Date: 20070717

Docket: T-840-05

Citation: 2007 FC 753

Vancouver, British Columbia, July 17, 2007

PRESENT: The Honourable Mr. Justice O'Reilly

BETWEEN:

ABBOTT LABORATORIES and
ABBOTT LABORATORIES LIMITED

Applicants

and

THE MINISTER OF HEALTH
and APOTEX INC.

Respondents

REASONS FOR JUDGMENT AND JUDGMENT

(Edited for public release)

[1] Abbott owns patents for an antibiotic called clarithromycin which it markets under the name "Biaxin". Although Abbott's patents do not expire for a number of years, Apotex wishes to market its own clarithromycin tablets.

[2] Abbott seeks an order prohibiting the Minister of Health from issuing to Apotex a Notice of Compliance under the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 until two of its patents expire. The Notice of Compliance would permit Apotex to put its tablets on the market. Apotex alleges that Abbott's patents are invalid and, therefore, that Abbott is not entitled to the prohibition order it seeks. Further, Apotex alleges that even if Abbott's patents were valid, it would not be infringing them by producing its own version of clarithromycin. To obtain a prohibition order Abbott must prove that Apotex's allegations are unjustified.

I. Issue

Has Abbott established that Apotex's allegations of invalidity and non-infringement of Canadian Patents No. 2,419,729 ('729) and No. 2,471,102 ('102) are unjustified?

[3] I have found that Abbott has failed to prove that Apotex's allegations of invalidity are unjustified. Therefore, I need not deal with Apotex's allegations of non-infringement.

II. Analysis

(a) Proceedings under the *Notice of Compliance (NOC) Regulations*

[4] Proceedings under these Regulations serve the limited purpose of providing an expeditious means of determining issues relating to the validity and scope of drug patents within the regulatory scheme governing manufacturers' rights to market their products in Canada: *Biovail Corporation* v. *Canada (Minister of National Health and Welfare)*, 2006 FC 784, [2006] F.C.J. No. 1179 (T.D.) (QL).]

(b) Burden of proof

[5] Abbott bears the legal burden of proving on a balance of probabilities that Apotex's allegations of invalidity are unjustified. Apotex shoulders an evidentiary burden. If it has presented sufficient evidence to give its allegations an air of reality, then it has rebutted the presumption that Abbott's patents are valid (*Patent Act*, R.S.C. 1985, c. P-4, s. 43(2); see Annex).

[6] Apotex has clearly met its evidentiary burden through the reports of its experts and references to scholarly articles and other patents. I cannot presume, therefore, that Abbott's patents are valid. I must determine whether Abbott has proved that Apotex's allegations are unjustified: *Abbott Laboratories* v. *Canada (Minister of Health)*, 2007 FCA 153, [2007] F.C.J. No. 543 (C.A.) (QL).

(c) The Abbott Patents

[7] The two Abbott patents in issue here have much in common. They describe two forms (Forms I and II) of clarithromycin and their respective properties, set out in detail the process of methylation, crystallization and recrystallization by which the base molecule (erythromycin) is converted to clarithromycin Forms I and II, cite the United States patents in which those procedures were previously disclosed, give numerous examples of the means by which Form I or Form II can be achieved, and provide graphs of the X-ray powder diffraction pattern (XRPD), infrared spectra (IR) and differential scanning calorimetry (DSC) for the two crystal forms of clarithromycin.

[8] The two patents differ in the following respects:

(i) The ‘729 Patent

[9] Abbott relies on claim 8 of the ‘729 patent. It claims Form I when prepared by the process described in claim 1 of the patent. That process involves the crystallization of clarithromycin from a syrup or semi-solid with the resulting product containing at least one residual solvent. Abbott asserts that its ‘729 patent contains a valid claim to Form I, when prepared in the prescribed manner.

[10] The specification of the ‘729 patent says that one embodiment of the invention is the process for producing Form I from a syrup or semi-solid, with the product containing at least one residual solvent. It also refers to a further embodiment of the invention being Form I itself, when prepared according to the prescribed process. These embodiments line up with claims 1 and 8 of the patent. It is agreed, however, that claim 1, being a claim for a process rather than for a medicine or for the use of a medicine, cannot be the subject of proceedings under the Regulations. Accordingly, I need only deal with claim 8.

(i) The ‘102 Patent

[11] Abbott relies on claim 9 of the ‘102 patent. It claims the use of Form II clarithromycin, with specified impurities, as an antibiotic.

[12] The specification of the patent states that one embodiment of the invention is Form II with impurities. In a preferred embodiment, the impurities are certain alkylated compounds. In a more preferred embodiment, the impurities are situated at specified locations of the clarithromycin molecule. In the most preferred embodiment, the impurities are identified and reside at three particular loci of the molecule. Abbott asserts claim 9 as it relates to the use of one of the most preferred embodiments of the patent as an antibiotic.

