Date: 20070606

Docket: T-775-06

Citation: 2007 FC 590

Ottawa, Ontario, June 6, 2007

PRESENT: The Honourable Mr. Justice O'Reilly

BETWEEN:

BAYER HEALTHCARE AG
and BAYER INC.

Applicants

and

SANDOZ CANADA INCORPORATED
and THE MINISTER OF HEALTH

Respondents

REASONS FOR JUDGMENT AND JUDGMENT

[1] The applicants Bayer Healthcare AG and Bayer Inc. have asked me to overturn a decision of the Minister of Health allowing the respondent Sandoz Canada Inc. to market an intravenous drug called ciprofloxacin. Bayer sells ciprofloxacin in a ready-to-use "mini-bag" format, whereas Sandoz intends to market a more concentrated version in glass vials. Bayer argues that Sandoz cannot go to market until it has met the requirements of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 and given Bayer a chance to bring proceedings to prohibit the Minister from letting Sandoz do so.

[2] Sandoz argues that it has no obligation to take the steps on which Bayer insists. The Minister takes the same position. They submit that the Minister's decision to issue a Notice of Compliance (NOC) allowing Sandoz to market its product was correct.

[3] I agree with the respondents. I must, therefore, dismiss this application for judicial review.

I. Issue

[4] Did the Minister err in deciding that the Regulations do not apply in the circumstances and, as a consequence, granting Sandoz an NOC for its product?

[5] Given that this case turns on an interpretation of the Regulations, I can overturn the Minister's decision if I conclude that he made an error of law.

[6] This judgment involves an analysis of ss. 5(1) and 5(1.1) of the Regulations, as they existed prior to October 2006; the former has now been amended and the latter has been repealed (SOR/2006-242). (Relevant enactments are set out in an Annex).

[7] Sandoz argued that Bayer does not have standing to bring this application. However, as the other issues have been decided in Sandoz' favour, I need not deal with this question. This should not be taken as a conclusion that I have rejected Sandoz' argument against Bayer's standing

II. Analysis

(a) The Regulatory Scheme

[8] An innovator drug company, such as Bayer, can protect the monopoly rights that flow from a drug patent by asking the Minister to list the patent on the Minister's register. The patent is listed in respect of the product for which the innovator sought and received approval from the Minister. Once a patent is listed, a generic drug company, such as Sandoz, that wants to produce a drug that is bioequivalent to the drug against which the innovator's patent is listed can either wait until the patent expires before getting an NOC or take other steps available to it under the Regulations (s. 5(1)). For example, it may address the innovator's patent by alleging that it is invalid, or by alleging that its drug will not infringe the patent. Once the innovator receives the generic's notice of allegation (NOA), it can apply to the Federal Court for an order prohibiting the Minister from granting the generic an NOC and, in doing so, keep the generic out of the market for 24 months while the proceedings unfold. (See *AstraZeneca Canada Inc*. v. *Canada (Minister of Health)*, 2006 SCC 49, at paras. 16-17.

(b) Factual Background

[9] In the 1990s, the Minister approved two drugs that Bayer had developed - "CIPRO I.V." and "CIPRO I.V. Minibags". Both contain ciprofloxacin. In 2004, the Minister granted Sandoz' predecessor, Sabex, an NOC for a drug called "Ciprofloxacin Injection USP". Soon after, the

Minister rescinded the NOC after Bayer pointed out that it had a patent listed on the register (Canadian Patent No. 1,282,006 – the ‘006 patent) in relation to its “CIPRO I.V. Minibags”, against which Sandoz had compared its product for bioequivalency.

[10] Given Bayer’s valid objection, the Minister sent Sabex a notice of non-compliance. In it, the Minister noted that Sabex would be entitled under the *Food and Drug Regulations*, C.R.C. 1978, c. 870, Part C, to compare its product to a drug sold in an equivalent jurisdiction, for which an NOC had previously been granted but which was no longer being marketed in Canada. Sabex took up that idea by applying for a second NOC, this time comparing its drug to Bayer’s CIPRO I.V., which Bayer marketed in the United States but no longer sold in Canada. Bayer had no patent listed against CIPRO I.V. on the Minister’s register.

[11] In 2006, the Minister issued an NOC to Sandoz (Sabex’s successor).

(c) Bayer’s Objections

[12] Bayer has raised two main arguments against the Minister’s decision:

[13] First, Bayer argues that the Minister should have obliged Sandoz to address the ‘006 patent before granting Sandoz an NOC. Bayer submits that Sandoz continues to compare its product to the Bayer minibag against which the ‘006 patent is listed and, therefore, that s. 5(1) of the Regulations

applies. Bayer suggests that the circumstances are no different now than in 2004 when the Minister refused to issue an NOC to Sabex.

[14] Second, Bayer argues that, even if the Minister was correct in his decision that Sandoz did not have to address the ‘006 patent before getting its NOC according to s. 5(1) of the Regulations, the Minister failed to consider the need to do so pursuant to s. 5(1.1).

[15] I will deal with each of these arguments in turn.

