Date: 20060316

Docket: T-2295-03

Citation: 2006 FC 341

Ottawa, Ontario, March 16, 2006

PRESENT: The Honourable Mr. Justice John A. O'Keefe

BETWEEN:

ABBOTT LABORATORIES and
ABBOTT LABORATORIES LIMITED

Applicants

- and -

THE MINISTER OF HEALTH and
PHARMASCIENCE INC.

Respondents

PUBLIC VERSION OF
REASONS FOR ORDER AND ORDER

O'KEEFE J.

[1] This is an application by the applicants, Abbott Laboratories and Abbott Laboratories Limited (collectively, Abbott), brought pursuant to subsection 6(2) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 for an order prohibiting the Minister of Health from issuing a notice of compliance (NOC) to Pharmascience Inc. for the production of

clarithromycin 250 mg or 500 mg tablets until after the expiration of Canadian Letters Patent Nos. 2,258,606, 2,261,732 , 2,277,274, 2,386,527, 2,386,534, 2,387,356, and 2,387,361 (collectively the Abbott patents).

[2] The applicants seek the following relief:

1. an order prohibiting the Minister from issuing an NOC to Pharmascience for the production of clarithromycin 250 mg or 500 mg tablets until after the expiration of the Abbott patents, and

2. costs of the application.

[3] The respondent, Pharmascience, requested that the application be dismissed with costs. Pharmascience also asked that damages be awarded pursuant to section 8 of the *NOC Regulations*.

Background

[4] Abbott Laboratories Limited (Abbott Canada) is a Canadian innovator pharmaceutical manufacturer that distributes and sells BIAXIN, an antibiotic used to treat infections. Abbott Laboratories (Abbott USA) is a company incorporated in the United States of America and is the parent of Abbott Canada.

[5] Abbott Canada sells clarithromycin in Canada, under the brand name BIAXIN, in 250 mg and 500 mg strength tablets pursuant to NOCs issued to Abbott Canada on May 8, 1992 and August 25, 1994.

[6] The active medicinal ingredient in BIAXIN is clarithromycin. Clarithromycin is a molecule that can be arranged in different crystal forms having different properties relating to their crystal structure. The Abbott patents, which are owned by Abbott USA, relate to specific clarithromycin forms, methods or processes for their manufacture, and their uses as an antibiotic. Abbott Canada, with the consent of Abbott USA, filed the Abbott patents with the Minister for listing on the patent register that is maintained by the Minister pursuant to the *NOC Regulations*.

[7] Pharmascience, a manufacturer of generic drugs, sought approval from the Minister to sell a generic version of BIAXIN in Canada. By letter dated October 22, 2003, Pharmascience sent a notice of allegation (NOA) to Abbott Canada pursuant to section 5 of the *NOC Regulations*. The NOA advised that Pharmascience had filed an abbreviated new drug submission (ANDS) for clarithromycin in 250 mg and 500 mg tablets, referencing the BIAXIN in 250 mg and 500 mg dosages for which NOCs were issued to Abbott Canada.

[8] The NOA alleged that all of the Abbott patents are invalid on numerous grounds, including: anticipation, obviousness, overly broad claims, insufficiency of description, ambiguous claims, and

lack of utility. The NOA cited numerous prior art references as the factual and legal basis for the allegations.

[9] Pharmascience also alleged that the Abbott patents are not eligible for listing on the patent register maintained by the Minister.

[10] In response to the NOA, Abbott commenced this proceeding by notice of application issued December 5, 2003. Abbott's position is that none of the allegations in the NOA are justified.

The Abbott Patents

[11] The Abbott patents relate to three particular crystal forms of compound 6-O-methylerythromycin A, namely Form 0, Form I and Form II, characterized by their powder x-ray diffraction patterns. The '606 patent discloses in its summary of invention:

> We have discovered that 6-O-methylerythromycin A can exist in at least two distinct crystalline forms, which for the sake of identification are designated "Form I" and "Form II". The crystal forms are identified by their infrared spectrum, differential scanning calorimetric thermogram and powder x-ray diffraction pattern. Form I and Form II crystals have an identical spectrum of antibacterial activity, but Form I crystals unexpectedly have an intrinsic rate of dissolution about three times that of Form II crystals. Investigations in our laboratory have revealed that 6-O-methylerythromycin A when recrystallized from ethanol, tetrahydrofuran, isopropyl acetate, and isopropanol, or mixtures of ethanol, tetrahydrofuran, isopropyl acetate, or isopropanol with other common organic solvents results in exclusive formation of Form I crystals, not identified hitherto before.