(d) Apotex's allegations of invalidity

[13] Apotex has presented numerous arguments suggesting that Abbott's patents are invalid. In broad terms, Apotex alleges that Abbott's patents do not disclose any invention. It makes the following more particular arguments:

(i) Anticipation: Others had disclosed the subject matter of Abbott's patents in public documents prior to the relevant date of July 29, 1996. Further, Abbott had disclosed its own invention to the public by virtue of its sale of Biaxin prior to 1996;

(ii) Obviousness: The subject-matter of Abbott's patents was an obvious derivation from common knowledge in the field;

(iii) Double-patenting: Abbott had already obtained patents for the same ostensible inventions and cannot get other valid patents without adding anything new;

(iv) Inutility: The subject matter of Abbott's patents is not patentable because it lacks the essential requirement of usefulness;

(v) Insufficiency: The Abbott patents do not disclose a means of producing what is claimed.

[14] In addition, in relation to the '729 patent, Apotex argues that Abbott's claim for Form I is invalid because Form I was a known product at the relevant date. It submits that one cannot obtain a valid patent for an old product even if the product is made by a new process. Apotex does not accept that the '729 patent sets out a new process but, even if it did, Apotex says the claim for Form I is untenable.

(e) Abbott's application for prohibition

[15] Abbott would be entitled to an order of prohibition only if Apotex failed to meet its evidentiary burden or if it proved that none of Apotex's allegations was justified. If Abbott failed to satisfy its burden in respect of any of Apotex's sustainable allegations, it could not obtain the requested order.

[16] I am not satisfied that all of Apotex's allegations are unsupportable or unjustified. Therefore, I cannot grant the order Abbott seeks. I am satisfied that at least one allegation of invalidity is justified in relation to each patent. Abbott has not discharged its burden to prove otherwise.

(f) Validity of the ‘729 Patent

[17] The ‘729 patent makes clear that the process of creating clarithromycin was not invented by Abbott. The patent refers to various prior United States patents owned by the Taisho Pharmaceutical Company. Further, the patent describes a process of crystallizing and recrystallizing clarithromycin for purposes of purification which follows standard chemical practices of dissolution in a solvent, heating, filtering, cooling and drying. When particular solvents are used this process yields clarithromycin in Form I.

[18] Further, Form I was disclosed well before July 29, 1996. For example, a European patent (no. 0041355), filed in 1981 and held by Taisho, described a process of crystallization and recrystallization using chloroform and diethyl ether. A similar process using chloroform and isopropyl ether was described in Morimoto, S., *et al*., “Chemical Modification of Erythromycins. I. Synthesis and Antibacterial Activity of 6-0-Methylerythromycins A” (1984) Vol. 37: No. 2, *Journal of Antibiotics*, 187-189.

[19] Apotex’s experts state that the processes described in these documents yield clarithromycin Form I. Dr. Peter Stang, Professor of Chemistry at the University of Utah, concluded that the chloroform/diethyl ether combination created Form I given that the XRPD, IR and DSC data for the resulting crystal correspond with the figures provided for Form I in the ‘729 patent. He also concluded that the chloroform/isopropyl ether combination yielded Form I on the same reasoning. Dr. Robin Harris, Professor Emeritus of Chemistry at Durham University, England,

agreed with both of those conclusions. Dr. Robert McClelland, retired Professor of Chemistry at the University of Toronto, also agreed. Apotex's experts also cited numerous occasions on which Abbott's experts had conceded that persons following the prior art would produce Form I when they recrystallized clarithromycin in ethanol.

[20] It is clear, therefore, that Form I was a known compound well before July 29, 1996. The question arises, therefore, whether Abbott can have a valid patent for a known product, even if it had developed a novel process for producing it (which is disputed). This same issue arose in another case dealing with an Abbott clarithromycin patent: *Abbott Laboratories* v. *Canada (Minister of Health)*, 2005 FC 1332, [2005] F.C.J. No. 1721 (T.D.) (QL). There, Justice Michael Phelan concluded that both Form II clarithromycin and the processes for making it were known well before 1996. He found the Abbott patent before him invalid on that basis. The Federal Court of Appeal upheld that conclusion (2007 FCA 153, [2007] F.C. No. 543 (C.A.) (QL)), relying on the reasoning in the case of *Hoffmann-La Roche & Co*. v. *Canada (Commissioner of Patents)*, [1955] S.C.R. 414. In *Hoffman-La Roche*, the Supreme Court of Canada held that a patent for a known product was invalid even if the process by which it was made was novel. The product would not meet the definition of an "invention" (although the process would). Justice Rand stated:

> The definition clause furnishes no warrant for treating a well known substance as being a "new and useful . . . composition of matter" because it has been produced by a certain process. The assumption is that the product of different processes is identical and no such constructive attribute can render the substance itself either new or useful. (At p. 417.)

