, for example, by the Supreme Court of Canada in *Borowski v. Canada (Attorney General)*, [1989] 1 S.C.R. 342 at 353-6. The essential question is as to whether there remains a live controversy or whether the Applicant by its actions has conceded the application of section 5 to the issue of an NOC for its 2 mg and 4 mg tablets. I should first confirm that I believe it was open to Servier to submit new evidence on this motion with respect to facts arising after the hearing of the application. It is implicit in the *Borowski* decision that at any time up to judgment there may be events which render the proceeding moot. Servier here put before the Court evidence which arguably could have that effect and it was incumbent on me to consider it.

[7] While the matter is not free from doubt, I have concluded that I cannot say with certainty that the actions of the Applicant have rendered the original application moot. As Justice Hughes has said in *Ferring Inc. v. Canada (Minister of Health)* 2007 FC 300, aff'm 2007 FCA 276, at paras. 81-84, whether an application for an NOC is or is not governed by section 5 of the PM (NOC) Regulations involves the jurisdiction and duty of the Minister. If the application comes within section 5 he may not issue the NOC, but if the application is otherwise correct and does not fall within section 5, he must issue the NOC. This is essentially a matter of jurisdiction and legal duty. In my view the Applicant cannot confer jurisdiction on the Minister to apply section 5 to its application through the filing of Form V's or a Notice of Allegation based on the assumption that section 5 is applicable to its 2 mg and 4 mg tablets.

[8] Servier also argues that the Applicant is estopped from maintaining a position that section 5 does not apply when it has taken another step based on an assumption that section 5 does apply – namely the sending of a Notice of Allegation under section 5. The precedents cited for this come from ordinary litigation and seem to involve some form of prejudice caused to the opposite party by a litigant changing his position. This is not conventional litigation nor is it apparent to me that the position of Servier has been prejudiced. The actions of the Applicant can be explained as, on the one hand, maintaining its position that the Minister has no authority to refuse its NOC application for 2 mg and 4 mg tablets, while on the other hand taking the necessary steps to pursue its application should it ultimately be held that section 5 does apply.

[9] I am therefore not prepared to dismiss the application on the grounds put forth in Servier's motion. At the same time I do not wish to encourage this kind of multifarious proceedings which consumes the time and resources of the Court and the parties. I will therefore dismiss Servier's motion without costs as I believe Servier raised a serious issue by this motion because of the Applicant's actions in pursuing multiple remedies concurrently.

Application for Judicial Review of Minister's Decision

[10] Essentially the Applicant argues that it did not compare its 2 mg and 4 mg dosages to the COVERSYL 2 mg and 4 mg drugs. While it asked for an NOC to be issued to cover its 2 mg and 4 mg and 8 mg dosages it says it only referred to bioavailability data in respect of the 8 mg dosage of Servier because it relied on bioavailability studies comparing its 2 and 4 mg dosages to COVERSYL 8 mg's by use of the proportionality policy.

[11] The decision of the Minister in question here is essentially a decision that within the terms of subsection 5 (1) of the PM (NOC) Regulations the Applicant in its ANDS in respect of 2 mg and 4 mg dosages of APO-Perindopril compared those drugs with or made reference to 2 mg and 4 mg dosages of COVERSYL for the purpose of demonstrating bioequivalence. In my view this is essentially a question of law as to the interpretation of section 5 in relation to the *Food and Drug Regulations* and the standard of review should be correctness: see *AstraZeneca Canada Inc. v. Canada (Minister of Health)*, [2006] 2 S.C.R. 560 at para. 25. While it has been held by the Federal Court of Appeal that a decision by the Minister as to whether one drug is the bioequivalent of

another is entitled to a high degree of deference (*Reddy-Cheminor Inc. v. Canada (Minister of Health)* 2004 FCA 102, para. 8), that is not the issue here. Rather the issue is as to whether the Applicant seeking an NOC for its 2 mg and 4 mg tablets on the basis of the testing and approval of COVERSYL 2 and 4 mg dosages was comparing its drugs with Servier's 2 and 4 mg drugs. I believe that solely involves the interpretation of the regulation and the standard of review is correctness.

[12] While, as noted below, I conclude that the Minister's decision was correct, if that is not the relevant standard for the same reasons I would conclude that the decision was reasonable. (The recent Supreme Court of Canada decision in *Dunsmuir v. New Brunswick*, [2008] S.C.J. No. 9 was decided after the present application was argued. To the extent that it would abolish the standard of patent unreasonableness (see paras. 43-50) it has no relevance to this present case. The majority does, however, indicate that many tribunal decisions on statutory interpretation are entitled to the deference implied in a standard of review of reasonableness (see *Dunsmuir* at paras. 66-71). The present determination by the Minister that subsection 5(1) of the PM (NOC) Regulations applies to the Applicant's ANDS may fall within that kind of decision of law. For the reasons stated, I do not find it necessary to decide which of the remaining standards applies here, as the Minister's decision meets both standards.)