[12] The ’274 patent discloses in its summary of invention:

> 6-O-methylerythromycin A can exist in a third crystal form, designated “form 0”. Form 0, I, and II crystals have an identical spectrum of antibacterial activity. 6-O-methylerythromycin A prepared by the various methods described in the patent literature summarized below, in which the compound is purified by recrystallization from ethanol, result in initial formation of the crystalline form 0 ethanolate. Form 0 solvates are also formed with tetrahydrofuran, isopropanol, and isopropyl acetate. The form 0 solvate is converted to the non-solvated form I by removing the solvent from the crystal lattice by drying at a temperature of from about 0ºC to about 50ºC. Form 0 is converted to the non-solvated crystal form II by heating under vacuum at a temperature of between about 70ºC and 110ºC.

[13] The following summaries of the Abbott patents are taken almost verbatim from the applicants’ factum.

’606 Patent

The ’606 patent claims Form II, characterized by a particular powder X-ray diffraction pattern.

’732 Patent

The ’732 Patent claims processes for the isolation of Form II using particular solvents, and to Form II when made by those processes (product-by-process claims).

’274 Patent

The ’274 patent claims Form 0, a solvated form of clarithromycin, a process for preparing Form 0 from certain solvents, and its uses as a therapeutic agent.

’527 Patent

The ’527 patent claims Form I, methods of preparation of Form I from Form 0 using select solvents, and isolating Form I. The patent also contains claims to a process for making Form II from Form I as a starting material.

’534 Patent

The ’534 patent claims different methods of preparing Form I, pharmaceutical compositions using Form I and uses of Form I.

’356 Patent

The ’356 patent claims methods of preparing Form 0, pharmaceutical compositions containing Form 0, and use claims as a therapeutic agent.

’361 Patent

The ’361 patent claims methods of preparing Form 0, pharmaceutical compositions containing Form 0, methods of use, and Form 0 for use in the preparation of Form II.

Experts

Abbott’s Experts

[14] Dr. Stephen Byrn received a Ph.D. in chemistry from the University of Illinois in 1970. He has been the Head of the Department of Industrial and Physical Pharmacy at Purdue University since 1994. He is a scientist, professor and author in the field of pharmaceutical chemistry and solid-

state chemistry. He consults extensively in the pharmaceutical industry and is widely published on issues relating to the crystal forms of drugs.

[15] Dr. Allan Myerson received a Ph.D. in chemical engineering from the University of Virginia in 1977. He has been the Provost of the Illinois Institute of Technology since January 2003. He consults in the pharmaceutical industry on designing processes to crystallize drugs, and he is also widely published in the area of crystallization.

[16] Dr. Jerry Atwood received a Ph.D. in chemistry from the University of Illinois in 1968. He has been a Professor and Chairman of the Department of Chemistry at the University of Missouri-Columbia since 1994. He has served as editor of numerous chemistry journals, and has published more than 580 articles. He considers himself an expert in the field of crystal growth, crystal engineering and polymer chemistry.

Pharmascience's Experts

[17] Dr. Craig J. Eckhardt received a Ph.D. in physical chemistry from Yale University in 1967. Since 1978 he has been professor of chemistry at the University of Nebraska. His research focuses on crystallization and characterization of crystals. He is widely published in the area of organic crystals.

[18] Dr. Mark D. Hollingsworth received a Ph.D. in organic chemistry from Yale University in 1985. He then completed postdoctoral studies at the University of Cambridge. He is currently an associate professor of chemistry at Kansas State University. He has acted as consultant to pharmaceutical companies in the area of crystal analysis and preparation of crystal forms, and he has published extensively in the field of organic synthesis of crystal forms.