[21] In the Federal Court of Appeal, Justice Karen Sharlow made it clear that the principle in *Hoffmann-La Roche* still applies in Canadian law. She held that Abbott could not have a valid claim

to Form II clarithromycin, even if it was created by a novel process, because Form II was a known product. Abbott argued that those who followed the prior art would not know which form of clarithromycin they had produced. But Justice Sharlow held that "the absence of that knowledge is legally irrelevant" given that "well established analytical techniques would have disclosed its presence if anyone had cared to look at the appropriate moment" (at para. 22).

[22] Justice Sharlow determined that a product was "known" if a hypothetical claim for its invention would be invalid for anticipation. In other words, if a person could get a valid patent for the product in issue, then it could not be said that the product was known. By that analysis, Abbott argues that its claim for Form I as created by the process set out in claim 1 of the patent is valid. It submits that a hypothetical patent for Form I would be valid because, although Form I had been disclosed in earlier publications, the disclosure was not enabling; that is, the prior references did not contain sufficient information to permit a person of ordinary skill and knowledge to understand "the nature of the invention and carry it into practical use without the aid of inventive genius but purely by mechanical skill" (*Free World Trust* v. *Électro-Santé Inc.*, [2000] 2 S.C.R. 1024, at para. 26, quoting H.G. Fox, *The Canadian Law and Practice Relating to Letters Patent for Inventions* (4th ed. 1969), at pp. 126-7).

[23] In my view, Abbott does not have a valid patent for Form I even if it was produced by a novel process. Form I is an old product. There are numerous prior art sources, cited above, that contained sufficient information to enable skilled workers to make it. The fact that they would not

have known that they had made that particular form of clarithromycin is, according to the Federal Court of Appeal, “legally irrelevant”.

[24] Therefore, Abbott has failed to discharge its burden of proof in relation to the ‘729 patent.

(f) Validity of the ‘102 patent

[25] Abbott concedes that Form II clarithromycin was a known substance before the relevant date of July 29, 1996. Indeed, as mentioned, the Federal Court of Appeal recently upheld a Federal Court finding that Form II was an old product as of that date: *Abbott Laboratories* v. *Canada (Minister of Health)*, above. The prior art showed that heating Form I created Form II on the way to the melting point of clarithromycin, around 225°C (Morimoto, S., *et al*., “Chemical Modification of Erythromycins. I. Synthesis and Antibacterial Activity of 6-0-Methylerythromycins A”, (1984) Vol. 37: No. 2, *Journal of Antibiotics*, 187-189). In addition, numerous other sources described the creation of clarithromycin Form II by crystallization in various solvents. Justice Phelan referred to the existence of five European patent applications dating back to 1980, as well as numerous articles in the *Journal of Antibiotics* from 1984 to 1993 that described how to make Form II.

[26] It is also clear on the evidence that the prior art disclosed clarithromycin containing the same impurities that are identified in the various embodiments and claims of the ‘102 patent. Dr. Stang concluded that “it would be obvious to a person skilled in the art that any prior preparation of clarithromycin . . . would have the same alkylated clarithromycin impurities recited in . . . the

‘102 patent”. Dr. McClelland agreed. He was of the view that the process described in Morimoto S., *et al*., above, as well as in other prior art documents, would have yielded clarithromycin (whether Form I or Form II) in the presence of the same impurities as identified in the ‘102 patent.

[27] Abbott does not dispute this evidence. Its principal argument is that, while Form II was known, no one had recognized its use as an antibiotic. Apotex suggests that this use was obvious since all of the prior art was inspired by the promising anti-bacterial activity of clarithromycin. Accordingly, using Form II clarithromycin as an antibiotic was not an invention and should not be patentable: *GlaxoSmithKline Inc.* v. *Canada (Minister of Health)*, 2004 FC 116, [2004] F.C.J. No. 191 (T.D.) (QL), at para. 28. In reply, Abbott suggests that while both the antibiotic properties of clarithromycin generally and the existence of Form II were well-known, no one had, in effect, put “two and two together”. Accordingly, Abbott maintains that no one knew that Form II could be used as an antibiotic.

[28] The argument on this point arose from the recent decision of Justice Sharlow, described above. That decision amounts to a binding conclusion that Form II was an old product and anticipated by prior art. Abbott attempted to save its patent by arguing that the *use* of Form II was an invention even if Form II itself was not. Given that this issue was raised for the first time during oral argument, there is little evidence in the record directly on point.