(i) *Did the Minister err in concluding that Sandoz did not have to address the ‘006 patent according to s. 5(1) of the Regulations?*

[16] Subsection 5(1) of the Regulations imposes certain obligations on a generic company seeking an NOC. Those obligations arise where:

(1) the generic compares its drug with, or makes reference to, another drug marketed in Canada by an innovator under an NOC in order to show that the generic’s drug is bioequivalent to the innovator’s drug (and, therefore, already proven to be safe and effective); and

(2) the innovator has submitted a patent list in respect of that drug.

[17] Where these circumstances exist, the generic company must either accept that it will not get an NOC for its drug until the innovator's patent expires, or address the innovator's patent by, for example, alleging that the patent is invalid or will not be infringed.

[18] Bayer argues that the conditions under s. 5(1) exist and, therefore, that the Minister should have required Sandoz to address the '006 patent before getting its NOC. I disagree.

[19] Sandoz did not compare its product with, or refer to, Bayer's mini-bag for purposes of showing bioequivalence with it. Nor could it have. While "bioequivalence" is not a defined term, s. 5(1) of the Regulations states that bioequivalence can be demonstrated "on the basis of pharmaceutical and, where applicable, bioavailability characteristics". In fact, a generic company can only obtain accelerated approval for a drug when the drug is the "pharmaceutical equivalent" of an innovator's product, and it must prove that equivalence (*Food and Drug Regulations,* s. C.08.002.1(1)(*a*), (2)(*c*)(i)). To be pharmaceutically equivalent, the two drugs must contain "identical amounts of the identical medicinal ingredients in comparable dosage forms" (s. C.08.001.1). Therefore, drugs can be demonstrated to be bioequivalent only if it can first be shown that they are pharmaceutically equivalent, in the sense that they contain the same amount of the same medicine. The Sandoz product is a concentrated solution. It does not contain the same amount of ciprofloxacin as the Bayer mini-bag. The drugs are neither pharmaceutically equivalent nor bioequivalent.

[20] The Bayer product is a ready-to-use mini-bag containing ciprofloxacin for use as an intravenous drip. It contains a concentration of 2 mg/ml. The Sandoz product is contained in a glass vial that must be diluted before it is administered to a patient intravenously. Its concentration of ciprofloxacin is 10 mg/ml. Bayer argued that the absolute amount of medicine could be the same in the two drugs, depending on the size of the container. For example, if the Bayer product was packaged in a 100 ml bag, the amount of ciprofloxacin would be 200 mg. If the Sandoz product was contained in a 20 ml vial, it too would have 200 mg of ciprofloxacin in it. Therefore, Bayer submits, the two products would contain the same amount of the same medicine and would then meet the definition of "pharmaceutical equivalents". I do not find this reasoning to be persuasive. It would only be if the two products were always marketed in these formats that they could be said to have the same amount of medicine in them. Further, at no point could one say that the two products had a comparable dosage form, no matter what size of container was used.

[21] In its drug submission, Sandoz does refer to the Bayer mini-bag, but not for purposes of showing bioequivalency with it. Rather, Sandoz suggests that an impurity contained in its product is tolerable given that the same impurity exists in Bayer's mini-bag. Clearly, this is not a comparison or reference "for the purpose of demonstrating bioequivalence". As mentioned, bioequivalence is a function of pharmaceutical and bioavailability characteristics, neither of which includes a drug's impurity profile. Drugs are pharmaceutically equivalent if they contain the same amount of the same medicine. Impurities are non-medicinal ingredients. Therefore, two drugs with the same impurity are not pharmaceutically equivalent if they differ in the amount of medicine they contain or their

dosage form.

[22] Given that the first circumstance referred to above is absent, s. 5(1) of the Regulations does not apply. As Justice Roger Hughes stated, "if there is no comparison or reference for the purpose of bioequivalence, section 5(1) is not triggered" (*Ferring Inc., et al* v. *Canada, et al*., 2007 FC 300, at para. 60).

[23] Further, Sandoz compares its product to a drug that is no longer marketed in Canada. There is no patent listed against that drug in Canada. Bayer used to have three patents listed in respect of a similar product, but none has been listed since 2004. Therefore, the second circumstance referred to above is also absent. Subsection 5(1) of the Regulations does not apply.

(i) *Did the Minister err in concluding that Sandoz did not have to address the '006 patent according to s. 5(1.1) of the Regulations?*

[24] Subsection 5(1.1) of the Regulations imposes similar obligations to those provided in s. 5(1). However, the cirumstances for its application are different. Subsection 5(1.1) applies where:

(1) the generic seeks an NOC for a drug containing the same medicine as another drug marketed in Canada by an innovator under an NOC;

(2) the innovator has submitted a patent list in respect of its drug; and

(3) the generic's drug has the same route of administration and a comparable strength and dosage form to the innovator's.

[25] Where these circumstances exist, the generic must, as under s. 5(1), either accept that it will not get an NOC for its drug until the innovator's patent expires, or address the innovator's patent by, for example, alleging that the patent is invalid or will not be infringed. According to Justice Binnie, s. 5(1.1) is directed to the situation where a drug company requests an NOC "for a drug which contains a medicine that it purports to copy from another generic but in fact copies from the innovator company that has filed the patent list." (*Bristol-Myers Squibb Co*. v. *Canada (Attorney General)*, [2005] 1 S.C.R. 533, at para. 69. Obviously, that is not the situation before me. However, I am satisfied that one of the circumstances expressly set out in s. 5(1.1) is not present here in any case.