[19] Dr. Ricardo F. Aroca received a Ph.D. in chemistry from Moscow State University in 1970. He has served as assistant professor and associate professor at the University of Toronto and the University of Chile. Since 1987, he has been a professor of chemistry at the University of Windsor.

Anticipation by Prior Art

[20] Of the numerous prior art references cited by Pharmascience in its NOA in support of its anticipation allegations, the two most important ones are references by Salem and Iwasaki.

[21] The article by Salem is titled “Clarithromycin” and was published in 1996 in the book “Analytical Profiles of Drug Substances and Excipients, Volume 24” edited by H. Brittain (the Salem reference). The Salem reference disclosed an x-ray powder diffraction pattern for clarithromycin based upon 2-theta values that are almost identical to the 2-theta values of the Form II clarithromycin claimed by the ’606 and the ’732 patents.

[22] The article by Iwasaki, Acta Cryst (1993) C49, 1227-1230, disclosed a methanol solvate of clarithromycin (the Iwasaki reference). This article was published in 1993.

Obviousness

[23] The NOA listed a multitude of prior art references which allegedly rendered the Abbott patents obvious. For example, to substantiate its claim that the ’732 patent is obvious, the NOA listed 24 prior art references. Abbott’s experts deposed that it is quite inconceivable that a skilled chemist would be able to combine those 24 references in order to arrive at Form II clarithromycin.

[24] The most important reference for obviousness is the Iwasaki reference which Pharmascience alleges renders obvious the claims to Form 0 in the ’274 patent. Form 0 is a solvated form of clarithromycin. In support of the obviousness allegations, Dr. Hollingsworth deposed:

> The Iwasaki article from 1993 discloses a methanol solvate of clarithromycin and its crystal structure. This crystal contains methanol bound within the crystal structure. This methanol is crystallographically ordered and hydrogen bonded to the lactone carbonyl group of clarithromycin.
>
> From this example, in which an alcohol (methanol) is hydrogen bonded to the clarithromycin, and because clarithromycin is a large, irregularly-shaped molecule with several hydrogen bond donors and acceptors, a typical organic chemist would [be] on the lookout for other solvated forms of clarithromycin, and would not be surprised by the presence of other solvates.

[25] Abbott's experts refuted Pharmascience's allegations by leading experimental evidence to demonstrate that following the teachings of Pharmascience's prior art references did not yield Form 0 solvate. Abbott's experts also adduced evidence with respect to the Iwasaki reference to support the following statements at paragraph 104 of the applicants' factum:

> Iwasaki did not make the Form 0 obvious because:
>
> (a) the structure of Iwasaki's methanol solvate is not the same as the structure of the Form 0 solvate in the '274 Patent;
>
> (b) the difference in the structure means that Iwasaki's solvate and Form 0 claimed in the '274 Patent have completely different characteristics.
>
> (c) that Iwasaki may have made clarithromycin from a methanolic solution "does not lead one directly and without difficulty to the existence of the Form 0 solvate."

[26] In addition, Dr. Byrn testified:

> The Iwasaki reference does not teach one skilled in the art anything about the stability of the Form 0 solvate. In fact, it is my understanding that the methanol solvate is much more stable than the Form 0 solvate. In many important respects, the Iwasaki reference teaches away from Form 0.

Issues

[27] Abbott raised the following issues in its oral presentations:

1. Whether the doctrine of *res judicata* (issue estoppel) applies to the '732 patent;

2. Whether the Salem article was prior art;

3. The "Modiano statements" (statements made in the European Patent Office);

4. Obviousness;

5. Prior sales;

6. Eligibility to be listed on the patent register;

7. Alleged anticipation by the Iwasaki article.

[28] Pharmascience, in its memorandum of fact and law, stated the issues as follows:

> There are 7 main issues in this application:
>
> (1) The effect of a summary proceeding on onus and estoppel;
>
> (2) the knowledge of the person skilled in the art;
>
> (3) Form II is old, anticipated, and product by process claim invalid;
>
> (4) Obviousness test permits basic analysis;
>
> (5) Patent validity grounds (insufficiency, claims broader);
>
> (6) Patents to a new process ('732 patent) and an intermediate ('274 patent) should not be listed;
>
> (7) Procedural issues (NOA, Abbott admissions, credibility).