[29] Apotex points to articles in which Form II was disclosed and its antibacterial effects were described (see Y. Watanabe, *et al*., “Chemical Modification of Erythromycins. IX. Selective

Methylation at the C-6 Hydroxyl Group of Erythromycin A Oxime Derivatives and Preparation of Clarithromycin" (1993) Vol. 4b: No. 4, *Journal of Antibiotics*, 647-660; S. Morimoto, *et al.*, "Chemical Modification of Erythromycins II. Synthesis and Antibacterial Activity of O-alkyl Derivatives of Erythromycin", (1990) Vol. 4.3: No. 3, *Journal of Antibiotics*, 286-294). It also asked me to draw a common-sense inference from the fact that all of the prior art was devoted to the development of clarithromycin for use as an antibiotic. Its use as an antibiotic was obvious to all of those involved in its study. In fact, it was the only known use for clarithromycin. Apotex refers to *Abbott Laboratories v. Canada (Minister of Health)*, 2007 FCA 187, in which Justice Marc Noël stated in relation to Form II: "Saying, in effect, that an antibiotic is used as an antibiotic adds nothing to the invention" (para. 43).

[30] In my view, Abbott cannot succeed in its argument that it invented the use of Form II as an antibiotic. First, there is nothing in the '102 patent itself that supports the contention that use of Form II as an antibiotic was an aspect of the invention. Nowhere is this claim reinforced by any discussion, disclosure, examples or data. In fact, the patent states that Forms I and II exhibit excellent and identical antibacterial activity. The only difference between them is that Form I dissolves more quickly. The patent notes that drugs currently on the market contain Form II and suggests that Form I would be a more economical and effective product. I see nothing that supports Abbott's assertion that the use of Form II as an antibiotic was an aspect of the invention disclosed by the '102 patent.

[31] Second, Abbott bears the onus of proof on the issue of validity and it has not tendered evidence supporting its position. For its part, Apotex has met its evidentiary burden by directing me to evidence showing that the use of Form II as an antibiotic was obvious in light of the prior art. Abbott has not proved that this allegation is unjustified.

[32] Abbott relies solely on the assertion that different crystal forms of a given substance can have different properties. For example, it notes that graphite and diamonds are both crystal forms of carbon, but obviously have different characteristics. Accordingly, Form II clarithromycin could have different chemical properties from Form I (and other crystal forms of clarithromycin). Abbott cites the following passage in another clarithromycin-related proceeding in support of this argument:

> Dr. Atwood points out that a substance may take on millions of crystalline forms. Although that substance may in itself be a medicine, some of the crystalline forms may not, because they cannot dissolve in the body. They may be no more beneficial than a penny swallowed by a child. Form 0 did not need to have medical value, as long as it could be converted into Form II which does. (*Abbott Laboratories* v. *Canada (Minister of Health)*, 2006 FC 120, [2006] F.C.J. No. 256 (T.D.) (QL), at para. 62); reversed on other grounds: 2007 FCA 73, [2007] F.C.J. No. 233 (C.A.) (QL)).

[33] Dr. Jerry Atwood, Professor of Chemistry at the University of Missouri-Columbia, whose opinion is cited in the passage quoted above, advises that it is not obvious that one crystal form of clarithromycin would be useful as an antibiotic just because another one was. I accept that different crystals can have different properties. But Abbott has offered no evidence to support its alleged invention. It has not shown that it discovered any particular therapeutic characteristics of Form II or any other properties that would be make it suitable for use as an antibiotic. Again, the patent itself suggests otherwise.

[34] In my view, therefore, Abbott has failed to discharge its burden of proof in relation to the ‘102 patent.

III. Disposition

[35] Abbott has not proved that the allegations of invalidity discussed above are unjustified. Therefore, I must dismiss Abbott’s request for an order of prohibition with costs.

JUDGMENT

THIS COURT'S JUDGMENT IS THAT:

1. Abbott's request for an order of prohibition is dismissed with costs to be calculated at the mid-point of Column IV.
2. The parties shall make any submissions regarding the need to edit these reasons before public release within ten days.

"James W. O'Reilly"
Judge

Annex “A”

Patent Act, R.S.C. 1985, c. P-4	*Loi sur les brevets*, L.R. 1985, ch. P-4
Validity of patent 43. (2) After the patent is issued, it shall, in the absence of any evidence to the contrary, be valid and avail the patentee and the legal representatives of the patentee for the term mentioned in section 44 or 45, whichever is applicable.	Validité 43. (2) Une fois délivré, le brevet est, sauf preuve contraire, valide et acquis au breveté ou à ses représentants légaux pour la période mentionnée aux articles 44 ou 45.

FEDERAL COURT
SOLICITORS OF RECORD

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