[13] I believe the Minister's interpretation here is correct for the reasons set out by the TPD in its letter of January 12, 2006 to the Chairman and CEO of the Applicant. Once must first understand the interconnection between the PM (NOC) Regulations and the *Food and Drug Regulations* as

quoted above. In section 2 of the PM (NOC) Regulations a “notice of compliance” is defined as the notice issued under section C.08.004 of the *Food and Drug Regulations*. Therefore to determine whether an ANDS compares the drug which is the subject of that ANDS with, or makes reference to, another drug for the purpose of demonstrating bioequivalence reference must be made to the requirements of the *Food and Drug Regulations*. By paragraph C.08.002.1 (1) (a) of those regulations an ANDS must make a “comparison with a Canadian reference product” which is the “pharmaceutical equivalent” of that product. The definition in section C.08.001.1 of “pharmaceutical equivalent” is that of a new drug that “contains identical amounts of the *identical medicinal ingredients in comparable dosage forms*.” [emphasis added]. By paragraph (a) of the definition of “Canadian reference product” in section C.08.001.1 such a product is any drug in respect of which a notice of compliance has been issued and which is marketed in Canada by the innovator of that drug, which in this case would include COVERSYL in 2 mg, 4 mg and 8 mg dosages. Thus, an ANDS must make a comparison with a “Canadian reference product” which is the pharmaceutical equivalent of that product, meaning that it must contain an identical amount of the identical medicinal ingredient in comparable dosages. This obviously means that where subsection 5(1) of the PM (NOC) Regulations refers to the comparison by a second person of its drug to another drug which has already been marketed in Canada, that must mean a reference (as required by subsection C.08.002.1 of the *Food and Drug Regulations*) to every pharmaceutical equivalent of drugs included in the ANDS, namely every dosage for which an NOC is sought. Further by paragraph C.08.002.1(b) the ANDS must show that the new drug is bioequivalent with the Canadian reference product which means every drug in respect of which the NOC is sought and which is marketed in Canada by the innovator of the drug. With respect to each of these dosages the

Applicant for an ANDS must show that the drug or drugs, each of which is the pharmaceutical equivalence of an existing drug on the market to which it must be compared, is bioequivalent with that "Canadian reference product" based on pharmaceutical and "where the Minister considers it necessary, bioavailability characteristics". The Minister, when he issues an NOC, must certify the equivalence of each dosage in the NOC to a Canadian reference product of comparable dosage: see subsection C.08.004(4).

[14] What the Applicant did here in its amended ANDS was to provide bioavailability studies comparing its dosages to the COVERSYL 8 mg dosage. The Minister applied the proportionality policy and allowed it to establish bioequivalence for the 2 mg and 4 mg tablets by this means. On this basis the Applicant contends that it had not made a comparison between its 2 mg and 4 mg dosages with those of COVERSYL. But for the reasons stated above it was obliged to make that comparison if it is to obtain an NOC for the 2 mg and 4 mg dosages. It appears to me that the directing minds of the Applicant have confused two things. There is an obligation to make a comparison as required by subsection 5(1) of the PM (NOC) Regulations, and sections C.08.001.1, C.08.002.1 (1) and C.08.004 (4) of the *Food and Drug Regulations*, with each pharmaceutical equivalent of the Canadian reference product. That means a comparison with each dosage covered by the patent. They have confused this requirement with the requirements for demonstrating bioequivalence of the Canadian reference products of each dosage which may be relaxed as they have been in the proportionality policy. This relaxation does not mean that the comparison is no longer required to each form of the drug protected by the patent.

[15] This is consistent with the policy of the Regulations which is to ensure that generic companies which wish to bypass normal testing requirements for each dosage of the drugs they wish to sell must compare those drugs in each dosage for which they seek an NOC to drugs already tested and marketed by innovator companies. The Federal Court of Appeal has struck down attempts to rely indirectly on the work of innovator companies by generic companies comparing their drugs to drugs of other generic companies which have already made the comparison to the drugs of the innovator company: see *Nu-Pharm v. Canada (Attorney General)*, [1998] F.C.J. No. 274; *Merck & Co. v. Nu-Pharm Inc.*, [2000] F.C.J. No. 380. What the Applicant seeks to do in this case would equally be an attempt to rely indirectly on the testing and approval of the 2 mg and 4 mg dosages of COVERSYL which are included on a patent list, and thus avoid the patent protection already afforded to those dosages.

Disposition

[16] This application will therefore be dismissed with costs to Servier and the Minister.

JUDGMENT

THIS COURT ORDERS AND ADJUDGES that

1. Servier Canada Inc. and ADIR's motion for summary dismissal of the application be dismissed without costs;

2. The application for judicial review of the decision of the Minister of Health applying the *Patented Medicines (Notice of Compliance) Regulations* to the Applicant's submission for a Notice of Compliance for Apo-Perindopril 2 mg and 4 mg tablets be dismissed with costs to the Minister of Health and Servier Canada Inc.

"Barry L. Strayer"
Deputy Judge

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-737-06
STYLE OF CAUSE:	**APOTEX INC. and THE MINISTER OF HEALTH and SERVIER CANADA INC. and ADIR**
PLACE OF HEARING:	Toronto
DATE OF HEARING:	November 27, 2007
REASONS FOR ORDER:	STRAYER, J.
DATED:	April 14, 2008

APPEARANCES:

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