Analysis and Decision

[29] Issue 1

Does *res judicata* (issue estoppel) apply with respect to the '732 Patent?

Abbott submitted that *res judicata* (issue estoppel) applies as Pharmascience raised the issue of the validity of the '732 patent before Justice Gibson in *Abbott Laboratories* v. *Canada (Minister of Health)* 2004 FC 1349, 36 C.P.R. (4th) 437 (*Pharmascience I*) and a final order of prohibition issued as a result of the Federal Court of Appeal upholding Justice Gibson's decision to grant the prohibition. Pharmascience submitted that the Pharmascience I case is different than the present case, hence the doctrine should not apply.

[30] In *Toronto (City of)* v. *Canadian Union of Pubic Employees, Local 79*, 2003 SCC 63, [2003] 3 S.C.R. 77, Justice Arbour, at paragraph 23, outlined the conditions that must be met for issue estoppel to apply:

> Issue estoppel is a branch of *res judicata* (the other branch being cause of action estoppel), which precludes the relitigation of issues previously decided in court in another proceeding. For issue estoppel to be successfully invoked, three preconditions must be met: (1) the issue must be the same as the one decided in the prior decision; (2) the prior judicial decision must have been final; and (3) the parties to both proceedings must be the same, or their privies (*Danyluk* v. *Ainsworth Technologies Inc.*, [2001] 2 S.C.R. 460, 2001 SCC 44, at para. 25 *per* Binnie J.). . . .

[31] Further, in *Danyluk* v. *Ainsworth Technologies Inc.*, 2001 SCC 44, [2001] 2 S.C.R. 460, Justice Binnie stated at paragraph 18:

> The law rightly seeks a finality to litigation. To advance that objective, it requires litigants to put their best foot forward to establish the truth of their allegations when first called upon to do so. A litigant, to use the vernacular, is only entitled to one bite at the cherry. The appellant chose the ESA as her forum. She lost. An

> issue, once decided, should not generally be re-litigated to the benefit of the losing party and the harassment of the winner. A person should only be vexed once in the same cause. Duplicative litigation, potential inconsistent results, undue costs, and inconclusive proceedings are to be avoided.

[32] It is with these legal principles in mind that the present case must be assessed to determine whether or not issue estoppel should be applied.

[33] *Pharmascience I* dealt with the '732 patent. Justice Gibson stated at paragraph 4 of this decision:

> On the foregoing factual basis, Pharmascience's Notice of Allegation alleges that its form II clarithromycin is produced by a process that does not infringe Canadian Letters Patent No. 2,261,732 and that, alternatively, if its clarithromycin is covered by Claims 16 to 21 of the Patent, then those claims are broader than the invention made and disclosed and thus the Patent is invalid.

[34] In the NOA filed by Pharmascience dated October 22, 2003, which is the NOA for the present application, the following is stated:

> **Legal basis**
>
> Abbott currently has seven patents listed on the register in respect of clarithromycin 250 mg and 500 mg tablets. PMS has already filed a Notice of Allegation with respect to Canadian Patent No. 2,261,732 (the '732 Patent) on the basis of non-infringement and alternatively invalidity due to the claims being broader than the invention if the patent is found to cover the PMS material.

> This Notice of Allegation relates to the invalidity of the '732 Patent (on the basis of obviousness and anticipation) and the invalidity of the six newly added patents: . . .

[35] The majority decision of the Federal Court of Appeal in *Procter & Gamble Pharmaceuticals Canada Inc.* v. *Canada (Minister of Health)*, 2003 FCA 467, [2004] 2 F.C.R. 85 stated as follows at paragraph 16:

> *Issue Estoppel*
>
> P&G submits that the question of whether the '376 patent is eligible for inclusion on the Patent Register is *res judicata* in that it is subject to the doctrine of issue estoppel. P&G says that in prior litigation between the same parties (*Procter & Gamble Pharmaceuticals Canada, Inc.* v. *Canada (Minister of Health)* (2001), 15 C.P.R. (4th) 496 (F.C.T.D.), affirmed (2002), 20 C.P.R. (4th) 1 (F.C.A.)), the issue of the eligibility of the '376 patent for inclusion on the Patent Register was or could have been raised. The prior proceeding involved a different proposed use for Genpharm's product. P&G says that it is not now open to Genpharm to raise this issue in these proceedings.