[26] Once again, it appears to me that s. 5(1.1) does not apply in this case, even though the first two of the three circumstances listed above may well exist: Sandoz' product contains ciprofloxacin, the same medicine as that in the Bayer mini-bags, against which Bayer has listed the '006 patent. However, the third circumstance is absent. The two drugs cannot be said to be of comparable strength or dosage form.

[27] The Sandoz product must be diluted before it is administered. Bayer argued that the Sandoz product would be diluted to 2 mg/ml before being given to a patient. At that point, the two drugs would have a comparable strength and dosage form and, in addition, the Sandoz product would infringe the '006 patent. In my view, the fact that the Sandoz product can be diluted to the same concentration as the Bayer mini-bag does not make the two products of "comparable strength". The

products should be compared when they are in the form in which they are marketed. Further, I note that the Sandoz product may be diluted to 2 mg/ml or to an even lower concentration (*e.g.* 1 mg/ml). Finally, Bayer can seek a remedy for patent infringement if it is of the view that the Sandoz product comes within the ‘006 patent at the point of administration.

[28] Therefore, s. 5(1.1) does not apply. Sandoz did not have to address the ‘006 patent before obtaining its NOC.

III. Conclusion

[29] The Regulations do not address the situation, that exists here, where a generic company wishes to market a product that is bioequivalent to a drug that is not marketed in Canada and for which no patent is listed. Accordingly, I can find no error in the Minister’s interpretation of the Regulations, or his decision to issue an NOC to Sandoz. I must, therefore, dismiss this application for judicial review with costs. The parties shall have 5 days to make submissions regarding the need to edit these reasons before they are released publicly.

JUDGMENT

THIS COURT'S JUDGMENT IS THAT:

1. This application for judicial review is dismissed with costs.

2. The parties may make submissions within five days of the date of this judgment regarding the need to edit the reasons before they are released publicly.

"James W. O'Reilly"
Judge

Annex

Patented Medicines (Notice of Compliance) Regulations, SOR/93-133

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,

(*a*) state that the 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 pursuant to paragraph 4(2)(*c*) is false,

(ii) the patent has expired,

(iii) the patent is not valid, or

(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.

(1.1) Subject to subsection (1.2), where subsection (1) does not apply and where a person files or has filed a submission for a

Règlement sur les médicaments brevetés (avis de conformité), DORS/93-133

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) 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 faite par la première personne aux termes de l'alinéa 4(2)*c*) est fausse,

(ii) le brevet est expiré,

(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

notice of compliance in respect of a drug that contains a medicine found in another drug that 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 included on the register in respect of the other drug containing the medicine, where the drug has the same route of administration and a comparable strength and dosage form,

(*a*) state that the 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 pursuant to paragraph 4(2)(*c*) is false,

(ii) the patent has expired,

(iii) the patent is not valid, or

(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.

de la drogue faisant l'objet de la demande d'avis de conformité.

(1.1) Sous réserve du paragraphe (1.2), lorsque le paragraphe (1) ne s'applique pas, la personne qui dépose ou a déposé une demande d'avis de conformité pour une drogue contenant un médicament que l'on trouve dans une autre drogue qui a été commercialisée au Canada par suite de la délivrance d'un avis de conformité à la première personne et à l'égard de laquelle une liste de brevets a été soumise doit inclure dans la demande, à l'égard de chaque brevet inscrit au registre visant cette autre drogue contenant ce médicament, lorsque celle-ci présente la même voie d'administration et une forme posologique et une concentration comparables :

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

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

(i) la déclaration faite par la première personne aux termes de l'alinéa 4(2)*c*) est fausse,

(ii) le brevet est expiré,

(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.

Food and Drug Regulations, C.R.C., c. 870

Règlement sur les aliments et drogues (C.R.C., ch. 870)

C.08.001.1. For the purposes of this Division,

"Canadian reference product" means

"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*)

C.08.001.1. Les définitions qui suivent s'appliquent au présent titre.

«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. (*pharmaceutical equivalent*)

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,

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

(2) An abbreviated new drug submission shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug, including the following:

…

(c) evidence from the comparative studies conducted in connection with the submission that the new drug is

(i) the pharmaceutical equivalent of the 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) la drogue nouvelle est un équivalent pharmaceutique du produit de référence canadien;

(2) La présentation abrégée de drogue nouvelle doit contenir suffisamment de renseignements et de matériel pour permettre au ministre d'évaluer l'innocuité et l'efficacité de la drogue nouvelle, notamment :

[…]

c) les éléments de preuve, provenant des études comparatives menées dans le cadre de la présentation, établissant que la drogue nouvelle :

(i) d'une part, est un équivalent pharmaceutique du produit de référence canadien,

FEDERAL COURT

NAME OF COUNSEL AND SOLICITORS OF RECORD

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