At paragraphs 23 to 25, the Court stated:

> [23] That is not the case here. Genpharm was aware of the '376 patent and the issue date shown on its face. As well, the Form IV patent list, the document on which P&G submitted the '376 patent to the Minister of Health for inclusion on the Patent Register, is a public document that shows on its face the date on which it was submitted. These were the only facts Genpharm needed to challenge the '376 patent's eligibility to be included on the Patent Register.
>
> [24] This case is about Genpharm not raising an issue in the first litigation, even though it had the necessary facts at the relevant time. I think Lord Shaw in *Hoystead* v. *Commissioner of Taxation*, [1926] A.C. 155 (H.L.) at 166, set out the law applicable to the circumstances here:

> Thirdly, the same principle -- namely, that of setting to rest rights of litigants, applies to the case where a point, fundamental to the decision, taken or assumed by the plaintiff and traversable by the defendant, has not been traversed. In that case also a defendant is bound by the judgment, although it may be true enough that subsequent light or ingenuity might suggest some traverse which had not been taken. The same principle of setting parties' rights to rest applies and estoppel occurs.

[25] Third, Genpharm argues that the doctrine of issue estoppel can only be used by a defendant or respondent to bar a plaintiff's or applicant's action or application. It cannot be used to bar a defendant or respondent from raising a defence that it failed to raise in an earlier proceeding. I do not agree. The doctrine of issue estoppel may be invoked by either party. In *Fidelitas Shipping Co.* v. *V/O Exportchleb*, [1965] 2 All E.R. 4 (C.A.) at 9, Lord Denning stated:

> But within one cause of action, there may be several issues raised which are necessary for the determination of the whole case. The rule then is that, once an issue has been raised and distinctly determined between the parties, then, as a general rule, neither party can be allowed to fight that issue all over again. The same issue cannot be raised by either of them again in the same or subsequent proceedings except in special circumstances . . . And within one issue, there may be several points available which go to aid one party or the other in his efforts to secure a determination of the issue in his favour. The rule then is that each party must use reasonable diligence to bring forward every point which he thinks would help him. If he omits to raise any particular point, from negligence, inadvertence, or even accident (which would or might have decided the issue in his favour), he may find himself shut out from raising that point again, at any rate in any case where the self-same issue arises in the same or subsequent proceedings.

> Lord Denning's statement has been approved not only by Ritchie J., writing for the majority of the Supreme Court, in *Grandview (Town)* v. *Doering*, [1976] 2 S.C.R. 621 at 637, but by this Court in *Merck & Co.* v. *Apotex Inc.*, [1999] F.C.J. No. 2022 (QL) [reported 5 C.P.R. (4th) 363], at para. 13 and by the Trial Division (as it then was) in *Apotex Inc.* v. *Canada (Attorney General)*, [1997] 1 F.C. 518 at 542, 71 C.P.R. (3d) 166, and *Richter Gedeon Vegyészeti Gyar Rt* v. *Apotex Inc.*, 2002 FCT 1284 [reported 23 C.P.R. (4th) 478], at para. 21. It is, therefore, open to P&G to plead that Genpharm is estopped from arguing that the '376 patent was not eligible for inclusion on the Patent Register.

[36] The case law indicates that a party is required to use reasonable diligence to bring forth in the first instance all points that relate to that issue. In this case, the issue is the invalidity of the ‘732 patent.

[37] Is the issue to be decided in this case the same as the issue decided in the *Pharmascience I* case?

A review of the *Pharmascience I* case discloses that the NOA filed by Pharmascience alleged that the claims were broader than the invention made and thus, patent ‘732 was invalid. Justice Gibson in this decision ruled that the patent was not invalid. At paragraphs 122 and 123, Justice Gibson stated:

> [122] Given the foregoing, I am satisfied that an interpretation of the disclosure of the ‘732 Patent in a manner that extends to include the process utilized or proposed to be utilized by Pharmascience’s supplier is reasonably open and does not result in the claims of that patent that are here in issue exceeding the scope of the disclosure on which those claims are based. In the result, to put it another way, I am satisfied that, on the evidence before the Court, Pharmascience has failed to discharge the evidentiary burden on it to justify the

> allegation of invalidity of the Claims 16 to 21 of the ‘732 Patent on the basis of overbreadth.
>
> **CONCLUSION**
>
> [123] In summary, I conclude that the Applicants have met the burden on them to demonstrate that Pharmascience’s Notice of Allegation fails to fulfil the requirements of the *Regulations* and, in the result, is insufficient to ground success by Pharmascience on this application. Further, I conclude that the Applicants have discharged the burden on them to demonstrate that Pharmascience’s allegations that its Clarithromycin tablets 250 mg and 500 mg for which it has sought approval to market in Canada in an Abbreviated New Drug Submission would, if that approval were granted, result in an infringement of the ‘732 Patent and, if it would result in an infringement of that Patent, then the Patent is not invalid by reason of overbreadth of Claims 16 to 21 of the Patent. Put another way, and more simply, the Applicants have been entirely successful on this application. In the result, an Order will go prohibiting the Respondent, the Minister of Health, from issuing Pharmascience a Notice of Compliance for Clarithromycin – 250 mg and 500 mg tablets until after the expiration of Canadian Letters Patent No. 2,261,732.

[38] In the present case, Pharmascience’s notice of allegation relates to the invalidity of the ‘732 patent and the invalidity of six newly added patents. I am satisfied that with respect to the ‘732 patent, the issue is the same as the issue decided in *Pharmascience I*.

[39] Was the prior judicial decision in *Pharmascience I* final?

The decision of Justice Gibson was upheld by the Federal Court of Appeal. Accordingly, the prior judicial decision was final.

[40] Were the parties to both proceedings the same?

A review of the styles of cause in both applications shows that the parties were the same in both proceedings.

[41] I am of the view that issue estoppel (one of the branches of *res judicata*) applies and therefore, the invalidity of the ‘732 patent cannot be relitigated. All of the points that could have been raised to show the invalidity of the ‘732 patent should have been raised when the invalidity of the ‘732 Patent was argued before Justice Gibson.

[42] Pharmascience submitted that Abbott did not raise the issue of *res judicata* in its notice of application. However, I note that Abbott raised the issue in its memorandum of fact and law and Pharmascience replied to the issue in its memorandum of fact and law. As well, both parties argued the issue of *res judicata* before me. This is sufficient to allow the issue to be raised.

[43] The respondent submitted that even if issue estoppel does apply, I should exercise my discretion and hear the application. I do not agree. There are not sufficient factors present to cause me to exercise my discretion to hear the case.

[44] Abbott submitted that once issue estoppel is accepted, then an order of prohibition must issue and this would end the matter. I agree that an order of prohibition must issue until after the expiration of the ‘732 patent.

Conclusion

[45] Because I have found that *res judicata* (issue estoppel) applies to the allegation respecting the ‘732 patent and the order of Justice Gibson in *Pharmascience I* granting prohibition with respect to this patent, I will issue an order pursuant to subsection 6(2) of the *NOC Regulations* prohibiting the Minister of Health from issuing to the respondent, Pharmascience Inc., NOCs for clarithromycin 250 mg or 500 mg tablets until after the expiration of the ‘732 patent.

[46] Abbott shall have its costs of the application.

ORDER

[47] **IT IS ORDERED that:**

1. The Minister of Health is prohibited, pursuant to subsection 6(2) of the *NOC Regulations*, from issuing to the respondent, Pharmascience Inc., notices of compliance for clarithromycin 250 mg and 500 mg tablets until after the expiry of Canadian Letters Patent No. 2,261,732.

2. Abbott shall have its costs of the application.

"John A. O'Keefe"
Judge

FEDERAL COURT

NAME OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	T-2295-03
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